

## Overactive Bladder Drugs, Botox or Neurostimulation?

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The Annual Women's Health Update

## Definition

- International Continence Society (ICS) definition of overactive bladder
- Urgency with or without urge incontinence, usually with increased frequency and nocturia
  - Frequency - >8 times in 24 hours
  - Nocturia - >1 time per night
  - Urge incontinence
  - Distinguish from stress or overflow

Table 1. Definitions of overactive bladder syndrome	
Detrusor overactivity	A urodynamic observation characterised by involuntary spontaneous or provoked detrusor contractions during the filling phase <sup>1,2</sup>
Nocturnal polyuria	An excess (>20-30%) proportion of urine excretion at night <sup>2</sup>
Polyuria	>40 mL urine/kg body weight during 24 hours
Postvoid residual volume	The volume of fluid remaining in the bladder at the completion of micturition <sup>2</sup>
Urgency	A sudden, compelling desire to void that is difficult to defer <sup>1,2</sup>
Urinary frequency	>8 micturitions/24 hours
Urgency urinary incontinence	Involuntary loss of urine associated with urgency <sup>2</sup>

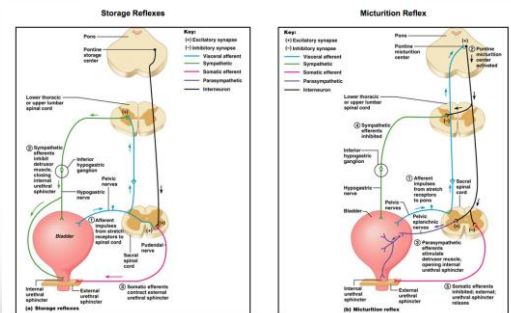
Overactive Bladder Syndrome. Management and treatment options.  
[www.racgp.org.au/afp/2012/november/overactive-bladder-syndrome](http://www.racgp.org.au/afp/2012/november/overactive-bladder-syndrome)

## Prevalence

- Prevalence 12-17%
- Increases with age
  - 22% men and women 70-74yo
  - 42% men and 31% women >75yo

## Impact

- Lower work productivity
- Travel and activity restriction
- Sexual dysfunction
- Depression
- Interrupted sleep
- Falls
- Fractures



<http://classes.midlandtech.edu/carterp/Courses/bio211/chap25/chap25.htm>

## Pathophysiology

- Detrusor muscle overactivity
  - Upregulation of muscarinic receptors M2, M3
  - Increased release of stretch-related acetylcholine
  - Supersensitivity to acetylcholine
  - Ischaemia, nerve injury, smooth muscle damage → DHIC

Banakhar M, Shajji T, Hassouna, M. Pathophysiology of overactive bladder. Int Urogynecol J (2012) 23:975-982

## Pathophysiology

- Bladder outlet obstruction or inflammation
  - Increased nerve growth factor and neuronal enlargement
  - Altered smooth muscle structure and function
  - Enhanced spinal micturition reflex

Banakhar M, Shajji T, Hassouna, M. Pathophysiology of overactive bladder. Int Urogynecol J (2012) 23:975-982

## Pathophysiology

- Neurogenic bladder
  - Damage cerebral inhibitory centre
  - Alter dopamine-glutamatergic mechanisms
  - Loss of inhibitory substantia nigra cells in basal ganglia
  - Increased mechanosensitivity of capsaicin-sensitive C fibers

Banakhar M, Shajji T, Hassouna, M. Pathophysiology of overactive bladder. Int Urogynecol J (2012) 23:975-982

## Differentials

- UTI
- Medications / caffeine
- Polydipsia / Nocturnal polyuria
- Constipation
- Reduced mobility
- Prolapse / Vaginitis
- BPH / Stricture
- Surgery / radiotherapy
- Pelvic mass
- Diverticulitis
- Endometriosis
- Diabetes
- Neurogenic bladder
- Malignancy
- Bladder stones
- Painful bladder syndrome

## Assessment

**Table 2. Investigations for overactive bladder syndrome**

### Initial investigations<sup>18</sup>

- Urinalysis to exclude infection, haematuria and glycosuria
- Urinary tract ultrasound and measurement of postresidual volume
- Frequency/volume chart for at least 3 days
- Bladder diary for a minimum of 3 days

### Secondary investigations<sup>19</sup>

- Urine cytology
- Urodynamic testing
- Cystoscopy
- Imaging of upper urinary tract or spine

Overactive Bladder Syndrome. Management and treatment options. www.racgp.org.au/afp/2012/november/overactive-bladder-syndrome

## Behavioural therapy

- Response rate
  - Initial 85%
  - 3 year 48%
- Reduction in number of incontinence episodes
  - Behavioral therapy 80.7%
  - Drug 68.5%
  - Placebo 39.4%

Holmes DM, Stone AR, Barry PR. Bladder training 3 years on. BJU (1983) 55:660-4. Burgio KL, Locher JL, Goode PS et al. Behavioural vs drug treatment for urge urinary incontinence in older women. JAMA (1998) 280:1995-2000.

## Behavioural therapy

- Dietary strategies
  - Caffeine, alcohol, irritants, avoid constipation
- Bladder retraining
  - Timed voids, deferral strategies, voids 3-4 hourly
- Fluid management
  - Adequate hydration 1.5L per day
- Pelvic floor muscle exercises

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## Pharmacotherapy

- Alpha blockers
- Anticholinergics – M3 antagonists
  - Non-selective – Oxybutynin
  - Selective M3 – Solifenacin
- Tricyclic antidepressants
  - Amitriptyline – not first-line
- Sympathomimetics – B3 agonists
  - Mirabegron

## Novel Therapy

- Botulinum toxin A (Botox)
- Posterior tibial nerve stimulation (PTNS)
- Sacral nerve modulation (SNM)

## Botulinum Toxin A

- PBS listing 2012, 2014
- Anticholinergics ineffective
- $\geq 14$  UUI episodes/week
- Achieve  $>50\%$  reduction in UUI episodes
- Willing to self-catheterise
- 100 IU DO, 200 IU NDO



Rovner E. Practical aspects of administration of onabotulinumtoxinA. Neurology and Urodynamics (2014) 33:S32-37.

## Botulinum Toxin A

- Onset 1-2/52, lasts 9-12/12
- Urinary retention risk
  - 36 of 552 patients (6.5%)
  - CISC required for  $<6$  weeks in  $>50\%$
  - Higher risk with DM
- 60-65% improved



Rovner E. Practical aspects of administration of onabotulinumtoxinA. Neurology and Urodynamics (2014) 33:S32-37.  
Cox L, Cameron AP. OnabotulinumtoxinA for the treatment of overactive bladder. Res Rep Urol (2014) 21:6:79-89

## PTNS

- FDA approved 2000
- Needle placement
- Weekly stimulation x12
- Monthly maintenance
- RCT PTNS vs sham
  - 54.5% vs 20.9%
- RCT PTNS vs tolterodine
  - 79.5% vs 54.8%



Johnsen N, Osborn D, Dmochowski R. The role of electrical stimulation techniques in the management of the male patient with urgency incontinence. Current Opinion Urol (2014) 24(6):560-5.

## SNM

- FDA approved 1997
- S3 nerve foramen
- Implant permanent lead with temporary extension wire for trial phase 1-2 weeks
- Implant pulse generator and battery if trial effective



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## SNM

- MRI contraindicated
- Response rate 33-88%
- High correlation between 1 and 5 year success rates – 84%



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## SNM

- 3 year study (Siegel)
  - 59% UUI patients significantly improved
  - 46% UUI patients completely dry
  - 56% urgency-frequency patients had >50% reduction in frequency
  - 70% retention patients had >50% reduction in catheter volume per catheterisation
- 5 year study (van Kerrebroeck)
  - 68% UUI patients, 56% urgency-frequency, 71% retention patients had >50% improvement from baseline

Kohli N, Patterson D. InterStim therapy: a contemporary approach to OAB. Rev Obst Gyn (2009) 2(1):18-27.

## SNM

- Complication risks
  - Pain at implant site
  - Lead migration
  - Wound complication
  - Bowel dysfunction
  - Generator problem
  - Infection
  - Battery life 5-7 years



Kohli N, Patterson D. InterStim therapy: a contemporary approach to OAB. Rev Obst Gyn (2009) 2(1):18-27.

## Take Home Messages

- Recognise and exclude differentials
- History and examination important
- Initiate behavioural therapy
- Drugs – anticholinergics, B3 agonists
- Adjuncts – urodynamic studies, cystoscopy
- Botox vs sacral neuromodulation