1. What is Overactive Bladder?

**OAB Symptom-Based Diagnosis**

"urinary urgency, with or without urge incontinence, usually with frequency and nocturia, in the absence of infection or other proven pathology”

ICS / IUGA 2010 (Haylen et al)

What is “Urinary Urgency”?

How is it different to just a strong desire to void
A “Strong Desire to Void” vs “Urgency”

**NORMAL BLADDER SENSATION**

<table>
<thead>
<tr>
<th>Volume (ml)</th>
<th>Feeling</th>
</tr>
</thead>
<tbody>
<tr>
<td>50</td>
<td>“No Sensation”</td>
</tr>
<tr>
<td>100</td>
<td>“First Sensation of Filling”</td>
</tr>
<tr>
<td>150</td>
<td>“First Desire to Void”</td>
</tr>
<tr>
<td>200</td>
<td>“Strong Desire”</td>
</tr>
<tr>
<td>300</td>
<td></td>
</tr>
<tr>
<td>400</td>
<td></td>
</tr>
</tbody>
</table>

50ml - “No Sensation”
100ml - “First Sensation of Filling”
150ml - “First Desire to Void”
200ml - “Strong Desire”

**NORMAL BLADDER SENSATION**

Like turning up a dimmer switch on a light

**So how does urgency differ??**

**NORMAL BLADDER SENSATION**

Like turning up a dimmer switch on a light

Sensation comes on SUDDENLY, with minimal warning
And it rarely relates to bladder fullness

Determining whether your patient has OAB??

You simply need to ask a few specific questions!!!

- “When you first get an urge to pass urine, does it usually start mild, like you could wait 30min if you had to, or does it change from nothing to a desperate urge to pass urine in an instant?”

- “If you were queuing up at the supermarket and suddenly got an urge to pass urine, could you wait till you have paid, or could the urge come on so suddenly that you would have to leave your shopping and race to the toilet?”

Prevalence of OAB

2011 EAU Guidelines on Urinary Incontinence

OAB (urgency) increases with age and affects:

- 10-26% of adult males
- 8-42% of adult females
A little note about SUI vs OAB

**STRESS INCONTINENCE**

Stress urinary incontinence

蓀OAB / URGENCY / URGE INCONTINENCE

But!!!!

Sub-urethral Slings
- TVT
- TOT / Monarc

~10-30% of ♀ developed new onset urgency / UUI after undergoing a sub-urethral sling for SUI

A little note about SUI vs OAB

**STRESS INCONTINENCE**

Stress urinary incontinence

蓀OAB / URGENCY / URGE INCONTINENCE

But!!!!

Sub-urethral Slings
- TVT
- TOT / Monarc

~10-30% of ♀ developed new onset urgency / UUI after undergoing a sub-urethral sling for SUI

GOING BACK TO THE ASSESSMENT OF OAB

Do we need to send a patient for **urodynamic testing** prior to starting any treatment? (or is it reasonable to treat simply on the presence of the symptom of urgency)

From www.iuga.org. Patient handout Urodynamics

Rates of DO in People with OAB-WET

<table>
<thead>
<tr>
<th>Study</th>
<th>N</th>
<th>Gender</th>
<th>DO (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Digesu et al 2003</td>
<td>843</td>
<td>♀ with OAB</td>
<td>54.2%</td>
</tr>
<tr>
<td>Sekido et al 2006</td>
<td>139</td>
<td>♂ &amp; ♀ with OAB</td>
<td>82%</td>
</tr>
<tr>
<td>Hashim &amp; Abrams, 2006</td>
<td>♂ &amp; ♀</td>
<td>♂ with OAB</td>
<td>90%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>♀ with OAB</td>
<td>43%</td>
</tr>
</tbody>
</table>

Pathophysiology behind Urinary Urgency in ♀

**Motor Dysfunctions**

Detrusor Overactivity

**Sensory Processing Dysfunction**

Increased release of sensory neurotransmitters through bladder wall

Research has now shown that the **pharmaceutical treatment of OAB (urgency)** has equal effectiveness irrespective of whether DO is then found on urodynamics!

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Word of Warning: a common clinical error regarding the link between urgency, frequency and nocturia….

It is commonly assumed that symptoms of

**Frequency & Nocturia**

- Often end up experiencing Urinary Frequency & Nocturia

**URINARY URGENCY**

**FREQUENCY NOCTURIA**

It is commonly assumed that symptoms of

**URINARY FREQUENCY**

eg voiding 10-12 times per day but without urgency

**CAUSES:**
- Incomplete bladder emptying / high post void residuals
- Low compliance / small capacity bladder eg after radiation therapy
- Excessive 24-hour urine production
  - eg diabetes mellitus / insipidus
- In these circumstance, treating with an antimuscarinic will probably make the person worse.

**NOCTURIA**

eg voiding 3-5 times through the night without day symptoms

- Most common cause is Nocturnal Polyuria (excessive urine production at night)
- Day time lower limb varicous pooling
- Pre-sleep medications → diuresis
- Secondary to Obstructive Sleep Apnea

---

**Management of OAB**

1. **Pharmaceutical Options**
   - Review of the antimuscarinics – success rates, side effects and patient compliance
   - Mirabegron – a new class of drug for OAB

2. **When patients don’t like the drugs!! - other conservative management of OAB**
   - Physiotherapy – Bladder Retraining, Urgency Inhibition, Non-surgical neuromodulation
   - Intravesical Botulinum Toxin

3. **When all else fails and nothing has worked!**
   - ‘Interstim’ - implanted Sacral Neuromodulation

---

**Anti-muscarinics: How do they work??**

**PHARMACEUTICAL MANAGEMENT**

- Antimuscarinics
- The new B3 Adreno-receptor agonist (B3 – AR)

**TRADITIONAL BELIEF**

- M receptors are located on Detrusor Smooth muscle cells in the bladder wall

- Blocking M-receptors on the Detrusor smooth muscle cells
- Blocks Involuntary Detrusor Contractions

It was this mechanism that meant health professionals believed you needed a the presence of “Detrusor Overactivity” to justify their use in patients with OAB….
M-Receptors are also found on the urothelium of the bladder (inside layer).

Blocking M-Receptors in bladder urothelium reduces the release of sensory neurotransmitters.

Reduced Sensation of Urgency during bladder filling.

CURRENT UNDERSTANDING

Muscarinic Subtypes in Other Effector Organs

- Variety of Muscarinic Receptors: M1, M2, M3
  - Bladder: M3
  - Brain: M1
  - Cardiac: M2
  - Salivary Glands: M1, M3
  - Gut: M2, M3

Impact of Non-Specific Antimuscarinics

Non-Specific Antimuscarinics block all M Receptors around the body (M1, M2, M3).

Muscarinic Subtypes in Other Effector Organs

- Bladder: M3
- Brain: M1
- Cardiac: M2
- Salivary Glands: M1, M3
- Gut: M2, M3
- Iris/ciliary body
- Lacrimal gland
- Salivary glands
- Stomach and esophagus
- Colon
- Bladder

- Dry mouth
- Dry eyes
- Constipation
- Dizziness
- Tachycardia
- Dyspepsia
- blurred vision
- Blurred vision
- Dry eyes

Impact of Non-Specific Antimuscarinics

- Dry mouth
- Dry eyes
- Constipation
- Dizziness

Anti-muscarinics: A Delicate Balance

<table>
<thead>
<tr>
<th>Efficacy</th>
<th>Side Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Increased Voiding Volumes</td>
<td>Dry Mouth</td>
</tr>
<tr>
<td>Less Frequency</td>
<td>Constipation</td>
</tr>
<tr>
<td>Less Urgency</td>
<td>Blurred Vision</td>
</tr>
<tr>
<td></td>
<td>Dizziness, cognitive changes</td>
</tr>
</tbody>
</table>

Antimuscarinics for OAB

There are lots of different anti-muscarinics approved for OAB

- Ditropan: Oxybutynin Hydrochloride - oral
- Oxytrol: Oxybutynin slow release patch
- Detrusitol: Tolterodine Tartrate - oral
- Enablex: Darifenacin Hydrobromide – oral slow release
- Vesicare: Solifenacin Succinate – oral slow release

MAIN DIFFERENCE???

How selective they are to the bladder

Oral Antimuscarinics (anticholinergics) summary from TGA Listing

- Ditropan
- Detrusitol
- Enablex
- Vesicare

Company

Active Ingredient

Dosage

Pregnancy

SIDE EFFECTS

Dry Mouth

Dry Eyes

Constipation

Dizziness

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### Oral Antimuscarinics (anticholinergics)

#### Summary from TGA Listing

<table>
<thead>
<tr>
<th>Company</th>
<th>Ditropan</th>
<th>Detrusitol</th>
<th>Enablex</th>
<th>Vesicare</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sanofi-Aventis Australia Pty Ltd</td>
<td>Hyoscine Hydrobromide</td>
<td>Toleridina Hydrobromide</td>
<td>Darifenacin Hydrochloride</td>
<td>Solifenacin Succinate</td>
</tr>
</tbody>
</table>

#### Dosage

<table>
<thead>
<tr>
<th>Pregnancy</th>
<th>Ditropan</th>
<th>Detrusitol</th>
<th>Enablex</th>
<th>Vesicare</th>
</tr>
</thead>
<tbody>
<tr>
<td>B1</td>
<td>2mg, 2/day</td>
<td>5mg, 2/day</td>
<td>1 x 7.5mg OR 1 x 15 mg</td>
<td>1 x 5mg OR 1 x 10mg</td>
</tr>
</tbody>
</table>

#### Side Effects

- Dry Mouth: **50-80%**
- Dry Eyes: **39% ; 24%**
- Constipation: **15 – 28%**
- Dizziness: **20 - 35%**

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THE GOOD NEWS….

These can be a very quick, easy and effective way to reduce a person’s symptoms…..

Great for the person who comes to your office saying:

“I am going on an overseas holiday in 3 weeks and I need my bladder under control before then”

But Do People Stay On Antimuscarinics?

Sexton, Notte, Maroulis et al 2011, Systematic Review

- 43% to 83% discontinue medication within 30 days
- Over half of patients never refill their initial prescription
- The rate of discontinuation continues to rise with time, with <2% uptake at 12 months.


Symptom Return after Cessation of Antimuscarinics…

Lee, Choo et al 2011 - ~2/3 Patients Relapse on Cessation of Rx

<table>
<thead>
<tr>
<th>Urgency Status</th>
<th>Urgency Incontinence</th>
<th>Day Frequency Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>40/108 (65%) signt. relapse</td>
<td>38/96 (68%) signt. relapse</td>
<td>70/108 (65%) signt. relapse</td>
</tr>
</tbody>
</table>


Mirabegron - “Myrbetriq”…

by Betmiga (Astellas).

- A new class of drug for OAB
- Not an Antimuscarinic
- β3 Adreno-Receptor Agonist (β3-AR)
- Mechanism
  - Facilitating sympathetic actions
  - (as opposed to Antimuscarinics which inhibit parasympathetic mechanisms)
  - Works by facilitating the detrusor relaxation mechanisms

Mirabegron - “Myrbetriq”…

by Betmiga (Astellas).

**Dosage:**
Start with 25mg / incr. to 50mg if required x 1 daily with or without food

**Time to Full Benefit:** ~8 weeks

**Duration of Treatment** Not curative (needs long term use)

**Side Effects**
- Possible increase in blood pressure
- Headache
- Nasopharyngitis (runny nose)
- Dizziness
- Nausea

Other options for treatment of OAB

1. Behaviour Retraining / Bladder Retraining
2. Conservative Neuromodulation Options
   - Tibial nerve stimulation
   - Percutaneous
   - Transcutaneous
   - Vaginal Stimulation
3. Intra-vesical Botulinum Toxin
4. Implanted Sacral Neuromodulation
What is Multicomponent Behaviour Retraining??

Wyman, Burgio and Newman 2009

“Teach a new response to urgency based on the use of pelvic floor muscle contraction to suppress urgency, control incontinence and restore a normal voiding interval”


How does Multicomponent Behaviour Retraining compare to Oxybutynin in effectiveness??

Medical therapy – Oxybutynin 72.7% reduction in incontinence

Behavioral therapy alone 57.5% reduction in incontinence – without any medication!

Combined Therapy 85-90% reduction in incontinence


Conservative Neuro-modulation Therapies

Tibial Nerve Stimulation

Percutaneous Tibial Nerve Stimulation

Transcutaneous Tibial Nerve Stimulation

Intravaginal Stimulation

PTNS

Percutaneous Tibial Nerve Stimulation

TREATMENT PROTOCOL
- 30 minutes stimulation
- 1/week
- 12 weeks

EFFECTIVENESS
6 Randomised Controlled Trials

> 4 RCT = PTNS vs Sham success rates ranging from 37 – 82%

> 2 RCT = PTNS vs Antimuscarinics PTNS equally effective

Transcutaneous Tibial Nerve Stimul’nt

Effectiveness - TTNS vs Oxybutynin

Souto et al 2014, February

SHORT TERM RESULTS 30min stim 2/week for 12 weeks

<table>
<thead>
<tr>
<th>SYMPTOM</th>
<th>TTNS 30min 2/wk</th>
<th>Oxybutynin Mean (SD)</th>
<th>P-value</th>
<th>b/w gps</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incontinence</td>
<td>94% → 11%</td>
<td>100% → 31%</td>
<td>p &lt; 0.001</td>
<td>p = 0.39</td>
</tr>
<tr>
<td>Frequency</td>
<td>12.7 → 8</td>
<td>11 → 7.9</td>
<td>p &lt; 0.001</td>
<td>p = 0.75</td>
</tr>
<tr>
<td>Nocturia</td>
<td>94% → 11%</td>
<td>84% → 5%</td>
<td>p &lt; 0.001</td>
<td>p = 0.24</td>
</tr>
</tbody>
</table>

All Groups significantly improved after treatment – with no difference between groups. TTNS equally effective as Oxybutynin


TTNS vs Oxybutynin

LONG TERM RESULTS

Both groups that included TTNS maintained their improvements at 3months after cessation of treatment

Whereas the oxybutynin only group had significant symptom return.


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Intra-Vaginal Stimulation (IVS) vs Antimuscarinic Therapy

3 COMPARISON STUDIES

1. Oxybutynin 5mg 2-3/day vs Intravaginal Neuromodulation
   - IVS outcome had equal/similar effectiveness to Antimuscarinic Therapy

2. Placebo vs Oxybutynin 2.5mg 3/day vs Intravaginal Neuromodulation
   - Placebo: resolved in 0.0%, improved in 9.5%, unchanged 90.5%
   - Oxybutynin: resolved in 8.7%, improved in 30.4%, unchanged 74%
   - E-Stim Gp: resolved in 16.7%, improved in 41.7%, unchanged 41.7%

3. Tolterodine 2mg b.d vs Intravaginal Neuromodulation
   - Results:
     - Oral Tolterodine: Effective – 76%; Cure – 40%
     - E-Stimulation: Effective – 74%; Cure – 37%
   - IVS outcome had equal/similar effectiveness to Anticholinergic Therapy

Little note for GPs…….
Where do you refer??

Finding a Physiotherapist with training in OAB, Pelvic Floor and Women's Health....

Women’s Health Training Associates

Physio Directory

http://www.whta.com.au

Over 300 Physiotherapists across the east coast of Australia and New Zealand with training in pelvic floor, bladder, bowel and sexual disorders.

BOTOX FOR THE BLADDER!

Effectiveness Botox Type A

Indication – OAB refractory to medical therapy

Covered within the PBS since 2014

Can be used for both neurogenic and idiopathic detrusor overactivity

Treatment Protocol:

- 100-300U Botox
- Injected at 10-30 different sites in bladder dome
- Performed under local or general anaesthesia

Generally ~80% of patients experience improvement

- Voids per day: 12-53% reduction
- Urgency Episodes/day: 28-70% reduction
- Incontinence Episodes/day: 35-87% reduction
- Max cystometric capacity: 45% increase

- Long term recurrence rate: 27-66%
- Mean duration of effect: 6-14months
- Average Inter-injection Interval: 14-23months

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Review Results Continued:

- Satisfaction Rates:
  - 93% state they would undergo the treatment again.

- Mild Side Effects:
  - Significant PV Residual: 19-43%
  - Requiring CISC: 4-43%
  - UTI: 10-43%

Whilst some pt’s have a temporary effect, others appear “cured” after 1-2 treatments.

Other options for treatment of OAB

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2. Conservative Neuromodulation Options
   - Tibial nerve stimulation
   - Vaginal Stimulation
   - Percutaneous
   - Transcutaneous
3. Intra-vesical Botulinum Toxin
4. Implanted Sacral Neuromodulation

Sacral Nerve Stimulation

Termiology
Sacral Nerve Stimulation → Sacral Neuromodulation

Aim
Corrections of inappropriate, unwanted or erroneous nerve signals

Principle
Impacts upon neural interfaces to produce benefit

SNS for Bladder and Bowel Control

An established therapy for patients with:
- urinary urge incontinence (OAB)
- urinary urgency-frequency (OAB)
- (non-obstructive urinary retention)
- (chronic faecal incontinence)

More than 100,000 patients worldwide have received SNS

SNS: surgical phenomenon

Neuromodulation - fast growing area of medicine
20 years experience

Procedure: bridging the divide
Conservative & potentially hazardous surgery

Evidence-based Medicine
RCT; unprecedented attentive / prolonged FU

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Adv Pelvic Floor – POP & SUI

SNS: patient info

The procedure: try before you buy
day-case; minor procedure; 2 stage (test / permanent implant)

Safety
Zero mortality Low morbidity; day-case; minor procedure

Effective
64-79% success rates – preserved in long-term

Sydney Colorectal + Pelvic Floor Centre

SNS: try before you buy

Test

Implant

Sydney Colorectal + Pelvic Floor Centre

SNS – XR position

Sydney Colorectal + Pelvic Floor Centre

SNS: patient info

The procedure: try before you buy
day-case; minor procedure; 2 stage (test / permanent implant)

Safety
Zero mortality Low morbidity; day-case; minor procedure

Effective
64-79% success rates – preserved in long-term

Sydney Colorectal + Pelvic Floor Centre

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1. Medtronic-sponsored research: InterStim Therapy Clinical Summary 2011.

SNS: Urge Incontinence (UI)

79% of urge incontinence patients achieved clinical success

64% of urgency-frequency patients achieved clinical success

77% of urinary retention patients achieved clinical success

Take home message

Persistent Symptoms – refer to specialist / MDT

SNS – minor, safe, success in 6-8/10