

# Treatment of Painful Bladder Syndrome and Pelvic Organ Prolapse

*Highlights of the 4th International Consultation on Incontinence,  
July 5-8, 2008, Paris, France*

[Rev Urol. 2009;11(1):28-32]

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**Key words:** Stress urinary incontinence • Pelvic organ prolapse • Pregnancy • Prostatectomy • Painful bladder syndrome • Interstitial cystitis

The purposes of the 4th International Consultation on Incontinence (ICI), attended by medical professionals with interest in all aspects of incontinence, were to (1) review the current state of knowledge on incontinence; (2) standardize response criteria and recommendations for clinical research on incontinence; (3) validate standard international instruments to evaluate incontinence in collaboration with the major associations involved in the field of incontinence; and (4) propose a widely accepted strategy for the practical diagnostic and therapeutic management of incontinence according

to the principles of evidence-based medicine.

Twenty-three committees were formed. Each committee was charged with a specific topic to assess what we know, what we think we know, what we do not know, and what we need to know. The consultation's methodology follows evidence-based principles, defined in collaboration with the Oxford and Cochrane groups. Here we report on 3 of these committees.

### Committee on Incontinence Pathophysiology<sup>1</sup>

The Committee on Incontinence Pathophysiology reviewed current understanding of the mechanisms underlying urinary continence and risk factors for incontinence, including gender, age, childbirth/parity, obesity, coughing, lifting, hysterectomy, and genetic factors. Periurethral collagen composition changes in women with stress urinary incontinence (SUI), including a lower ratio of type I to type III collagen, were highlighted.

Changes in elastic fiber metabolism and gene expression have been associated with pelvic organ prolapse (POP), and there are age-related changes to the pelvic floor musculature, including a loss of rhabdosphincter muscle mass. Recent studies reported increased levels of matrix metalloproteinases in women with POP.

Recent research highlighted by this committee includes reports that cystocele correction will cure SUI in approximately 66% of patients. It is recommended that POP reduction be performed as a part of formal urodynamics because POP reduction unmasks occult SUI rates of 23% to 63% during testing, and pessary reduction seems to be the best predictor of post-surgical elevated postvoid residuals.

### Assessment of Stress Incontinence

Recent urodynamic studies were described, including the association of the relationship between opening bladder pressure and intrinsic

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sphincter deficiency with lower urethral resistance pressures in women with SUI. Women with SUI were also shown to have reduced pelvic floor muscle activity and lower urethral closure pressures after repeated coughs. Ultrasonographic sphincter volume correlated with the degree of incontinence during videourodynamics; however, results on urethral vasculature in SUI were conflicting.

### *Pelvic Floor and Pregnancy*

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poses to postpartum urge incontinence. Early postpartum prevalence rates are 9% to 31%. Specific perinatal risk factors include parity, birth weight, and type of delivery. Episiotomy did not seem to be protective. Episiotomy is associated with increased postoperative pain and bleeding and a higher incidence of 3rd- and 4th-degree perineal tears with midline episiotomy.

Cesarean delivery seems to be protective, but this effect diminishes with further deliveries. One recent study showed a 35% incidence of stage II POP after secondary cesarean delivery, compared with 32% after vaginal delivery. A different study showed reduced POP and POP symptoms after cesarean delivery compared with vaginal delivery.

Most of the damage to the pelvic floor seems to be associated with the first pregnancy and delivery. Epidural analgesia is associated with a higher rate of perineal injury due to prolonged second stage of labor and increased use of instrument delivery. However, there does not seem to be an increased incidence of postpartum SUI.

### *Risk Factors of Prolapse*

POP risk factors include childbirth, parity, obesity, and hysterectomy. Hysterectomy was associated with a more than 5-fold increased risk of POP. Colposuspension and sacrospinous ligament fixation also increased risk of subsequent POP. Estrogen therapy may promote urge incontinence but not POP. There may also be genetic factors involved in POP: an increased incidence is noted in relatives with POP. POP is common in patients with connective tissue disorders, such as Ehlers-Danlos syndrome.

### *Incontinence in Men*

Detrusor overactivity and overactive bladder in men is often secondary to prostatic obstruction, and detrusor overactivity may resolve in 70% of patients after bladder outlet obstruction is treated. Changes in neurotransmission and mechanical properties of the bladder may contribute to persistent detrusor overactivity in some men. SUI is seen almost exclusively in men with a history of prostate surgery or neurologic disease. The etiologies of postprostatectomy incontinence include direct injury, thermal injury, nerve injury, or damage from ablative technologies or radiation.

Level 2 evidence from the US Agency for Health Care Policy and Research 1994 Clinical Guidelines gave a prevalence of 2.1% for post-transurethral resection of prostate (TURP) SUI. Level 1 evidence exists showing no differences in rates of incontinence after TURP versus potassium-titanyl-phosphate laser prostatectomy and TURP versus holmium laser resection. Post-TURP incontinence is much more common

after treatments for prostate cancer, including brachytherapy and external beam radiotherapy.

Rates of incontinence after radical prostatectomy are variable and depend on definitions, surgeon expertise, and method of data collection. Medicare data from 1988 to 1990 showed that 31% of patients wore pads or clamps. Numbers from centers of excellence are generally much better, generally less than 10%.

Level 1 evidence did not show a difference in incontinence outcomes with laparoscopic versus open radical prostatectomy. Data are accumulating with respect to robotic radical prostatectomy and are generally similar to data for open surgery.

### **Committee on Painful Bladder Syndrome<sup>2</sup>**

Committee chairman Professor Philip Hanno was unable to attend the ICI meeting; the committee report was instead presented by Professor Jørgen Nordling from Denmark. He opened with a brief history of the name and proposed changing the name to Bladder Pain Syndrome, in accordance with the name change proposal by ESSIC, the European Society for the Study of IC/PBS (interstitial cystitis/painful bladder syndrome), of which he is chairman. The committee reviewed definitions and criteria used over the years, including the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) criteria, the International Continence Society (ICS) definition, and most recently the ESSIC definition, with an explanation of the ESSIC classification system based on findings at cystoscopy, hydrodistention, and biopsy, and whether these investigations have been performed.

This committee emphasized that disorders associated with IC/PBS are being inadequately investigated. These associated disorders did not

form part of the classic NIDDK diagnostic criteria and have not been considered as part of the routine history or physical examination for IC/PBS. These associated disorders should be explored because there is no agreed-upon pathognomonic bladder pathology to suggest that they are solely end-organ disorders. The outcomes of well-designed, multicenter, placebo-controlled trials directed at the bladder have been disappointing.

Although there has been increasing interest in IC/PBS and associated disorders, they have largely been investigated by specialists in the associated diseases. The committee concluded that when properly investigated, it can be demonstrated that there are many symptom-based chronic pain disorders significantly associated with IC/PBS.

Confusable diseases must be excluded as the cause of the symptoms. The long list of confusable diseases can be excluded in stages by a detailed medical history and focused physical examination, urinalysis and culture, flow, pressure-flow, and ultrasound examinations, cystoscopy, and biopsy. Currently, no questionnaire has either the specificity or sensitivity to be used in clinical diagnosis. A variety of questionnaires can be used for following the course of the disease, assessing the severity of the disease, or as a primary endpoint in clinical treatment studies to measure overall improvement.

Recommended treatments for IC/PBS are graded from A (highest) to D (lowest), and levels of evidence from 1 (highest) to 4 (lowest). Grading is based on evidence from published studies, which may differ from unpublished evidence from clinical practice.

Conservative therapies for IC/PBS include physical therapy (evidence level 2), behavior modification (evidence level 3), stress reduction

(evidence level 4), and dietary manipulation (evidence level 4). All of these received a grade C recommendation.

#### *Pharmacotherapy*

**Antihistamines.** Hydroxyzine had level 1b evidence but a grade D recommendation. Antihistamine blocks neuronal activation of mast cells. Antihistamines have been shown to have good therapeutic effects by several noncontrolled studies, but an NIDDK study in 2003 showed no significant benefit.

**Pentosan polysulfate sodium.** There have been 5 randomized, controlled trials of pentosan polysulfate sodium (PPS), with mixed results. The committee awarded PPS level 1 evidence but a grade D recommendation owing to conflicting level 1 evidence.

**Antidepressants.** Amitriptyline had level 2 evidence and a grade B recommendation. There has been 1 randomized, controlled trial and several noncontrolled studies. The theoretical mechanisms of amitriptyline include central and peripheral anticholinergic action, sedative action, blocking of H1-histaminergic receptors, and analgesic action (inhibition of reuptake of serotonin and norepinephrine). Desipramine and doxepin had level 3 evidence and a grade C recommendation.

**Immunosuppressants.** Cyclosporine had level 3 evidence and a grade C recommendation. There have been 3 uncontrolled studies and 1 study comparing cyclosporine with PPS. Cyclosporine seems to improve pain and frequency but has potentially serious side effects and should only be considered in severe, intractable patients.

**IPD-1151T.** Suplatast tosilate (IPD-1151T) suppresses helper T cells producing interleukin-4 and -5. Only 1 uncontrolled study has been reported, but a large-scale, placebo-controlled study is under way.

#### *Intravesical Treatment*

Intravesical treatments, with evidence level and treatment grade, include the following:

- Capsaicin, resiniferatoxin: 1 D
- Bacillus Calmette-Guérin: 1 D
- Dimethyl sulfoxide: 2 B
- Lidocaine: 2 C
- Heparin: 3 C
- Hyaluronic acid: 4 D
- Chondroitin sulfate: 4 D
- PPS: 4 D
- Oxybutynin: 4 D
- Botulinum toxin: 4 D

#### *Bladder Distention*

Bladder distention has been used for many years, not only as a diagnostic tool but also for the treatment of IC patients. However, most studies are retrospective and uncontrolled, and evidence is conflicting. For bladder distention the level of evidence was 3 and treatment grade was C.

#### *Sacral Neuromodulation*

Sacral neuromodulation for IC/PBS patients is still an investigational procedure. The committee emphasized that strict patient selection and detailed discussion with the patient, including providing the patient with reported long-term results, are essential.

#### *Hunner's Lesion (Ulcer)-Directed Therapy*

Transurethral resection, coagulation, and laser ablation of Hunner's lesion (ulcer) were given an evidence level of 3 and a grade C recommendation.

#### *Surgery*

The committee gave the following evidence levels and recommendation grades in the field of surgery: hydrodistention, 3 C; Hunner's lesion resection/fulguration, 3 C; bladder augmentation/cystoplasty (end-stage disease), 3 C; diversion with or without cystectomy, 3 C.

### *Cystoplasty*

There is some evidence that cystoplasty with supratrigonal resection may benefit selected patients with end-stage classic IC/PBS (with Hunner's lesion). There is no evidence that subtrigonal cystectomy with cystoplasty has any outcome advantage over supratrigonal cystectomy, but it is associated with more complications and poorer functional bladder rehabilitation.

Recommendations by the Committee on Painful Bladder Syndrome included the following: treatment decisions should be based as far as possible on placebo-controlled, randomized, controlled trials; treatment should be guided by patient-driven outcomes; start with the least invasive treatments; approach surgical therapies with caution; add or subtract treatments on the basis of results in individual patients; consider more extensive evaluation and invasive therapies in patients who have failed oral and intravesical treatments. Unproven therapies should be given within the framework of clinical trials; irreversible surgery should be a last resort, with rare exceptions.

Recommended first-line treatments include conservative therapy, patient education, dietary modification, non-prescription analgesics, and pelvic floor relaxation, while addressing treatment of pain. Second-line treatment includes oral therapies, intravesical therapies, and physical therapy, while addressing treatment of pain. Third-line treatment includes cystoscopy under anesthesia with bladder distention and fulguration of Hunner's lesion, while addressing treatment of pain. Fourth-line treatment includes neuromodulation, intramural botulinum toxin, and pharmacologic management, while addressing treatment of pain, and diversion with or without cystectomy and substitution cystoplasty.

The committee suggested that a screening tool with adequate sensitivity and specificity be developed and that epidemiologic studies should be conducted in the population aimed at detecting incidence and prevalence and at identifying risk factors. A patient database should be established in different regions with long-term follow-up for the purpose of understanding the natural history of the disease and to examine differences in the natural history of the disease between regions.

Patients who also have pain syndromes or autoimmune diseases may have different pathophysiology, natural history, and treatment responses from patients who do not have associated disorders. Subgrouping patients would allow better treatment strategies to be developed but may also answer the question of whether this is an end-organ disease of the bladder or a systemic condition.

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A simple tool should be developed for nonspecialists to pick out patients with concomitant disorders. Researchers should test the concept that categorizes all types of pelvic pain into one "chronic urologic pelvic pain syndrome," bearing in mind that some patients have symptoms involving multiple pelvic organs, concurrently or sequentially. According to the committee, a practical, multidisciplinary care model that includes physicians in charge, dieticians, physiotherapists, pain specialists, psychologists, psychiatrists, and patient support groups should be developed.

### **Committee on Surgery for Pelvic Organ Prolapse<sup>3</sup>**

The session started when the chairperson, Dr. Linda Brubaker, conveyed the

committee's disappointment that only a few randomized clinical trials were published since the last ICI meeting. They also thought that the medical profession may be too quick in adoption of new technologies and procedures that are not evidence based. Issues such as indication for prolapse surgery and valid, universally accepted outcome measures are still unmet needs. There is a lack of data regarding the best "primary" repair and ways to minimize postoperative complications, including urgency and dyspareunia.

### *Repair POP With Mesh*

The use of mesh in POP repair is exciting but controversial. If mesh is used for the primary repair, what operation should be performed for recurrence? Are more complications associated with subsequent repairs if mesh was used for the primary repair? What is the ideal mesh to use? Unfor-

tunately at this point there are no answers to these questions. One unique material (Gore-Tex®) was singled out, for which erosion rates are significantly higher than with other materials. Colpectomy and colpocleisis were recommended for women who are not sexually active. The committee noted a low rate of "sexual regret" in women undergoing these procedures.

### *Absorbable and Nonabsorbable Mesh*

Two randomized clinical trials were reviewed that reported conflicting evidence with the use of absorbable mesh with anterior colporrhaphy. Three trials (level 1 evidence) support the use of nonabsorbable synthetic mesh with anterior repairs, but not enough evidence exists to support use

in apical or posterior repairs. Mesh extrusion rates are 5% to 17%.

With respect to apical suspensions, there is no evidence supporting the superiority of sacrospinous fixation versus uterosacral ligament suspension. The former technique has higher rates of anterior compartment recurrence, and the latter shows higher rates of ureteral compromise. There is level 3 evidence on the use of mesh (mostly prefabricated kits), which supports its use in apical repairs.

### *Vaginal Vault Prolapse*

The committee reviewed 3 randomized, controlled trials comparing abdominal versus vaginal approaches. Better anatomic outcomes were obtained abdominally but with a higher cost and morbidity. There is level 1 evidence to recommend using synthetic graft material over biologic material to bridge the apex of the vagina to the sacrum during abdominal sacrocolpopexy (ASC). Concomitant hysterectomy (3- to 5-fold increased risk) and smoking history increase the risk of mesh extrusion/erosion.

There are not yet enough data to support superiority of laparoscopic or robotic-assisted approaches. There is controversy regarding the role of concomitant hysterectomy with vault prolapse repair, and the use of hysteropexy is rising in popularity. As stated above, the risk of mesh erosion with the combined procedure is significantly higher.

The committee noted a single level-1 trial that showed inferior outcomes with uterine-preserving procedures, although there are level 2 to 3 data with conflicting results. The committee also believed that current urodynamic testing with prolapse reduction was insufficient for predicting postoperative SUI but that there is an increased risk of de novo SUI if occult SUI exists preoperatively.

### *Posterior and Apical Repairs*

There was level 2 evidence comparing site-specific repair versus fascial plication; success rates were 67% versus 86%, respectively ( $P = .001$ ). Level 3 evidence was presented on the use of polypropylene mesh for posterior repairs, showing high rates of extrusion and dyspareunia. The committee recommended against the use of mesh in this procedure.

A grade A recommendation was given for the use of ASC for apical prolapse and for the use of synthetic mesh over biologic graft for this procedure. Synthetic graft improves 1-year outcomes for anterior repairs, but this benefit must be weighed against the risk of mesh complications. Transvaginal repair is preferred over transanal repair for posterior prolapse.

A grade B recommendation was given for a concomitant Burch procedure at the time of ASC in women without preoperative SUI. Because concomitant hysterectomy at the time of ASC increases the risk of mesh erosion, the committee also gave a grade B recommendation for consideration of alternative plans. For anterior repairs with hysterectomy, avoiding mesh is reasonable.

Sacrospinous fixation and uterosacral ligament suspension were recommended equally for the vaginal approach to vault prolapse (grade B). For posterior repairs, there are no data supporting the use of synthetic mesh; porcine dermis repair is inferior to the other techniques (grade B). Levator plication should be used with caution in sexually active women owing to increased rates of dyspareunia (grade B). The committee's grade C recommendations were for the consideration of apical suspension at the time of any vaginal prolapse repair. Outcomes with fascial plication are superior to those with site-specific repair in the posterior compartment.

In 1 study, porcine dermis was superior to traditional anterior colporrhaphy.

The committee also recommended against the use of mesh in vaginal repairs if an intraoperative proctotomy occurred. The committee found insufficient evidence to support any technique of primary prolapse repair or for specific vaginal procedures. There is also not enough evidence to provide guidance regarding the use of mesh after intraoperative cystotomy. The committee also stated that an anatomic finding, in the absence of symptoms, is rarely an indication for surgery, and that surgical alternatives should be presented to women considering prolapse repair.

### *Future Perspectives*

Trials are needed regarding the optimal repair of posthysterectomy prolapse, comparing the use of mesh versus native tissue for apical repairs, and comparing different techniques for apical suspension. Studies are needed concerning surgical approaches after primary mesh repair failure. Better-validated outcome measures are needed to assess anatomic and functional outcomes after surgery. The committee encouraged the creation and use of registries for new devices to allow proper data collection and to determine the safety and efficacy of these products. ■

### References

1. Koelbl H, Nitti VW; for the Committee on Incontinence Pathophysiology. Report of the Committee on Incontinence Pathophysiology. Presented at: 4th International Consultation on Incontinence; July 5-8, 2008; Paris, France.
2. Hanno P; for the Committee on Painful Bladder Syndrome. Report of the Committee on Painful Bladder Syndrome. Presented at: 4th International Consultation on Incontinence; July 5-8, 2008; Paris, France.
3. Brubaker L; for the Committee on Surgery for Pelvic Organ Prolapse. Report of the Committee on Surgery for Pelvic Organ Prolapse. Presented at: 4th International Consultation on Incontinence; July 5-8, 2008; Paris, France.