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A PUBLICATION OF THE
ASSOCIATION OF REPRODUCTIVE HEALTH PROFESSIONALS



August 2004

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Interstitial cystitis (IC) is a chronic pelvic pain symptom of bladder origin, characterized by urinary frequency, urgency, and pelvic pain. Recent research is demonstrating that many women – possibly as many as 1 in 4.5 – are suffering from this bladder-related condition that, until recently, was poorly understood. Many practitioners are unclear as to how best to diagnose or manage this condition; consequently, women suffer with IC for an average of 5 to 7 years before they are correctly diagnosed. Although the specific pathophysiology remains unknown, research has identified a lower urinary epithelial dysfunction in the bladder of many patients with IC. This finding has led to important advances in diagnosis and management, enabling women (and men) to receive accurate diagnoses of IC early in the disease process, before it has compromised their quality of life.

This publication is based upon information presented by C. Lowell Parsons, MD, a leading urologist and researcher at the 2003 ARHP annual meeting held in La Jolla, California. The purpose of this publication is to provide clinicians with the most current information regarding this common syndrome, and to facilitate consideration of the bladder as a source of chronic pelvic pain.

My sincere thanks to the members of our advisory committee for their time and expertise: C. Lowell Parsons, MD; Chris Rause, MSN; and Lee Shulman, MD.

Wayne C. Shields
ARHP President and CEO

LEARNING OBJECTIVES

After completing this *Clinical Proceedings*, participants will be able to:

1. Identify the signs and symptoms of chronic pelvic pain of bladder origin.
2. Discuss the epidemiology and demographics of chronic pelvic pain and interstitial cystitis in women and men.
3. Discuss the theories underlying the pathophysiology of interstitial cystitis.
4. Discuss the impact of IC on quality of life.
5. Identify the role of the PUF, PST, cystoscopy with hydro-distention in the diagnosis of IC.
6. Identify pharmacologic and nonpharmacologic management options for IC.
7. Discuss the relationship between IC and chronic nonbacterial prostatitis in men.

This publication has been made possible by an unrestricted educational grant from Ortho-McNeil Pharmaceutical, Inc.



INTRODUCTION

Interstitial cystitis (IC) is a chronic disease of the urinary bladder. The symptoms, including urinary frequency, urinary urgency, and pelvic discomfort or pain, in the absence of defined etiology, can range in severity from mild and intermittent to chronic and severe (Table 1). Although actual prevalence data are not known, recent studies suggest that this syndrome is far more common than previously believed and may affect as many as one in 4.5 women and 9 percent of men. In women, the absence of a definitive diagnostic test for IC often results in misdiagnosis of these symptoms as urinary tract infection (UTI), endometriosis, or yeast vulvovaginitis; in men, it is most often misdiagnosed as chronic non-bacterial prostatitis. The urinary symptomatology clearly indicates bladder involvement; however, the accompanying pelvic pain may be experienced anywhere throughout the genitourinary region and further confounds the diagnosis. In many women, IC remains incorrectly diagnosed and managed for an average of five to seven years. It is likely that male IC patients experience a similar delay in the recognition of their disease.

TABLE 1. Chronic Pelvic Pain of Bladder Origin: Interstitial Cystitis

- Urinary urgency + frequency + pelvic pain
 - Pain may ↑ with bladder filling, ↓ with emptying
- Absence of defined bacterial etiology
- Nocturia
 - Mild (2X) to Severe (>12X)
- Pain associated with sexual intimacy
- Pain often increases 1 week before menstruation

Numerous theories have been proposed to explain the pathophysiology of IC, which is believed to have a multifactorial pathogenesis. One popular hypothesis suggests that IC results from an abnormality in the bladder epithelium. The intravesical Potassium Sensitivity Test (PST), which appears to detect this bladder epithelial abnormality, has been increasingly relied upon—often in conjunction with the Pelvic Pain Urgency and Frequency (PUF) Patient Symptom Scale—to support a diagnosis of IC.

Clinicians need to become more aware of IC as a possible cause underlying chronic pelvic pain or pain of bladder origin.

ABBREVIATIONS AND ACRONYMS

CP	chronic prostatitis
CPP	chronic pelvic pain
CPPS	chronic pelvic pain syndrome
CPT	Current Procedural Terminology
DMSO	dimethyl sulfoxide
FDA	Food and Drug Administration
GAG	glycosaminoglycan
IC	interstitial cystitis
KCl	potassium chloride
LUDE	lower urinary dysfunctional epithelium
NBP	non-bacterial prostatitis
NIDDK	National Institute of Diabetes and Digestive and Kidney Diseases
NIH	National Institutes of Health
OAB	overactive bladder
PID	pelvic inflammatory disease
PPS	pentosan polysulfate sodium
PST	Potassium Sensitivity Test
PUF	Pelvic Pain Urgency and Frequency (Patient Symptom Scale)
RUTI	recurrent urinary tract infection
STI	sexually transmitted infection
TCA	tricyclic antidepressants
UTI	urinary tract infection



INTERSTITIAL CYSTITIS IN WOMEN

EPIDEMIOLOGY AND MAGNITUDE

It is estimated that at least 9 million women in the United States suffer from chronic pelvic pain (CPP), described as pain in the lower abdomen, vulva, urethra, vagina, medial thighs and/or perineum, often in conjunction with unrecognized voiding symptoms (urinary urgency and frequency) and dyspareunia. Common etiologies often ascribed to CPP include endometriosis, pelvic inflammatory disease (PID), dysmenorrhea, and post-surgical scarring/adhesions, as well as diseases or conditions of the urinary tract or bowel. The ramifications of CPP are significant: CPP is an indication for nearly one in five hysterectomies and is the underlying reason for more than one in 10 gynecologic referrals (Table 2). The gynecologist rarely considers that CPP may have a genitourinary origin.

TABLE 2. Consequences of CPP

Affects ~9 million women
10% to 12% outpatient gynecologist referrals
5% to 10% laparoscopies
— No overt pelvic pathology in 60% of cases
Indication for nearly 1 in 5 hysterectomies

Recently reported studies have demonstrated that the source of the chronic pelvic pain for many women diagnosed with these conditions is actually of bladder origin and that the women suffer from interstitial cystitis. In fact, research has demonstrated that 60 percent of diagnostic laparoscopies for chronic pelvic pain are associated with undefined pelvic pathology, often because the source of the pelvic pain is of bladder origin.^{1,2} Contrary to popular beliefs, IC is a common cause of CPP: 80 to 85 percent of women with an unidentified etiology of CPP have pain of bladder origin.³ Studies also have determined that nearly 40 percent of women undergoing laparoscopy for undefined pelvic pain have no endometriosis.⁴

Currently, approximately 700,000 women are diagnosed with interstitial cystitis each year (Table 3). However, it is believed that, at minimum, another 1 to 2 million women—and possibly as many as 7 million women—are affected by (but not yet diagnosed with) this syndrome.³ In other words, at least one in nine women, and possibly as many as one in 4.5 women, suffer from interstitial cystitis.⁵ The majority of patients with IC are Caucasian women with a

median age at diagnosis of 42 to 46 years.^{6,7} Many of these women first experience the cluster of symptoms associated with IC (i.e., urinary urgency, frequency, and pelvic pain) while they are in their 30s or younger. Women see an average of eight physicians over a five- to seven-year period before a correct diagnosis of IC is made. Consequently, the impact to quality of life can be, and often is, significant: 60 percent of women with IC report dyspareunia, nearly 50 percent are unable to work full-time, and the majority report sleep disturbances (Table 4).⁸ Patients with IC score lower on quality-of-life inventories than patients on dialysis, and many have concomitant emotional concerns, including a greater likelihood of suicidal ideation, than do patients without IC. The need for prompt identification and diagnosis of IC, along with effective management, is readily apparent.

TABLE 3. Interstitial Cystitis: Scope of the Problem⁹

700,000 women diagnosed with IC/year
— Up to 7 million women afflicted but not yet diagnosed
~1 in 4.5 women
— Majority Caucasian
— Median age at diagnosis: 42–46 years
— Suffer ~5–7 years until accurate diagnosis
— See ~8 physicians before accurate diagnosis
~9% of men

TABLE 4. Consequences of IC

60% of patients report dyspareunia
~50% unable to work full-time
~70% report sleep disturbances
Score lower on quality-of-life inventories than dialysis patients
Concomitant emotional concerns

PATHOPHYSIOLOGY

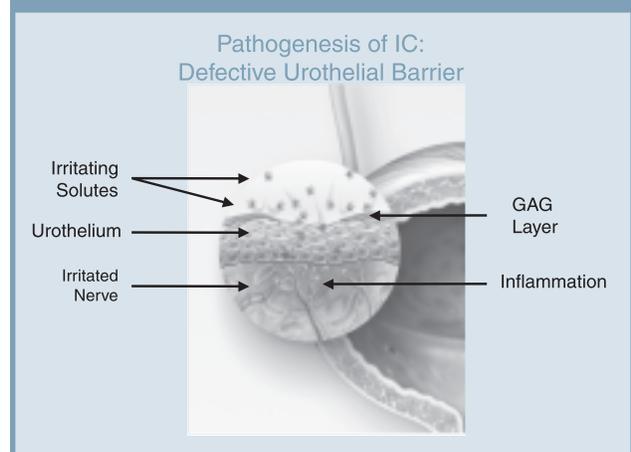
Interstitial cystitis is believed to have a multifactorial pathogenesis. Patients with IC have significantly reduced



levels of the urinary glycoprotein GP51 and increased levels of the neuropeptide Substance P; in addition, antiproliferative factor is present in the majority of patients who have severe IC. There remains the unlikely possibility that as-yet undetectable microbes may be causative, but it is doubtful that IC is the result of autoimmune processes.

In one recent theory of IC pathogenesis, which incorporates most reported data, epithelial dysfunction plays a major role. Epithelial impermeability depends on a healthy mucus (glycosaminoglycan layer) which, when present and healthy, makes the epithelium quite impermeable. If the bladder epithelium becomes more permeable, urinary solutes are allowed to diffuse into the bladder wall (Figure 1). Potassium is probably the major toxin, because its leakage into the bladder wall will depolarize nerves and muscles and injure tissue. This will result in neural upregulation, mast cell activation, and, over time, destruction of muscle and blood vessels in the bladder wall. Hence, a lower urinary dysfunctional epithelium, coupled with potassium recycling, would explain the myriad clinical observations in IC patients.

FIGURE 1. Damaged Epithelial (glycosaminoglycan [GAG]) Structure – Suggested IC Pathology¹⁰



DIAGNOSIS

Differential Diagnosis

Interstitial cystitis is a chronic progressive disorder of the lower urinary tract that presents as urinary frequency, urgency, or pelvic pain in any combination in the absence of defined etiology or overt bladder pathology such as infection. The pelvic pain can range from none to mild/intermittent to severe. Urologic symptoms do not necessarily worsen with bladder filling or emptying; they may just be present. Most patients with IC (75 percent) complain of dyspareunia, and some will have nocturia ranging from mild (voiding less often than twice per night)

to severe (voiding at least 12 times per night). Research has demonstrated that IC patients with more severe IC average 16.5 voids per day, compared with 6.5 voids per day among healthy patients.¹¹ Typically, a total of nine or more voids in a 24-hour period is consistent with IC.³ Many women report an increase in pelvic pain or frequency one week before menses, and many women experience dysmenorrhea. Sixty percent of women and men with IC report pain during and/or after sexual activity.⁸ Allergic conditions, certain foods or beverages, and physical and emotional stress may exacerbate symptoms.

The diagnosis of IC depends upon the presenting signs and symptoms. Primarily, the only other diagnoses to consider are urinary tract infection and, if hematuria is present, a rare but possible bladder cancer. The acute onset of symptoms may be suggestive of bladder or urinary tract infection (this can readily be ruled out), sexually transmitted infections (STIs), including gonorrhea, chlamydia, and mycoplasma, and/or vaginal infections. IC should be suspected among women with any of the following conditions:

- Recurrent UTI (RUTI), because most women diagnosed with recurrent UTI are not infected but are having IC symptom flares
- Overactive bladder (OAB), because most of these women have sensory urgency that usually responds only minimally or not at all to anticholinergic treatment
- A history or suspicion of endometriosis
- Premenstrual pain or dysmenorrhea
- Dyspareunia and/or pain and/or frequency/urgency surrounding intercourse

Research now indicates that IC should be suspected in all women who present with cyclical or noncyclical chronic pelvic pain, whether or not urinary frequency or urgency is present, in the absence of definable pathology.

Diagnostic Process

The diagnosis of IC is not difficult and is based upon presenting signs and symptoms and an absence of other bladder pathology. A patient history of urinary frequency and urgency, pain or discomfort in the pelvic area, and flares associated with sexual activity are strongly suggestive of IC. The pelvic pain can be experienced throughout the genitourinary area, including the lower abdomen, inguinal area, labia, vaginal-perineal region, lower back, or the medial aspect of the thighs, often confusing a diagnosis (Table 5). Normal urinalysis, sterile urine culture, and negative cytology rule out urinary tract infection and bladder cancer, the only significant diagnoses associated with these presenting signs and



symptoms. When IC is suspected, useful information can be obtained by having the patient keep a voiding log (Table 6). Physical examination can detect anterior vaginal wall tenderness in symptomatic patients who currently have pain. This is perhaps the most valuable and only physical finding. Although prolapse may be present, in general, it has nothing to do with the patient's symptoms. In patients who have hematuria and in men over age 45, one can consider office cystoscopy and upper urinary tract imaging to rule out genitourinary cancer. Males over the age of 55 years also may require assessment for bladder outlet obstruction.

TABLE 5. Location of Pain in IC¹²

Location of Pain	% Affected
Dysuria	47
Urethral/vaginal	71
Above pubic bone	67
Lower abdomen	45
Lower back	42
Vaginal	52
Inguinal	23

TABLE 6. Diagnosis of IC

- No definitive test for IC
- Initial process
 - Patient history + physical examination + urinalysis/culture
 - Voiding log
- Cystoscopy with/without hydrodistention
- Patient questionnaire (PUF)
- Potassium Sensitivity Test Additional tests
 - Pelvic or transvaginal ultrasound
 - Intravenous pyelogram
 - Cystometrogram

IC cannot be diagnosed histologically. Cystoscopy with or without hydrodistention (under anesthesia) is routinely performed on any patient with micro- or gross hematuria to rule out any bladder abnormalities but is of limited benefit and therefore not required for the diagnosis of IC.¹³ Fewer than 1 percent of patients with severe disease will have the classic sign of erythematous patches (Hunner's ulcers) upon cystoscopy; most patients will have no lesions visible upon routine inspection of the bladder.⁷ Petechial hemorrhages also have been identified

in healthy patients. Cystoscopy with hydrodistention has been shown to improve symptoms in 30 to 60 percent of patients with milder cases of IC within two to four weeks, after an initial period during which symptoms worsen, and is therefore considered to be an initial short-term therapeutic option. However, some risks are associated with the procedure, including the risk of small bladder tears and the very rare risk of significant bladder perforation requiring catheter drainage or open surgical repair.

Two recent significant additions to the diagnostic armamentarium include the written screening questionnaire—the Pelvic Pain Urgency and Frequency Patient Symptom Scale—and the Potassium Sensitivity Test. These two tools represent the first real advances in diagnosis in many years and are helpful, but not necessary, in diagnosing IC. Although neither is sufficient alone to conclusively diagnose IC, a high PUF score in combination with a positive PST is strongly suggestive of IC. In fact, recent data suggest that high PUF scores are strongly correlated with a positive PST. Thus, a high PUF score alone may be considered sufficient to initiate IC therapy.

Pelvic Pain Urgency and Frequency Patient Symptom Scale

The Pelvic Pain Urgency and Frequency Patient Symptom Scale is an eight-question symptom scale that measures both the presence and severity of symptoms and much a patient is bothered by the symptoms (*Patient Symptom Scale*, inside back cover). The maximum score is 35. The PUF is more specific to IC symptoms than any other available questionnaire; it addresses both urologic and gynecologic symptoms.

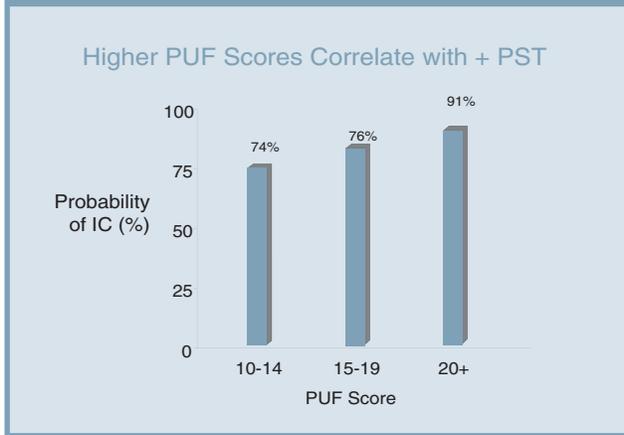
One-third of its questions address frequency (day and night), a symptom that is not covered by any other urologic questionnaire; one-third address urgency (a separate symptom); and one-third address pelvic pain. In addition, two questions concern symptom flares with sexual activity. An overwhelming majority of healthy/control subjects have low PUF scores (<2); in contrast, high symptom, bother, and total scores (10+ points) are highly suggestive of IC (Figure 2). Recent data indicate that any patient who scores ≥ 5 on the PUF has a 55 percent chance of having IC.¹⁴ The PUF can lead to early identification of patients with a high likelihood of having IC and can help distinguish IC from other abdomenopelvic conditions. It should be administered to all patients who present with chronic pelvic pain, including those with recurrent UTIs and chronic prostatitis, and a score of 5 or more makes IC a likely diagnosis.

Intravesical Potassium Sensitivity Test

The intravesical Potassium Sensitivity Test was developed primarily to test the scientific hypothesis that



FIGURE 2. Higher PUF Scores Correlate with Positive PST (IC)¹⁴



potassium plays a significant role in generating bladder symptoms. It was also developed to identify patients with abnormal epithelial permeability that allows potassium to leak and be absorbed into the bladder epithelium, causing pain, inflammation, and ultimately tissue destruction. Patients with a healthy bladder typically do not absorb or react with pain or urgency to potassium chloride, whereas patients with IC will respond with significant discomfort or pain upon the introduction of potassium (Table 7). Trials consistently demonstrate a highly significant difference between IC patients and control subjects in response to the PST. A positive response to the PST is therefore a definitive sign of a bladder component, such as IC, underlying the pelvic pain.¹² However, because the PST has also been shown to be positive in other bladder diseases, including acute bacterial cystitis and radiation cystitis, these conditions must be ruled out. As a result of all the recent PST findings, the new term “lower urinary dysfunctional epithelium” (LUDE) has been introduced to focus on the fact that the disease we call interstitial cystitis is from LUDE and, as such, may be part of a bigger problem that affects all of the lower urinary tract—the bladder, the prostatic ducts, and the urethra. In all these structures, epithelial dysfunction followed by potassium cycling can generate symptoms. Unlike cystoscopy with hydrodistention under anesthesia, the PST can be performed in an office by a non-urologist. Patients with IC are very “volume sensitive” and can experience significant sensory urgency with a rapid

TABLE 7. Potassium Sensitivity Tests in Patients with IC¹²

	N	+ PST N (%)
Patients	2,148	1,696 (79)
Controls	188	3 (1.6)

introduction of any solution into the bladder. The PST test involves the very slow introduction of 40 cc of room-temperature sterile water—over a two- to three-minute time period—into the bladder through a thin catheter (e.g., a LoFric® catheter or a #10 French pediatric tube used as a catheter). This establishes a baseline of pain/urgency after filling of the bladder, using a scale from 0 (lowest) to 5 (most severe pain) (Table 8). After the water is left in the bladder for five minutes, it is emptied through the catheter and the 40 cc of potassium chloride solution (KCl) is instilled. The patient is asked to re-evaluate the level of pain and urgency; any increase in pain or urgency by ≥ 2 points above 0 suggests IC. The solution can be held in the bladder for up to five minutes for patients who have no immediate reactions. Any response of 2 or more points is a positive PST, provided that the KCl solution is identified as the more provocative solution. Patients who respond significantly to the introduction of just water are considered likely to have IC, because water should not affect a normal bladder. The PST has a rapid recovery time (minutes), although it may cause significant and immediate (albeit temporary) discomfort or flare-ups. It should be noted that this procedure can be coded for reimbursement.

An overwhelming majority of patients with genitourinary symptoms and/or IC have a positive PST; however, a

TABLE 8. Potassium Sensitivity Test

Measures epithelial permeability
Procedure (outpatient basis by non-urologists)
– Introduce H ₂ O into bladder – score pain or urgency on a scale of 0–5
– Introduce KCl into bladder – re-evaluate pain or urgency
– Any score in pain or urgency ≥ 2 suggests IC if patient also rates KCl as more provocative than water
Rapid recovery time (minutes)
Role of PST in diagnosis
– Healthy patients do not respond with pain/urgency to H ₂ O or KCl
– Majority of patients with IC have positive PST (>78%)
– Majority of patients with pelvic pain have positive PST (80%)
Positive PST:
– Definitive sign that CPP has bladder component
– Not sufficient to conclusively diagnose IC
– Also positive in radiation cystitis and acute bacterial cystitis
Negative PST: Does not rule out IC



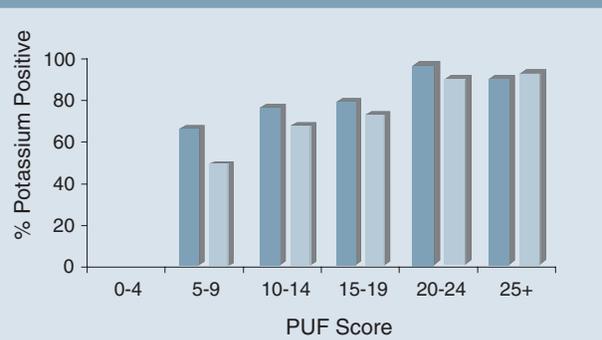
positive PST is not sufficient to conclusively diagnose IC.¹² A negative PST occurs when a patient has no pain or urgency response to the procedure. However, a negative PST does not rule out IC, because up to 60 percent of patient with a negative PST meet the research/diagnostic criteria for IC established by the National Institutes of Health.¹² False negatives can occur in patients who have had recent intravesical dimethyl sulfoxide (DMSO) or heparin therapy, recent hydrodistention, or are on pain medications or already maximally stimulated.¹²

Research has identified many previously unrecognized gynecologic cases of IC through the use of the PST. In a recent study, gynecologists administered the PST to women with gynecologic chronic pelvic pain who had been diagnosed with a wide variety of ailments, including endometriosis, recurrent UTI, vulvar vestibulitis/vulvodynia, and urgency-frequency syndrome. Although only 1 percent of the women had been diagnosed originally with IC, 81 percent³ to 85 percent¹⁵ tested positive on the PST, suggesting that IC can masquerade as a variety of other complaints (Table 9). Of a total of >2,200 PSTs performed on IC patients, 78 percent were positive, in contrast to <3 percent in healthy individuals.^{16,12} These data highlight the value of the PST in the diagnosis of CPP syndromes and IC. In addition, the data indicate that all patients who present with pelvic pain should be evaluated for a bladder-based condition, such as IC, as part of the standard work-up, because most of them appear to have IC.

Research has clearly demonstrated a high correlation between a high PUF score and the likelihood of a positive PST in gynecology patients with pelvic pain, as well as

urology patients suspected of having IC. In a recent study, 91 percent of women with PUF scores >20 had a positive PST, as did 76 percent of women with PUF scores 15–19, 74 percent of women with PUF scores of 10–14, and 55 percent of patients with a PUF score >5 (Figure 3).¹⁴ In comparison, control patients typically have low PUF scores (<2) and 0 percent positive PST results. Eighty-four percent of patients who score >15 on the PUF will have a positive PST. The high correlation between these two diagnostic measures ultimately may enable clinicians to minimize use of the PST for diagnostic purposes. The PUF can be used as the primary screening tool, reserving the PST for those patients with lower PUF scores (e.g., 5–8) whose clinical presentation is suggestive of IC or for those in whom the diagnosis is unclear.

FIGURE 3. PUF Scores and Potassium-Positive Reaction: Gynecologic Versus Genitourinary Cases¹⁴



N=334. In Press Urology; Parsons et. al
PUF=pain/urgency/frequency, maroon=Gyn, orange=GU.

TABLE 9. Initial Clinical Diagnoses and Potassium Test Results for Patients with Pelvic Pain³

Initial Clinical Diagnosis	No.	Median Age (y)	Patients with +PST ^a (%)
Pelvic pain	93	35	71 (76%)
Vulvar vestibulitis/vulvodynia	45	36	37 (82%)
Dyspareunia	28	40	25 (89%)
Urgency-frequency syndrome	24	41	18 (75%)
Endometriosis	22	33	19 (86%)
Recurrent urinary tract infection	15	31	12 (80%)
Yeast vaginitis	7	38	6 (86%)
Other ^b	6	39	5 (83%)
IC	4	35	4 (100%)
Total	244	36	197 (81%)

^aThere were no statistically significant differences between any groups (P>0.5 for all comparisons, Fisher exact test). The only groups with sufficient subjects available for meaningful, statistical power were those with pelvic pain, vulvar vestibulitis/vulvodynia, endometriosis, and dyspareunia.

^bUrethral syndrome (3 patients), detrusor instability (1 patient), pelvic floor dysfunction (1 patient), and urinary incontinence (1 patient).



MANAGEMENT OPTIONS

Numerous and diverse treatment approaches have been used for the management of IC. The two main goals of treatment are to correct the epithelial dysfunction and to inhibit neural hyperactivities; for many patients, control of allergies is also indicated. Currently, the Food and Drug Administration (FDA) has approved only two drugs for the management of IC: traditional intravesical instillations with DMSO and oral treatment with pentosan polysulfate sodium (PPS). Younger patients (aged 18–25 years) with short-duration disease typically require treatment for 10–12 months; response to treatment takes longer in patients who have a long history of the disease. Responses typically take about 1.5 months for every year the patient has had symptoms of the disease. Additional therapeutic options include a variety of intravesical and oral agents to manage the pain and inflammation associated with IC, often in conjunction with specific diet and behavioral interventions. Surgery remains a last resort for those patients with severe disease who have not responded to any other therapies.

Principles of Therapy

For successful management of IC, a multimodal treatment regimen based on three principles is recommended:

- *Restore epithelial impermeability* with heparinoid therapy; the only approved oral agent is PPS.
- *Downregulate neural hyperactivity* with tricyclic antidepressants (TCAs). When TCAs are not tolerated, selective serotonin reuptake inhibitors are helpful. Anticholinergic drugs have some limited benefit.
- *Control allergies* with hydroxyzine, which stabilizes mast cells and inhibits their degranulation.

In patients who are slow to respond, therapy with an agent such as PPS should not be stopped. Instead, additional medications should be incorporated into the regimen as described in the second and third points.

FDA-APPROVED TREATMENTS

Oral Pentosan Polysulfate Sodium

Pentosan polysulfate sodium (Elmiron®) is the only oral agent approved for the relief of bladder pain or discomfort associated with IC. PPS is similar in chemistry and structure to the naturally occurring glycosaminoglycan layer (mucus layer) (Table 10). It is believed to play a role

in replenishing the defective GAG layer, thereby restoring the epithelial impermeability, which then prevents irritating solutes (primarily potassium) from reaching the epithelial cells. As such, the effects of oral PPS on the bladder epithelium have been likened to the way Pepto Bismol® is used to treat gastrointestinal distress; PPS coats the epithelium and makes it impermeable. PPS therapy also appears to increase bladder capacity and volume per void. PPS may have possible anti-inflammatory properties and a potentially stabilizing effect on mast cells, or even detoxifying cations in urine that could injure the anionic bladder mucus. Finally, successful PPS treatment reduces potassium sensitivity as measured by the PST.

The FDA-recommended dosage of oral PPS is 300 mg/day, taken as three 100-mg capsules. Patient compliance can be enhanced with a dosing regimen of 200 mg twice daily; however, this is not FDA indicated. Patients with decreased urinary frequency may require three to six months of therapy before pain relief is obtained; other patients may experience symptomatic relief within two to four months. Nevertheless, most clinicians who specialize in IC recommend that patients remain on oral PPS indefinitely. When therapy is not successful after six to nine months, additional treatments may be added to the PPS. PPS is well tolerated and has no known drug/drug interactions. Oral PPS is associated with infrequent, mild, and transient side effects including headache, alopecia (completely reversible), and minor gastrointestinal discomfort; approximately 1 percent of patients experience

TABLE 10. Oral Pentosan Polysulfate Sodium

Only oral drug approved for IC (1996)
Similar in chemistry/structure to GAG
Mechanisms of action
Plays role in replenishing defective GAG layer → “Coats the bladder epithelium, protects it from irritating urinary solutes”
Dosage: Three 100-mg capsules per day
Course duration: 10–12 months in short-duration disease; longer in patients with long history of IC symptoms
Side effects: Well-tolerated agent with mild/transient adverse effects

slight liver function changes that are not associated with jaundice or other clinical signs or symptoms and resolve spontaneously.

Clinical trials have demonstrated the efficacy of oral PPS versus placebo in reducing the pain, urgency, frequency, and nocturia of IC.^{17,18} Early research involving patients with severe IC found that PPS reduced pain by at least 50 percent versus placebo after three months of treatment, affording patients significant improvement in their quality



of life (Figure 4).¹⁹ A more recent dose-ranging 32-week study demonstrated excellent patient response to the FDA-approved dose of 300 mg/day PPS.²⁰ In addition, duration of therapy was shown to be much more significant to clinical improvement than therapy dosage, and ongoing use provides increasing symptomatic improvement (Figure 5).

Patients receiving oral PPS therapy need to establish realistic expectations of the treatment. Patients with at least moderate IC often have a significant GAG defect that requires a minimum of three to six months of treatment before oral PPS can exert its effect and allow the bladder sensory nerves to downregulate. Studies that demonstrate even a moderate response to PPS (28 percent to 62 percent¹⁸) in shorter treatment durations highlight the efficacy of this agent, which is enhanced with ongoing use, especially more than eight months.¹⁷

FIGURE 4. PPS Demonstrates Significant Improvement of Symptoms¹⁹

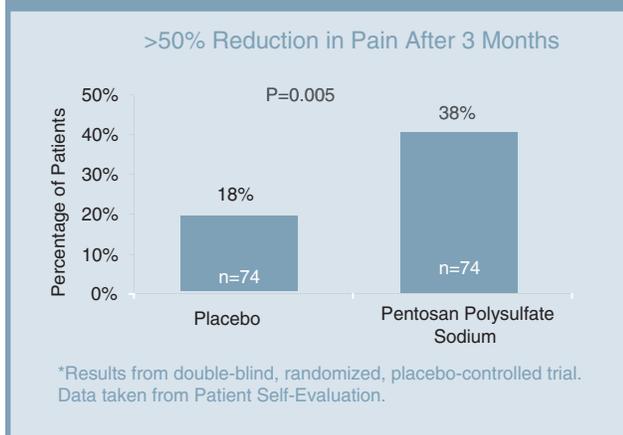
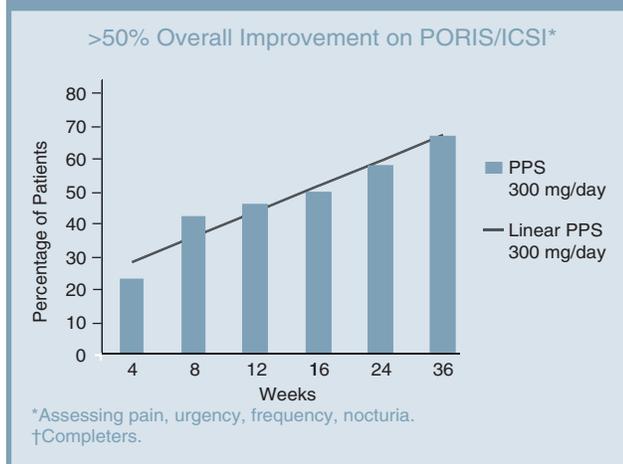


FIGURE 5. PPS – Symptomatic Improvement Increases with Duration of Dose²⁰



Intravesical Dimethyl Sulfoxide

The first and only other therapy approved by the FDA for the management of IC is bladder instillation with dimethyl sulfoxide and RIMSO-50, a 50 percent aqueous solution of DMSO. DMSO is an anti-inflammatory analgesic agent with muscle-relaxing properties (Table 11). The mechanism of action of DMSO remains unknown; however, DMSO has been shown to increase the reflex firing of pelvic nerve efferent axons and to increase bladder capacity.

DMSO is instilled through a catheter and retained in the bladder for five to 10 minutes before being expelled. Each treatment course lasts six to eight weeks and involves weekly or biweekly instillations either in a clinician's office or, by highly motivated patients, through self-catheterization at home. Bladder instillation with DMSO can provide at least moderate symptomatic relief and sustained remissions.²¹ Repeat treatment courses are often necessary, but the efficacy of this therapy disappears rapidly in most patients. DMSO has a good safety profile, although it can leave a garlic-like taste or odor that remains on the breath or skin for up to 72 hours after

TABLE 11. Dimethyl Sulfoxide

- Only agent approved for bladder instillation
- Anti-inflammatory analgesic
- Muscle-relaxing properties
- In-office or self-catheterization
- Treatments administered once/week or once every other week
- Each treatment course = 6 – 8 weeks
- Procedure
 - 4 Insertion of catheter
 - 4 DMSO passed into bladder and retained for ~15 minutes
- Adverse effects: garlic-like taste or odor on breath or skin

treatment.²² Patients are required to undergo blood testing, including kidney and liver function tests, every six months.

Alternative Pharmacologic Therapies

Numerous alternative intravesical and oral agents have been used in the treatment of IC, albeit without specific FDA indications (Table 12). The two intravesical options—heparin sulfate and PPS—focus specifically on reducing the epithelial dysfunction of IC, whereas the oral agents are used to alleviate the pain or inflammation of IC.¹⁶ Heparin is a sulfated polysaccharide, similar to those normally found in the bladder epithelium, which has beneficial anti-adherence actions that protect against bacterial invasion. Intravesical instillation of heparin



sulfate, either as monotherapy or as combination therapy (often with DMSO), corrects the mucosal defect and restores the injured urothelium.

TABLE 12. Second-Line Therapies

Intravesical Heparin	
Oral agents	
Antibiotics	Analgesics
Anticholinergics	Antidepressants
Antihistamines	
Diet/behavioral interventions	
Bladder training techniques	
Surgery	

Patients with concurrent UTI or STI often require oral antibiotics, and patients with concurrent overactive bladder may benefit from prescription anticholinergic agents. It should be noted that neither antibiotics nor anticholinergics are effective specifically for the management of IC. Analgesics, such as aspirin and acetaminophen (possibly with codeine for patients with severe disease), are often recommended to help alleviate pain; however, non-steroidal anti-inflammatory agents have very limited efficacy in IC patients. Tricyclic antidepressants (such as amitriptyline)²³ and antihistamines (particularly hydroxyzine)²⁴ may be taken at bedtime to help the patient sleep. In addition, antihistamines (primarily hydroxyzine) have been shown to suppress mast cell degranulation. Hormone therapy (in the form of oral contraceptives or gonadotrophin analogues) also has been used for some women, especially in reducing the frequency of the menses, given that IC flares typically the week before the period. Because the patients experience more relief of their symptoms when their periods are less frequent, it may be beneficial for them to take continuous birth control pills on a schedule that produces menses only twice per year.

Non-pharmacologic Interventions

Non-pharmacologic therapies, including diet and behavioral interventions, are often recommended to supplement the relief provided by traditional pharmacologic therapies, because they are rarely sufficient alone for most patients. Women are instructed to avoid foods high in potassium that can exacerbate symptoms, including tomatoes, citrus fruits, chocolate, and coffee. Avoiding spicy foods also is recommended.

Behavioral interventions focus predominantly on bladder training techniques and may afford some symptomatic relief for patients with (at most) mild-to-moderate pain. Patients can be trained to institute scheduled voiding

patterns, maintained through relaxation and distraction techniques. This is not to be attempted until patients have begun to respond to oral pharmacologic treatments. Gentle stretching and pelvic floor relaxation exercises also may be of benefit. Tricyclic antidepressants can be started to help women manage the pain and/or concomitant anxiety and depression associated with IC.

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THE RELATIONSHIP BETWEEN IC, CHRONIC PROSTATITIS, AND LOWER URINARY TRACT DYSFUNCTIONAL EPITHELIUM

Interstitial cystitis is not just a disease of women. In evaluating men with lower urinary tract symptoms, the specific diagnosis often has been based on the exact location of the patient's pain: urethral pain was ascribed to urethritis, urgency/frequency with bladder pain was attributed to a cystitis, and penile tip/perineal pain associated with sexual intercourse led to a diagnosis of prostatitis. However, these apparently disparate conditions all may be part of the continuum of lower urinary epithelial dysfunction. The consequence of this dysfunction is an abnormal permeability of the urothelium, which allows the normally high levels of urinary potassium to diffuse directly into the interstitium, thereby depolarizing sensory nerves. The result is urgency, pain, or both. As noted, this epithelial dysfunction can be detected through the use of the Potassium Sensitivity Test (PST). LUDE disease encompasses not only the majority of IC cases but also a substantial number of cases of chronic prostatitis/chronic pelvic pain in men.

Prostatitis is the most common diagnosis among men under age 50 years and the third most common genitourinary disease in men over age 50 years.¹ In the United States, approximately 9 to 16 percent of men aged 40 to 79 years are diagnosed with prostatitis,^{2,3} and 2 to 10 percent of men have at least mild-to-moderate symptoms of prostatitis.⁴ The National Institute of Diabetes, Digestive and Kidney Diseases (NIDDK) of the National Institutes of Health (NIH) established a classification system for prostatitis in 1995 (reconfirmed in 1998) that defined four categories of prostatitis (Table 13). The first two categories, acute bacterial prostatitis (Category I) and chronic bacterial prostatitis (Category II), arise from a bacterial infection and are treated with antimicrobial agents. Category IV, asymptomatic inflammatory prostatitis, is frequently identified when a male is undergoing evaluation for other urogenital concerns (e.g., infertility or prostate cancer). Category III, the largest category, encompasses cases of chronic non-bacterial prostatitis (NBP) and chronic pelvic pain syndrome (CPPS), also known as chronic prostatitis (CP), which has been subdivided into inflammatory (Category IIIA) and non-inflammatory (Category IIIB) CPPS. This category is most similar to IC; in fact, it is believed that many men diagnosed with NBP (CP/CPPS) have concurrent IC. The overwhelming majority of men diagnosed as having prostatitis have NBP or CP/CPPS.⁵ CP/CPPS accounts for 2 to 8 million physician visits each year^{1,6} and is the reason

for 8 percent of visits to a urologist (Table 14).¹ CP/CPPS is the fourth most common diagnosis at urology visits.⁷ The overall prevalence of CP/CPPS, estimated at 9 percent, is equivalent to that of ischemic heart disease or diabetes and more that of asthma.² Currently, approximately 300,000 males are diagnosed with interstitial cystitis each year; however, it is likely that the majority of men with NBP or CP/CPPS—more than 9 million men—have IC, either alone or in combination with prostatitis or urethritis.

TABLE 13. NIDDK Classifications/Definitions Prostatitis⁸

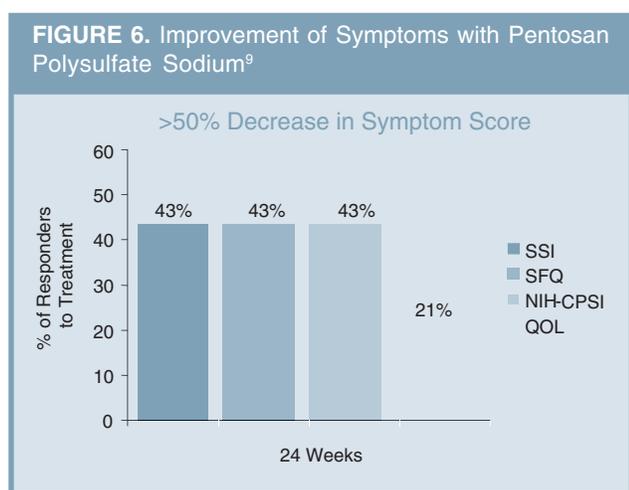
- Category I:** Acute bacterial prostatitis; acute infection of the prostate
- Category II:** Chronic bacterial prostatitis; recurrent infection of the prostate
- Category III:** Chronic non-bacterial prostatitis/chronic pelvic pain syndrome
 - IIIA:** Inflammatory chronic pelvic pain syndrome (white cells are found in semen, expressed prostatic secretions, or voided bladder urine)
 - IIIB:** Non-inflammatory chronic pelvic pain syndrome (no white blood cells are found)
- Category IV:** Asymptomatic inflammatory prostatitis (no subjective symptoms; white blood cells are found in prostate secretions or prostate tissue during evaluation for other disorders)

TABLE 14. Epidemiology of CP/CPPS in Men

- Prostatitis**
 - Most common diagnosis in men <50 years old
 - Third most common genitourinary diagnosis in men >50 years old
 - 9% of men aged 40 to 79 years (in United States)
 - 2% to 6% men have at least mild-to-moderate symptoms
- CP/CPPS**
 - Overall prevalence 9%²
 - Similar to ischemic heart disease/diabetes
 - Accounts for 2 to 7 million physician visits/year^{1,6}
 - Accounts for 8% of urologic visits
 - Fourth most common diagnosis at urology visits⁷



Data from a recent chronic prostatitis treatment study support this concept. In a recent prospective, multicenter, open-label clinical trial, 32 men diagnosed with Category IIIA prostatitis (CP/CPSP) were treated with PPS (100 mg tid) for six months.⁹ PPS therapy was associated with a significant reduction in symptom frequency and severity and a significant improvement in patients' quality of life; 43 percent of the patients reported more than 50 percent clinical improvement (Figure 6). Because PPS is believed to aid in restoring or repairing the urothelial mucus, its efficacy in reducing CP/CPSP symptoms may indicate that CP/CPSP and IC share the same underlying pathophysiology, a lower urinary epithelial dysfunction that may involve both bladder and prostate.¹⁰



To place male IC in perspective, it is necessary to emphasize several points. First, frequency and urgency are primarily a bladder symptom. Dysuria is a urethral symptom. Because bladder pain can be felt anywhere in the pelvis, its origin may not be obvious. The clinical advisors believe LUDE (as reviewed above) can affect the entire lower urinary tract, so that patients may have both IC and prostatitis concomitantly. Although an epithelial dysfunction may be present in urethral and/or prostatic tissues as well as in the bladder, many men who have received a diagnosis of CP/CPSP may have a bladder-origin pathology as the actual source of their symptoms. Pain that originates in the bladder can refer to the rectum, groin, perineum, lower abdomen, scrotum, testes, and/or penis as well as to other locations in the pelvis. The analogue for this is the female (no prostate), whose bladder-generated pain refers to all these **same** regions.

IC in men is characterized by frequency and urgency of urination (which is a bladder symptom) and pelvic pain (which may be from either the bladder or the prostate) in the absence of defined bacterial etiology. Patients also may report pain at the groin, testicles, or tip of the penis; urethral burning; and dyspareunia (Table 15). As is seen in women, men with IC may experience constipation or irritable bowel

syndrome, a slow urinary stream, and low back pain. Frequently, men with IC are initially misdiagnosed as having chronic prostatitis/CPSP, benign prostatic hyperplasia, or epididymitis because of the similarities in clinical presentation: urinary frequency, dysuria, and suprapubic discomfort. Table 16 delineates the numerous similarities between CP/CPSP and IC in men. Both syndromes are characterized by a negative urine culture, pelvic discomfort or pain, and dyspareunia. It is important to bear in mind that many of the men may have either IC only or both problems. In the past, the diagnosis was made by tradition and habit in such cases. Traditionally, chronic prostatitis was the most likely diagnosis for a man who presented to a clinician with

TABLE 15. Location of Pain in Prostatitis¹¹

Location of Pain	% Affected ^a
Dysuria	78
Perineal	27
Lower abdomen	42
Testicular	50
Scrotal	36
Rectal	33
Post-void	50

^a N=43

symptoms of intermittent genitourinary pain, symptom flares associated with sexual activity, and no evidence of bacterial infection. It is now becoming recognized that IC is underdiagnosed in the male population, and that IC may be present in as many as one in 20 men in the United States.¹⁰

Diagnosis of IC in men is similar to that of diagnosis in women, focusing on patient history, presenting signs and symptoms, and ruling out infection or cancer through urinalysis, culture, and cytology. The PUF or the NIH Chronic Prostatitis Symptoms Index can be used to assess prostatitis symptoms (Table 17).

The PST is also applicable for male patients. As with healthy women, healthy men rarely respond to potassium in the bladder. However, the majority of males with either IC or prostatitis exhibit potassium sensitivity as measured by the PST. In fact, recent research indicates similar rates of positive potassium sensitivity tests among men diagnosed with prostatitis and IC (~84 percent and 79 percent, respectively).¹¹ PUF scores also correlate highly with a positive PST in men (unpublished data).

Management of IC in men is also similar to that in women. As mentioned, a six-month regimen of PPS (100 mg tid) produced a significant decrease in frequency and severity of symptoms in CP/CPSP patients.⁹ Anecdotal evidence suggests that male IC patients receive the greatest benefit



TABLE 16. Relationship Between CP/CPPS and IC in Men

	CP/CPPS	IC
Symptoms	Urinary urgency	Urinary urgency
	Urinary frequency	Urinary frequency
	Nocturia	Nocturia
	Pelvic pain/testicular/penile pain	Pelvic pain
	Ejaculatory pain/orchialgia	Dyspareunia
Etiology	Effects of urine toxicity	Effects of urine toxicity
	Neurogenic	Neurogenic
	Occult organisms	Occult organisms
Pain with bladder filling	~45% of patients	Almost always
Glomerulations with hypersensitive disorders	Frequent	Frequent
Urine culture	Negative	Negative
Office cystoscopy	No abnormalities	No abnormalities
Levator spasm	Frequently seen	Frequently seen
Non-relaxing pelvic floor	50% patients	70% patients
Signs of inflammation	Variable	Variable
Effect of diet	Can exacerbate symptoms	Can exacerbate symptoms

from PPS 600 mg/day in two or three divided doses. It should be noted that prescribing PPS at a dose above 300 mg/day is an off-label use of the drug.

In conclusion, men 50 years of age or younger who present with urgency/frequency and/or pelvic pain are likely to have LUDE disease, the consequence being a problem with potassium management in the lower urinary tract. In such patients, the disease may affect any number or combination of organs in the lower urinary tract—the bladder, urethra, or prostate. This will be reflected in the patient’s symptomatology. IC, urethritis, and prostatitis are all part of the continuum of LUDE, and a patient may have one or more of these problems simultaneously. By understanding the disease process and use of the PST, IC in these patients can be effectively diagnosed and managed—often with the use of PPS.

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TABLE 17. NIH-Chronic Prostatitis Symptoms Index

Pain or Discomfort

1. In the last week, have you experienced any pain or discomfort in the following areas?
- a. Area between rectum and testicles (perineum)
 - b. Testicles
 - c. Tip of the penis (not related to urination)
 - d. Below your waist, in your pubic or bladder area
2. In the last week, have you experienced:
- | | | |
|--|---------------------------------------|---------------------------------------|
| | <u>Yes</u> | <u>No</u> |
| a. Pain or burning during urination? | <input type="checkbox"/> ₁ | <input type="checkbox"/> ₀ |
| b. Pain or discomfort during or after sexual climax (ejaculation)? | <input type="checkbox"/> ₁ | <input type="checkbox"/> ₀ |
3. How often have you had pain or discomfort in any of these areas over the last week?
- | | | |
|---|---------------------------------------|---------------------------------------|
| | <u>Yes</u> | <u>No</u> |
| <input type="checkbox"/> ₀ Never | <input type="checkbox"/> ₁ | <input type="checkbox"/> ₀ |
| <input type="checkbox"/> ₁ Rarely | <input type="checkbox"/> ₁ | <input type="checkbox"/> ₀ |
| <input type="checkbox"/> ₂ Sometimes | <input type="checkbox"/> ₁ | <input type="checkbox"/> ₀ |
| <input type="checkbox"/> ₃ Often | <input type="checkbox"/> ₁ | <input type="checkbox"/> ₀ |
| <input type="checkbox"/> ₄ Usually | <input type="checkbox"/> ₁ | <input type="checkbox"/> ₀ |
| <input type="checkbox"/> ₅ Always | <input type="checkbox"/> ₁ | <input type="checkbox"/> ₀ |
4. Which number best describes your AVERAGE pain or discomfort on the days that you had it, over the last week?
-
- 1 2 3 4 5 6 7 8 9 10
- No pain Pain as bad as you can imagine

Urination

5. How often have you had a sensation of not emptying your bladder completely after you finished urinating, over the last week?
- ₀ Not at all
 - ₁ Less than 1 time in 5
 - ₂ Less than half the time
 - ₃ About half the time
 - ₄ More than half the time
 - ₅ Almost always

6. How often have you had to urinate less than 2 hours after you finished urinating, over the last week?
- ₀ Not at all
 - ₁ Less than 1 time in 5
 - ₂ Less than half the time
 - ₃ About half the time
 - ₄ More than half the time
 - ₅ Almost always

Impact of Symptoms

7. How much have your symptoms kept you from doing the kinds of things you would usually do, over the last week?
- ₀ None
 - ₁ Only a little
 - ₂ Some
 - ₃ A lot
8. How much did you think about your symptoms, over the last week?
- ₀ Not at all
 - ₁ Less than 1 time in 5
 - ₂ Less than half the time
 - ₃ About half the time

Quality of Life

9. If you were to spend the rest of your life with your symptoms just the way they have been during the last week, how would you feel about that?
- ₀ Delighted
 - ₁ Pleased
 - ₂ Mostly satisfied
 - ₃ Mixed (about equally satisfied and dissatisfied)
 - ₄ Mostly dissatisfied
 - ₅ Unhappy
 - ₆ Terrible

Scoring the NIH-Chronic Prostatitis Symptom Index Domains
 Pain: Total of items 1a, 1b, 1c, 1d, 2a, 2b, 3, & 4 = _____
 Urinary Symptoms: Total of items 5 & 6 = _____
 Quality of Life Impact: Total of items 7, 8, & 9 = _____



ESTABLISHING AN IC TREATMENT CENTER

The number of patients who have IC is significantly greater than previously believed. As a result, clinicians and their support staff need to be appropriately educated about the diagnosis and management of this under-diagnosed and undertreated chronic pain syndrome. Figure 7 presents a diagnostic and treatment algorithm to assist in this process. Table 18 identifies the key Current Procedural Terminology (CPT) codes that pertain to the diagnostic procedures associated with IC; all diagnostic procedures are reimbursable. It is important that the clinician's office provide not only medical management but also emotional support to patients with IC. Patient information and advocacy groups such as the Interstitial Cystitis Association and Interstitial Cystitis Network also can support patients as they deal with the chronicity and pain of IC.

FIGURE 7. Guidelines: Diagnosis and Treatment Algorithm for Interstitial Cystitis

Clinical presentation	Urgency + frequency ± pain		
Diagnostic assessment	History Physical examination Urinalysis Urine culture		
Diagnostic results	↓ Neg pain	↓ + Pain	↓ ±Pain
	Neg exam	- Culture	+Culture
	Neg culture		
Diagnosis	OAB	IC/CPPS	UTI
Treatment	PPS, Intravesical DMSO Antibiotics		
If treatment failure, suspect	RUTI Resistant uropathogens IC		

TABLE 18. Interstitial Cystitis: Appropriate 2003 CPT Codes^a

Purpose of Visit/Procedure	CPT Code(s)
New patient (comprehensive)	99204/99205
Established patient (detailed or comprehensive)	99214-99215
Initial consult (Level 4 or 5)	99244 or 99245
Follow-up visits (1 st and 3 rd month)	99213/99214
Second opinion	99274 or 99275
Urinalysis	8100
Cytology	88151
Urine culture	87076, 87088, P9612 87181/87184
Cystourethroscopy	52000
Urethral/ bladder catheterization (simple)	51701
Bladder instillation	51700
PST solution	J3480
DMSO	J1212
Therapeutic solution ^b	J1644 for heparin J2000 for lidocaine
Bladder irrigation, simple and/or instillation	51700
Non-imaging pelvic ultrasound	51798
Cystoscopy	52000
Hydrodistention	52260
Catheter supplies	A4353

^aCPT= Current Procedural Terminology; KCl = potassium chloride; PPS = pentosan polysulfate sodium; PST = Potassium Sensitivity Test.

^bIn addition to heparin, the solution includes 10 cc of 1% lidocaine or 16 cc of 2% lidocaine and 3 cc of 8.4% sodium bicarbonate (not billable). PPS 100 to 200 mg (not billable) may be substituted for heparin. (Note: Intravesical use of PPS is an off-label use of this product.)

^a N=43



CONCLUSION

Interstitial cystitis remains a common yet frequently unrecognized cause of chronic pelvic pain among gynecologic and urologic patients. The clinical manifestations of urinary urgency and frequency and (chronic) pelvic pain are too frequently misdiagnosed as either urinary tract infection or endometriosis in women and chronic prostatitis in men; consequently, a majority of patients continue to suffer for years until an accurate diagnosis of IC is obtained. The recent addition of both the Pelvic Pain Urgency and Frequency (PUF) Patient Symptom Scale and the Potassium Sensitivity Test (PST) should facilitate faster identification and diagnosis of IC, as long as clinicians keep IC “top of mind” for patients who present with this complex of symptoms.

The U.S. Food and Drug Administration currently has approved only two treatments approved for the management of IC: oral pentosan polysulfate sodium (PPS) and weekly/biweekly bladder instillation with dimethyl sulfoxide (DMSO). PPS increases bladder capacity and volume per void and acts as a buffer in the

bladder epithelium, soothing the inflammation and reducing potassium sensitivity. Oral PPS reduces pain by 50 percent within three months of treatment initiation and has a good safety profile. Similarly, bladder instillation with DMSO provides patients with at least moderate symptomatic relief. Other pharmacologic (analgesics, antihistamines, and tricyclic antidepressants) and non-pharmacologic (diet and behavior) interventions may be used to supplement traditional therapies. Surgery is reserved for only the most severe cases that have failed all other treatments.

The impact of IC on a patient’s quality of life can be significant. Early diagnosis and appropriate management are imperative. All male and female patients presenting with chronic pelvic pain and urinary urgency/frequency in the absence of overt bladder pathology should be evaluated for the possibility that the pain is of bladder origin, caused by interstitial cystitis. In women and men under the age of 55 years, interstitial cystitis may be the chief cause of the symptoms of urinary urgency/frequency and/or pelvic pain.

Pelvic Pain and Urgency/Frequency Patient Symptom Scale

Patient's name: _____ Today's date: _____

For each question, please circle the answer that best describes your experience.

	0	1	2	3	4	SCORE
1. How many times do you go to the bathroom during waking hours?	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, to what extent does it usually bother you?	None	Mild	Moderate	Severe		_____
3. Are you currently sexually active? YES ___ NO ___						_____
4. a. If you are sexually active, do you now have or have you ever had pain or urgency to urinate during or after sexual intercourse?	Never	Occasionally	Usually	Always		_____
b. Has pain or urgency ever made you avoid sexual intercourse?	Never	Occasionally	Usually	Always		_____
5. Do you have pain associated with your bladder or in your pelvis, vagina, lower abdomen, urethra, perineum, testes, or scrotum?	Never	Occasionally	Usually	Always		_____
6. Do you still have urgency shortly after urinating?	Never	Occasionally	Usually	Always		_____
7. a. When you have pain, is it usually ___?		Mild	Moderate	Severe		_____
b. How often does your pain bother you?	Never	Occasionally	Usually	Always		_____
8. a. When you have urgency, is it usually ___?		Mild	Moderate	Severe		_____
b. How often does your urgency bother you?	Never	Occasionally	Usually	Always		_____

Total score ranges are from 1 to 35.

Total Score = _____

A total score of 10-14 = 74% likelihood of positive PST; 15-19 = 76%; 20+ = 91% potassium positive



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Parsons: Speaker and consultant for Ortho-McNeil Pharmaceutical, Inc.

Rause: Has no significant relationships to disclose.

Shulman: Speaker and consultant for Ortho-McNeil Pharmaceutical, Inc.; received grant/research support from Wyeth Pharmaceuticals and Berlex Laboratories.

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