Differential diagnosis of chronic pelvic pain in women: the urologist's approach

Sophie G. Fletcher and Philippe E. Zimmern

Abstract | Chronic pelvic pain in women can be caused by a host of gynecological, gastrointestinal, musculoskeletal, neurologic, as well as urologic disorders. An initial broad differential diagnosis is essential. At times, overlapping symptoms and vague physical findings necessitate a multidisciplinary diagnostic approach. A thorough history, which is careful to characterize all aspects of the patient's symptoms, can usually direct the differential toward the bladder when this organ is the source of the pain. Interstitial cystitis/painful bladder syndrome (IC/PBS) should be included in the differential diagnosis, but it should not be used as an expeditious diagnosis when pain coexists with frequency and urgency. Multiple other urologic conditions such as overactive bladder, urinary tract infection, urethral diverticulum, periurethral masses (Skene gland cyst or abscess), and even urethral stricture disease, have overlapping symptom complexes with IC/PBS, and they must not be overlooked as they are much more easily diagnosed and treated. By using a stepwise approach and an evidence-based thought process, the obscurity of chronic bladder and urethral pain can evolve into a progressively narrowing differential.

Fletcher, S. G. & Zimmern, P. E. *Nat. Rev. Urol.* **6**, 557–562 (2009); advance online publication 1 September 2009; doi:10.1038/nrurol.2009.178

Introduction

Chronic pelvic pain (CPP) is a challenging clinical entity that is an important issue in the health care of women. Three different operational definitions of CPP have been used in the literature: durational, anatomic, and affective-behavioral. A useful clinical definition is noncyclic pain that lasts 6 months or more; is localized to the pelvis, the anterior abdominal wall at or below the umbilicus, or the buttocks; and is of sufficient severity to cause functional disability or require medical care. Depending upon its definition, CPP is estimated to have a prevalence of 3.8% in women aged 15–73 years, which is higher than the prevalence of migraine (2.1%) and is similar to that of asthma (3.7%) or back pain (4.1%).[1] In the USA, a large poll found that 16% of women with CPP had experienced either constant or intermittent pelvic pain during the preceding 6 months, and direct costs of health care for this disorder are estimated at US$880 million per year.[2] CPP can be caused by a host of gynecological, gastrointestinal, musculoskeletal, neurologic, as well as urologic disorders (Box 1). Sexual abuse and depression have also been implicated as potential causes.[3,4] An initial broad differential diagnosis is essential; at times, overlapping symptoms and vague physical findings necessitate a multidisciplinary approach. Our goal with this Review is to present an up-to-date, evidence-based guide to the evaluation of women who present to the urologist's office with a chief complaint of CPP.

Competing interests
The authors declare no competing interests.

Painful problems of the bladder

The first question that the urologist needs to answer when a patient presents with CPP is whether the pain is of urologic etiology. Painful problems of the bladder in women such as interstitial cystitis (IC) and painful bladder syndrome (PBS) present with a variety of symptoms, which are all too often shared with other urological disorders such as overactive bladder (OAB), urinary tract infection (UTI), urethral diverticulum, periurethral masses (Skene gland cyst or abscess), and even urethral stricture disease. The diagnosis of IC is further confused by changes made to diagnostic criteria during the past 20 years, and because there still are no universally accepted criteria for a definitive diagnosis.

The International Continence Society (ICS) has defined IC as "the complaint of suprapubic pain related to bladder filling, accompanied by other symptoms such as increased daytime and night-time frequency, in the absence of proven urinary tract infection or other pathology."[5] This definition highlights pain as an integral part of IC, hence the ICS has recommended the term 'painful bladder syndrome' (PBS); over the past several years, the nomenclature has evolved to include PBS with IC, as 'IC/PBS'. This term includes the entire symptom complex: bladder or pelvic pain, and urinary frequency or urgency, in the absence of any identifiable pathology.[5,6] IC/PBS has few physical signs, no pathognomonic histopathology, no characteristic urodynamic parameters, and no diagnostic laboratory tests, much less an identifiable etiology. The evaluation of patients with suspected IC/PBS can be lengthy and frustrating for both patient and physician. IC/PBS should be included in the differential diagnosis of CPP, but it should not

Department of Urology, The Methodist Hospital, Houston, TX, USA (**S. G. Fletcher**).
Department of Urology, University of Texas Southwestern Medical Center, Dallas, TX, USA (**P. E. Zimmern**).

Correspondence:
S. G. Fletcher,
The Methodist Hospital,
Department of Urology,
6560 Fannin,
Suite 2100, Houston,
TX 77030, USA
sgfletcher@tmhs.org

Key points

- Chronic pelvic pain (CPP) is a challenging clinical entity that is an important issue in the health care of women
- The differential diagnosis for CPP of urologic etiology includes urinary tract infection, urethral diverticulum, periurethral masses, urethral stricture disease, pelvic floor dysfunction, interstitial cystitis and painful bladder syndrome
- Voiding symptoms of urgency, frequency and nocturia are commonly reported in patients who are complaining of bladder or urethral pain
- No one particular diagnostic technique can be used to evaluate CPP; of paramount importance is the patient's history, which can substantially narrow the differential diagnosis and initiate appropriate referral
- Using a stepwise approach and an evidence-based thought process can help guide the history, physical examination, and ancillary testing in the best interests of the patient

be used as an expeditious diagnosis when pain coexists with frequency and urgency.

No time course for symptoms is specified in the ICS definition of IC/PBS, probably because the natural history of the disease is unknown. Seventy percent of patients report having only one symptom (either pain, or urinary frequency or urgency) at onset, and the mean time to emergence of all symptoms is 11 months.[7] The 1988 US National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) criteria for the definition of IC state that duration of symptoms less than 9 months excludes a diagnosis of IC; however, no minimum duration of symptoms is provided. Consensus panels have since recommended that a duration of symptoms of as little as 6 weeks is sufficient to consider a diagnosis of IC/PBS.[8]

History

The evaluation of women with CPP can be exhaustive, and often it is difficult to afford the time or office resources for an extensive patient interview. An accurate history, however, can rule out several other diagnoses, and can direct subsequent investigations. Often, just establishing a time course of symptoms can be challenging.

Pain associated with hormonal changes is usually attributed to endometriosis or adenomyosis. However, pain in IC/PBS will also fluctuate with hormone levels, and this fact should not be overlooked.[9] Pain relieved by antibiotic use is most suggestive of chronic UTI, or less commonly urethral diverticulum. Although reported anecdotally, little evidence in the literature demonstrates relief of IC/PBS symptoms with antibiotic use. A pilot study of 50 women with the diagnosis of IC who were randomized to either sequential antibiotics or placebo found an overall improvement rate of 48% in the treatment arm versus 24% for placebo ($P = 0.14$), with no differences noted in terms of relief of pain and urgency ($P = 0.22$). Notably, 80% of women in the treatment group experienced adverse effects compared to 40% in the placebo group ($P = 0.009$).[10] Another study of 104 women with IC/PBS demonstrated that regardless of symptom flares, the incidence of culture-confirmed recurrent bacteriuria over a 24-month period was 6.6%—a rate not appreciably different from that of the general population.[11] In accordance with the ICS definition of IC/PBS, urine cultures must be obtained, and the patients must be thoroughly evaluated for chronic UTI when IC/PBS is suspected.

A history of pelvic infections, traumatic childbirth, intrauterine device or pelvic surgery should raise concern for various conditions such as adhesions, pelvic floor muscle dysfunction and obstructive voiding. Finally, a full psychosocial history should be obtained for all patients, with questions regarding sexual abuse and depression.[3,4] Discovery of either of these entities might prompt a psychiatric referral, in order to help the patient find appropriate evaluation and treatment.

The history should also focus on the characteristics of the pain, including location, quality, duration, and modifying factors. Any association with urination, bowel movements, menses, and sexual activity should be determined, as it might guide the differential diagnosis. Visceral pain is usually not well localized, and patients can have difficulty differentiating whether visceral abdominopelvic pain is of gynecologic, urologic, or intestinal origin. Careful identification of a source of pain outside the bladder or urethra should lead to a more appropriate referral, when indicated. It can be useful to have the patient mark the location of her pain on a pain map, as this might elucidate a distribution of pain suggestive of a nonvisceral source.[12,13] In women with IC/PBS, suprapubic pain is prominent, and some urologists believe that it is necessary to the diagnosis, but many patients report additional sites of pain including the urethra, genitalia and lower back.[13–15] In a large study investigating sites of pain in patients with IC/PBS, 66% of patients reported two or more pain sites, with the suprapubic region being the most common; however, isolated sharp and burning urethral pain was seen in 31% of patients.[13] Another study demonstrated that 85% of patients with IC/PBS have concomitant vulvodynia. This possibility should not be overlooked; if vulvodynia is suspected, referral to a gynecologist can be considered for help with treatment.[16]

Voiding symptoms of urgency, frequency and nocturia are commonly reported in patients who are complaining of bladder or urethral pain. OAB very commonly overlaps with IC/PBS in this regard, although the frequency, urgency and urge urinary incontinence of OAB is rarely associated with pain.[17] Unlike the urgency of OAB, described as "a sudden compelling desire to pass urine, which is difficult to defer",[5] the urgency of IC/PBS is associated with pain, and rarely associated with incontinence.[17] Periurethral masses such as Skene gland cysts or abscesses, and urethral diverticula, are also associated with dysuria and lower urinary tract symptoms (LUTS). In one series, 40% of women referred to a specialty urology clinic for further evaluation of pelvic pain were found to have a periurethral mass as the etiology.[18] Careful physical

examination, cystoscopy and imaging studies such as MRI can usually lead to the proper diagnosis in these cases. Finally, urethral stricture disease is a rare entity in women, which can also be a cause of LUTS, dysuria, elevated postvoid residual volumes, and chronic UTI.[19,20]

Screening questionnaires and voiding diaries can be very helpful in determining symptoms and assessing their impact on quality of life. The Pelvic Pain and Urgency/Frequency Symptom Scale and the O'Leary–Sant IC symptom and problem indices are commonly used.[21,22] Both surveys characterize pain, urinary urgency, frequency, nocturia, and the impact of these symptoms on daily life; the former also includes questions regarding sexual dysfunction. These tools might also serve to elucidate symptoms that the patient failed to mention during history taking. Voiding diaries provide helpful information regarding frequency, incontinence, voiding volumes, as well as the consumption of fluids, in particular caffeine and alcohol. Dietary triggers of pain are an important feature of IC/PBS, with up to 85% of women reporting worsening of their symptoms after ingesting certain foods or beverages. Such foods commonly include caffeinated, carbonated and alcoholic beverages, fruit juices, and chocolate.[9,23]

Physical examination

Physical examination is most useful for identifying areas of tenderness, and particularly the presence of any masses along the urethra or anterior vaginal wall. Genitourinary examination should proceed slowly so as not to exacerbate symptoms, which would make the remainder of the examination difficult. A moistened cotton swab should be used to elicit point tenderness at the vulva, which is suggestive of vulvodynia. Similar tenderness at the urethral meatus suggests Skene gland cyst or abscess. If previous vaginal or pelvic surgeries are in the patient's history, possible extrusion of mesh or suture should be investigated. Trigger points for pain can be encountered along areas of scarring from previous anterior or posterior prolapse repair sites, but they can also be encountered along the levator muscles laterally as signs of myofascial dysfunction. The anterior vaginal wall and area along the urethra should be inspected and palpated for any nodules, masses or point tenderness. Both Skene gland cysts and urethral diverticuli are associated with symptoms of frequency, urgency, dysuria, dyspareunia and discharge. If point tenderness is encountered and a diverticulum is suspected, MRI should be performed for diagnosis and operative planning.[24,25] Palpation of the bladder to elicit bladder base tenderness is also essential. Tenderness here can steer the differential toward IC/PBS; however, the possibility of endometriosis, irritable bowel syndrome or pelvic floor dysfunction should not be discounted in this setting.

Laboratory tests

Urine culture is an essential component of the work-up in the setting of bladder or urethral pain. If possible, the

Box 1 | Selected differential diagnosis of CPP

Gastrointestinal
- Celiac disease
- Colitis
- Colon cancer
- Inflammatory bowel disease
- Irritable bowel syndrome
- Proctodynia

Gynecologic
- Adhesions
- Adenomyosis
- Adnexal cysts
- Chronic endometriosis
- Gynecologic malignancies
- Leiomyata
- Pelvic congestion syndrome
- Pelvic inflammatory disease

Musculoskeletal
- Degenerative disc disease
- Fibromyalgia
- Myofascial pain

Neurologic
- Nerve entrapment
- Neurologic dysfunction

Urologic

Bladder
- Bladder malignancy
- Chronic UTI
- IC/PBS
- Erosion of mesh or suture
- Urolithiasis
- Trigonitis

Urethra
- Urethral diverticulum
- Skene duct cyst
- Erosion of mesh or suture
- Urethral caruncle
- Urethral prolapse
- Stricture
- Urethral condylomata
- Urethral leiomyoma
- Fibroepithelial polyp
- Periurethral granuloma
- Urethral hemangioma

Vagina
- Vulvodynia
- Gartner duct cyst
- Bartholin gland cyst
- Vaginal implants of endometriosis

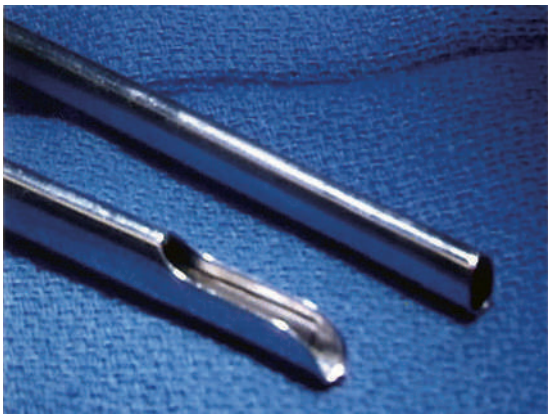

Figure 1 | The female cystoscope. The 'female cystoscope' (right), or 'female urethroscope', is a 17.5 Fr cystoscope with a blunt rather than beveled end, as is seen on the normal cystoscope (left). This design allows very good vision of the entire urethral wall on urethroscopy.

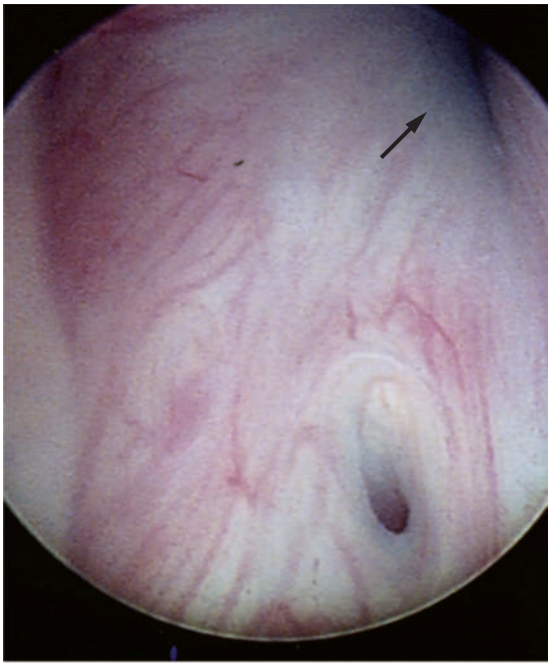

Figure 2 | Ostium of urethral diverticulum elucidated on cystourethroscopy. The urethral lumen can be seen in the upper right hand corner of the image (arrow).

patient's past culture results from outside laboratories should be reviewed as well, to assess for culture-proven bacteriuria and sensitivities. Additionally, urine cytology should be sent for analysis if genitourinary malignancy is suspected. Currently, no urinary marker is available for the diagnosis of IC/PBS. However, a number of urine components have altered levels in patients with IC/PBS, including eosinophil cationic protein, glycoprotein-51, antiproliferative factor and several inflammatory markers. The utility of these molecules as markers for the diagnosis of IC/PBS is currently under study.[26]

Cystoscopy

Cystourethroscopy in the setting of pelvic pain is preferably performed with a 'female cystoscope' (Figure 1) or a flexible cystoscope in order to best visualize the urethra as well as the bladder. Direct visualization is indispensable in women with bladder or urethral pain, especially for identifying eroded mesh or suture from a previous surgery, the ostium of a urethral diverticulum (Figure 2),[18] or the narrow caliber of the urethra in urethral stricture disease.[19] Cystoscopy is also imperative for the exclusion of pathology such as transitional cell carcinoma, or carcinoma *in situ* of the bladder in all patients with a history of gross hematuria in the absence of UTI.

The diagnostic approach to IC/PBS has changed over the past decade, becoming more dependent on symptoms, and less reliant on cystoscopic findings or histopathology.[27] Cystoscopy with hydrodistension, part of the diagnostic approach developed by the NIDDK, has been used as a gold standard diagnostic test for IC.[28] The primary cystoscopic features of IC, according to these guidelines, are glomerulations and Hunner ulcers. However, not all patients with symptoms of IC/PBS have glomerulations, and not all patients with glomerulations have IC/PBS.[27,29] In addition, no clear definition exists for Hunner ulcer, and its identification suffers from poor interobserver agreement.[30] In general, cystoscopic findings do not correlate with the degree of pain or urinary symptoms.[31] Biopsy is not diagnostic of IC, and has little diagnostic value in general when evaluating women with chronic bladder or urethral pain.[29]

Similarly, the potassium chloride sensitivity test is not a reliable tool for the diagnosis of IC/PBS. This test consists of instilling a solution of potassium chloride into the bladder, with resultant pain indicating IC/PBS. The test relies on the assumption that all patients with IC/PBS have a permeable glycosaminoglycan barrier at the urothelium. In addition, the test causes pain in a patient population already experiencing pain, and assessment of severity of pain is subjective. Level I evidence supporting the use of the test is sparse, and the sensitivity and specificity of the test varies between studies.[32–34] Teichman and Nielsen-Omeis[34] found the test to be only 60% accurate for the diagnosis of IC, with a 40% false-negative rate. A more recent study reported sensitivity and specificity of 73% and 83%, respectively.[32] Across studies, sample sizes are small, outcome measures vary, and definitions of IC/PBS are different.[35,36] The less painful, less invasive, and more accurate approach to diagnosing IC/PBS is to use clinical findings. A thorough characterization of the patient's urinary urgency, frequency and bladder pain, with exclusion of other urological conditions, is the most useful and reliable means of diagnosing IC/PBS.

Urodynamics

Urodynamic testing is essential in the evaluation of certain voiding disorders, but findings are not likely to contribute to the diagnosis of a painful bladder condition

such as IC/PBS. In this setting, urodynamic studies are most useful for the identification of other disorders such as obstructive voiding. Entities associated with urethral pain or dysuria that can cause bladder outlet obstruction in women are anti-incontinence procedures, suture or mesh from previous incontinence or prolapse surgery, malignancy, meatal stenosis, fibrosis, Skene gland cyst or abscess, and urethral stricture.[37] The exact urodynamic definition of bladder outlet obstruction is debated,[38–41] and urodynamics alone cannot be used to make the diagnosis. However, a high-pressure low-flow combination during the pressure-flow phase can be suggestive of these obstructive entities, and can direct further testing such as cystoscopy, voiding cystourethrography (VCUG) or MRI.

Although studied, little evidence supports an association between urodynamic findings and the diagnosis of IC/PBS. Nigro *et al.*[42] discovered a negative association between the volume at first desire to void on urodynamics and the presence of Hunner ulcers on cystoscopy. However, others investigators have failed to demonstrate urodynamic correlates of global measures of bodily pain and health.[43] In comparisons between patients with IC/PBS and control patients with OAB, the consensus was that patients with IC/PBS experience greater early filling sensation with a decreased bladder capacity.[44–46] This observation is not surprising, given that the urgency of IC/PBS is associated with pain,[17] and the suprapubic pain of IC/PBS is improved during and immediately after urination in 53% and 71% of patients, respectively.[9] To date, no consensus exists regarding the use of urodynamic data to diagnose, or exclude the diagnosis of IC/PBS. Thus, IC/PBS remains a diagnosis of exclusion based mainly on symptoms, and urodynamic studies should be seen as a means by which to exclude other pathologies, as opposed to identify IC/PBS itself.

In some cases, video urodynamics can be helpful in showing urethral anatomy while voiding. Video urodynamics identified 41% of urethral diverticula in patients who underwent evaluation for refractory lower urinary tract symptoms.[18] As VCUG does not have a particularly high sensitivity for the detection of urethral diverticula, any index of suspicion should instigate further evaluation with MRI.[24]

Imaging

Performing routine pelvic ultrasonography or MRI for every woman who presents with complaints of chronic bladder or urethral pain is neither efficient nor effective. Pelvic ultrasonography can be helpful in elucidating gynecologic sources of pelvic pain, prompting an appropriate referral. MRI is extremely useful for identifying and delineating the margins of urethral diverticulum. Foster *et al.*[24] demonstrated that MRI was 100% sensitive for urethral diverticula whereas other imaging modalities (CT, endovaginal ultrasonography, intravenous pyelography, and VCUG) were less accurate. The complexity and extent of the diverticula studied were rarely misjudged with MRI, leading to improved surgical planning and lower rates of recurrence. Furthermore, noncommunicating intraurethral wall diverticula in women have been reported, which were diagnosed only via MRI, and not by cystoscopy or VCUG (Figure 3).[25]

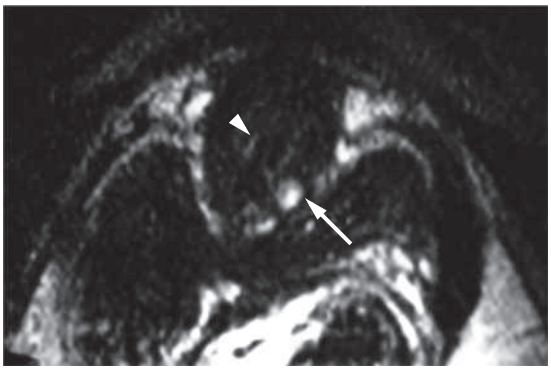

Figure 3 | Noncommunicating urethral diverticulum diagnosed via pelvic MRI. The image shows the noncommunicating diverticulum (long arrow) and the urethral lumen (arrowhead).

Conclusions

CPP in women is a serious problem, and one that is encountered frequently by urologists. Initially, a broad diagnostic approach that considers the various etiologies of multiple organ systems is warranted; this can necessitate multidisciplinary investigation and require one or more referrals to other specialties before the patient has been fully evaluated. A thorough history, which carefully characterizes all aspects of the patient's symptoms, can usually direct the differential, and identify the bladder as the source of pain in appropriate cases. IC/PBS should be included in the differential diagnosis, but it should not be used as an expeditious diagnosis when pain coexists with frequency and urgency. Multiple other urologic conditions have overlapping symptom complexes with IC/PBS, and they must not be overlooked, as they are much more easily diagnosed and treated. By using a stepwise approach and an evidence-based thought process, the obscurity of chronic bladder and urethral pain can evolve into a progressively narrowing differential.

Review criteria

The Cochrane Library, EMBASE and MEDLINE databases were queried via OVID and PubMed. The keywords used were "pelvic pain", "chronic pelvic pain", "bladder pain", "urethral pain", "dysuria", "periurethral mass", "interstitial cystitis", "painful bladder syndrome", and "IC/PBS". Generally, only publications from the past 5 years were selected for inclusion, but commonly referenced and highly regarded older publications were not excluded. Reference lists of articles identified by this search strategy were also examined to identify additional sources.

1. Zondervan, K. T. *et al.* Prevalence and incidence of chronic pelvic pain in primary care: evidence from a national general practice database. *Br. J. Obstet. Gynaecol.* **106**, 1149–1155 (1999).
2. Mathias, S. D., Kuppermann, M., Liberman, R. F., Lipschutz, R. C. & Steege, J. F. Chronic pelvic pain: prevalence, health-related quality of life, and economic correlates. *Obstet. Gynecol.* **87**, 321–327 (1996).
3. Lampe, A. *et al.* Chronic pelvic pain and previous sexual abuse. *Obstet. Gynecol.* **96**, 929–933 (2000).
4. Walling, M. K. *et al.* Abuse history and chronic pain in women: I. Prevalences of sexual abuse and physical abuse. *Obstet. Gynecol.* **84**, 193–199 (1994).
5. Abrams, P. *et al.* The standardisation of terminology of lower urinary tract function: report from the Standardisation Sub-committee of the International Continence Society. *Am. J. Obstet. Gynecol.* **187**, 116–126 (2002).
6. Hanno, P. International Consultation on IC—Rome, September 2004/Forging an international consensus: progress in painful bladder syndrome/interstitial cystitis. *Int. J. Urogynecol. Pelvic Floor Dysfunct.* **16 (Suppl. 1)**, S2–S34 (2005).
7. Porru, D. *et al.* Different clinical presentations of interstitial cystitis syndrome. *Int. J. Urogynecol. Pelvic Floor Dysfunct.* **15**, 198–202 (2004).
8. Forrest, J. B. & Mishell, D. R. Jr. Breaking the cycle of pain in interstitial cystitis/painful bladder syndrome: toward standardization of early diagnosis and treatment: consensus panel recommendations. *J. Reprod. Med.* **54**, 3–14 (2009).
9. Warren, J. W. *et al.* Evidence-based criteria for pain of interstitial cystitis/painful bladder syndrome in women. *Urology* **71**, 444–448 (2008).
10. Warren, J. W. *et al.* Pilot study of sequential oral antibiotics for the treatment of interstitial cystitis. *J. Urol.* **163**, 1685–1688 (2000).
11. Stanford, E. & McMurphy, C. There is a low incidence of recurrent bacteriuria in painful bladder syndrome/interstitial cystitis patients followed longitudinally. *Int. Urogynecol. J. Pelvic Floor Dysfunct.* **18**, 551–554 (2007).
12. Jensen, M. P. & Karoly, P. in *Handbook of Pain Assessment* (eds Turk, D. C. & Melzack, R.) 135–151 (Guilford Press, New York, 1992).
13. Warren, J. W. *et al.* Sites of pain from interstitial cystitis/painful bladder syndrome. *J. Urol.* **180**, 1373–1377 (2008).
14. Simon, L. J., Landis, J. R., Erickson, D. R. & Nyberg, L. M. The Interstitial Cystitis Data Base Study: concepts and preliminary baseline descriptive statistics. *Urology* **49**, 64–75 (1997).
15. FitzGerald, M. P., Brensinger, C., Brubaker, L. & Propert, K. What is the pain of interstitial cystitis like? *Int. Urogynecol. J. Pelvic Floor Dysfunct.* **17**, 69–72 (2006).
16. Gardella, B. *et al.* Insight into urogynecologic features of women with interstitial cystitis/painful bladder syndrome. *Eur. Urol.* **54**, 1145–1151 (2008).
17. Abrams, P., Hanno, P. & Wein, A. Overactive bladder and painful bladder syndrome: there need not be confusion. *Neurourol. Urodyn.* **24**, 149–150 (2005).
18. Blaivas, J. G., Flisser, A. J., Bleustein, C. B. & Panagopoulos, G. Periurethral masses: etiology and diagnosis in a large series of women. *Obstet. Gynecol.* **103**, 842–847 (2004).
19. Migliari, R. *et al.* Dorsal buccal mucosa graft urethroplasty for female urethral strictures. *J. Urol.* **176**, 1473–1476 (2006).
20. Lorenzo, A. J., Zimmern, P., Lemack, G. E. & Nurenberg, P. Endorectal coil magnetic resonance imaging for diagnosis of urethral and periurethral pathologic findings in women. *Urology* **61**, 1129–1133 (2003).
21. O'Leary, M. P., Sant, G. R., Fowler, F. J. Jr, Whitmore, K. E. & Spolarich-Kroll, J. The interstitial cystitis symptom index and problem index. *Urology* **49**, 58–63 (1997).
22. Parsons, C. L. *et al.* Increased prevalence of interstitial cystitis: previously unrecognized urologic and gynecologic cases identified using a new symptom questionnaire and intravesical potassium sensitivity. *Urology* **60**, 573–578 (2002).
23. Koziol, J. A. Epidemiology of interstitial cystitis. *Urol. Clin. North Am.* **21**, 7–20 (1994).
24. Foster, R. T., Amundsen, C. L. & Webster, G. D. The utility of magnetic resonance imaging for diagnosis and surgical planning before transvaginal periurethral diverticulectomy in women. *Int. Urogynecol. J. Pelvic Floor Dysfunct.* **18**, 315–319 (2007).
25. Daneshgari, F., Zimmern, P. E. & Jacomides, L. Magnetic resonance imaging detection of symptomatic noncommunicating intraurethral wall diverticula in women. *J. Urol.* **161**, 1259–1261 (1999).
26. Erickson, D. R. Urine markers of interstitial cystitis. *Urology* **57**, 15–21 (2001).
27. Hanno, P. M., Landis, J. R., Matthews-Cook, Y., Kusek, J. & Nyberg, L. Jr. The diagnosis of interstitial cystitis revisited: lessons learned from the National Institutes of Health Interstitial Cystitis Database study. *J. Urol.* **161**, 553–557 (1999).
28. Gillenwater, J. Y. & Wein, A. J. Summary of the National Institute of Arthritis, Diabetes, Digestive and Kidney Diseases Workshop on Interstitial Cystitis, National Institutes of Health, Bethesda, Maryland, August 28–29, 1987. *J. Urol.* **140**, 203–206 (1988).
29. Denson, M. A., Griebling, T. L., Cohen, M. B. & Kreder, K. J. Comparison of cystoscopic and histological findings in patients with suspected interstitial cystitis. *J. Urol.* **164**, 1908–1911 (2000).
30. Bade, J., Ishizuka, O. & Yoshida, M. Future research needs for the definition/diagnosis of interstitial cystitis. *Int. J. Urol.* **10 (Suppl.)**, S31–S34 (2003).
31. Messing, E. *et al.* Associations among cystoscopic findings and symptoms and physical examination findings in women enrolled in the Interstitial Cystitis Data Base (ICDB) Study. *Urology* **49**, 81–85 (1997).
32. Daha, L. K. *et al.* Comparative assessment of maximal bladder capacity, 0.9% NaCl versus 0.2 M KCl, for the diagnosis of interstitial cystitis: a prospective controlled study. *J. Urol.* **170**, 807–809 (2003).
33. Chambers, G. K., Fenster, H. N., Cripps, S., Jens, M. & Taylor, D. An assessment of the use of intravesical potassium in the diagnosis of interstitial cystitis. *J. Urol.* **162**, 699–701 (1999).
34. Teichman, J. M. & Nielsen-Omeis, B. J. Potassium leak test predicts outcome in interstitial cystitis. *J. Urol.* **161**, 1791–1794 (1999).
35. Dimitrakov, J. & Guthrie, D. Genetics and phenotyping of urological chronic pelvic pain syndrome. *J. Urol.* **181**, 1550–1557 (2009).
36. Evans, R. J. & Sant, G. R. Current diagnosis of interstitial cystitis: an evolving paradigm. *Urology* **69 (4 Suppl.)**, 64–72 (2007).
37. Goldman, H. B. & Zimmern, P. E. The treatment of female bladder outlet obstruction. *BJU Int.* **98 (Suppl. 1)**, 17–23 (2006).
38. Groutz, A., Blaivas, J. G. & Chaikin, D. C. Bladder outlet obstruction in women: definition and characteristics. *Neurourol. Urodyn.* **19**, 213–220 (2000).
39. Kuo, H. C. Videourodynamic characteristics and lower urinary tract symptoms of female bladder outlet obstruction. *Urology* **66**, 1005–1009 (2005).
40. Nitti, V. W., Tu, L. M. & Gitlin, J. Diagnosing bladder outlet obstruction in women. *J. Urol.* **161**, 1535–1540 (1999).
41. Defreitas, G. A., Zimmern, P. E., Lemack, G. E. & Shariat, S. F. Refining diagnosis of anatomic female bladder outlet obstruction: comparison of pressure-flow study parameters in clinically obstructed women with those of normal controls. *Urology* **64**, 675–679 (2004).
42. Nigro, D. A. *et al.* Associations among cystoscopic and urodynamic findings for women enrolled in the Interstitial Cystitis Data Base (ICDB) Study. *Urology* **49**, 86–92 (1997).
43. Kirkemo, A. *et al.* Associations among urodynamic findings and symptoms in women enrolled in the Interstitial Cystitis Data Base (ICDB) Study. *Urology* **49**, 76–80 (1997).
44. Kim, S. H., Kim, T. B., Kim, S. W. & Oh, S. J. Urodynamic findings of the painful bladder syndrome/interstitial cystitis: a comparison with idiopathic overactive bladder. *J. Urol.* **181**, 2550–2554 (2009).
45. Philip, J., Willmott, S. & Irwin, P. Interstitial cystitis versus detrusor overactivity: a comparative, randomized, controlled study of cystometry using saline and 0.3 M potassium chloride. *J. Urol.* **175**, 566–570 (2006).
46. Kuo, H. C. Urodynamic study and potassium sensitivity test for women with frequency-urgency syndrome and interstitial cystitis. *Urol. Int.* **71**, 61–65 (2003).

Acknowledgments

This work was supported by the Felecia Cain Fellowship Endowment for Female Pelvic Medicine, Reconstructive Surgery and Neurourology.