



## Overactive bladder

### Introduction

The symptoms of an overactive bladder (OAB) have been reported to occur in as many as 1 in 3 women over 75 years of age and 1 in 15 women over 40 years. About half of these women are affected by incontinence<sup>1</sup>. There is a significant underreporting of symptoms because of embarrassment on the part of the patient and lack of awareness on the part of care takers. Women go to their doctors only when these symptoms become bothersome or embarrassing, or when they are concerned about a serious underlying problem.

OAB is a term given to a collection of common lower urinary tract symptoms, namely frequency and urgency with or without urge incontinence<sup>2</sup>. It has also been called the urge syndrome<sup>3</sup>. This symptom complex is not a diagnosis but the clinical end result of several possible etiologies. It is used to imply a possible underlying detrusor over-activity without the need to resort to urodynamic studies. It is treated in much the same way as detrusor over-activity. The latter is a urodynamic observation characterized by involuntary detrusor contractions during the filling phase which may be spontaneous or provoked while the subject is trying to inhibit micturition<sup>4</sup>.

### Etiopathology

Sometimes, a discrete disease process initiates the cascade leading to overactive vesical function. Anatomic and inflammatory sources may include infection, interstitial cystitis, urethrotrigonitis, urolithiasis, and neoplasia. Common neurologic triggers include cerebral vascular accidents, intracranial lesions, and Parkinsonism. However, idiopathic detrusor instability implies the exclusion of an identifiable primary trigger. Though all forms of the overactive bladder share the common trait of poor accommodation with filling, they may not share a common underlying pathophysiology. For lack of a more precise explanation, the idiopathic OAB has been often characterized as the product of a disordered micturition reflex, a regression to primitive voiding patterns marked by fullness at low volume, automatic emptying, and lack of inhibition. Numerous theories have been put forth to explain this regression. The underlying disorder may lie in the sensory (predominance of plurinergic receptors or oversensitive stretch receptors), neurogenic, or myogenic

components. The common theme is a change in the property of the detrusor smooth muscle that predisposes the bladder to unstable contractions due to a reduction in the functional innervation of the bladder wall.

### Clinical evaluation

A woman's history is the cornerstone on which the evaluation rests. History should be taken in a systematic and prescribed format. Hematuria, pain, and obstructive features point to a physically identifiable etiology and should be vigorously pursued. The purpose of history taking is to look for the etiological factors and comorbidity. Important information includes past pelvic surgery, especially for incontinence, past neurologic conditions, and the use of medications, particularly those with anticholinergic, antidepressant, psychotropic, or alpha-blockade effect. Results of previous evaluation and medical and surgical treatment should be obtained. Bowel and sexual dysfunction should be looked for. History also helps to differentiate urge incontinence from other etiologies of incontinence to some extent.

Questionnaires that quantify symptoms and determine the effect on quality of life have been recommended in the assessment of OAB. Validated incontinence questionnaires include the Incontinence Impact Questionnaire and the Urological Distress Inventory<sup>5</sup>.

A urinary diary recorded by the patient for 1 to 7 days is a reliable and reproducible objective assessment of symptoms and should be performed in any patient with significant urge symptoms. In addition to providing information on bladder behavior and the severity of incontinence, the urinary diary may suggest the particular type of urinary disorder, reveal excessive fluid intake, and serve as a useful baseline for ongoing treatment.

Clinical examination should be performed to assess pelvic organ prolapse, estrogen status, presence of infection, or a pelvic mass. An assessment of pelvic floor strength using digital examination or a perineometer during voluntary contraction of the levator muscle is of great importance in evaluating and teaching pelvic floor exercises. The clinical sign of stress incontinence has a positive predictive value of 91%<sup>6</sup>. However 40% of these patients will have an additional

urodynamic diagnosis of detrusor instability or hypersensitive bladder or voiding dysfunction. Neurologic assessment should focus on the sacral spinal cord segments S2 to S4, which provide the nerve supply to the lower urinary tract.

### Investigations

Perineal pad testing is a simple noninvasive method of confirmation and quantification of urine leakage and is used to evaluate treatment modalities for incontinence. Pad testing can be of short (20 minutes to 2 hours) or long duration (24 to 48 hours). The test-retest variability of the short-term pad test is considerable (up to 150%). The long-term test has a test-retest variability of 7%. The 1 hour pad test will show a weight gain of less than 1 g and a 24 hour test of less than 10 g in continent women <sup>7</sup>.

Postvoid residual urine measurement is important in women at high risk for voiding dysfunction. A residual urine greater than 30 mL measured by ultrasound 1 minute after a normal void of 200 mL or more, and confirmed on more than one occasion, is considered significant <sup>8</sup>. Postvoid residue can be measured by traditional urethral catheterization, which is cheap but carries a 1% risk of infection. More centers now opt for ultrasound because of its noninvasive nature and ability to pick up other pathology such as calculi, diverticuli, and carcinoma.

About 15% of women with classic symptoms of bladder overactivity have stress incontinence on urodynamics and vice-versa <sup>9</sup>. Urodynamic evaluation is recommended in women with mixed symptomatology, when conservative treatment has failed, before incontinence surgery, and in neurogenic patients. Women with bladder overactivity symptoms can show variable findings on filling cystometry.

The bladder may show unstable phasic contractions (of any amplitude) that cannot be suppressed (detrusor instability), a tonic rise in bladder pressure (reduced bladder compliance), or a stable but low capacity as a result of pain or urgency; or it may have normal function (stable, normal compliance, good capacity). The incidence of unstable contractions is increased by making filling cystometry more provocative (eg, faster filling speed, change in posture from supine to standing, ice-water filling, and hand washing). Ambulatory urodynamic studies have been used to advantage in women with bladder overactivity symptoms. Between 10 and 30% of patients with urge symptoms and negative routine cystometry show detrusor instability on ambulatory urodynamics <sup>10</sup>. It also eliminates the need for orthograde bladder filling, which makes it a more physiological process.

Women who have hematuria, pain, and previous urological surgery should be evaluated with a cystourethroscopy early in the course of management. Neurophysiological studies are at present experimental and research oriented. They are directed towards studying the nerve and motor unit of the detrusor muscle.

### Treatment

Options for managing the OAB are broadly divided into bladder retraining, medicines and surgery. General advice should include managing fluid intake. Women should be advised to consume between 1 and 1.5 liters of fluids in any 24 hour period. Simply cutting down on the volume or altering the times at which majority of fluids are consumed can reduce symptoms substantially to improve the quality of life. Caffeine and alcohol are known bladder irritants and are best minimized or substituted by decaffeinated or nonalcoholic beverages. Advice from an incontinence advisor about the use of pads, general hygiene and measures to minimize the risk of infection is invaluable and is sometimes all that women are looking for. Surgical treatment modalities such as bladder diversion, augmentation (clam cystoplasty), denervation and continent pouch formation play a minor role in managing bladder over-activity and are usually a last resort.

Bladder retraining is based on the ability to suppress urinary urge and to extend the times between voiding. Predetermined times for voiding are recommended even though the woman may be incontinent between these times. The efficacy of bladder retraining is increased when pelvic floor exercises are concomitantly taught. Biofeedback techniques such as visual analogue scales can be used with bladder retraining exercises in a broader behavioral modifications program for these women. Cure rates with bladder retraining have been reported to be between 44 and 90%. They do not have any physical side effects. However, there is a need for a specialist trainer as well as a willing and understanding patient for this to succeed.

Neuromodulation is one of the newer treatment modalities under evaluation <sup>11</sup>. Various methods such as the SANS (Stoller Afferent Nerve Stimulator), peripheral sacral nerve stimulation, and the more invasive interstim central sacral nerve stimulation are being studied.

### Pharmacotherapy

For most women, pharmacotherapy will be used alone or in conjunction with other modalities in the treatment of bladder overactivity. A wide variety of therapeutic preparations are available. It is difficult to compare them because of the high placebo effect (30-40%) and since the response to any drug is likely to be in the region of 60% the difference will

probably be small. The focus, then, is on enhancing compliance and keeping side-effects to a minimum. To achieve these goals, there has been a move towards sustained release preparations which allow once-a-day dosing of existing agents. Newer drug delivery modalities such as intravesical therapy with vanilloids, capsaicin, and resiniferatoxin are on the horizon. With the presently available drugs, medical therapy aims to –

- Inhibit bladder contractility (anticholinergic agents, muscolotropic agents, and tricyclic antidepressants)
- Increase outlet resistance (alpha adrenergic agonists)
- Decrease urine production (desmopressin)
- Improve local tissue health (estrogens).

Anticholinergic drugs are directed towards the M<sub>2</sub> and M<sub>3</sub> receptors in the bladder. Acetylcholine released from the postganglionic parasympathetic nerve terminals acts on these receptors to initiate detrusor contractions. The M<sub>3</sub> receptors are thought to mediate the main part of this effect. But these are also found in the salivary glands and bowel. The common side effects, therefore, include dry mouth and eyes, constipation, tachycardia, and retention of urine. Anticholinergic drugs are contraindicated in women with glaucoma only if it is untreated closed angle glaucoma. Currently available anticholinergic drugs include oxybutinin, tolterodine and trospium. Oxybutinin has direct muscle relaxing and local anesthetic actions in addition to being antimuscarinic. It is usually started in a low dose (2.5 mg twice a day) which is increased to the usually therapeutic dose of 5 mg four times a day. Tolterodine can be similarly increased to 2 mg twice a day. The limiting factor with both these drugs is the occurrence of side effects. Extended release preparation of oxybutinin and long acting preparation of tolterodine can be used to achieve and sustain the therapeutic dose. These drugs have been compared in randomized, double blind, placebo controlled trials and found to have similar clinical efficacy. However, tolterodine had fewer side effects, particularly dry mouth<sup>12</sup>. Trospium has also been shown to have similar results (equal efficacy and fewer side effects) in comparison with oxybutinin<sup>13</sup>. Newer agents such as darifenacin and solifenacin are designed specifically for the overactive bladder and should be available in the near future.

Propiverene has anticholinergic and calcium channel blocking actions but its use is limited by severe side effects. Tricyclic antidepressants (imipramine) are not used as first line agents due to the risk of orthostatic hypotension and ventricular arrhythmia. They are useful in treating symptoms of nocturia and adult nocturnal enuresis. Estrogen is frequently prescribed in the treatment of detrusor incontinence, despite the fact

that there is little evidence to support its use.

## Conclusion

A better understanding of the symptom complex of bladder overactivity is emerging. Rational investigations on the ground work of a detailed clinical evaluation allow the identification of patients with this common problem. Most patients can be treated with conservative means and pharmacotherapy. Newer agents and delivery systems are set to change the present clinical algorithms in the management of the overactive bladder.

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