Case

- 51 yo female presents to you for follow-up of her HTN, Asthma, Chol. At the end of the visit, she complains of urinary incontinence and needing to wear pads.
- You are the first person she has told about this and she is very embarrassed about it.
Case

- She reports frequent “episodes” of needing to urinate suddenly and rushes to bathroom
- Sometimes she leaks before she can get there or as soon as she stands up to rush there
- She is urinating more frequently than usual and awakes at night to urinate
The next best step in management is:

- A. Initial trial of an oral antimuscarinic
- B. Moderate fluid intake and avoid caffeine and alcohol
- C. Obtain additional history and evaluation
- D. Kegel exercises
- E. Tell her she should use pads and stop whining because the condition is not life threatening
The next best step in management is:

- A. Initial trial of an oral antimuscarinic
- B. Moderate fluid intake and avoid caffeine and alcohol
- C. Obtain additional history and evaluation
- D. Kegel exercises
- E. Tell her she should use pads and stop whining because the condition is not life threatening
Case

• You question her further:
• She reports leakage every time she coughs or sneezes. This is frequent due to her asthma and seasonal allergies
• Also leaks during P 90X workouts (after seeing the infomercial)
• 4-5 large pads per day, soaked.
Question

• What symptoms does the patient report?
  – A. Urge incontinence and stress incontinence
  – B. Nocturia, urgency, urge incontinence, stress incontinence
  – C. Frequency, urgency, stress incontinence
  – D. Frequency, urgency, nocturia, urge incontinence, stress incontinence
  – E. None of the above
• What symptoms does the patient report?
  – A. Urge incontinence and stress incontinence
  – B. Nocturia, urgency, urge incontinence, stress incontinence
  – C. Frequency, urgency, stress incontinence
  – D. Frequency, urgency, nocturia, urge incontinence, stress incontinence
  – E. None of the above
Definitions and Evaluation
Definition/Types of Incontinence

• The involuntary loss of urine
• First Step: establish pattern of incontinence
  – Urge Incontinence / (Overactive Bladder)
  – Stress Incontinence
  – Mixed Incontinence
  – Overflow Incontinence
Definition: “Overactive Bladder”

ICS Definition of Overactive Bladder, 2010:

“Urgency with or without urge incontinence, usually with frequency and nocturia, in the absence of urinary tract infection or other obvious pathology”

Abrams et al, 2002
Evaluation/Diagnosis of OAB

• Minimum evaluation of uncomplicated patient includes:
  – Careful history
  – Physical Exam
  – Urinalysis

• Additional assessment
  – Ucx, PVR, bladder diary, symptom questionnaires

• NOT recommended for initial evaluation
  – Cystoscopy, urodynamics, renal/bladder sonogram

AUA/SUFU Guideline, 2012
Stress Incontinence

• The complaint of involuntary leakage on effort or exertion, or on sneezing or coughing

• Minimum Evaluation:
  – History and physical exam
  – Objective demonstration of SUI
    • Cough or Valsalva leak test (supine or standing)
  – Assessment of PVR
  – Urinalysis/Ucx, if indicated

AUA Guideline on SUI, 2009
Abrams et al., 2002
Mixed and Overflow Incontinence

• Mixed Urinary Incontinence
  – Presence of both stress and urge incontinence
  – Involuntary leakage associated with both urgency and exertion, effort, sneezing, coughing

• Overflow Incontinence
  – Continuous incontinence due to a full bladder
  – Can present similar to stress incontinence
  – Elevated PVR, often painful

Abrams et al, 2002
### Urinary Incontinence: Symptoms

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Stress</th>
<th>Urge</th>
<th>Mixed</th>
<th>Overflow</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leak with cough, sneeze, exercise</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Leak with urgency</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Frequent urination, nocturia</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Continuous leakage</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>+</td>
</tr>
</tbody>
</table>

Clinical Pearl: Severe, total gravitational stress incontinence (“incontinence of non-resistance”) will also report continuous leakage and so will urinary fistula.
Bladder Functional Anatomy

"Smooth Sphincter" (BN/Prox Urethra)

"Striated" Sphincter

Pelvic Floor

Beta-Adrenergic

Body

Muscarinic Ach

Base

Alpha-Adrenergic

Outlet
Case

- What is the minimum required workup on this patient?
  - A. History and physical
  - B. History, physical, U/A
  - C. History, physical, U/A, PVR
  - D. History, physical, U/A, PVR, Renal sonogram
  - E. History alone
Case Answer

• What is the minimum required workup on this patient?
  – A. History and physical
  – B. History, physical, U/A
  – C. History, physical, U/A, PVR
  – D. History, physical, U/A, PVR, Renal sonogram
  – E. History alone
Scope of the Problem

• 2008:
  – Overactive Bladder: 10.7% of population
  – Urinary Incontinence: 8.2% of population

• 2018 Estimate:
  – Overactive Bladder: 20.1% of population
  – Urinary Incontinence: 21.6% of population

• Highly prevalent diseases
  – Will double over next decade
  – Over 1 billion people afflicted worldwide

Irwin et al., 2011
Prevalence in U.S. Women

Markland et al., 2011
Prevalence of incontinence is increasing in both men and women.
Overactive Bladder / Urge Incontinence
Economic Burden

• U.S. National cost of OAB with incontinence
  – 2007: $65.9 billion
  – 2015: $76.2 billion
  – 2020: $82.6 billion

• Perspective:
  – Osteoporosis 2008: $22 billion
  – Breast Cancer 2010: $16.5 billion
  – Colon Cancer 2010: 14.1 billion
  – Lung Cancer 2010: 12.1 billion

Coyne et al., 2014
Blume and Curtis, 2011
NCI: www.cancer.gov
Epidemiology

- Age specific OAB prevalence similar in men and women
  - 16% men vs. 16.9% women
  - 11% men vs. 13% women

- Prevalence increases with age

  Stewart et al, 2003 (NOBLE Study)
  Irwin et al, 2006 (EPIC Study)
Age Specific OAB Prevalence

Stewart et al, 2003
Epidemiology: Urge Incontinence

• Gender-based differences identified

• Higher prevalence of OAB with incontinence in women:
  – Female: 9.3% OAB wet vs. 7.6% OAB dry
  – Male: 2.6% OAB wet vs. 13.4% OAB dry

• Steeper age-related increase in urge incontinence in women:
  – Age 44 women vs. age 64 men

Stewart et al, 2003
Epidemiology: Dry Urgency

- Higher prevalence of urgency without incontinence in men
- Rises steeply between ages 45-55
- More gradual rise in women

Stewart et al, 2003
Natural History of OAB

- OAB tends to be chronic, progressive disease

Diagram showing the longitudinal study of women and men.
Etiology

- Precise mechanisms of OAB not fully understood
- Especially true for sensation of urgency
  - Subjective human experience
  - Modified by other disease states
  - Difficult to make animal model of “urgency”
- Neurogenic Overactive Bladder
  - Animal models exist
Classical Model of OAB
Urgency: Afferent Pathways

- Urothelial sensitization of afferent nerves
  - Area of active investigation
  - Urothelium has capacity to release non-neuronal acetylcholine and other neurotransmitters (ATP, NO) that may modulate afferent nerve firing

- Role of bladder interstitial cells
  - Currently unclear, but may have modulatory role in afferent nerve firing

- Firing of afferent nerve at given level of distention is modifiable (concept of “gain”)

De Groat W.C., 2009
Hypotheses

- **Neurogenic Hypothesis**
  - Detrusor overactivity arises from generalized, nerve-mediated excitation of detrusor muscle

- **Myogenic Hypothesis**
  - Increased probability of spontaneous contraction and/or propagation of activity between muscle cells

- Not mutually exclusive
OAB Management

• AUA Guideline: Diagnosis and Treatment of Adult Overactive Bladder

• General guidelines for management of female incontinence
  – International Consultation on Incontinence (ICI)
  – National Institute for Health and Clinical Excellence (NICE), UK

• Helpful evidence-based approach to management
Urge Incontinence

• First Line
  – Behavior / lifestyle changes, kegels

• Second Line
  – Antimuscarinics, Beta-3 agonists

• Third Line
  – Neuromodulation
  – Intravesical Botox

• Fourth Line
  – Surgery: Augmentation cystoplasty
Management

- Bladder Diary / Frequency Volume Chart
- Principal objective means of evaluating frequency/urgency symptoms
  - Functional bladder capacity
  - Mean voided volumes
  - Voids per day / night
  - Accidents per day / night
- Foundation for starting therapy
- Means of tracking progress (or lack of it)
Conservative Management

- Lifestyle changes and behavior modifications
- Relative paucity of Level 1 evidence
- Considered first line treatment by all modern guidelines panels
- Minimal to no risk for patient with reasonable outcomes
- Grade A recommendation from ICI as first line treatment
Two Basic Types of Therapy

• **Habit changes**
  – Dietary modifications
  – Timed voiding routine

• **Training Techniques**
  – Urgency suppression
  – Bladder Training
  – Delayed Voiding
  – Pelvic Floor Muscle Training (PFMT)
    • With or without biofeedback
  – Multicomponent Behavioral Training
Dietary Modification

- Reduction/elimination of caffeine
  - Diuretic, promotes UDC’s in vitro
  - Increases urinary frequency / urgency sx’s
  - Little Level 1 evidence that improves continence

- Smoking cessation
  - Higher risk of OAB/LUTS in smokers
  - Little data demonstrating cessation improves continence
Lifestyle Changes

• Weight Reduction
  – BMI positively correlates with SUI and OAB sx
  – BMI > 30 independent risk factor OAB in women
  – Weight loss improves female urge and stress incontinence

• Avoiding Constipation
  – Improves frequency and urgency in elderly

Osborn et al, 2013
Subak, 2005
Wyman et al, 2009

Charach, 2005
Wyman et al, 2009
**Fluid Management**

- Excessive fluid intake worsens frequency and urgency symptoms
- Normalizing fluid intake reduces these symptoms
- Excessive fluid restriction can also worsen OAB symptoms in some patients
- High-concentrated urine = potential irritant
- “Normal” intake recommended (ICI, NICE)
  - Required intake varies greatly depending upon environment and activity

“8 glasses per day” is a baseless convention, not supported by literature

Panel on Dietary Reference Intakes
For Electrolytes and Water, IOM, 2005
Osmoregulation / Homeostasis

Very Narrow Range: 280-295 mOsm/kg water
<table>
<thead>
<tr>
<th>Technique</th>
<th>Description</th>
<th>Symptom</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Habit changes (managing symptoms and promoting bladder health)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lifestyle modification</td>
<td>Diet, fluid, bowel and weight management; smoking cessation</td>
<td>X</td>
</tr>
<tr>
<td>Timed voiding*</td>
<td>Urination at a fixed interval that avoids the symptom (useful for urgency and UI not associated with frequency)</td>
<td>X</td>
</tr>
<tr>
<td><strong>Training techniques (managing symptoms)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urgency control techniques</td>
<td>Deep breathing and using complex mental tasks (reciting poetry, counting backwards from 100 by 7 s etc.) to ignore urgency</td>
<td>X</td>
</tr>
<tr>
<td>Bladder training</td>
<td>Progressively increasing interval between voidings; utilises distraction and relaxation techniques to gradually increase the time between urinations</td>
<td>X</td>
</tr>
<tr>
<td>Multicomponent behavioural training*</td>
<td>Teaching to not rush to bathroom in response to urgency and use of PFM contractions to suppress bladder contraction and delay voiding, with use of pelvic floor muscle exercises</td>
<td>X</td>
</tr>
<tr>
<td>Pelvic floor muscle training</td>
<td>Daily regimen of pelvic floor muscle contractions to maintain or build strength and endurance</td>
<td>X</td>
</tr>
<tr>
<td>Delayed voiding*</td>
<td>Progressively increasing interval between onset of urgency and voiding</td>
<td>X</td>
</tr>
</tbody>
</table>

Wyman et al, 2009
Pelvic Floor Muscle Training

• PFM strength assessed and taught by provider
  – No consensus or proper protocol
• Weak or poor control of PFM candidates for biofeedback, physical therapy
• Cochrane Meta-analysis Data, 2010
  – Pelvic floor muscle training vs. no treatment
  – Best in 3 months, supervised PFMT
  – Recommended inclusion in first line treatment for stress, urge, or mixed incontinence
Numerous studies support combination of behavior modification and antimuscarinic therapy for OAB treatment:

- Improves overall objective outcome
- Improves patient-reported satisfaction


Mattiason et al., *BJU Int.* 2003, 91: 54-60.
Drug Classes Used in OAB

- Antimuscarinics
- Membrane Channel Agents
- Antidepressants
- Alpha-Blockers
- Beta-3 Agonists
- PDE-5 Inhibitors
- COX Inhibitors

- Toxins
  - Botulinum Toxin
  - Vanilloids

- Hormones
  - Estrogen
  - Desmopressin
Antimuscarinics

- Antimuscarinics mainstay of medical therapy, Grade A recommendation from ICI, 2008
- Compounds approved in U.S.:

<table>
<thead>
<tr>
<th>Antimuscarinic</th>
<th>Delivery</th>
<th>Dosing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oxybutynin IR / ER</td>
<td>Oral</td>
<td>BID-TID / QD</td>
</tr>
<tr>
<td>Oxybutynin Patch</td>
<td>Transdermal</td>
<td>BIW</td>
</tr>
<tr>
<td>Oxybutynin Gel</td>
<td>Transdermal</td>
<td>QD</td>
</tr>
<tr>
<td>Tolterodine IR / ER</td>
<td>Oral</td>
<td>BID / QD</td>
</tr>
<tr>
<td>Fesoterodine</td>
<td>Oral</td>
<td>QD</td>
</tr>
<tr>
<td>Trospium IR / ER</td>
<td>Oral</td>
<td>BID / QD</td>
</tr>
<tr>
<td>Darafenacin</td>
<td>Oral</td>
<td>QD</td>
</tr>
<tr>
<td>Solafenacin</td>
<td>Oral</td>
<td>QD</td>
</tr>
</tbody>
</table>
Mechanism of Action

- *Competitive* antagonist of muscarinic acetylcholine receptor
- Reduce detrusor contractility during storage phase of micturition
  - Parasympathetic (voiding) nerves are quiescent
  - Massive release of Ach during voiding able to overcome competitive action drug (except at very high dosages)
**Mechanism of Action**

1. Competes with neuronally released acetylcholine – Possibly more important for high dose therapy
2. Also, likely competes with non-neuronally released (e.g. urothelial) acetylcholine – Possible inhibition of abnormal afferent activity leading to OAB symptoms

The definitive mechanism of action is still under investigation

De Groat W.C., 2009
Muscarinic Receptors

- Bladder contains M1, M2, M3 receptors
  - M3 mediate detrusor contraction
  - M2 greatly outnumber M3 receptors
    - M2 likely also facilitate bladder contraction
- No evidence that M3 selectivity beneficial
  - Darifenacin most M3-selective
Properties

• Tertiary Amines
  – Oxybutynin, tolterodine, fesoterodine, solafenacin, darafenacin
  – Lipophilic: cross blood-brain barrier
  – Well absorbed from GI tract

• Quaternary Ammonium (Trospium)
  – Limited entry into CNS
  – Low CNS side effects
  – Not as well absorbed
Antimuscarinic Effects

- Compared to Placebo:
  - Reduced daily urgency and UUI episodes
  - Reduced voids per day
  - Increased daily voided volumes
  - Increased number of patients returning to total continence
  - Improve patient-reported HRQoL

Chapple et al, 2008
## Adverse Events Greater than Placebo

<table>
<thead>
<tr>
<th>Event</th>
<th>Treatment %</th>
<th>Placebo %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any Adverse Event</td>
<td>53.4</td>
<td>39.9</td>
</tr>
<tr>
<td>Any Dry Mouth</td>
<td>29.6</td>
<td>7.6</td>
</tr>
<tr>
<td>Pruritis</td>
<td>15.4</td>
<td>5.2</td>
</tr>
<tr>
<td>Constipation</td>
<td>7.7</td>
<td>3.9</td>
</tr>
<tr>
<td>Erythema</td>
<td>6.9</td>
<td>2.0</td>
</tr>
<tr>
<td>Headache</td>
<td>5.9</td>
<td>4.9</td>
</tr>
<tr>
<td>UTI</td>
<td>5.0</td>
<td>3.6</td>
</tr>
<tr>
<td>Dyspepsia</td>
<td>4.7</td>
<td>2.1</td>
</tr>
<tr>
<td>Blurred vision</td>
<td>3.8</td>
<td>2.6</td>
</tr>
<tr>
<td>Dizzyness</td>
<td>3.5</td>
<td>2.5</td>
</tr>
<tr>
<td>Somnolence</td>
<td>3.1</td>
<td>1.9</td>
</tr>
<tr>
<td>Sweating</td>
<td>1.8</td>
<td>0.0</td>
</tr>
<tr>
<td>Fatigue</td>
<td>1.6</td>
<td>0.6</td>
</tr>
<tr>
<td>Urinary Retention</td>
<td>1.1</td>
<td>0.2</td>
</tr>
</tbody>
</table>
Which Antimuscarinic to Use?

- No firm data demonstrating consistent superiority of one agent over another
- Other factors should guide therapy:
  - Side effects, cost, ease of administration
  - Individualized treatment
- NICE Guidelines, 1996:
  - First line: generic oxybutynin IR
  - Select alternative agent if side effects poorly tolerated
Which Antimuscarinic?

- Review of RCTs:
  - Oxybutynin IR highest RR for withdrawal and adverse events
- ER formulations favored over IR
  - Fewer side effects, same or better efficacy
- Oral vs. Transdermal (patch)
  - Transdermal = less dry mouth, constipation
  - Transdermal = skin site reactions, withdrawal

Chapple et al, 2008
Other AUA Recommendations

- Poor symptom control or side effects:
  - Modify dose
  - Alternative agent
    - Alternative antimuscarinic
    - Beta-3 agonist
- Manage constipation or dry mouth before abandoning antimuscarinic therapy

AUA/SUFU OAB Guideline, 2012
Other AUA Recommendations

• Antimuscarinic cautions:
  – Contraindicated in narrow-angle glaucoma
  – Other medications with anti-cholinergic properties
  – Frail, elderly patients

• Refer patients uncontrolled on medical / behavioral management for third line options.

AUA/SUFU OAB Guideline, 2012
Mirabegron: Beta-3 Agonist

- Binds bladder beta-3 receptors resulting in relaxation of detrusor
- Once daily dosing
  - 25mg and 50 mg doses approved in U.S.
- Multiple RCTs demonstrate vs. placebo
  - >50% reduction in incontinent episodes
  - Reduction in urinary frequency (8x/24h)
  - 12 week endpoints

Chapple et al, 2014
Mirabegron Adverse Events

• Pooled RCT data:
  – Dry mouth, constipation same as a placebo
  – Most common reasons for discontinuation of antimuscarinics

• Most common AEs:
  – Hypertension (7.3%)
  – Nasopharyngitis (3.4%)
  – UTI (3.0%)
Intravesical Botulinum Toxin (BTX)

• Neurotoxin protein produced by C. botulinum
  – Most potent neurotoxin known
• Blocks acetylcholine release at both somatic and autonomic nerve terminals
  – Prevents fusion of Ach-containing vesicles with neuronal cell membrane = blocks transmission
Mechanism: Botox-A

• Muscle is partially denervated until new innervation occurs (block efferents)
  – Long duration of action

• Mechanism probably more complex
  – Release of *urothelial* neurotransmitters blocked (acetylcholine, substance P, ATP)
  – Possibly blocks *afferent pathways* involved in OAB (peripheral afferent desensitization)
Urodynamic Effects of BTX-A

- Increased bladder capacity
- Increased bladder compliance
- Reduced maximum detrusor pressure during bladder contraction
- Reduced maximum urinary flow rate
- Increased PVR

Schurch et al, 2005
Sahai et al, 2009
Efficacy of Intravesical Botox

- RCT’s idiopathic OAB:
  - Significant reduction daily UI
  - Significant reduction in voids per day
  - Significant improvement in patient-reported QoL (UDI-6/UDI)

- RCT Objective outcomes:
  - Increased mean bladder capacity
  - Increased volume per void
  - (more robust to placebo effects)

Anger et al, 2010
Chapple, 2014
Urinary Retention Risk

<table>
<thead>
<tr>
<th></th>
<th>Idiopathic OAB (100U)</th>
<th>Neurogenic OAB (200U)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CIC (%)</td>
<td>6.5%</td>
<td>30.6%</td>
</tr>
<tr>
<td>Median duration (Days)</td>
<td>63 days</td>
<td>289 days</td>
</tr>
</tbody>
</table>

Must be willing/able to CIC to be considered for intravesical botox
## Overall Adverse Events (100U)

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>Percentage (N=552)</th>
</tr>
</thead>
<tbody>
<tr>
<td>UTI</td>
<td>18%</td>
</tr>
<tr>
<td>Dysuria</td>
<td>9%</td>
</tr>
<tr>
<td>Urinary Retention</td>
<td>6%</td>
</tr>
<tr>
<td>Bacteriuria</td>
<td>4%</td>
</tr>
<tr>
<td>Elevated PVR</td>
<td>3%</td>
</tr>
</tbody>
</table>
Botox Adverse Events

• Generalized Weakness (Rare)
  – Systemic dissemination (“flaccid paralysis”)
  – Swallowing, breathing problems reported

• Allergic Reaction (Rare)
  – Tachyphylaxis has been reported

• Resistance to treatment
  – 30% antibody-mediated
  – Use lowest dose, wait at least 3 months

• Caution in patients:
  – Dysfunction of neuromuscular junction

Leong et al, 2010
## Long Term Follow-Up

- **Need for repeated injection**

<table>
<thead>
<tr>
<th>Authors</th>
<th>Duration of Improvement</th>
<th>Interval Between Injections</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sahai et al</td>
<td>6 months</td>
<td>--</td>
</tr>
<tr>
<td>Brubaker et al</td>
<td>26 months</td>
<td>--</td>
</tr>
<tr>
<td>Kalsi et al</td>
<td>14 months</td>
<td>1.9 years</td>
</tr>
<tr>
<td>Khan et al</td>
<td></td>
<td>14 months</td>
</tr>
<tr>
<td>Schmid et al</td>
<td>9 months</td>
<td>13.5 months</td>
</tr>
</tbody>
</table>
FDA Approved Urologic Uses

- Neurogenic detrusor overactivity
  - Dose 200U
- Idiopathic OAB
  - Dose 100U
- Long term efficacy and side effects
- Events associated with repeated administration
Sacral Neuromodulation

• FDA-Approved Therapy for
  – Urge Urinary Incontinence
  – Urgency-Frequency Syndrome
  – Non-obstructive Urinary Retention

• Reserved for patients refractory to behavior modification and medical therapy
  – Or unable to tolerate

• MRI contraindicated
Sacral Neuromodulation

- Mechanism of action remains unclear
- Restores balance of excitatory and inhibitory stimuli affecting the detrusor

Two main hypotheses:
1. Somatic afferent stimulation suppresses interneuronal transmission in bladder reflex pathway
2. Suppression of bladder efferent preganglionic neurons

Leng and Chancellor, 2005
Clinical Efficacy

- Urge Incontinence (Schmidt et al, 1999):
  - 73% reduction incontinence / 24h
  - 82% reduction number pads / 24h
  - Sustained effect at 18mo follow-up
Clinical Efficacy

- Urgency/Frequency (Hassouna et al, 2000):
  - 46% reduction in number voids / 24h
  - 92% increase in voided volumes
  - 27% reduction in degree of urgency
  - Sustained effect at 2 years post implant
Efficacy is Maintained Over Time

- Maintained 18–24mo in early RCTs
- 5–year data (van Kerrebroeck et al, 2007)
  - 152 implanted patients
  - Followed annually 5 years
  - Leaks per day = 58% success
  - Pads per day = 61% success
  - Effect maintained over 5 years
  - Voided volume: 56% success
  - Daily Voids: 40% success
  - Degree of Urgency: 56% success
InSite Trial

• RCT Sacral Neuromodulation vs. Medication
  – 147 subjects randomized
  – All failed at least 1 medication, but not all
• Success = >50% reduction in symptoms

<table>
<thead>
<tr>
<th></th>
<th>Neuromodulation</th>
<th>Medical Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall OAB Response</td>
<td>76%</td>
<td>49%</td>
</tr>
<tr>
<td>Urge Incontinence</td>
<td>71%</td>
<td>47%</td>
</tr>
<tr>
<td>Urinary Frequency</td>
<td>61%</td>
<td>37%</td>
</tr>
</tbody>
</table>

Seigel et al, 2014
InSite Trial

• Implication:
• Patients refractory to antimuscarinics may benefit more from neuromodulation than continued medical therapy
Problem: Adverse Events/Revisions

- Adverse events are common
- Significant differences in reporting

<table>
<thead>
<tr>
<th>Problem</th>
<th>% Adverse Events</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain at Implant Site</td>
<td>3-42%</td>
</tr>
<tr>
<td>Other Device-related Pain</td>
<td>3-43%</td>
</tr>
<tr>
<td>Lead Migration</td>
<td>1-21%</td>
</tr>
<tr>
<td>Bowel Dysfunction</td>
<td>4-7%</td>
</tr>
<tr>
<td>Infection</td>
<td>4-10%</td>
</tr>
</tbody>
</table>

Adapted from Leong et al, 2010
Revision

• At 1.5-3y follow-up (Seigel, 2000):
  – 33% of implanted devices required surgical revision to resolve adverse event
  – 10.5% explanted for lack of efficacy

• At 5y follow-up (van Kerrebroeck et al, 2007)
  – 39.5% revised to resolve adverse event
  – 6% explanted for lack of efficacy or adverse event
Tibial Nerve Stimulation

- Less invasive form of neuromodulation
  - Needle placed into SP6 acupuncture point
  - 12 weekly 30 minute sessions
  - Maintenance therapy for responders

- 60-81% positive response rate across all trials

- Only 1 sham-controlled RCT
  - 54% improved vs. 21% sham control

- Objective outcome similar to tolterodine ER

- Durability over 12mo in 1 study

Peters et al, 2010
Peters et al, 2009
MacDiarmid et al, 2010
Augmentation Cystoplasty

- Poor compliance and refractory DO
  - Neurogenic vs. non-neurogenic
- Excellent outcomes
  - 93% dry rate in non-neurogenic patients
- CIC required in 39% non-neurogenic patients
  - Stoma vs. no stoma must be discussed preop

Reyblat and Ginsberg, 2010
Augmentation Cystoplasty: Complications

- Potential metabolic/electrolyte complications
  - Common source of exam questions
- Potential CRF
  - Assess baseline creatinine
- UTI: 4-46%
- Stones: 10-33%
- Perforation: 6-9%
- Carcinoma: very low risk

Reyblat and Ginsberg, 2010
• 56 yo female on oxybutynin IR 5mg 3x per day. She reports resolution of incontinence, but is skipping doses due to constipation. Which intervention is **NOT** recommended:
  – A. Reduce dose of oxybutynin
  – B. Trial of neuromodulation
  – C. Administer a stool softener
  – D. Change to extended release oxybutynin
  – E. Try an alternative antimuscarinic
Question

- 56 yo female on oxybutynin IR 5mg 3x per day. She reports resolution of incontinence, but is skipping doses due to constipation. Which intervention is NOT recommended:
  - A. Reduce dose of oxybutynin
  - B. Trial of neuromodulation
  - C. Administer a stool softener
  - D. Change to extended release oxybutynin
  - E. Try an alternative antimuscarinic
Stress Incontinence
Stress Incontinence

- Estimated total U.S. cost $13.2 billion
  - 70% routine care (MD visits, buying pads)
  - 14% nursing home admission
  - 9% treatment
  - 6% complications
  - 1% diagnosis

Chong et al., 2011
Epidemiology: Stress Incontinence
Prevalence Increases in Pregnancy
Conceptual Model
Etiology: Risk Factors

- Age
- Vaginal Delivery
- Parity
- Family History (i.e. genetics)
- Obesity / BMI
- Diabetes
- HRT
- Surgery / Hysterectomy
Etiology

- Primary zone of continence in men and women is urethral sphincter
  - Mid-urethra in females
  - Membranous urethra in males
- Stress incontinence caused by incompetence of the urethral sphincter
- Leakage across sphincter when bladder / abdominal pressure greater than pressure exerted by urethra.
Stress Incontinence Treatment

1. Behavior Modification
   - Pelvic Floor ("Kegel") Exercises
   - Increase tone of pelvic floor and external urethral sphincter
   - Non-invasive treatment for both male and female stress incontinence
   - Useful for all forms of urethral incontinence

   - No FDA-approved medication
   - Primarily surgical disease
Male and Female SUI Treatment

• First Line
  – Kegels

• Second Line
  Female
  Urethral sling
  Urethral bulking

  Male
  Artificial Sphincter
  Male Urethral Sling
Summary

• OAB and SUI highly prevalent diseases
• Significant healthcare cost
• Expected to increase over next decade
• Patients commonly do not seek care
  – PCP must screen
• Within scope of the PCPs
  – Guidelines in place
Summary

• Establish pattern of incontinence
  – Good H&P, +/- PVR, U/A if applicable

• Initial trial of therapy
  – Behavior / lifestyle
  – Kegels

• Add medical management (OAB)
  – Antimuscarinic, beta-3 agonist

• Refer failures to Female Pelvic Medicine and Reconstructive Surgery (FPMRS) specialist
Thank You!

ctwiss@surgery.arizona.edu