Current Concepts in Evaluation and Management of Overactive Bladder

Melissa R. Kaufman, MD, PhD, FACS, ASEL-IA
Civil Aviation Medical Association
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Disclosures

Boston Scientific Inc. – National Principal Investigator
Cook Myosite Inc. – Global Principal Investigator
Valencia Technologies – Data Safety Monitoring Board
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Disclosures
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Goals

- Explain care pathways for evaluation and management
- Identify when overactive bladder (OAB) become “refractory”
- Describe management option of refractory OAB
  - Onabotulinumtoxin A
  - Neuromodulation
- Introduce novel concepts for OAB treatment
Goals
Terminology

- OAB: Urgency, with or without urgency incontinence
- Hallmark symptom - urgency
- Sudden compelling desire to void which is difficult to defer
- Usually with frequency and nocturia
- Due primarily to failure of storage
Physiology of the lower urinary tract

• Storage
• Evacuation
• Role of central nervous system
• Role of lower urinary tract anatomy
Storage

- Accommodate urinary volume
- Maintain continence
- Maintain low intravesical pressures
- Protect upper tracts
- Provide appropriate sensations of filling
- Viscoelastic properties of bladder
- Tonic contraction of outlet
Emptying

- Coordinated event
- Voluntary control
- Sustained detrusor contraction
  - Appropriate duration, strength to allow complete emptying
Normal bladder function

• Compliance
  • Bladder wall stretch with filling without increase in pressure
• Capacity
• Stability
• Low pressure, no abnormal contractions, closed sphincter
• Emptying: detrusor contraction, opening of sphincter
Normal bladder function

- Neurophysiology
  - Sacral reflex arc S2-S4
  - Thoracolumbar sympathetic system T12-L1
  - Pontine micturition center
  - Higher brain stem centers: inhibitory input
  - Coordinated sphincter relaxation

- Injury results in disorderly storage and micturition reflexes
Neurophysiology of bladder

- Parasympathetic
  - Acetylcholine
  - Sacral cord - pelvic nerve - ganglia in pelvic plexus and detrusor

- Sympathetic
  - Norepinephrine
  - Lumbar cord - hypogastric nerve - pelvic plexus and pelvic organs

- Somatic
  - Acetylcholine
  - Onuf’s nucleus - pudendal nerve - external urethral sphincter
Normal bladder function

- **Parasympathetic** contributes to **EMPTYING**
  - Contracts detrusor muscle
  - Relaxes internal urethral sphincter

- **Sympathetic** contributes to **STORAGE**
  - Relaxes detrusor muscle
  - Contracts internal urethral sphincter

- **Somatic**
  - Parasympathetic activated - relaxes the external urethral sphincter
  - Sympathetic activated - contracts the external urethral sphincter
Sympathetic: storage

**Hypogastric Nerve**
- Contracts urethra
- Relaxes bladder

**Pontine Micturition Center**

**SYM**

$T_{10}-L_2$

$S_2-S_4$

**Onuf’s nucleus**

**Pudendal nerve**

+$\beta_3$

+$\alpha_1$

+$N$
Sympathetic: storage
Parasympathetic: emptying

- **Onuf’s nucleus**
  - **S2-S4**

- **Pelvic Nerve**
  - Contracts detrusor
  - Inhibits urethra

- **Pontine Micturition Center**
  - **T10-L2**
  - SYM

- **PSYM**
  - Onuf’s nucleus
Parasympathetic: emptying
Wein’s classification of function

- Fill/Store
  - Bladder
  - Urethra/outlet
  - Both

- Emptying/voiding
  - Bladder
  - Urethra/outlet
  - Both
Spectrum of lower urinary tract dysfunction

- SUI
- Mixed (UUI+SUI)
- UUI

Overactive Bladder

- Urgency
- Frequency
- Nocturia
Spectrum of lower urinary tract dysfunction

AUA OAB guidelines: focus on pathways

Care pathways: established concept

- "Get with the Guidelines" (AHA and ASA)
- Stroke
- Heart failure
- Myocardial infarction
- Diabetes protocols
- Medicare core measures
**PQRS for incontinence**

**Physician Quality Reporting System for Incontinence.** As currently written, in 2015 the reporting program shifted from a voluntary program to a **mandatory** one in which penalties will be assessed for failure to participate.

**Urinary Incontinence: Plan of Care for Urinary Incontinence in Women Aged 65 Years and Older:**

Percentage of female patients aged 65 years and older with a diagnosis of urinary incontinence with a **documented plan of care for urinary incontinence** at least once within 12 months.

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Centers for Medicare & Medicaid Services. 2014 Physician Quality Reporting System (PQRS)
Why focus on incontinence?

Why focus on incontinence?

• 37 million with OAB = 1 in 6 Americans
• 18 million with fecal incontinence (FI) = 1 in 12 Americans
• UI and FI - over 50% of nursing home residents
• U.S. economic cost of OAB is $12.6 billion (year 2000 dollars)

Why focus on incontinence?
Hidden condition: QOL impact

- Self-manage
  - Frequent voiding
  - Fluid restriction
  - Pads
- 2 years prior to seeking treatment
- 30% of patients who seek treatment receive no assessment
QOL impact
Effects of urinary incontinence

• Significant negative impact on both overall and health-related QOL
  • Social isolation
  • Depression
  • Psychological distress
  • Increased caregiver burden
  • Skin inflammation / breakdown
  • Sleep disturbance
  • Increased risk urinary tract infection (UTI)
  • Limitation or avoidance of sexual activity
  • Increased risk of mortality (falls, fractures, skin breakdown)
AUA guidelines evaluation

- History
- Physical
- Urinalysis
# Urinalysis

<table>
<thead>
<tr>
<th>Condition</th>
<th>Action</th>
<th>Decision</th>
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</thead>
<tbody>
<tr>
<td>Hematuria</td>
<td>Submit all pertinent medical information and status report.</td>
<td>If no underlying condition found after urology evaluation – <strong>Issue</strong> and submit evaluation to the FAA.</td>
</tr>
<tr>
<td>Proteinuria and Glycosuria</td>
<td>Submit all pertinent medical records; current status to include names and dosage of medication(s) and side effects</td>
<td>Trace or 1+ protein and glucose intolerance ruled out – <strong>Issue</strong></td>
</tr>
</tbody>
</table>

**Vanderbilt University Medical Center**

**Department of Urology**
AUA guidelines evaluation

- May consider
  - Urine culture
  - Postvoid residual
  - Bladder diary
  - Symptom questionnaire
  - Urodynamics
  - Cystoscopy
  - Imaging
Potential etiologies of OAB

• Myogenic
  • Detrusor dysfunction due to hypoxia
  • Metabolic syndrome
• Neurogenic
  • Decreased central inhibition
• Urothelial
  • Disrupted cell signaling
  • Hormonal
• Idiopathic
Differential diagnosis of OAB

- Prolapse
- Outlet obstruction
- Atrophic vaginitis
- Pelvic floor dysfunction
- Interstitial cystitis
- Diabetic cystopathy
- Fluid intake
- Medications
- Malignancy
- UTI
- Stress incontinence
OAB history

- **Triggers**
  - “Key in the door”, hand washing
  - Rising from the seated position
  - Coughing, walking, jumping
  - Supine leakage
- **“Urge Syndrome” symptoms**
  - Frequency
  - Nocturia
  - Urgency
  - Urge incontinence
OAB physical exam

- Abdominal
- Back / Spine
- Neurological
- Pelvic
Treatment options

- Behavioral therapy
- Pharmacologic therapy
- Combined behavioral and pharmacologic
- Minimally invasive therapies
  - Botulinum A-toxin
  - Tibial nerve stimulation
  - Sacral neuromodulation
- Surgery
Treatment options
Pilots and incontinence
Maximum absorbency garment
“Do it in the suit”
First line therapies

• Behavioral therapies
  • Bladder training
  • Bladder control strategies
  • Pelvic floor muscle training
  • Fluid management
  • Weight loss

• Patient counseling regarding OAB symptoms
  • Tailored to individual
  • Expectations and setting realistic goals
Fluid and dietary modification

• Fluid restriction often counterproductive
  • Concentrated urine is irritating
  • Increased urgency and frequency
• Drink small amounts often
• Avoid bladder irritants
  • Coffee and tea, carbonated beverages, chocolate, spicy and tomato-based foods
• Avoid constipation
  • Increased fiber and fluid intake
Behavioral therapies

- Education
- Timed Voiding
- Delayed Voiding
- Pelvic Floor Exercises
- Reinforcement

Behavioral Modification
Miss-behavioral therapies
Second line therapies

- Antimuscarinics
  - Oxybutynin (Ditropan)
  - Oxybutynin transdermal (Oxytrol)
  - Tolterodine (Detrol)
  - Darifenacin (Enablex) – M3 receptor
  - Solifenacin (Vesicar) – M3 receptor
  - Trospium chloride (Sanctura) – does not cross blood brain barrier
- β-3 adrenergic receptor agonists
  - Mirabegron (Myrbetriq)
Pharmacologic therapy

- Anticholinergics
- β-3 adrenergic agonists
- Alpha blockers
- Tricyclic antidepressants: Imipramine

Muscarinic receptors

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<tr>
<th>Receptor</th>
<th>Organs</th>
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<tr>
<td>$M_1$</td>
<td>salivary glands, enteric nerves</td>
</tr>
<tr>
<td>$M_2$</td>
<td>heart, smooth muscle</td>
</tr>
<tr>
<td>$M_3$</td>
<td>smooth muscle, salivary glands</td>
</tr>
<tr>
<td>$M_4$</td>
<td>brain (diffuse), lung</td>
</tr>
<tr>
<td>$M_5$</td>
<td>brain (substantia nigra), eye</td>
</tr>
</tbody>
</table>
Muscarinic receptors

- Bladder distribution
  - M2 80%, M3 20%

- M3 - most important in normal function
  - Selective agents with diminished SE profile

- M2 - More important with pathology
Anticholinergic side effects

- Dry mouth
- Constipation
- Dry eyes
- Blurred vision
- Dyspepsia
- UTI
- Urinary retention
- Impaired cognitive function
Adverse effects

Oxybutynin*

- Dry Mouth: 71%
- Dizziness: 17%
- Constipation: 15%
- Somnolence: 14%
- Nausea: 12%
- Blurred Vision: 10%
Adverse effects

Tolterodine*

- Dry Mouth: 35%
- Constipation: 7%
- Headache: 7%
- Dizziness: 5%
- Abdominal Pain: 5%
Low molecular weight anticholinergics

- Lipophilic with neutral charge properties
- Easily penetrate into CNS

<table>
<thead>
<tr>
<th>Property</th>
<th>Darifenacin</th>
<th>Fesoterodine</th>
<th>Oxybutynin</th>
<th>Propiverine</th>
<th>Solifenacin</th>
<th>Tolterodine</th>
<th>Trospium</th>
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<tr>
<td>Molecular weight</td>
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<td>Lipophilic</td>
<td>Hydrophilic</td>
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<td>Neutral</td>
<td>Positive</td>
<td>Positive</td>
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<tr>
<td>P-gp substrate</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
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</table>
Commonly prescribed drugs are tied to nearly 50% higher dementia risk in older adults.

By Jacqueline Howard, CNN
Updated 5:54 AM ET, Tue June 25, 2019

What are anticholinergic drugs and should you be worried about a link to dementia?

Elinor Aspegren, USA TODAY
Published 3:24 p.m. ET June 26, 2019 | Updated 9:04 a.m. ET June 27, 2019

These drugs in your bathroom increase With Long-Term risk of dementia

By Meera Jagannathan
Published: July 1, 2019 4:58 a.m. ET

A study showed commonly prescribed medications may be linked to a higher chance of dementia. USATODAY
Anticholinergic drugs and risk of dementia: case-control study

Kathryn Richardson,¹ Chris Fox,² Ian Maidment,³ Nicholas Steel,² Yoon K Loke,² Antony Arthur,¹ Phylo K Myint,⁴ Carlota M Grossi,¹ Katharina Mattishent,² Kathleen Bennett,⁵ Noll L Campbell,⁶ Malaz Boustani,⁷ Louise Robinson,⁸ Carol Brayne,⁹ Fiona E Matthews,¹⁰ George M Savva¹

Anticholinergic Drug Exposure and the Risk of Dementia A Nested Case-Control Study

Carol A. C. Coupland, PhD; Trevor Hill, MSc; Tom Dening, MD; Richard Morriss, MD; Michael Moore, MSc; Julia Hippisley-Cox, MD
Richardson et al.

- Nested case-control study in UK
- Age 65 to 99
- Exclusion criteria: Motor neuron disease, HIV/AIDS, multiple sclerosis, Down syndrome, alcohol abuse
- 40,770 cases diagnosed with dementia between 4/2006 and 7/2015 and 283,933 matched controls
Richardson et al.

- Dose-response effect

<table>
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<tr>
<th>DDDs (ACB 2)</th>
<th>Adjusted Odds Ratio (95% CI)</th>
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<tr>
<td>0</td>
<td>1.00</td>
</tr>
<tr>
<td>&gt;0 to 13</td>
<td>1.02 (0.94 to 1.11)</td>
</tr>
<tr>
<td>14 to 89</td>
<td>1.07 (0.94 to 1.23)</td>
</tr>
<tr>
<td>90 to 364</td>
<td>1.20 (1.03 to 1.40)</td>
</tr>
<tr>
<td>365 to 1459</td>
<td>1.18 (0.99 to 1.39)</td>
</tr>
<tr>
<td>&gt;1460</td>
<td>1.57 (1.18 to 2.09)</td>
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</tbody>
</table>
Richardson et al.

- Antidepressant, antiparkinson, and urological drugs
  - Associated with future incidence of dementia
- Antipsychotic, gastrointestinal, and respiratory drugs
  - Not associated with future incidence of dementia
- Urological drugs: Adjusted OR 1.18 (1.13 to 1.23)
### Richardson et al.

- Urological drugs

<table>
<thead>
<tr>
<th>Exposure Period Before Index Date</th>
<th>Odds Ratio (95% CI)</th>
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<td>15 to 20 years</td>
<td>1.27 (1.09 to 1.48)</td>
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<tr>
<td>10 to 15 years</td>
<td>1.22 (1.13 to 1.32)</td>
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<tr>
<td>4 to 10 years</td>
<td>1.23 (1.18 to 1.29)</td>
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</table>
Anticholinergic Drug Exposure and the Risk of Dementia: A Nested Case-Control Study

Carol A. C. Coupland, PhD; Trevor Hill, MSc; Tom Dening, MD; Richard Morriss, MD; Michael Moore, MSc; Julia Hippisley-Cox, MD
• Nested case-control study in UK
• Age 55+
• Exclusion criteria: Huntington/Parkinson/Creutzfeldt-Jakob/HIV/multiple sclerosis
• 58,769 cases diagnosed with dementia and 225,574 matched controls
Odds Ratio (95% CI) for Bladder Antimuscarinics

- **Unadjusted**
- **Adjusted for Other Drug Types**
- **Fully Adjusted**

<table>
<thead>
<tr>
<th>Use Case</th>
<th>Odds Ratio</th>
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<tr>
<td>Nonuse</td>
<td>Unadjusted</td>
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<tr>
<td>1 to 90</td>
<td>Adjusted</td>
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<tr>
<td>91 to 365</td>
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<tr>
<td>366 to 1095</td>
<td></td>
</tr>
<tr>
<td>&gt;1095</td>
<td></td>
</tr>
</tbody>
</table>
Coupland et al.

- Associations strongest:
  - Antidepressants, antiparkinson drugs, antipsychotics, bladder antimuscarinics, and antiepileptic drugs

- No significantly increased risks:
  - Antihistamines, skeletal muscle relaxants, GI antispasmodics, antiarrhythmics, or bronchodilators

- Associations were stronger:
  - Diagnosed before age 80; vascular dementia vs Alzheimer’s
• Similar for exposure windows of 3-13 years and 5-20 years
• If causal, 10% of dementia diagnoses attributable to anticholinergics
Urology consensus statement

• Behavioral therapies should be instituted first
• Counsel patients on risk of cognitive impairment, dementia
• Use the lowest effective dose
• Decrease dosage of other anticholinergics
• Consider β-3 agonists/botulinum toxin/neuromodulation
**FAA guidance**

- Anticholinergics
  - Do not issue

<table>
<thead>
<tr>
<th></th>
<th>Genitourinary</th>
<th>Bladder</th>
<th>N</th>
<th>NOT ALLOWED</th>
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<tbody>
<tr>
<td></td>
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<td></td>
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</tr>
<tr>
<td>Detrol</td>
<td>tolterodine tartrate</td>
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<td>Ditropan</td>
<td>oxybutynin</td>
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<tr>
<td>Ditropan XL</td>
<td>oxybutynin</td>
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<tr>
<td>Sanctura</td>
<td>trospium</td>
<td></td>
<td></td>
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</table>
**FAA guidance**

- Anticholinergics
  - Do not issue
  - Even for agents that do not cross the blood-brain barrier

<table>
<thead>
<tr>
<th>Sanctura</th>
<th>trospium</th>
<th>Genitourinary</th>
<th>Bladder</th>
<th>N</th>
<th>NOT ALLOWED</th>
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</thead>
</table>
FAA guidance

- β-3 adrenergic receptor agonist
  - Allowed
  - 2-week observation period

<table>
<thead>
<tr>
<th>Myrbetriq</th>
<th>mirabegron</th>
<th>Genitourinary</th>
<th>Bladder</th>
<th>Y</th>
<th>ALLOWED but requires 2 week observation and physician status report</th>
</tr>
</thead>
</table>
Mirebegrón (Myrbetriq)

- β-3 adrenergic receptor (AR)
  - Bladder, adipose, heart, blood vessels, gut, uterus, liver
- 97% in bladder is β-3 subtype
$\beta_3$ adrenergic receptor agonist
Mirebegron (Myrbetriq)

- Can increase blood pressure
- Caution in patients also taking antimuscarinic
  - Urinary retention
- CYP2D6 inhibitor – dose adjustment may be needed
  - Metoprolol and desipramine
Mirebegenron (Myrbetriq)

<table>
<thead>
<tr>
<th>Number of patients</th>
<th>Placebo (%)</th>
<th>Myrbetriq 25 mg (%)</th>
<th>Myrbetriq 50 mg (%)</th>
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<tr>
<td>Hypertension*</td>
<td>7.6</td>
<td>11.3</td>
<td>7.5</td>
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<tr>
<td>Nasopharyngitis</td>
<td>2.5</td>
<td>3.5</td>
<td>3.9</td>
</tr>
<tr>
<td>Urinary tract infection</td>
<td>1.8</td>
<td>4.2</td>
<td>2.9</td>
</tr>
<tr>
<td>Headache</td>
<td>3.0</td>
<td>2.1</td>
<td>3.2</td>
</tr>
<tr>
<td>Constipation</td>
<td>1.4</td>
<td>1.6</td>
<td>1.6</td>
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<tr>
<td>Upper respiratory tract infection</td>
<td>1.7</td>
<td>2.1</td>
<td>1.5</td>
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<tr>
<td>Arthralgia</td>
<td>1.1</td>
<td>1.6</td>
<td>1.3</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>1.3</td>
<td>1.2</td>
<td>1.5</td>
</tr>
<tr>
<td>Tachycardia</td>
<td>0.6</td>
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<td>1.2</td>
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<tr>
<td>Abdominal pain</td>
<td>0.7</td>
<td>1.4</td>
<td>0.6</td>
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<tr>
<td>Fatigue</td>
<td>1.0</td>
<td>1.4</td>
<td>1.2</td>
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Mirebegenron (Myrbetriq)

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<th>Myrbetriq 50 mg (%)</th>
<th>Active Control (%)</th>
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<tr>
<td>Number of patients</td>
<td>812</td>
<td>812</td>
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<tr>
<td>Hypertension</td>
<td>9.2</td>
<td>9.6</td>
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<tr>
<td>Urinary tract infection</td>
<td>5.9</td>
<td>6.4</td>
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<tr>
<td>Headache</td>
<td>4.1</td>
<td>2.5</td>
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<tr>
<td>Nasopharyngitis</td>
<td>3.9</td>
<td>3.1</td>
</tr>
<tr>
<td>Back pain</td>
<td>2.8</td>
<td>1.6</td>
</tr>
<tr>
<td>Constipation</td>
<td>2.8</td>
<td>2.7</td>
</tr>
<tr>
<td>Dry mouth</td>
<td>2.8</td>
<td>8.6</td>
</tr>
<tr>
<td>Dizziness</td>
<td>2.7</td>
<td>2.6</td>
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<td>Sinusitis</td>
<td>2.7</td>
<td>1.5</td>
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<tr>
<td>Influenza</td>
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<td>3.4</td>
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<tr>
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<tr>
<td>Cystitis</td>
<td>2.1</td>
<td>2.3</td>
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</table>
Adherence to OAB medications

- 72% of patients not adherent to medications at 6 months
- Climbs to 82% at 12 months

~90% of OAB patients lost

- Of the 37.4 million patients with OAB...

![Chart showing patient distribution]

Anticholinergic purgatory
Small % move to advanced therapies

Case Study #1 – Group of 8 Physicians

- Total OAB Patients: 365
- Total Office Visits: 4,300
- Total OAB Scripts: 15,645

1.8% of all OAB patients

Case Study #2 – Group of 14 Physicians

- Total OAB Patients: 3,188
- Total Office Visits: 6,258
- Total OAB Scripts: 12,200

5.8% of all OAB patients
Third line therapies

- Severe refractory OAB symptoms
- Not candidates for second-line therapy
- Onabotulinumtoxin-A
- Neuromodulation
  - Sacral nerve modulation
  - Peripheral tibial nerve stimulation
Botulinum toxin

- Neurotoxin
- Derived from a gram-positive coccus *Clostridium botulinum*
- Commonly use the serotype 'A' strain
- Inhibits Ach release from presynaptic nerve terminal
- Induces detrusor muscle relaxation
Onabotulinum toxin A

- Neurogenic detrusor overactivity and non-neurogenic OAB
- The patient must be able and willing to:
  - return for post-void residual evaluation
  - perform self-catheterization
- Effects diminish over time
  - Repeat injections
  - Duration averages 3 -6 months
Reduction in UI episodes
Reduction in UI episodes

≥50% Reduction

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<thead>
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<th>% Patients</th>
<th>0</th>
<th>10</th>
<th>20</th>
<th>30</th>
<th>40</th>
<th>50</th>
<th>60</th>
<th>70</th>
<th>80</th>
<th>90</th>
<th>100</th>
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<tr>
<td>57.5</td>
<td>28.9</td>
<td>33.2</td>
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100% Reduction

<table>
<thead>
<tr>
<th>% Patients</th>
<th>0</th>
<th>10</th>
<th>20</th>
<th>30</th>
<th>40</th>
<th>50</th>
<th>60</th>
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</tr>
</thead>
<tbody>
<tr>
<td>22.9</td>
<td>6.5</td>
<td>10.3</td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

Botox complications

- Retention defined by >200 with symptoms or >349 cc

<table>
<thead>
<tr>
<th>Adverse event</th>
<th>BOTOX® 100 U (N= 552)</th>
<th>Placebo (N= 542)</th>
</tr>
</thead>
<tbody>
<tr>
<td>UTI</td>
<td>18%</td>
<td>6%</td>
</tr>
<tr>
<td>Dysuria</td>
<td>9%</td>
<td>7%</td>
</tr>
<tr>
<td>Urinary retention*</td>
<td>6%</td>
<td>0%</td>
</tr>
<tr>
<td>Bacteriuria</td>
<td>4%</td>
<td>2%</td>
</tr>
<tr>
<td>Elevated residual urine volume*</td>
<td>3%</td>
<td>0%</td>
</tr>
</tbody>
</table>
**ABC trial: anticholinergic v. Botox**

- RCT, double blinded
  - Placebo med or placebo injection
- No difference in mean UUI episodes
- Completely dry
  - 27% Botox
  - 13% medications
- Side effects
  - UTIs/intermittent catheterization in Botox (13%/6%)
  - Dry mouth/constipation in medications

Real world retention rates

- 160 patients treated for OAB
  - Mean age 64
  - 24% men
- Rate of urinary retention 35%
  - Defined by initiation of intermittent catheterization or catheter placement
  - Correlated to increased preoperative PVR

Botox future directions

• Intravesical Botox gel
• Currently initiating Phase II clinical trial
FAA guidance

- Botox for bladder indications
  - Allowed
  - No flying for 72 hours after each injection
Peripheral tibial nerve stimulation

- PTNS based on retrograde stimulation of sacral nerves
- Tibial nerve accessed with percutaneous needle
- 30 minutes of stimulation 1x week for 12 weeks
- Improvements (54%) maintained with on-going treatment
- Adverse events are relatively uncommon and mild
PTNS future directions

- Valencia Technologies eCoin™
- Fully-implantable device
- No external power supply
- Feasibility study
  - 46 patients
  - 70% responder rate, 20% dry rate
- Pivotal study now enrolling
PTNS future directions

- Bluewind Medical RENOVA™
- Implantable with direct incision or percutaneous delivery device
- Daily self-administered session with wearable stimulator
Sacral neuromodulation

- Mechanism of action both afferent and efferent stimulation
- Somatic, pelvic, hypogastric
- Modulates storage and micturition reflex pathways
- Urgency/frequency (68%)
- Non-obstructive retention (71%)
- Fecal incontinence (89%)
Implant

• Test stimulation period
  • 3 to 7 days (in-office PNE)
  • Up to 14 days (Stage 1)

• Choosing the test
  • Based on frequency of symptoms
  • Based on patient preference
  • Based on patient body habitus
Fluoroscopic guidance
Fluoroscopic guidance
Fluoroscopic guidance
Percutaneous approach
### Motor and sensory response

<table>
<thead>
<tr>
<th>Nerve Innervation</th>
<th>Pelvic Floor</th>
<th>Foot/calf/leg</th>
<th>Sensation</th>
</tr>
</thead>
<tbody>
<tr>
<td>S2 Primary somatic contributor of pudendal nerve for external sphincter, leg, foot</td>
<td>“clamp”** of anal sphincter</td>
<td>Leg/hip rotation, plantar flexion of entire foot, contraction of calf</td>
<td>Contraction of base of penis, vagina</td>
</tr>
<tr>
<td>S3 Virtually all pelvic autonomic functions and striated muscle (levator ani)</td>
<td>“bellows”*** of perineum</td>
<td>Plantar flexion of great toe, occasionally other toes</td>
<td>Pulling in rectum, extending forward to scrotum or labia</td>
</tr>
<tr>
<td>S4 Pelvic autonomic and somatic No leg or foot</td>
<td>“bellows”***</td>
<td>No lower extremity motor stimulation</td>
<td>Pulling in rectum only</td>
</tr>
</tbody>
</table>

* Clamp: contraction of anal sphincter and, in males, retraction of base of penis. Move buttocks aside and look for anterior/posterior shortening of the perineal structures.

** Bellows: lifting and dropping of pelvic floor. Look for deepening and flattening of buttock groove.
SNM complications

- 40% complication rate in 5 years
- Adverse events
  - Pain at the stimulator and lead sites
  - Lead migration
  - Infection/irritation
  - Electric shock
  - Need for additional surgeries (> 30% of patients)
  - Periodic battery replacement
  - Diagnostic spinal MRI is contraindicated

Sutherland, Neurourol Urodyn 2007
SNM considerations

- Safety & effectiveness have not been established for:
  - bilateral stimulation
  - pregnancy, unborn fetus, and delivery
  - patients with neurological disease origins
  - pediatric use under the age of 16 (urinary) and age of 18 (bowel)
  - Pilots!!
FAA guidance

- Likely defer?
- FAA Pacemaker Protocol Worksheet?
- Considerations
  - Electromagnetic interference
  - Security screening
  - Unanticipated stimulation
  - Can turn off device

Figure 1. Approaching security gates.
Considerations with neuromodulation
Future directions

- Axonics implantable
  - Rechargeable (1-hour q 2 weeks)
  - 15-year time to battery replacement
  - Tined lead designed to minimize migration
Future directions

• Neuspera
  • Mid-field technology
  • Evanescent and propagating electromagnetic waves to power implanted medical devices

• Neuvectra
  • Implanted lead with constant current technology
End stage patient options

• Indwelling catheter/suprapubic catheter
• Rare cases of severe, refractory, complicated OAB patients
  • Augmentation enterocystoplasty
  • Urinary diversion
Future directions

- Amphora
  - Selective bladder denervation
  - Radiofrequency ablation at trigone
  - Cystoscopic approach

Conclusions

- Crucial to employ care pathways for evaluation and management
- Initiate behavioral, pharmacologic therapies
- Recognize failure of first-line therapy
- Refer early for advanced therapies
  - Onabotulinumtoxin A
  - Neuromodulation
- Future relies on understanding of pathophysiology
Conclusions: FAA guidance

- Anticholinergics
  - Do not issue
- β–3 adrenergic receptor agonists
  - Allowed with 2-week observation period and physician status report
- Botox injections
  - Not disqualifying for bladder, no flying within 72 hours after injection
- Tibial nerve stimulation
  - No guidance
- Sacral neuromodulation implants
  - Likely exclusion but potential special issuance?
Conclusions: FAA guidance
Questions?
Thank you!

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615-300-1360