

Male Pelvic Pain: Beyond Urology and Chronic Prostatitis

Jeannette M. Potts*

Vista Urology & Pelvic Pain Partners, 2998 South Bascom Avenue, Suite 100, San Jose, CA 94125, USA

Abstract: Chronic pelvic pain in men has often been misdiagnosed as prostatitis. After excluding serious or acute urological, neurological or colorectal conditions, it is essential to approach these patients with a much more comprehensive criteria. Thoughtful interview and methodical physical examination can very often reveal pelvic floor muscle dysfunction, Myofascial pain syndromes, Functional Somatic Syndrome/Central Sensitization Syndromes and/or psychosocial distress. One must be aware that many of these syndromes frequently overlap. Acknowledgement of these conditions and validation of both their physical and psychological distress is paramount to creating trust and confidence in the patient. These are the cornerstones for empowerment and self-care required in the management of chronic pelvic pain.

Keywords: Central sensitization syndromes, chronic pelvic pain, empowerment, functional somatic syndromes, myofascial pain syndrome, myofascial trigger points, neuroendocrine dysfunction, pelvic floor muscle dysfunction, prostatitis, self-care.

INTRODUCTION

Taxonomy is the science of classification. In medicine, this technique is essential for promoting accuracy in describing clinical conditions and guiding treatments as well as research. The outdated and erroneous misuse of urological and inflammatory terminology to describe, classify and study this condition in men has led to misunderstanding, misdiagnosis, mistreatment and misappropriation of research funding.

Male pelvic pain continues to be erroneously approached as an urological condition and even worse, as an infectious or inflammatory malady of the prostate gland.

Although growing numbers of studies demonstrate a changing focus away from the prostate, research and treatment remain in the realm of urologists, who perpetuate the prostatocentricism through their persistent reference to the Prostatitis Classification System and the Categorization of male pelvic pain within the designation of Category 3 Prostatitis: Chronic (non-bacterial) Prostatitis/Chronic Pelvic Pain Syndrome. Published studies, as recently as 2015, continue to use the National Institutes of Health- Chronic Prostatitis Symptom Index (NIH-CPSI) as the research tool for inclusion criteria and instrument for assessing progress. Even more confusing, is the application of NIH-CPSI for studies testing the efficacy of therapies which neither address infection nor prostate disease, *e.g.* physical therapy, stress management, biofeedback.

Imagine applying similarly flawed taxonomy to a condition like headache. And headache would be subcategorized within the NIH Encephalitis Classification System, as

Category 3, non-infectious encephalitis/Chronic Headache syndrome [1] ...Then imagine all physicians evaluating and treating all types of headache as an infectious process in the brain.... This would be unacceptable, and yet this manner of approach and description persist in urology and primary care.

Taxonomy has indeed a very strong direct as well as indirect influence on our professional behavior. Erroneous organ specific labels for these conditions, perpetuate a narrow focus for both doctors and their patients, while hindering a more comprehensive approach for care and research.

This may also have ramifications in terms of insurance and reimbursement factors, since one of the potential obstacles to comprehensive care is the time afforded to physicians in the busy clinical setting. Narrowing the focus and spending less time with patients contributes to the vicious reimbursement cycle.

The broad differential diagnosis of male pelvic pain requires a comprehensive approach. After excluding serious or acute pathological conditions of the colon, rectum, neurological system or urinary tract, the physician should consider dynamic or functional conditions such as pelvic muscle dysfunction, Myofascial trigger points, pudendal neuralgia and functional somatic syndromes, also described as central sensitization syndromes. Patients may have one or more of these conditions, and often, I have found that patients do indeed have overlapping syndromes. Anxiety and stress play a predisposing and/or perpetuating role in pelvic pain as well.

In this setting, physicians are genuinely challenged to employ the art of healing, requiring an ongoing intellectual curiosity, compassion and creativity. Perhaps in more than any other field, a physician's EQ (Emotional Quotient) can be as significant as his academic credentials.

*Address correspondence to this author at the 2998 South Bascom Avenue, Suite 100, San Jose, CA 94125, USA; Tel: 650-996-3761; Fax: 408-703 4134; E-mail: DrPotts@VistaUrology.com

Either because of biopsychosocial predispositions or because of secondary depression and hopelessness due to the burden of pain, patients find themselves no longer in the “driver’s seat” and may assume a role of victimization. This response to a painful or chronic condition must be identified and addressed, as it greatly influences a patient’s confidence in the diagnostic process and impacts compliance with therapy, most of which involves self care.

This author has long believed that patient empowerment is the cornerstone to treating this condition in most patients. It is essential to make the correct diagnosis, but more importantly, the patient should bear witness to the formulation of that diagnosis. Only then, can the patient regain confidence and begin taking steps towards his recovery. We should never discount the influence of our level of engagement and compassion. We must be mindful of our professional behavior as having either a placebo or nocebo effect on patients. Therapeutic empowerment of patients can only be derived in a positive, supportive environment.

PELVIC PAIN IN MEN IS NOT PROSTATITIS

The very same members of the consensus panel who established the NIH classification system, readily acknowledged and stated that Category 3 Prostatitis represented the most common form of the symptomatic disease, 90-95%, and yet could not be proven to be an infection nor malady of the prostate gland.

Studies to demonstrate a prostocentric cause for the symptoms fail to show a correlation.

As early as 1963, an investigator observed that antibiotics afforded no better response than placebo among men with symptoms of prostatitis [2]. This has been corroborated by many investigators since then.

In a randomized, placebo-controlled trial 6 weeks of levofloxacin therapy for chronic prostatitis yielded no advantage over placebo [3], and a subsequent trial found that neither ciprofloxacin, the alpha-blocker tamsulosin, nor their combination reduced symptoms of chronic prostatitis compared with placebo [4].

There has been no correlation between symptom severity and the results of localization cultures, when using the Meares- Stamey technique otherwise known as the four glass test [5]. (The 4-glass test involves collection of sequential urine specimens before and after prostate massage and of prostatic fluid during prostate massage) [6].

Localization cultures can be even more misleading in the CPPS population as demonstrated in yet another, relatively large study in which normal controls were just as likely as men with chronic prostatitis/CPPS to have positive localization cultures (about 8% in both groups) [7]. Even prior to this publication, some specialists shared similar observations, which led to one of the most important recommendations made by the Giessen Consensus Group in 2002: Antibiotics were to be withheld until a second localization culture corroborated the same organism [8].

Localization testing to identify inflammation in either the expressed prostatic secretions (EPS) or in semen are simi-

larly nonspecific. Patient symptom severity is not correlated to presence or degree of inflammation detected in these specimens [9]. Indeed, abnormally high white blood cell counts have been identified among asymptomatic men. For example, many asymptomatic men seeking care for infertility have leukocytospermia. While infection is one potential cause of leukocytospermia, it can also occur in the setting of neurological trauma or in the setting of varicoceles [10]. In another example, among asymptomatic men with elevated PSA, 42% were found to have abnormally high white blood cell counts in their EPS, and subsequent prostate biopsies in this cohort showed a 50% incidence of histologically proven inflammation [11].

In 2013, researchers demonstrated no differences in bacterial cultures when comparing symptomatic patients with controls. Using state of the art microbial detection methods, 257 patients with either presumed Category 3 prostatitis or Interstitial Cystitis/Bladder Pain Syndrome and 261 asymptomatic controls were tested for uropathogens and compared. (Sixty percent of the subjects were males.) This provides the latest and best evidence regarding the absence of a microbiological contribution to Urologic Pelvic Pain Syndromes [12].

Chronic Orchalgia defined as either constant or intermittent scrotal or testicular pain is a common component or frequently diagnosed manifestation of Chronic Pelvic Pain in men. Unfortunately, it too, is approached as an infectious disorder and too commonly treated “empirically” with long repeated courses of antibiotics. In a related study, 55 men diagnosed with chronic scrotal pain syndrome (CSPS), were thoroughly evaluated by means of history, physical examination, scrotal ultrasound and methodical microbiological investigation. This consisted of urine localization study (four glass test), semen cultures and PCR tests for *Chlamydia trachomatis*, *Ureaplasma urealyticum*, *Mycoplasma hominis* and *Gonorrhea*. Only 22% demonstrated evidence of any organisms of clinical significance, leading the investigators to conclude that there is no evidence for the widely held belief that CSPS is the result of a chronic bacterial infection, therefore, “widespread use of antibiotics for this condition is unjustified” [13].

I’d also like to share my observation of investigations conducted by the NIH-NIDDK over the past 15 years. These did not include urine culture as entrance criteria for patients with presumed NIH Category 3 prostatitis. A single negative urinalysis sufficed as adequate screening prior to informed consent in pregabalin trial [14], alfuzosin trial [15], and physical therapy trial [16]. Study designs were formulated by a consensus of prostatitis experts, and no patients developed a urinary tract infection during non-antibiotic trials.

Besides antibiotics, other prostatocentric therapies are prescribed to men with CPPS. Investigators followed 100 patients with chronic prostatitis over 1 year, during which time they received sequential monotherapies that included antibiotics, alpha-blockers, and anti-androgen therapies [17]. One third of patients showed only modest symptom improvement, while only 19% experienced significant improvement. (Placebo responses are often similar). This is one

of my favorite studies, as it seems to have methodically dissociated the prostatocentric therapies from men with CPPS symptoms.

EVEN WHEN LOWER URINARY TRACT SYMPTOMS ARE ASSOCIATED WITH PELVIC PAIN, IT IS NOT DUE TO PROSTATE PATHOLOGY

In the past, LUTS in this setting was considered to be a manifestation of urinary tract infection or sexually transmitted disease, and later as “an acquired voiding dysfunction associated with prostatitis and/or prostatodynia” [18]. The voiding dysfunction described shares many characteristics of the “non-neurogenic neurogenic bladder,” observed by Hinman, “in boys with ureteral damage attributed to voiding dysfunction, which was not associated with anatomical or neurological abnormality” [19].

A study of 1768 men and 981 women, who volunteered during a health evaluation in Austria, was conducted to prove that LUTS associated with CP/CPPS could be unrelated to a prostate condition. The volunteers completed the National Institutes of Health Chronic Prostatitis Symptom Index (CPSI), with the female homolog of each male anatomical term for female participants, and International Prostate Symptom Score (IPSS), as well as a pelvic pain query. The prevalence of symptoms suggestive of CPPS in this selected population was 5.7% in women and 2.7% in men, and was higher in premenopausal women ($p = 0.03$). Storage symptoms were higher in women up to 60 years, and voiding symptoms were higher in men above 60 years of age. Further, mean IPSS scores were also significantly higher among women. The preponderance of LUTS and pain in the female cohort supports the conclusion that “other causes apart from the prostate are most likely to be involved” in CP/CPPS and LUTS diagnosed in men [20].

In 1994, Kaplan evaluated men previously “misdiagnosed” with chronic nonbacterial prostatitis. Among these men he observed a high incidence of bladder neck obstruction, which was associated with perineal pain in many. LUTS and pain resolved with bladder neck incision [21]. In a subsequent study of men 50 years of age or younger with voiding dysfunction, urodynamic testing revealed bladder neck obstruction (54%), pseudodyssynergia (contraction of the external sphincter during voiding) (DSD)(24%), impaired bladder contractility (17%), and acontractile bladder (5%) [22]. In a subsequent study, men with urodynamic evidence of pseudoDSD, 83% were successfully treated with biofeedback alone [23]. The investigators also noted that >90% of the patients were first born males, which may indicate a possible biopsychosocial predisposition for this disorder, whether it be called non-bacterial prostatitis, CP/CPPS, UCPP or pseudoDSD.

In a Chinese study of 113 CPP patients between ages of 18 to 48, nearly 20% were found to have urodynamic evidence of [non-neurogenic] DSD or pseudoDSD. This was characterized as low Q max, high detrusor pressure and high urethral pressures [24]. These patients, too, responded well to biofeedback.

Because of their success in the management of LUTS associated with BPH, alpha-blockers have been studied

rather extensively for the treatment of CPP. Further justification for the study of alpha-blockers for CPP is also based on the observation that these agents block $\alpha 1$ -mediated signaling in the lower urinary tract and the central nervous system, which may lead to improvement of both LUTS and pain in men with UCPP [25]. The effectiveness of alpha-blocker therapy for CPP, however, remains controversial as illustrated by one systematic review of six randomized, placebo-controlled trials comprising 386 patients with CP/CPPS. Four of the six trials showed a statistically significant improvement in symptom scores with alpha-blocker therapy, but two of these trials demonstrated no significant difference in quality-of-life scores. Of remaining two studies, one showed no difference between alpha-blocker therapy and placebo and the other had limitations in statistical methodology. The authors noted that these trials used differing alpha-blockers (no head-to-head studies have been reported) and lacked uniformity in how they defined significant change [26].

A subsequent NIH sponsored trial comparing the alpha-blocker alfuzosin with placebo in 272 UCPP patients, showed no difference in symptom scores, with both groups experiencing response rates of 49% and GRA improvement of 34.8% vs 33.6%, respectively [27].

A meta-analysis, published in JAMA in January 2011, provoked continued controversy. In this study, the pooled response rates favored alpha-blockers alone or in combination with antibiotics for the management of CP/CPPS. This meta-analysis also employed a research tool, which meticulously assessed the phenomenon of publication bias. The authors acknowledged that these pooled response rates “may be inflated given the evidence for publication bias” [28]. This statement was not included in the abstract and was excluded from article highlights in other periodicals, which was potentially misleading, perpetuating overuse/misuse of antibiotics or alpha-blockers in this setting. Furthermore, treatments, which may be more beneficial for some patients, such as physiotherapy or phytotherapy, were not included in this analysis.

Silodosin, a highly selective $\alpha 1A$ -adrenoceptor antagonist was also studied in the treatment of CP/CPPS. A total 151 patients were divided into three groups comparing 4 mg silodosin against an 8 mg dose and placebo. Silodosin at 4 mg was shown to be more effective than placebo in improving CPSI (statistical significance achieved within the urinary symptom and quality of life impact domains). GRA was also significantly greater for the treatment group (56% for 4 mg silodosin vs. 34% for placebo) [29]. The differences in treatment effects observed in this and other alpha-blocker studies, as explained by the authors, may be due to differences in study design, α -blockers and study population.

Improved patient phenotyping may perhaps, lead to better patient selection for some therapies such as alpha blockers and improved outcomes for certain subgroups.

The UPOINT classification system offers a first step towards a more ideal approach to men with pelvic pain. The nomogram represents U for Urinary, P for psychological, O for organ (prostate), I for infection, N for neurological and T for tenderness [of muscles]. The authors of this construct

point out the benefits of treating patients according to the subclassifications to better tailor therapy [30].

While the authors should be applauded for widening the scope of our approach to these patients, they still cannot seem to extricate themselves from “O” (the prostate organ) nor the “I” for infection. By definition, Category 3 Prostatitis is non-bacterial, and as mentioned before, not proven to be caused by any malady of the prostate gland. Additionally, the N for neurological is poorly defined, as it is meant to somehow encompass the role of functional somatic syndromes and perhaps other neuralgias or nerve entrapment syndromes such as Pudendal Neuralgia. And finally, T for tenderness does not do justice to the very broad and specialized field of physical medicine and the detection of Myofascial trigger points, which are clearly different from “tender” points. The UPOINT system does not address or explain the treatment or release of the trigger points. There is no acknowledgement of “T” or the elusion of Myofascial Pain Syndromes as a single domain, which can be causing symptoms in the other domains. Moreover, rather than treating each component of the patients’ symptomatology via the nomogram, it may be of greater benefit to treat Myofascial trigger points in order to relieve urinary symptoms (U), perceived pain in the bladder or prostate (O) and relieve pelvic muscle tension, which can exacerbate nerve entrapment (N). Likewise, exercises and stretching to enhance the treatment and durability of manual trigger point release can be empowering and therefore improve patients’ psychological well-being (P).

DYSORGASMIA AND POST EJACULATION PAIN ARE FREQUENTLY ASSOCIATED WITH CPPS, NOT PROSTATITIS

While many continue to diagnose dysorgasmia (pain with orgasm) and pain following ejaculation as “prostatitis” [31], this symptom is more commonly a component of CPP particularly in the setting of pelvic muscle floor dysfunction or Pudendal Neuralgia.

Approximately 50% of men with CPP also suffer from orgasmic or post-ejaculatory pain. A Turkish study published in 2011 found that 37% of men with CPP had painful ejaculations as compared to zero in controls [32]. A review of the literature demonstrates a range cited between 40 and 70% [33]. In our small series of 36 consecutive patients with CPP, 25 had dysorgasmia, post ejaculatory pain and/or other sexual dysfunction. Forty-five percent of the patients improved with physical therapy focusing on manual release of myofascial trigger points and pelvic floor relaxation [34]. Anderson *et al.* studied 133 men, among whom 92% had sexual dysfunction (including 56% who had ejaculatory pain). Greater than 77% improved with specialized physical therapy [35].

After evaluating hundreds of men with this condition, I began to notice a pattern. Many men who suffered from this condition are likewise troubled by the decrease or absence in semen volume. Their anxiety exacerbated by their wondering if there is a blockage or a back up of semen. Anecdotally speaking, many patients who recovered from CPP by employing the approach of pelvic floor physical therapy, reported improved sexual functioning, disappearance of pain and a return of normal ejaculatory volume and force.

Over the years, I have also had several patients who practice Martial Arts or Eastern Religions. These ASYMPTOMATIC men have shared with me their experience of preserving Chi [Energy]. They do not ejaculate during sexual activities. But they do climax. What they describe, essentially, is a form of volitional retrograde ejaculation, whereby the pelvic floor muscles are tightly contracted during orgasm, changing the variance in outlet resistance to reverse. That is, the point of least resistance is no longer out the urethra, but instead, the bladder neck, leading to retrograde ejaculation. Further research revealed that some men find this practice very painful and need to give up the practice.

Listening carefully to men with CPP and learning more about my other patients’ practices, allowed me to make the connection between these phenomena and to formulate my theory of Ejaculatory Dyssynergia [36]. This would explain the pain and decrease in ejaculated volume during flares and the coincidence of pain relief with normal ejaculation, including the perception of improved force and volume of ejaculation as well as enhanced pleasure.

PELVIC PAIN IN MEN

A Multifaceted Condition: One or a Combination of All of these

Pelvic Floor Muscle Dysfunction and Myofascial Trigger Points

When patients present with pain that can be associated with urinary symptoms, defecatory dysfunction and sexual symptoms, it should be no surprise that for most patients, the pelvic floor support structures and musculature are promoting the symptomatology. I ask students and patients alike, to imagine this extraordinary hammock, carrying the urinary and anal sphincters within a beautifully choreographed weaving of muscles, and then to imagine when one or more of those fibers is tense, non elastic, knotted or broken. Without proper attention, more and more of those fibers over compensate and eventually malfunction, hence the recruitment of larger and larger areas of pain or dysfunction. This is why we sometimes see patients with recent urinary symptoms and painful ejaculation, who began their odyssey years ago in the department of colorectal surgery with a non-healing fissure.

We must learn from other specialties as various forms of Physical Therapy have been employed with success for the treatment of analogous pain syndromes diagnosed by gynecologists and colorectal surgeons. Several urologists have applied these principles in the assessment and treatment of men with symptoms of prostatitis or CPP (See Table 1).

In 2004, Clemens and colleagues employed biofeedback and pelvic floor reeducation/ bladder training for men with chronic pelvic pain syndrome. Fourteen of the 19 men enrolled in the study underwent pre-treatment urodynamics. The various urodynamic findings (detrusor instability, hypersensitivity to filling, pseudo-dyssynergia), however, did not predict treatment results [37]. Overall, there were statistically significant improvements in all symptom parameters measured by AUA symptom score, 10-point visual analog pain and urgency scores, and voiding logs. Interestingly,

Table 1. Myofascial physical therapy definitions.

Myofascial Trigger Point: Taut bands or tender nodules that can be detected on examination which may cause painful contractions and/or referred pain when palpated or twitch responses. Areas in which trigger points are located exhibit weakness and limited range of motion.
Myofascial Trigger Point Release: A form of manual physical therapy, which addresses hyperirritable points on muscles or taut bands, which are responsible for pain or restricted movement. The release or treatment is done by compressing, strumming or stripping muscle fibers manually or digitally.
Biofeedback: A technique used to control certain anxiety states or tension with the use of an external device, in this case Surface EMG's which are used to train patients to relax their muscles.
Skin Rolling: A simple technique to free subcutaneous fascia. The skin is gently picked up and pulled away from underlying structures. The skin is then released from the fingertips and adjacent skin is lifted. This is done repeatedly over afflicted body regions.
Injection Therapy: A more immediate means of inactivating a trigger point. Helpful for patients who may not have access to further skilled manual therapy, or for those with limited treatment times. Myotoxic substances should be avoided.
Dry Needling: A form of "injection" therapy, without injectable substance. May be safer and less damaging to muscle fibers. Effleurage: A massage technique which involves sliding or gliding over the body with continuous motion.
Theracane: A self massage tool, which is the same size and shape of a walking cane, which can be used to more easily or comfortably reach trigger points in the back, flank or buttocks.

only half of the patients completed the full treatment course prescribed as 6 sessions.

Biofeedback was again the therapeutic modality in a series by Cornel and colleagues, in Holland [38]. Thirty-one of 33 men initially recruited completed the program, which included weekly and bi-weekly physical therapy up to 6-8 treatment sessions. These patients responded quite favorably as demonstrated by the improvement in NIH- Chronic Prostatitis Symptom index (pre-treatment mean, 23.6; post-treatment mean, 11.4) and pelvic floor electromyogram measurements during rest which improved from mean 4.9 mV at initial visit, to mean 1.7 mV. (Normal resting tone <2.0 mV).

Pelvic floor myofascial trigger point release of the pelvic floor was studied for the treatment of interstitial cystitis and [urinary] urgency frequency syndrome. In this series by Weiss, 7 of the 52 patients were men. Of 42 patients with urgency-frequency syndrome, 83% of patients experienced either complete resolution or moderate to marked relief of their symptoms. Of 10 patients diagnosed with interstitial cystitis, 70% reported moderate to marked improvement [39]. The author believes that pelvic floor physical therapy "arrests the neurogenic trigger leading to bladder changes, decreases central nervous system sensitivity and alleviates pain due to dysfunctional muscles."

More recently, Anderson and colleagues employed Myofascial Trigger Point release and paradoxical (progressive relaxation in the setting of complete acceptance of the painful symptoms) relaxation for the treatment of 138 men diagnosed with CP/CPPS, refractory to "traditional" therapy [40]. Patients received a minimum of weekly treatments for 4 weeks, but some received biweekly treatments for 8 weeks thereafter. Approximately half of the patients treated had clinical improvements associated with a 25% or greater decrease in all symptom scores, which included NIH-CPSI and PPSS. According to Global Response Assessment, 72% of patients reported marked or moderate improvement. The authors proposed a new understanding of UCPPS, in which certain types of pelvic pain reflect a "self-feeding state of

tension in the pelvic floor, perpetuated by cycles of tension, anxiety and pain."

In 2008, we completed a NIH sponsored multicenter trial, testing the feasibility of "manual" PT for the treatment of UCPPS in men and women. This was a randomized single-blinded clinical trial evaluating either Myofascial Physical Therapy (MPT)- targeted trigger point release and connective tissue manipulation (CTM) focusing on the muscles and connective tissues of the pelvic floor, hip girdle, and abdomen or Global Therapeutic Massage (GTM)- non-specific somatic treatment with full-body Western massage. Patients received weekly treatments for 10 weeks, and were evaluated within two weeks after the last treatment. Forty-seven patients were randomized, including 23 (49%) men and 24 (51%) women. Twenty-four (51%) patients were randomized to GTM, 23 (49%) to MPT; 44 (94%) patients completed the study. The trial proved feasibility of manual treatments and excellent adherence to protocol. More importantly, the trial showed a statistically significant difference in the benefit of Myofascial Physical Therapy over Global Therapeutic Massage. The response rate of 57% in the MPT group was significantly higher than the rate of 21% in the GTM treatment group ($p=0.03$). Even more striking was the significantly greater response of men to either modality when compared to women in this study [41]. Among men, 67% responded favorably to MPT, while 44% responded to GTM, which was the same response rate women had to MPT. GTM had minimal benefit for women.

A Functional Somatic Syndrome or, More Accurately, Central Sensitivity Syndrome

In 2001, this author found a strong correlation between the diagnosis of non-bacterial prostatitis and Functional Somatic Syndromes (FSS). A review of 100 randomly selected cases demonstrated that 65% of men seeking second opinion for CP/CPPS met the criteria for overlapping diagnoses considered to be FSS. Other diagnoses among these patients included: IBS (35%), chronic headache (36%), FM (5%), non-specific rheumatological symptoms (21%), and psychological disturbances (48%) [42].

These results are especially compelling when analyzed in the context of the general population, in which the lifetime prevalence of FSS is only 4%.

The inspiration for this chart review had come from a paper published in the *Lancet* in 1999. It had been given to me by a good friend and colleague, Dr. Leonard Calabrese, at the Cleveland Clinic. As was intended, this article expanded my curiosity and broadened my view of CP/CPSS.

In this article, by Wessley and colleagues, FSS are defined as a constellation of symptoms, which are persistent and distressing, and which after appropriate medical assessment, cannot be explained in terms of a conventionally defined medical disease [43]. These conditions are estimated to represent 35% of patients seeking outpatient consultation in every medical and surgical clinic (See Table 2). Wessley and colleagues state, that there are FSS diagnoses in every organ system and in every medical specialty. They believe this is simply a by-product of medical subspecialization and that, we may in fact be dealing with a single global syndrome, given different names by different specialists. The review did acknowledge Interstitial Cystitis as urology's brand of FSS, but did not mention prostatitis. Like myself, however, others have begun to notice the association between FSS and CP/CPSS.

Self reported medical problems were compared between 463 CP/CPSS patients and 121 controls. Domains queried included Gastroenterology, Cardiovascular, Neurological, Lymphatic, Infectious and Psychological. The CP/CPSS group reported dramatically higher incidence of co-morbidities (P values < 0.008) [44]. The significantly higher reported co-morbidities in the CP/CPSS group, is consistent with the patients' real or perceived tendency to suffer with overlapping diseases.

The first systematic exploration of the connection between UCPS and other disorders (in women) was reported

by Alagiri in 1997 [45]. They found, "Allergies, irritable bowel syndrome, and sensitive skin were the most common diseases in the interstitial cystitis population". They appropriately concluded that, "Interstitial cystitis has, as yet, an unexplained association with certain other chronic disease and pain syndromes."

Clauw and colleagues examined cohorts of patients with FM, IC, and healthy controls [46]. They found that IC patients shared many characteristics of FM patients. They were much more likely than controls to have systemic tender points and to report fatigue, musculoskeletal, gastrointestinal, and cardiopulmonary symptoms. In yet another investigation, a twin control study demonstrated the aggregation of overlapping syndromes among the 127 co-twin individuals diagnosed with CFS. When compared to their non-fatigued co-twin, there was a significantly higher prevalence of FM, IBS, chronic abacterial prostatitis, pelvic pain and interstitial cystitis in the CFS twin [47].

Central sensitization or a Central Sensitivity Syndrome (CSS) is one of the best explanations for the phenomenon of FSS, which have both visceral and somatic manifestations. Sensitization is caused by chemical and anatomical changes leading to hyperexcitability in the dorsal horn cells from persistent afferent C fiber bombardment by painful stimuli. The presence of sensitization expands the pain field and creates a neuroanatomical basis for pain persistence and recurrence in the presence of minimal or no discernable pathology. This process will eventually cause a local up-regulation and central "wind up" that creates a neuroanatomical basis for pain persistence in the presence of minimal disease or stimuli.

While recognition of FSS continues to lag, even more compelling mechanisms for CSS and its role in our daily clinical practices has become elucidated. In yet another milestone, Yunus advances the insights of Wessley to explain

Table 2. Functional somatic syndromes by medical specialty. (additions made to Wessley's original published in *Lancet*, 1999.)

Psychology	Affective disorders
Rheumatology	Fibromyalgia
Neurology	Migraine and tension headache, Cognitive difficulties
Infectious Disease	Chronic Fatigue Syndrome, Night sweats, Sick Building Syndrome, Gulf War Illness
Gastroenterology	Irritable Bowel Syndrome, Spastic colon, Globus Syndrome, Non-ulcer dyspepsia
Cardiovascular	Non cardiac chest pain, Mitral valve prolapse, Neurally mediated hypotension
Respiratory	Hyperventilation syndrome
Ear, nose and throat	Vestibular complaints, Vasomotor rhinitis, Globus syndrome, Temporomandibular Dysfunction
Dermatological	Non-dermatomal parasthesias
Allergy	Multiple chemical sensitivity
Gynecology	Premenstrual syndrome, Vulvodynia
Colorectal	Proctalgia fugax, Levator Ani Syndrome
Urology	Interstitial Cystitis/ Painful Bladder Syndrome, Female Urethral Syndrome, Chronic [Abacterial] Prostatitis, Prostatodynia, Chronic Pelvic Pain Syndrome

and justify the use of Central Sensitivity Syndrome for conditions previously designated FSS [48]. (In terms of taxonomy and the implications of our medical terminology, Dr. Yunus is as passionate about the misuse of a FSS as this author is about the overuse of the term prostatitis!) Not only does he convincingly amalgamate strong evidence from various subspecialty studies, but also unifies specific CPP conditions such as Myofascial pain syndromes and psychological distress within the definition of CSS. This inspires improved ways to approach patient care and research. And like Wessley, he presents yet another compelling call to action... as all manifestations of CSS represent the majority of outpatient consultations, as listed in Table 2.

Yilmaz and colleagues were able to detect differences in Autonomic nervous system functioning in men with CPPS. Comparing Blood pressure and heart rate variability among CPP patients and controls during rest, supine positioning or standing, revealed a significant decrease in the parasympathetic component of heart rate variability and an increase in the sympathetic component with postural change [49]. Interestingly, the sympathetic component in men with CPPS did not demonstrate the expected increase upon standing from the supine position. But this may have led to the compensatory increase in blood pressure seen in the CPPS patients. There was also higher mean BP in supine and standing positions in the CPPS group compared to controls, representing increased peripheral vascular sympathetic tone in the CPPS group. These findings suggest cardiovascular autonomic dysregulation in men with CPPS.

The concept of central sensitization is gaining recognition in the urological community; however, it is still detrimental to continue perpetuating a link between an infectious or inflammatory assault on the prostate as the trigger, when in fact, triggers for men with pelvic pain include many other urological as well as non-urological causes: Passage of kidney stones, changes in sexual functioning, obsessive masturbation, vasectomy, cycling, running, anal fissure disease, hemorrhoidectomy, sports or other orthopedic trauma, etc.

Recognizing the broad spectrum of potential triggers helps to better elucidate potential pathophysiology and expand our treatment repertoire. For example, I had seen a man who had experienced scrotal pain for over five years. So terrific was his pain that he underwent an orchiectomy, which unfortunately afforded him no relief of symptoms. Upon further review of his history, I discovered that he had a skiing accident about 9 months prior to the onset of scrotal pain. Although his broken ankle had healed well, his gait was never completely corrected, causing asymmetrical stress to his knees, hips and pelvis. He had developed trigger points with referred pain to the ipsilateral scrotum. His pain was resolved after physical therapy and aggressive home exercise, stretching and orthotics.

Chronic Pelvic Pain Syndromes are prevalent conditions causing significant morbidity and health care burden. For decades, CPPS was evaluated and managed as an end organ diagnosis or urological condition, with little benefit to patients. We believe CPP should be approached more comprehensively as a more common and plausible FSS or Central Sensitivity Syndrome [50].

Pelvic Floor Dysfunction, Stress and Anxiety

The role of psycho-social factors has been studied in this group of patients, revealing higher levels of hypochondriasis, somatization, depression and decreased social support [51]. Others have observed statistically higher incidence of fear of prostate cancer among these patients. These men were also found to have greater difficulty using public toilet, greater incidence of suicidal ideation and were described as more busy, nervous and meticulous [52].

In a later study, patients with chronic prostatitis/chronic pelvic pain syndrome (174) were compared with 72 male controls. Mental health disorders were identified in 13% of the CP/CPSP cases and 4% of controls (OR 2.0, $p = 0.04$) Medications for anxiety, depression or stress were being taken by 18% of patients but only by 7% of controls. Depression and panic disorder were also significantly more common in men with pelvic pain conditions than in controls [53].

The causes for and the perpetuation of CPP are multifactorial. Cognitive/behavioral and environmental variables can be significant predictors of patient adjustment in chronic pain. Men ($n = 253$) from a North American multi-institutional NIH-funded Chronic Prostatitis Cohort Study in 6 US (and 1 Canadian) centers participated in a survey examining pain and disability. Measures included demographics, urinary symptoms, depression, pain, disability, catastrophizing, control over pain, pain-contingent rest, social support, and solicitous responses from a significant other. Regressions showed that urinary symptoms, depression, and helplessness catastrophizing, predicted overall pain. Cognitive/behavioral variables of catastrophizing and pain-contingent rest, respectively, predicted greater pain and disability. Catastrophic helplessness was a prominent pain predictor [54]. The patients' coping and adaptive skills may influence the predisposition or perpetuation of symptoms in CP/CPSP patients, as well as perceived quality of life.

These observations, for example, could provide insights for cognitive therapy and patient self-care regimens.

Other investigators examined whether perceived stress was associated longitudinally with pain intensity and pain-related disability. A cohort of 224 men with CP/CPSP were followed for one year. Perceived stress and pain intensity measures were done at 1,3, 6 and 12 months after diagnosis. Greater perceived stress during the 6 months after the health care visit was associated with greater pain intensity ($p = .03$) and disability ($p = .003$) at 12 months, even after controlling for age, symptom duration, and pain and disability during the first 6 months [55].

Chronic stress may have a role in initiating or exacerbating pain syndromes including CP/CPSP. To that end, Anderson and colleagues demonstrated potential disturbances in psycho-social profiles and hypothalamic-pituitary-adrenal (HPA) function among patients with CP/CPSP. Forty-five men with CP/CPSP and 20 age-matched controls completed the Type A personality test, Perceived Stress Scale, Beck Anxiety Inventory and the Brief Symptom Inventory for Distress and Physical Symptoms. Saliva samples were collected at specific times over a two day period in order to measure

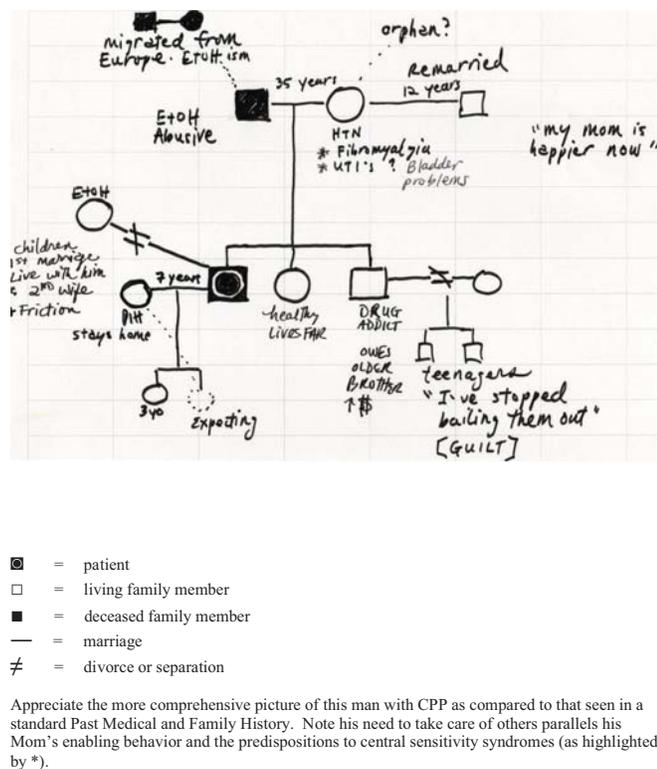


Fig. (1). A sample genogram.

free cortisol, reflecting secretory activity of the hypothalamic-pituitary-adrenal axis. Perceived stress and anxiety were significantly higher among men with CP/CPSPs than controls, as were all other psycho-social variables. Men with chronic pelvic pain syndrome had significantly increased awakening cortisol responses, mean slope of 0.85 vs 0.59 for controls ($p < 0.05$) [56].

As also reviewed and summarized by Yunus [47], CSS are highly correlated to HPA axis dysfunction and hyperexcitability of the central neurons. We would expect, therefore, neuroendocrine dysfunction in this cohort of patients, which explains both the precipitating and perpetuating influences of stress and the bidirectional cascade of this vicious cycle.

Obviously, it is essential to address the psychosocial aspects of CPP, whether these factors play a role in the initiation, perpetuation or exacerbation of symptoms associated with CPP. As previously described, Anderson and colleagues combined myofascial trigger point release with paradoxical relaxation therapy to successfully treat men with CPP [14]. The authors see this combination as “essentially one method with two aspects: Intrapelvic Physiotherapy restores and rehabilitates the pelvic tissue; Paradoxical Relaxation Therapy aims to deeply relax the pelvic floor, and extinguish the habit of focusing unnecessary tension in the pelvic muscles [57].”

The importance of therapy to address patient stress and anxiety is underscored by another study, in which patients were treated with nothing but stress management therapy. Of 110 patients, 86% reported that they were “better,” “much better,” or “cured” with stress therapy alone [58].

Evaluating Men with CPP

The patient interview is a two way street. After acquiring pertinent history, the interview should create a setting in which the patient senses compassion and trust [59]. Physicians must develop their own approach to acknowledging a patient's level of stress, anxiety and depressive symptoms, without discounting the physical aspects of the patient's complaints. In my experience, men suffering from CPP require validation of their physical complaints before addressing the psychological or emotional contributions to this syndrome. It is important to remember, “Physical disease and psychiatric disorder coexist and assessment of their relative contribution is not feasible...” [60]. It is frequently impossible and therefore futile to differentiate “the chicken or the egg;” psychological and emotional factors associated with CPP should be addressed simultaneously.

Particular attention should be paid to the presence of Functional Somatic Syndromes and CSS, or signs and symptoms of overlapping syndromes during the Review of Systems. Through this type of interview, the physician can more easily enlighten his patient about the possible interrelatedness of these conditions.

I frequently employ a family practice tool in my clinic, that is, the genogram. This involves constructing a diagram depicting family relations and other important relationships. It affords much more detail than a family history, capturing positive and negative social interactions, patterns, learned behaviors, etc. Sometimes birth order, sibling rivalry and gender expectations reveal factors, which act as invisible barriers to patients' self care and healing. A sample genogram is shown in Fig. (1).

History and physical should focus on athletic, occupational and other lifestyle risk factors, which may cause repetitive injury and musculoskeletal pain. Many times, there is not one inciting factor, but rather an accumulation of risk factors or micro-traumas that are often not elucidated until after the initial evaluation.

A simple flow chart, depicted in Fig. (2), illustrates the multiple facets to be considered in the evaluation of men

with CPP, beginning with the exclusion of very uncommon prostatic infections. While the differential diagnosis can be quite extensive (see Table 3), the most commonly found disorders in men with CPP include FSS or CSS, Pelvic floor dysfunction and Myofascial Pain Syndromes.

The examiner should be aware of characteristic referral patterns caused by myofascial trigger points, though variability exists between patients. These patterns can be confirmed

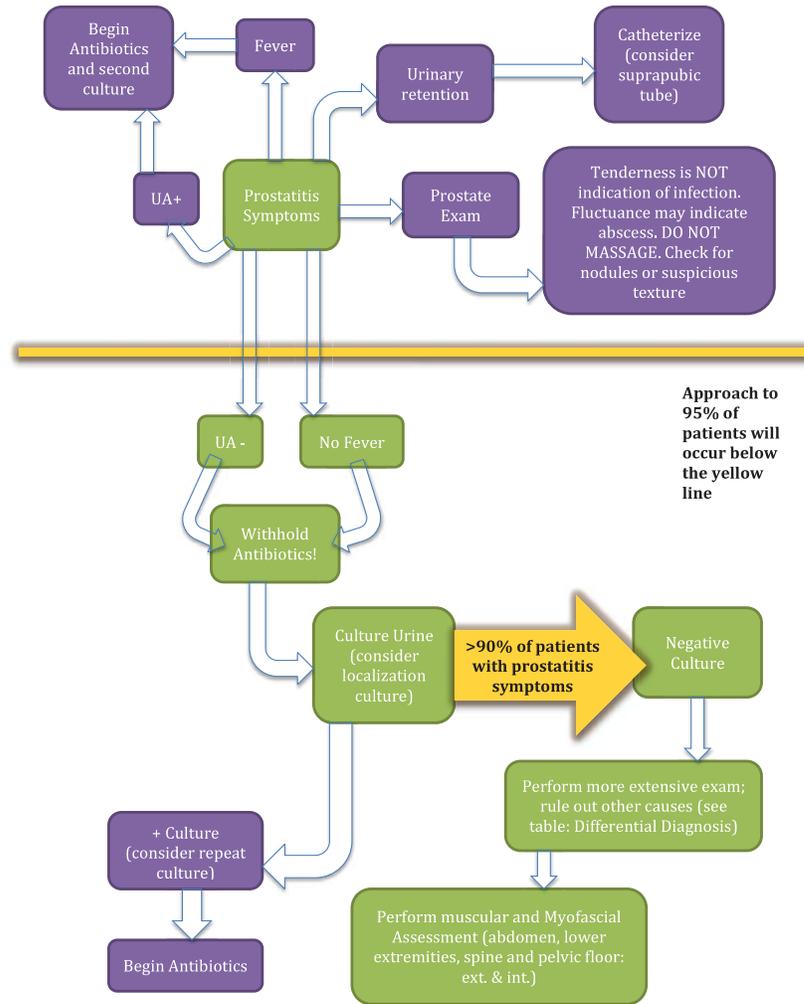


Fig. (2). Basic evaluation scheme for Men with “prostatitis symptoms”.

Table 3. Differential diagnosis of male chronic pelvic pain.

Infection: Sexually transmitted diseases, chronic bacterial prostatitis, fungal infection
Gastrointestinal: Appendicitis, diverticulitis, constipation, anal fissures, hemorrhoids
Abdominal wall defects: Inguinal or ventral wall hernias, Myofascial Trigger Points
Musculoskeletal: Neoplasm (primary or metastatic), degenerative joint disease of the hips, sacroileitis, leg length disparity, athletic or orthopedic issues, Pelvic floor dysfunction, Myofascial Pelvic Pain Syndrome
Neurologic: Low thoracic or lumbar herniated nucleus pulposus, lumbar stenosis, Parkinson disease, diabetic cystopathy, demyelinating disease, Pudendal Neuralgia
Central Sensitivity Syndromes: See functional somatic syndrome Table 2
Urologic: Renal calculi, varicocele, epididymitis, testicular neoplasm, interstitial cystitis

during physical examination. Patients are often helpful by offering feedback during the exam, with respect to location of trigger points and character of referred pain [61].

In addition to complete physical and genitourinary examination, methodical evaluation of back, abdominal wall and pelvic floor muscles should be performed. I believe this part of the evaluation is best performed with the patient in a supine lithotomy position, allowing for thorough examination of the external and internal muscles of the pelvic floor [62]. I methodically examine the coccyx for range of motion and pain as well as corresponding tension or knots in the levator ani muscle groups. The obturator internus is palpated and provocative testing can be applied by having the patient externally rotate against the resistance of the examiner's other hand. Alcock's canal should be gently explored to test for Tinel sign, indicating Pudendal nerve hypersensitivity. Further testing may reveal nerve irritability with referred pain patterns in the distribution of the pudendal nerve branches.

The patient is repositioned to assess posture, pelvic obliquity and leg length symmetry along with strength, flexibility and range of motion. Careful palpation of abdominal wall, pelvic floor and thigh muscles may reveal taut bands characteristic of trigger points with associated twitch response and/or pain [63].

Obviously, the prostate is also examined for nodules and texture changes. Urinalysis is performed to exclude bacteriuria, funguria, pyuria or hematuria. Localization cultures should be considered in patients who have had previously documented positive bacterial urine cultures or past episodes associated with fever. Localization cultures should be performed to guide future evaluation, treatment and more importantly avoid or discontinue unnecessary antibiotics. Prescribing antibiotics empirically is very rarely appropriate and inexcusable without first performing localization cultures. History will also guide the appropriateness of STI testing. In addition to testing for Chlamydia and Gonorrhea, microscopic exam of the VBI may reveal Trichomoniasis, and one may consider testing for Ureaplasma urealyticum and Mycoplasma hominis [64].

Treatment, Empowerment and Self Care

Unfortunately, this author is unable to recommend a specific therapy or management strategy for what is usually termed "Chronic [abacterial] Prostatitis," because the literature only reports the effects of various modalities in a cohort of patients who were inadequately evaluated. Patients in studies using alpha blockers [27], cox-2 inhibitors [65], or neuromodulating agents such as Lyrica [14], did not undergo interviews to exclude CSS or possible pelvic floor or Myofascial syndromes. Moreover, the qualifying physical examinations for these patients did not take into account orthopedic, neuromuscular or meticulous pelvic floor muscle or structural evaluation. The results of such studies imply a narrow diagnosis of chronic prostatitis or prostatodynia (Painful prostate without evidence of inflammation in the EPS), and are therefore not interpretable for the diverse group of conditions found in men with CPP. Our patients surely deserve more comprehensive and thoughtful evaluations, which would more appropriately guide his physician in

prescribing therapies. As mentioned earlier, improved phenotyping of our patients, through more methodical evaluation, could lead to more compelling results in most modalities previously studied. For instance, if the NIH sponsored trial studying the alpha-blocker alfuzosin had excluded patients with obvious pelvic floor dysfunction or Myofascial pain Syndromes, the results may have shown a benefit for the drug when compared to the placebo. Instead, the drug and placebo performed equally in alleviating symptoms. We must always remind ourselves that translation of academic data to the clinical setting requires an understanding of the methodology used in trials. Sometimes results are not translatable to patients in our clinics.

As observed by Wessley and later by Yunus, regardless of the type of CSS diagnosed, patients respond favorably to similar factors. These include: Empathy, Engagement of caregiver, Explanation of the physiological nature of symptoms, Limitation of investigations, Emphasis on management rather than cure, Anti-depressants, Cognitive behavioral therapy and Exercise. These qualities and interventions should be similarly considered for the man suffering from CPP.

Patient empowerment is paramount to management of symptoms of CPP. For men who are diagnosed with pelvic floor muscle dysfunction and/or Myofascial trigger points, empowerment begins with muscle and postural re-education to prevent further tissue compromise and to increase patient awareness and enhance balance and muscle tone [66].

Physical therapy for men with CPP involves connective tissue manipulation (CTM) and trigger point release to all body wall tissues of abdomen, back, buttocks and thighs that are found to contain myofascial trigger points or other connective tissue abnormalities. In the prone position, CMT can be applied posteriorly, from inferior thoracic level 10 to the popliteal creases. These techniques are applied until the therapist notices a favorable texture change within the affected tissue [61].

After repositioning into the supine position, CTM can be applied to anterior tissues. This allows the inclusion of the thighs; laterally, anteriorly, and medially from the knee up to and including the thigh crease. CTM can be performed on the abdominal wall from the supra-pubic rim to the anterior costal cartilages, with a concentration of manual interventions to focus on the peri-umbilical tissues. This usually involves a skin rolling technique, which should be taught to patients as part of their self care regimen. Manual trigger point release techniques are utilized to treat any noted trigger points or scars in the anterior or posterior lower quadrants. Options for the treatment of trigger points include manual release, manual stretching with and without cold spray, myofascial release, muscle play, dry needling or injection therapy. Therapy for dysfunctional muscles includes stripping, strumming, skin rolling and effleurage [67]. Sometimes, Myofascial trigger point release requires adjuvant therapies, which include dry needling or injection therapies. Self care of the external trigger points can be performed using a tennis ball against the wall or against the floor. A theracane can also be employed by the patient to reach his own trigger points comfortably and apply pressure according to his own leverage and tolerance.

Transrectal treatment of the soft tissues of the pelvic floor with CTM can be done with the patient in supine lithotomy, lateral Sims or prone positions depending on the patient's trigger point locations, comfort of the patient and ergonomics of the therapist. Regions evaluated and treated include periurethral tissues, white line, muscle origins and insertions. Myofascial manipulation to each muscle group is performed with the focus on restrictive bands and trigger points. Self care for internal trigger points has been both challenging and controversial. In 2011, investigators did prove feasibility and safety of an internal wand which comes equipped with a pressure gauge, allowing patients to measure the amount of pressure applied and to gradually titrate gentle force against the trigger points [68]. Of course, this requires special individualized instruction, as yet not available to the public.

Providing a form of biofeedback to patients by observing their progress in recruiting muscles and relaxing the pelvic floor helps patients to learn valuable pelvic floor "drop" techniques which has been shown to help diminish pain as well as extinguish urinary urgency [40].

Severe discomfort may prohibit or limit transrectal therapy, but can be employed as treatments progress. However, I have also found that some patients improve without internal therapy, as the external therapies along with patient exercise and stretching at home can lead to what I call a beneficial cascading effect on the pelvic floor muscles.

Encouraging patients to resume some form of physical activity cannot be overemphasized. (Some patients are so frightened by the pain that they require medical permission to engage in any form of exercise). Walking, for example, can lead to a positive feedback, whereby the stride increases, gait normalizes and the patient in essence is providing his own pelvic floor muscle strengthening and lengthening.

Home exercise programs are tailored according to the patient's condition, his lifestyle and abilities. These are prescribed to promote further muscle lengthening and pelvic floor reeducation as well as enhance durability of PT.

In the book, *A Headache in the Pelvis*, Anderson and Wise provide patients with much needed validation. Their valuable insights educate patients about the pathophysiology of most pelvic pain syndromes along with specific anatomical information which empowers patients to seek a non-urological approach to their diagnosis and to accept subsequent responsibility for the regimen involving physical therapy, self care and specialized relaxation techniques mentioned earlier in the chapter.

Healing Male Pelvic Pain, by Isa Herrera, includes many photographs to help guide patients through various exercises and stretches targeting muscle groups usually implicated in CPP [69]. The author provides an urological and pelvic floor overview along with detailed instructions for exercise and self care. Some exercises and poses are adopted from traditional yoga practices. In addition to *A Headache in the Pelvis*, I also recommend this book, which helps relieve the loneliness and catastrophizing experienced by so many men with CPP. Both books are very accessible and inspiring.

Acupuncture has been considered by some experts as an ancient form of neuromodulation, and therefore, a potential treatment option for some patients with pelvic pain. In a trial conducted in China, 44 CPP patients were randomized to acupuncture therapy, while 45 patients were randomized to sham therapy. Acupuncture therapy was performed twice weekly over a 10 week study period and consisted of nothing more than 4 acupoint punctures without any stimulation or adjuvant therapies. The sham treatment was performed at similar time intervals; the needles were all placed superficially and 15 mm to the left of the designated acupoints. Favorable response to acupuncture and sham were 73% and 47%, respectively (relative risk [RR] 1.81, 95% confidence interval [CI], 1.3–3.1, $p=0.02$). At 24 weeks after completing therapy, durability was appreciated in 32% of acupuncture group participants and 13% of sham group participants (RR 2.39, 95% CI, 1.0–5.6, $p=0.04$) [70].

A variety of stress management and psychological counseling options should be made available to men with CPP. These psychologically based alternatives should be explained as a synergistic part of medical modalities and physical interventions. Over 20 years of practice I have noted that some of my patients are comfortable with church based counseling and support, while others have found solace in meditation and yoga [58]. Still others have remedied their anxiety through a series of relaxation tapes, guided imagery or the paradoxical relaxation techniques as described in "A Headache in the Pelvis," by Wise and Anderson [27].

In the early 20th century, Edmund Jacobson, "the father of relaxation therapy", developed progressive relaxation techniques. Based on his work and other more contemporary psychologists, Dr. Wise developed Paradoxical Relaxation. While employing some of the Jacobson's progressive relaxation methods, Dr. Wise incorporates forgiveness and acceptance into his practice. Simply summarized, the paradox in this version of relaxation, is the acceptance and embracing of one's pelvic pain rather than fighting or resenting it. In his book entitled *Paradoxical Relaxation*, the development, rationale and instruction for this form of self-care is beautifully detailed [71]. The author emphasizes the need to practice these techniques regularly so as to be prepared for the inevitable flare-ups, which occur during recovery. He uses the metaphor of trying to build a well while trying to put out a house fire. A well, of course, must be in place in order to be prepared for such events.

Some institutions provide psychological support to men through programs such as "Executive Coaching," which may afford patients a more comfortable avenue toward psychotherapy. Some relaxation techniques might also be incorporated with physiotherapy using biofeedback, creative visualization, deep breathing and hand warming techniques.

It is not feasible for clinicians to conduct all of these types of treatments; however, clinicians must be familiar with and conversant about the options and resources available to each patient. Patients should be convinced and therefore confident about their management strategies. Because there is no "quick fix" for CPP, I believe the patient's investment must be derived, in part, from his physician's level of engagement.

CONCLUSION

Men suffering from Chronic Pelvic Pain deserve a more compassionate and comprehensive approach, incorporating the lessons learned from other subspecialties. We must also consistently apply the concepts of central sensitization as they apply directly to pain perception, neuroendocrine dysfunction and stress and to Myofascial and pelvic floor muscle dysfunction which can affect defecation, voiding and sexual activity. Management often requires a component of self care, which can be very challenging for patients with chronic and debilitating conditions such as this. Patient empowerment derived from a positive physician-patient relationship is essential to therapy.

CONFLICT OF INTEREST

I had been a consultant for New Pelvic Pain Technologies from 2012-2014.

ACKNOWLEDGEMENT

Declared none.

REFERENCES

- [1] Potts JM. Male Pelvic Pain Syndrome: Escaping the snare of prostatocentric thinking. *Curr Bladder Dysfunct Report*, Springer Science, January, 2015.
- [2] Gonder MJ. Prostatitis *Lancet* 1963; 83:305-6
- [3] Nickel JC, Downey J, Clark J, *et al.* Levofloxacin for chronic prostatitis/chronic pelvic pain syndrome in men: a randomized placebo- controlled multicenter trial. *Urology* 2003; 62:614-7.
- [4] Alexander RB, Propert KJ, Schaeffer AJ, *et al.* Ciprofloxacin or tamsulosin in men with chronic prostatitis/chronic pelvic pain syndrome: a randomized, double-blind trial. *Ann Intern Med* 2004; 141: 581-9.
- [5] Schaeffer AJ, Knauss JS, Landis JR, *et al.* Leukocyte and bacterial counts do not correlate with severity of symptoms in men with chronic prostatitis: the National Institutes of Health Chronic Prostatitis Cohort Study. *J Urol* 2002; 168:1048-53.
- [6] Meares EM, Stamey TA. Bacteriologic localization patterns in bacterial prostatitis and urethritis. *Invest Urol* 1968; 5:492-518.
- [7] Nickel JC, Alexander RB, Schaeffer AJ, *et al.* Leukocytes and bacteria in men with chronic prostatitis/chronic pelvic pain syndrome compared to asymptomatic controls. *J Urol* 2003; 170:818-22.
- [8] Nickel JC. Recommendations for the evaluation of patients with prostatitis. *World J Urol*. 2003; 21(2):75-81.
- [9] Schaeffer, AJ, Knauss, JS, Landis, JR, *et al.* Leukocyte and bacterial counts do not correlate with severity of symptoms in men with chronic prostatitis: the national institutes of health chronic prostatitis cohort study. *J Urol* 2002; 168:1048-53.
- [10] Sharma RK, Pasqualotto FF, Nelson DR, *et al.* Role of leukocytospermia in oxidative stress. *J Androl* 22:575-83.
- [11] Potts: Prospective Identification of NIH-Category IV prostatitis in men with elevated PSA levels. *J Urol* 2000; 164: 1550-53
- [12] Nickel JC, Stephens A, Chen J, *et al.* Application of State-of-the-Art Methods to Search for Microbial Contributions to the Etiology of Urological Chronic Pelvic Pain Syndrome (UCPPS) Abstract 1147, presented at American Urologic Association Annual Meeting, 2013.
- [13] Strebel RT, Schmidt C, Beatrice J, Sulser T. Chronic scrotal pain syndrome (CSPS): the widespread use of antibiotics is not justified. *Andrology*. 2013 Jan;1(1):155-9.
- [14] Pontari MA1, Krieger JN, Litwin MS, *et al.* Pregabalin for the treatment of men with chronic prostatitis/chronic pelvic pain syndrome: a randomized controlled trial. *Arch Intern Med*. 2010; 170(17):1586-93.
- [15] Nickel JC, Krieger JN, McNaughton-Collins M, *et al.* Alfuzosin and symptoms of chronic prostatitis- chronic pelvic pain syndrome, *NEJM*, 2008; 359: 2663-73.
- [16] Fitzgerald M, Anderson R, Potts J, *et al.* UPPCRN: Randomized multicenter feasibility trial of myofascial physical therapy for the treatment of urologic chronic pelvic pain syndromes. *J Urol*, 182: 570-580, 2009.
- [17] Nickel JC, Downey J, Ardern D, Clark J, Nickel K. Failure of a monotherapy strategy for difficult chronic prostatitis/chronic pelvic pain syndrome. *J Urol* 2004; 172: 551-4.
- [18] Meares EM, Jr: Acute and chronic prostatitis: Diagnosis and treatment. *Infect Dis Clin North Am* 1987; I: 855-73.
- [19] Hinman F, Baumann FW: Vesical and ureteral damage from voiding dysfunction in boys without neurological or obstructive disease. *J Urol* 1973; 167:1069-73.
- [20] Marszalek M, Wehrberger C, Temml C, *et al.* Chronic Pelvic Pain and Lower Urinary Tract Symptoms in Both Sexes: Analysis of 2749 Participants of an Urban Health Screening Project. *European Urology* 2009; 499-508.
- [21] Kaplan SA, Te AE, Jacobs BZ. Urodynamic evidence of vesical neck obstruction in men misdiagnosed with chronic nonbacterial prostatitis and the therapeutic role of endoscopic incision of the bladder neck. *J Urol* 1994; 152:2063-65.
- [22] Kaplan SA, Ikeguchi EF, Santarosa RP, *et al.* Etiology of voiding dysfunction in men less than 50 years of age. *Urology* 1996; 47: 836-9.
- [23] Kaplan SA, Santarosa RP, D'Alisera PM, *et al.* Pseudodyssynergia (contraction of the external sphincter during voiding) misdiagnosed as chronic non-bacterial prostatitis and the role of biofeedback as a therapeutic option. *J Urol* 1997; 157:2234-37
- [24] Zu XB1, Ye ZQ, Zhou SW, Qi L, Yang ZQ. Chronic prostatitis with non-neurogenic detrusor sphincter dyssynergia: diagnosis and treatment. *Zhonghua Nan Ke Xue* 2010; 16(2):146-9.
- [25] Nickel JC. Role of alpha1-blockers in chronic prostatitis syndromes. *BJU Int*. 2008; 101(suppl).
- [26] Mishra VC, Browne J, Emberton M. Role of alpha-blockers in type III prostatitis: a systematic review of the literature. *J Urol* 2007; 177: 25-30.
- [27] Nickel JC, Krieger JN, McNaughton-Collins M, *et al.* Alfuzosin and symptoms of chronic prostatitis- chronic pelvic pain syndrome, *NEJM* 2008; 359:2663-73.
- [28] Anothaisintawee T, Attia J, Nickel JC, Thammakraisorn S, Numthavaj P, McEvoy M, Thakkinstian A. Management of chronic prostatitis/chronic pelvic pain syndrome: a systematic review and network meta-analysis. *JAMA* 2011 5;305(1):78-86
- [29] Nickel JC, O'Leary M, Lepor H, *et al.* Silodosin for Men With Chronic Prostatitis/Chronic Pelvic Pain Syndrome: Results of a Phase II Multicenter, Double-Blind, Placebo Controlled Study. *J Urol* 2011; Pages 125-31.
- [30] Shoskes DA, Nickel JC, Dolinga R *et al* Clinical phenotyping of patients with chronic prostatitis/ chronic pelvic pain syndrome and correlation with symptom severity. *Urology* 2009; 73: 538.
- [31] Nickel JC, Elhilali M, Emberton M, Vallancien G. The Alf-One Study Group. The beneficial effect of alfuzosin 10 mg once daily in real life practice on lower urinary tract symptoms, quality of life and sexual dysfunction in men with LUTS and painful ejaculation. *BJU Int* 2006; 97: 1242-1246.
- [32] Sönmez NC, Kiremit MC, Guney S *et al.* Sexual dysfunction in type III chronic prostatitis (CP) and chronic pelvic pain syndrome (CPPS) observed in Turkish patients. *Int Urol Nephrol*. 2011 Jun; 43(2):309-14.
- [33] Magri V, Wagenlehner F, Perletti G, Schneider S, Marras E, Naber KG, Weidner W. Use of the UPOINT chronic prostatitis/chronic pelvic pain syndrome classification in European patient cohorts: sexual function domain improves correlations. *J Urol*. 2010 Dec;184(6):2339-45.
- [34] Potts JM, and Decker S. Specialized physiotherapy for sexual discomfort and dysorgasmia associated with UCPPS. Presented at the 6th Annual Meeting of the International Society for Men's Health, Nice, France, 2010.
- [35] Anderson RU, Wise D, Sawyer T, Chan CA. Sexual dysfunction in men with chronic prostatitis/chronic pelvic pain syndrome: improvement after trigger point release and paradoxical relaxation training. *J Urol* 2006;176:1534-8.
- [36] Potts, JM (Blog) <http://www.pelvicpainrehab.com/male-pelvic-pain/1994/shedding-light-on-male-pelvic-pain-and-sexual-dysfunction/>
- [37] Clemens, J.Q., Nadler, R.B., Schaeffer, A.J., Belani, J, Albaugh, J, and Bushman, W. Biofeedback, pelvic floor re-education, and

- bladder training for male chronic pelvic pain syndrome. *Urol* 2000; 56 (6): 951-5.
- [38] Cornel, E.B., van Haarst, E.P. Browning-Groote Schaarsberg, R.W.M., Geels, J. The effect of biofeedback physical therapy in men with chronic pelvic pain syndrome type III. *Euro Urol* 2005; 47: 607-11.
- [39] Weiss, J.M. Pelvic floor myofascial trigger points: manual therapy for interstitial cystitis and the urgency-frequency syndrome. *J Urol*, 2001; 166: 2226-2231.
- [40] Anderson, R.U., Wise, D., Sawyer, T, Chan, C. Integration of myofascial trigger point release and paradoxical relation training treatment of chronic pelvic pain in men. *J. Urol* 2005; 174: 155-160.
- [41] Fitzgerald MP, Anderson RA, Potts JM *et al.* Randomized Multicenter Feasibility Trial of Myofascial Physical Therapy for the treatment of Urologic Chronic Pelvic Pain Syndromes. *J Urol* 2009; 182: 570-580.
- [42] Potts JM, Moritz N, Everson D, *et al.* Chronic abacterial prostatitis: a functional somatic syndrome, Presented at: Annual Meeting of the American Urological Association; June 2, 2001.
- [43] Wessley S, Nimnuin C, Sharpe M. Functional somatic syndromes: one or many? *Lancet* 1999; 354: 936-9.
- [44] Pontari MA, McNaughton-Collins M, O'leary MP, *et al.* A case-control study of risk factors in men with chronic pelvic pain syndrome. *BJU Int.* 2005; 96(4): 559-65.
- [45] Alagiri M, Chottiner S, Ratner V, *et al.* Interstitial cystitis: unexplained associations with other chronic disease and pain syndromes. *Urology* 1997; 49: 52-57.
- [46] Clauw DJ, Schmidt M, Radulovic D, *et al.* The relationship between fibromyalgia and interstitial cystitis. *J Psychiatr Res.* 1997; 31(1):125-31.
- [47] Aaron LA, Herrell R, Ashton S, *et al.* Comorbid clinical conditions in chronic fatigue: a co-twin control study. *J Gen Int Med* 2001; 16:24-31.
- [48] Yunus, M B. Fibromyalgia and Overlapping Disorders: The Unifying Concept of Central Sensitivity Syndromes. *Semin Arthritis Rheum* 2007; 36: 339-56.
- [49] Yilmaz U, Liu YW, Berger RE, Yang CC. Autonomic Nervous System Changes in Men With Chronic Pelvic Pain Syndrome. *J Urol* 2007; 2170-2174.
- [50] Potts JM, Payne CK. Critical Review: Urologic Chronic Pelvic Pain in Men and Women. *Pain.* 2012; 153(4):755-8.
- [51] Berghuis JP, Heiman JR, Rothman I, Berger RE Psychological and physical factors involved in chronic idiopathic prostatitis. *J Psychosom Res* 1996; 41(4): 313-25.
- [52] Mehik A, Hellstrom P, Sarpola A, Lukkarinen O, Jarvelin MR. Fears, sexual disturbances and personality features in men with prostatitis: a population-based cross-sectional study in Finland. *BJU Int* 2001; 88:35-38.
- [53] Clemens JQ, Brown SO, Calhoun EA. Mental health diagnoses in patients with interstitial cystitis/painful bladder syndrome and chronic prostatitis/chronic pelvic pain syndrome: a case/control study. *J Urol* 2008;180(4):1378-82.
- [54] Tripp, DA, Nickel, JC, Wang, Y, Litwin, MS, McNaughton-Collins, M, Landis, JR., Alexander, R.B., Schaeffer, AJ, O'Leary, MP, Pontari, MA., Fowler, Jr., JE, Nyberg, LM., Kusek, JW. NIH-CPCRN Study Group: Catastrophizing and pain-contingent rest predict patient adjustment in men with chronic prostatitis/chronic pelvic pain syndrome. *J of Pain* 2006; 7(10):697-708.
- [55] Ullrich PM, Turner JA, Ciol M, Berger R. Stress is associated with subsequent pain and disability among men with nonbacterial prostatitis/pelvic pain. *Ann Behav Med.* 2005; 30(2): 112-8.
- [56] Anderson RU, Orenberg EK, Chan CA, Morey A, Flores V. Psychometric profiles and hypothalamic-pituitary-adrenal axis function in men with chronic prostatitis/chronic pelvic pain syndrome. *J Urol* 2008; 179(3): 956-60.
- [57] Wise D, Anderson R. A Headache in the Pelvis, Occidental, California: National Center for Pelvic Pain Research. Pages 2003; 106-33.
- [58] Miller HC. Stress Prostatitis *Urology.* 1988; 32(6): 507-10.
- [59] Potts, Non-pharmacological approach to men with chronic pelvic pain syndrome. *Curr Prostate Reports* 2009; 7:79-84.
- [60] Kellner R: Psychosomatic syndromes, somatization and somatoform disorders. *Psychother Psychosom.* 1994; 61(1-2):4-24.
- [61] Benjamin, PJ, Tappan, FM. Handbook of healing massage techniques – classic, holistic, and emerging methods. Pearson Education, Inc. 2005.
- [62] Potts J. Physical Therapy for CP/CPSPS, in Shoskes (editor) Prostatitis, Humana Press, 2008.
- [63] Travell JG. Myofascial pain and dysfunction: the trigger point manual. Baltimore: Williams and Wilkins; 1983.
- [64] Potts JM, Sharma R, Pasqualotto F, *et al.* Association of Ureaplasma urealyticum with abnormal reactive oxygen species levels and absence of leukocytospermia. *J Urol* 2000; 163: 1775-8.
- [65] Nickel JC, Pontari M, Moon T, *et al.* A randomized, placebo controlled, multicenter study to evaluate the safety and efficacy of rofecoxib in the treatment of chronic nonbacterial prostatitis. *J Urol.* 2003; 169(4):1401-5.
- [66] Potts, J.M. and O'Dougherty, E. Pelvic floor physical therapy for patients with prostatitis. *Cur Urol Rep* 2000; 1:155-8.
- [67] Kotarinos RK, CP/CPSPS pelvic floor dysfunction: evaluation and treatment. GU-IT IS Humana Press, 2007.
- [68] Anderson R, Wise D, Sawyer T, Nathanson BH. Safety and effectiveness of an internal pelvic myofascial trigger point wand for urologic chronic pelvic pain syndrome. *Clin J Pain.* 2011; 27(9):764-8.
- [69] Herrera I, Ending Male Pelvic Pain. Duplex Publishing, New York. 2013.
- [70] Lee SW, Liong ML, Yuen KH, *et al.* Acupuncture versus sham acupuncture for chronic prostatitis/chronic pelvic pain. *Am J Med* 2008; 121(1):79.
- [71] Wise D, Paradoxical Relaxation: the theory and practice of dissolving anxiety by accepting it. Occidental, CA: National Center for Pelvic Pain Research 2010.