**Evaluation and Treatment of Overactive Bladder**

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**Urinary Incontinence**

- **Common**  
  - 25% reproductive age women  
  - 40% postmenopausal women  
- **Chronic - social seclusion**  
  - Profound effect of QOL  
  - 3x Nursing home admits, falls & fractures  
- **Costly**  
  - $26 billion annually  
  - *More than all cancer care for women*

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**Overactive Bladder (OAB) Overview**

Prevalence: 8-31% of women

- **Frequency**: frequent urination, >8x per day
- **Urgency**: sudden compelling desire to void; difficult to defer
- **Nocturia**: need to wake during sleep to void, usually considered problematic >2x per night
- **Urgency urinary incontinence (UUI)**: involuntary leakage of urine usually associated with urgency


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**Stress vs. Urge Incontinence**

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Stress UI</th>
<th>OAB/Urge UI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Precipitant</td>
<td>activity</td>
<td>urgency</td>
</tr>
<tr>
<td>Timing</td>
<td>immediate</td>
<td>delayed</td>
</tr>
<tr>
<td>Amount</td>
<td>small-mod</td>
<td>large</td>
</tr>
<tr>
<td>Frequency</td>
<td>rare</td>
<td>common</td>
</tr>
<tr>
<td>Nocturia</td>
<td>rare</td>
<td>common</td>
</tr>
</tbody>
</table>
Causes of OAB

- Idiopathic in majority
  - Most likely involuntary detrusor contractions
- Other possibilities
  - Multiple sclerosis, other neurologic diseases
  - Post stroke
  - Parkinson’s
  - Spinal cord injury


Modifiable Contributing Factors for OAB

- UTI
- Constipation
- Diabetes
- Obesity
- Mobility impairment
- Sleep apnea
- Drugs: caffeine, diuretics, ACE inhibitors, sedatives, hypnotics

OAB Impact

- Not limited to urinary incontinence (UI)
  - OAB Dry: frequency, urgency, +/- nocturia
  - OAB Wet: OAB dry + UUI
- Women and men
- Increasing prevalence with age
- Significant impact on QOL
- Weekly UUI - ↑ risk
  - Falls 26%
  - Fracture 34%


OAB Is not Adequately Diagnosed or Treated

- Despite benefits to the patient
  - Improved overall QOL
  - Potential reduction in falls and fractures
  - Improvement in sleep
  - Reduced costs
  - Patient related
  - Health care system
- Few women seek care, and providers often do not assess or treat OAB
  - How can we help more women with OAB?
Diagnostic Aspects of Incontinence Study (DAISy)

- Multi-center study (N=301)
- 3 Incontinence Questions (3 IQ) vs. Extended Evaluation
  - US, UK, WHO: Clinical Practice Guidelines
  - Extensive History
  - Exam: Neuro S2-S4, Pelvic exam
  - Tests: PVR, Cough Stress Test, UA
  - 3-Day Diary

Brown JS et al. Annals Internal Med 2006;144:715

3 Incontinence Questions (3 IQ)

1. During the last 3 months, have you leaked urine, even a small amount?
   - Yes
   - No ➔ Questionnaire Completed.
2. During the last 3 months, did you leak urine: (Check ALL that apply.)
   - When you were performing some physical activity such as coughing, sneezing, lifting or exercise?
   - When you had the urge or the feeling that you needed to empty your bladder but you could not get to the toilet fast enough?
   - Without physical activity and without a sense of urgency?
3. During the last 3 months, did you leak urine most often: (Check only ONE)
   - When you were performing some physical activity such as coughing, sneezing, lifting or exercise? [STRESS]
   - When you had the urge or the feeling that you needed to empty your bladder but you could not get to the toilet fast enough? [URGENCY]
   - Without physical activity and without a sense of urgency? [OTHER]
   - About equally as often with physical activity as with a sense of urgency? [MIXED]

Accuracy of 3 IQ Compared to Extended Evaluation

<table>
<thead>
<tr>
<th></th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>LR+</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urge UI</td>
<td>0.75</td>
<td>0.77</td>
<td>0.79</td>
<td>3.26</td>
</tr>
<tr>
<td>Stress UI</td>
<td>0.86</td>
<td>0.60</td>
<td>0.74</td>
<td>2.13</td>
</tr>
</tbody>
</table>

> Similar to other diagnostic tests

Brown JS. Annals 2006

VALIDATION OF 3IQ

- 3IQ: simple, inexpensive, feasible
  - Reproducible (kappa 70% for urge and stress)
  - Acceptable accuracy for classification of incontinence type
- Include a urinalysis (UA) in the evaluation
- Take Home Message
  - 3IQ is a good test for type of UI in women
  - With 3IQ + UA, the risk of missed Dx and Rx is low

Initial Visit & Therapy for UUI

1. Simple Diagnosis - 3 IQ, UA
2. Patient information
   - *Educate and Empower* (self-help)
3. Treat modifiable factors
4. Reasonable expectations
   - *Ask patient what she wants!*
5. 50% reduction in incontinence
   - Pelvic-floor muscle exercises
   - Bladder-control strategies
   - Taught with a booklet

Burgio KL. JAMA 2002;288:2293; Goode PS. JAMA. 2003;290:345

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Urinary Diary

- Simple form for recording voids, incontinent episodes, fluid intake
- *Excellent education & intervention!*
  - ↓ UI episodes by 25-45%
- Very useful in planning therapy
  - fluid adjustment
  - timing and type of medications

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National Association For Continence: Patient Resources

- Web site: [www.nafc.org](http://www.nafc.org)
- Phone: 1-800-BLADDER
- Diagnostic quiz
- Disease state and treatment information
- FAQs
- Q&A forum

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**URINARY DIARY EXAMPLE**

<table>
<thead>
<tr>
<th>TIME</th>
<th>URINATE IN TOILET</th>
<th>LEAKING ACCIDENT</th>
<th>REASON FOR ACCIDENT</th>
<th>FLUID INTAKE TYPE</th>
<th>AMOUNT</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 a.m.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7 a.m.</td>
<td>XX</td>
<td></td>
<td></td>
<td>Tea</td>
<td>1 cup</td>
</tr>
<tr>
<td>8 a.m.</td>
<td></td>
<td>X</td>
<td>Sudden Urge</td>
<td>OJ</td>
<td>4 oz.</td>
</tr>
<tr>
<td>9 a.m.</td>
<td></td>
<td>X</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10 a.m.</td>
<td>X</td>
<td></td>
<td>Sudden Urge</td>
<td>Water</td>
<td>8 oz.</td>
</tr>
<tr>
<td>11 a.m.</td>
<td></td>
<td>X</td>
<td>Cough</td>
<td></td>
<td></td>
</tr>
<tr>
<td>12 noon</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 p.m.</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2 p.m.</td>
<td></td>
<td></td>
<td></td>
<td>Coffee</td>
<td>1 cup</td>
</tr>
<tr>
<td>3 p.m.</td>
<td>XX</td>
<td>X</td>
<td>On my way to bathroom</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4 p.m.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5 p.m.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Behavioral Treatment for UI

1. Fluids management
2. Avoid Caffeine
3. Pelvic Floor Exercises
   - Squeeze your bottom like you are trying to hold back gas (should feel around your vagina as well)
   - Hold for 2 seconds and relax for 2 seconds (increase each by 1 second each week until 10 seconds each)

4. Bladder control strategies
   - Urge control — “Freeze and Squeeze”
   - Stress control — “Squeeze before you Sneeze” (lift, etc.)

Verbal and written instructions


Meta-analysis: PFMT vs. no Rx

- 12 RCT of 672 women
  - moderate to high risk of bias
  - variation in interventions used, study populations, and outcome measures.
- ↑ report of cure or improvement with PFMT
  - better continence specific quality of life
  - less leakage on office pad test.
  - longer training period a greater benefit

Dumoulin C, Hay-Smith J. Cochrane Database Syst Rev 2010

Patient Information vs. Behavioral Rx

- 222 women with Urge UI: RCT

<table>
<thead>
<tr>
<th>Method</th>
<th>Improvement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biofeedback</td>
<td>63%</td>
</tr>
<tr>
<td>Verbal/vaginal instruct</td>
<td>69%</td>
</tr>
<tr>
<td>Self-help booklet</td>
<td>59%</td>
</tr>
</tbody>
</table>

Not statistically different

Bottom line: Educate & Empower!

Burgio KL. JAMA. 2002;288:2293

Bladder Training

- Re-establishing voluntary control
- Schedule voids q 30-60 minutes
- Diary, relaxation, urge suppression
- RCT demonstrated:
  - ≥ 50% improvement in 75% of participants
- Stress and Urge UI

Fantyl 1991
OAB Medications:
Patient-Directed Balance

- Relax the bladder
- Symptom relief
- Balance:

![Improved OAB](image)

Side effects

**Adverse effects:**
- dry mouth
- constipation
- drowsiness
- headache
- dizziness

**Contraindications:**
- narrow angle glaucoma
- hepatic/renal disease

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**Cochrane Review**

**OAB Drug Effectiveness**

- 61 RCTs; 12,000 adults; 9 meds
- Medication vs. placebo (RR, 95% CI)
  - Cure or improvement: 1.39 (1.28, 1.51)
  - UI episodes/dy: 0.54 (0.41, 0.67)
  - Voids/dy: 0.69 (0.54, 0.84)
  - Improved QOL: 3.00 (2.70, 3.34)
  - Dry mouth: 3.00 (2.70, 3.34)
  - No increase in withdrawal


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**Pharmacologic Therapies Indicated for OAB with or without UUI**

<table>
<thead>
<tr>
<th>Compound</th>
<th>Usual Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oxybutynin chloride (Ditropan, Ortho-McNeil-Janssen Pharmaceuticals)</td>
<td>5 mg by mouth 3-4 times daily</td>
</tr>
<tr>
<td>Oxybutynin chloride extended release (Ditropan XL, Ortho-McNeil-Janssen Pharmaceuticals and available as generic formulation)</td>
<td>5, 10, or 15 mg by mouth once daily</td>
</tr>
<tr>
<td>Oxybutynin transdermal patch (Oxytrol, Watson Pharmaceuticals)</td>
<td>One patch applied twice weekly</td>
</tr>
<tr>
<td>Oxybutynin gel 10% (Gelnique, Watson Pharmaceuticals)</td>
<td>One sachet applied daily</td>
</tr>
<tr>
<td>Tolterodine tartrate (Detrol, Pfizer)</td>
<td>2 mg by mouth twice daily</td>
</tr>
<tr>
<td>Tolterodine tartrate long-acting (Detrol LA, Pfizer)</td>
<td>4 mg by mouth once daily</td>
</tr>
<tr>
<td>Fesoterodine fumarate (Toviaz, Pfizer)*</td>
<td>4 or 8 mg by mouth once daily</td>
</tr>
<tr>
<td>Solifenacin succinate (Vesicare, Astellas Pharmaceuticals)</td>
<td>5 or 10 mg by mouth once daily</td>
</tr>
<tr>
<td>Trosplum chloride (Sanctura, Allergan)</td>
<td>20 mg by mouth twice daily</td>
</tr>
<tr>
<td>Trosplum chloride extended release (Sanctura XR, Allergan)</td>
<td>60 mg by mouth once daily</td>
</tr>
<tr>
<td>Darifenacin (Enablex, Novartis Pharmaceuticals)</td>
<td>7.5 or 13 mg by mouth once daily</td>
</tr>
</tbody>
</table>

* Tolterodine is the active metabolite of fesoterodine.

### Behavioral Rx vs. Medications

- 197 women with Urge UI: RCT
  - Biofeedback/behavioral $\downarrow$ UI 81%*,+  
  - Medication 69%*  
  - Placebo 40%  
  * P < 0.05 vs. medication; + P < 0.05 vs. control
- Greater satisfaction in behavioral group

**Bottom line: Educate & Empower**


### Which Rx First?

- Combo treatment: Makes sense
  - Behavioral to drug 84%  
  - Drug to behavioral 89%

**Bottom line: Be creative!**


### When to Refer

- Persistent, bothersome symptoms after 2-3 mo trials with behavioral treatment, drug treatment or both
- Patient not satisfied with treatment outcome
- UTI > 2 in 12 mo, PVR > 200 cc, hematuria, neurological symptoms, failure to isolate pelvic floor muscles in a patient who desires PFMT, prolapse $\geq$ hymen
- Refer to a specialist  
  - Urogynecologist  
  - Urologist  
  - Physical therapist/continence specialist  
- Refer to a specialist

### Refractory OAB

- Next treatment options:  
  - Intensive behavioral therapy with biofeedback  
    - Possible electrical stimulation  
  - Sacral nerve neuromodulation  
  - Posterior tibial nerve stimulation  
  - Botulinum toxin type A injection

**Sacral Nerve modulation**

- Refractory UUI
- Temporary, percutaneous SN test stimulation ➔ permanent, surgically implanted lead (S3 foramen) and neurostimulator (InterStim, Medtronic)
- In two multicenter trials:
  - 3 years, N=41: 59% had > 50% reduction in UUI/dy (46% dry) at 3 years
  - 5 years, N=152: UUI/dy decreased from 10 to 4
  - Voids/day decreased and volume voided increased

Siegle SW. Urology. 2000;56:87-91; van Kerrebroeck PE. J Urol. 2007;178:2029-34

**Percutaneous Tibial Nerve Stimulation**

- Electrostimulation of the PTN by a fine needle inserted near the ankle
- Rx for 30 minutes, weekly x 12 weeks
- RCT 220 adults with OAB: PTNS vs. sham
  - PTNS had sig. ↓ frequency, nocturia, mod/severe urgency, and UUI episodes vs. sham
- RCT 35 women with UUI PTNS vs. Placebo needle:
  - 71% vs. 0% had > 50 reduction in UIEF


**Intravesical Botulinum Toxin**

- Refractory OAB
- Placebo controlled RCT, BTX had 3.9 (95% CI 1.6, 6.2) fewer UI episodes/dy
- ↑ PVR, retention, UTI
- Not FDA approved


**Example of Results of Urodynamic Testing in a Woman with Severe Urgency Urinary Incontinence**

Think Outside the Bladder!

UI: Who is at Risk?

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral estrogen</td>
<td>90%</td>
</tr>
<tr>
<td>Stroke</td>
<td>90%</td>
</tr>
<tr>
<td>Diabetes</td>
<td>70%</td>
</tr>
<tr>
<td>BMI (per 5 units)</td>
<td>60%</td>
</tr>
<tr>
<td>Poor overall health</td>
<td>60%</td>
</tr>
<tr>
<td>Hysterectomy</td>
<td>40%</td>
</tr>
<tr>
<td>COPD</td>
<td>40%</td>
</tr>
<tr>
<td>Age (per 5 years)</td>
<td>30%</td>
</tr>
<tr>
<td>Live birth</td>
<td>30%</td>
</tr>
</tbody>
</table>


Estrogen Therapy for UI

- ↓ UI with estrogen Rx in observational studies
  - Receptors in urethra, bladder
- 7 RCTs oral CEE/MPA vs. placebo (N=15,593)
  - HERS & WHI
- For Stress, Urge, & Mixed UI:
  - Prevalent UI: ↑ frequency 40 - 50% (4 mo → 4 yrs)
  - Incident UI at 1 yr: ↑ 15% to 2-fold

Bottom line: oral HT not for prevention or Rx of UI


Weight Reduction & UI

- In women about 200 lbs:
  - Weight loss: > 5% or 30 lbs
  - > 50% ↓ in incontinence episodes
- Effective therapy for UI
- Unique motivator for weight loss
- Public Health Implications

Subak 2002; Subak 2006
**Weight Reduction & UI**

Program to Reduce Incontinence by Diet & Exercise
- NIDDK-funded RCT 338 obese women with UI
- 6-month lifestyle intervention vs. control

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Control</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight</td>
<td>- 8.2%</td>
<td>- 1.8%</td>
</tr>
<tr>
<td>Total UI</td>
<td>- 46%</td>
<td>- 25%</td>
</tr>
</tbody>
</table>

*Wt Loss similar to medications...*


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**DM: Independent Risk Factor for UI**

- **1.5 million women** with Type 2 DM have UI
- DM associated with:
  - 2-fold ↑ in UI prevalence & incidence
  - ↑ UI severity
  - ↑ bother, QOL impact

*If DM prevented, eliminate 17% of UI and 50% of severe UI*

- **Women with pre-diabetes**: similar findings!

Nurses Health Study (Liford 2005); NHANES 2001-2 (Brown 2006); Brown 1999; Ebbesen 2007

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**Diabetes Prevention Trial**

DPP

- **Lifestyle** N = 1,079
- **Metformin** N = 1,073
- **Placebo** N = 1,082

UI: 38%*  UI: 48%  UI: 46%

Knowler. NEJM 2002; Brown JS. Diabetes Care 2005

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**DPP UI Summary**

Among women with pre-diabetes:
- Weight loss and exercise: ↓ UI
- Weight change accounted for treatment effect

**DPP-Outcomes Study:**
- Long-term effects for prevention and early disease

Brown Diabetes Care 2005
**UI Treatment Effectiveness**

- Placebo 20-40%
- Behavioral 40-80%
- Pharmacological 40-70%
  - Side effects, discontinuation 50%
- Weight Loss 50-60%
- Surgery 80-100%
  - Long-term cure 50%

*Non-surgical treatments similar!*

**Summary and Conclusion**

Incontinence is common and treatable

- Simple diagnosis: 3IQ and UA
- Simple treatments: *Info ± Rx*
- Ask patient what they want!
- Combine treatments, flexibility
- Refer if no improvement in 2–6 months

*Educate and Empower!*

[www.ucsf.edu/wcc](http://www.ucsf.edu/wcc)