Gotta Go?  
Urinary Incontinence in the Elderly

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Objectives

• Discuss the etiology and pathophysiology of urinary incontinence (UI).

• Evaluate pharmacologic and non-pharmacologic treatment options for urinary incontinence.

• Create patient-specific recommendations for the treatment of urinary incontinence based on available efficacy and safety data.

Epidemiology

Adapted from: Essentials of Clinical Geriatrics, 2013.
Consequences of Incontinence

<table>
<thead>
<tr>
<th>Economic</th>
<th>Medical</th>
<th>Psychosocial</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cost of supplies, medications, home health aide/care at home, nursing facility</td>
<td>Risk of cystitis, urosepsis, pressure sores, perineal rashes, sleep disturbances, dehydration, falls</td>
<td>Embarrassment, isolation, depression, predisposition to institutionalization</td>
</tr>
</tbody>
</table>

The Aging Urinary Tract

<table>
<thead>
<tr>
<th>Physiologic Change</th>
<th>Results In...</th>
</tr>
</thead>
<tbody>
<tr>
<td>↓ bladder elasticity</td>
<td>Less capacity for volume</td>
</tr>
<tr>
<td>↑ residual volume</td>
<td>Incomplete emptying</td>
</tr>
<tr>
<td>↑ nocturnal sodium and fluid excretion</td>
<td>Nighttime awakening to urinate</td>
</tr>
<tr>
<td>↑ urethral resistance (men)</td>
<td>Weak stream, difficulty urinating</td>
</tr>
<tr>
<td>↓ urethral resistance (women, ↓ estrogen)</td>
<td>Urgency, going too much</td>
</tr>
<tr>
<td>Weakened pelvic floor muscles</td>
<td>Increased pressure on the bladder</td>
</tr>
<tr>
<td>↑ involuntary bladder contractions</td>
<td>Urgency, got to go NOW!</td>
</tr>
</tbody>
</table>

All contribute, but none alone precipitates incontinence

Anatomy & Pathophysiology
**Pathophysiology: Storage Phase**

- **Sympathetic Nervous System** (α-adrenergic)
- **Parasympathetic Nervous System**
- **Somatic Nervous System**

**Bladder**
- **Ureters**
- **Internal Sphincter**
- **External Sphincter**

**Bladder Neck**
- **Contraction (Closed)**
- **Relaxation (Open)**

**Pathophysiology: Voiding Phase**

- **Sympathetic Nervous System** (α-adrenergic)
- **Parasympathetic Nervous System**
- **Somatic Nervous System**

**Bladder**
- **Ureters**
- **Internal Sphincter**
- **External Sphincter**

**Bladder Neck**
- **Contraction (Closed)**
- **Relaxation (Open)**

**Pathophysiology: Summary**

- **Bladder Filling**
  - Sensation to void
  - Normal desire to void
- **Bladder Pressure**

**Picture credit:** [SketchyMedicine.com](http://sketchymedicine.com/2011/10/neural-control-of-micturition/)
### Evaluation & Diagnosis

**HISTORY**
- Symptoms (onset, type, frequency, timing)
- Bladder record
- Comorbidities, lifestyle, medications, environment
- Patient perception of incontinence

**PHYSICAL**
- Mobility issues
- Gynecological and urological evaluation
- Tests
  - Catheterization or bladder ultrasound (residual volumes)
  - Cystoscopy and flow studies
  - Urinary stress test
  - UA and urine cultures
  - Blood chemistries
  - Renal function
  - Postprandial glucose

### Goals of Therapy

- Minimize signs and symptoms most bothersome to the patient
  1. Non-pharmacologic techniques
  2. Medications
  3. Surgical intervention
- Set realistic expectations
  - Total elimination of symptoms may not be feasible
  - Communicate most common side effects
  - Balance patient goals, expectations, and risks

### Classification: Acute/Transient

- Recent onset
- Associated with acute medical problem
  - Heart failure
  - Acute confusion or altered mental status
  - Surgical procedures
Reversible Causes

• Delirium or Dementia
• Infections
• Atrophic vaginitis, urethritis, atonic bladder
• Psychological or Pharmaceuticals
• Endocrine (diabetes, hypothyroidism) or Excessive urine output/fluid intake
• Restricted mobility or Retention
• Stool impaction

Medication-Induced Incontinence

<table>
<thead>
<tr>
<th>Stress</th>
<th>• α-blockers</th>
<th>• Atypical antipsychotics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urge</td>
<td>• ACE inhibitors</td>
<td>• Hormone replacement</td>
</tr>
<tr>
<td></td>
<td>• Antidepressants</td>
<td>• Direct or indirect parasympathomimetics (cholinesterase inhibitors)</td>
</tr>
<tr>
<td>Overflow</td>
<td>• Anticholinergics</td>
<td>• α-agonists</td>
</tr>
<tr>
<td></td>
<td>• Antiparkinson drugs</td>
<td>• Opioids</td>
</tr>
<tr>
<td></td>
<td>• β-blockers</td>
<td>• Calcium channel blockers</td>
</tr>
<tr>
<td>Functional</td>
<td>• H1-antagonists</td>
<td>• Opioids</td>
</tr>
<tr>
<td></td>
<td>• Antipsychotics</td>
<td>• Alcohol</td>
</tr>
<tr>
<td></td>
<td>• Benzodiazepines</td>
<td></td>
</tr>
</tbody>
</table>

Increase Urine Production

• Diuretics
• Lithium
• NSAIDs

Treatment of Acute/Transient UI

• Identify and treat underlying cause
• Treat symptoms and patient needs
• Remove, reduce, substitute offending medication
• Attend to surgical complication, impaction, etc.
• Improve mood and mental status
• Antibiotics for infection or vaginitis
Case BW

- BW is a 72-year-old female who presents to the clinic complaining of increased frequency (every 2 hours), urgency, and moderate leakage
- PMH includes diabetes, uncontrolled hypertension, osteoporosis, and hypothyroidism
- Medications include metformin, HCTZ, amlodipine, calcium + vitamin D, and levothyroxine
- When asking her about OTC use, she mentions needing to take Miralax daily

Case BW, cont.

After removing the potential acute causes of UI, BW continues to have symptoms. She mentions that she has leakage when she sneezes and often needs to “race to the ladies room” throughout the day.

How would you classify BW’s incontinence?

a) Urge
b) Stress
c) Overflow
d) Mixed

Classification: Chronic/Persistent

<table>
<thead>
<tr>
<th>Cause</th>
<th>Urge</th>
<th>Stress</th>
<th>Overflow</th>
<th>Functional</th>
</tr>
</thead>
<tbody>
<tr>
<td>Detrusor muscle overactivity</td>
<td>Bladder distension due to obstruction (BPH, fecal impaction)</td>
<td>Incontinence with coughing, sneezing, laughing, exercise, activities that increase abdominal pressure, frequency</td>
<td>Underlying physical or mental impairment impacting ability to toilet</td>
<td></td>
</tr>
<tr>
<td>Weakened pelvic floor muscles</td>
<td></td>
<td>Incomplete voiding, frequency, urgency, hesitancy, abdominal fullness, straining</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Mixed = usually combination of urge and stress incontinence
Urge Urinary Incontinence (UUI)

- Involuntary voiding preceded by a brief warning
- Causes:
  - Detrusor muscle instability (involuntary contraction)
  - Two hypotheses
    - Neurogenic
    - Myogenic
- Overactive bladder (OAB)
  - Syndrome including urgency, frequency, and nocturia
  - With or without urge incontinence

UUI Treatment Strategy

- Identify and mitigate any reversible causes
- Non-pharmacologic
  - Lifestyle (e.g., diet, behavior)
  - Surgical
- Pharmacologic
  - Expectation of 4-6 week response
  - If no response, can switch to another agent in same class

Non-pharmacologic Treatment of UUI

- Diet (monitoring fluid, caffeine, bladder irritants)
- Exercise and weight loss
- Smoking cessation
- Scheduling regimens:
  - Timed voiding
  - Bladder training and scheduling
- Muscle rehabilitation:
  - Pelvic floor muscle exercises (e.g., Kegel exercises)
  - Biofeedback, electrical stimulation
  - Acupuncture
- External urine collection (men only)
- Surgery
**Non-pharmacologic Treatment of UUI**

- Urinary prosthesis (women)
  - Draws urine out of the bladder and blocks urine flow out
  - Inserted by physician, then by patient or caregiver
  - Replace every 29 days
  - Use remote control to void

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**UUI Treatment Targets**

![Diagram of UUI treatment targets](http://www.thedailynarrative.com/wp-content/uploads/2014/10/20141014-FG30001014FD-A.png)

**UUI Treatment Targets: Non-selective**

<table>
<thead>
<tr>
<th>Receptor</th>
<th>Anatomical Location</th>
<th>Result of Antagonism</th>
</tr>
</thead>
<tbody>
<tr>
<td>M1</td>
<td>Brain</td>
<td>Cognitive impairment</td>
</tr>
<tr>
<td></td>
<td>Gt tract</td>
<td>Constipation, dry mouth</td>
</tr>
<tr>
<td>M2</td>
<td>Brain</td>
<td>Cognitive impairment</td>
</tr>
<tr>
<td></td>
<td>Heart</td>
<td>Tachycardia</td>
</tr>
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<tr>
<td></td>
<td>Urinary tract</td>
<td>Bladder relaxation, sphincter closing</td>
</tr>
<tr>
<td>M3</td>
<td>Gt tract</td>
<td>Constipation, dry mouth</td>
</tr>
<tr>
<td></td>
<td>Ophthalmologic</td>
<td>Mydriasis</td>
</tr>
<tr>
<td>M4</td>
<td>Brain</td>
<td>Balance impairment</td>
</tr>
</tbody>
</table>

Adapted from Zimmerman K, 2015.
UUI Treatment: Anticholinergics

- Reduce cholinergic transmission to bladder, inhibit involuntary detrusor contraction, increase bladder capacity, decrease frequency of urination
- Side effects: dry mouth, visual disturbances, constipation, dry skin
- Precautions – arrhythmias, cardiovascular disease, GI motility issues, dementia, and elderly
- Contraindications – GI obstruction, closed and narrow angle glaucoma

UUI Treatment: Efficacy

- Anticholinergics have a modest benefit over placebo
  - Reduction in 0.6 episodes/day
  - 50% of patients still unhappy or frustrated with symptoms after treatment
- 60-70% of women discontinue within 6 months
- Similar efficacy between agents although limited head-to-head trials between agents
- Extended-release agents have lower rates of adverse effects than immediate release agents

Non-selective Anticholinergics

<table>
<thead>
<tr>
<th>Medication</th>
<th>Formulations</th>
<th>Adverse Effects</th>
<th>Additional Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oxybutynin</td>
<td>IR tablets (Ditropan®)</td>
<td>MOST</td>
<td>Reference standard Gradual dose escalation</td>
</tr>
<tr>
<td></td>
<td>ER tablets (Ditropan XL®)</td>
<td></td>
<td>Better tolerated than IR</td>
</tr>
<tr>
<td></td>
<td>Patch (Oxytrol®)</td>
<td></td>
<td>DTC for women only Bypasses 1st pass</td>
</tr>
<tr>
<td></td>
<td>Gel (Gelique®)</td>
<td></td>
<td>Bypasses 1st pass</td>
</tr>
<tr>
<td>Tolerodine</td>
<td>IR tablets (Detrol®)</td>
<td></td>
<td>CYP3A4 metabolism Renal dose adjustments</td>
</tr>
<tr>
<td></td>
<td>ER capsules (Detrol® LA)</td>
<td></td>
<td>Better tolerated than IR</td>
</tr>
<tr>
<td></td>
<td>ER tablets (Toviaz®)</td>
<td></td>
<td>Adjustment for renal impairment and 3A4 inhibitors</td>
</tr>
<tr>
<td>Fesoterodine</td>
<td>ER tablets (Toviaz®)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>IR tablets (Sanctura®)</td>
<td></td>
<td>Dose adjustment for CrCl &lt; 30 ml/min</td>
</tr>
<tr>
<td></td>
<td>ER tablets (Sanctura XR®)</td>
<td></td>
<td>Better tolerated than IR Avoid in renal impairment</td>
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CYP2D6 > CYP3A4 metabolism Renal dose adjustments
### UUI Treatment Targets: Selective

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### Selective Anticholinergics

#### Solifenacin
- **IR tablets (Vesicare®)**
- **M3 selectivity > M2**
- **Efficacy**
  - Non-inferior to oxybutynin IR
  - Superior to tolterodine IR
- **Side effects:**
  - Less than oxybutynin and tolterodine
  - More than darifenacin
- **Maximum 5 mg/day**
  - Renal impairment (CrCl < 30)
  - Moderate and severe hepatic impairment

#### Darifenacin
- **ER tablets (Enablex®)**
- **Truly selective for M3**
- **Efficacy**
  - Non-inferior to oxybutynin IR
  - More effective than tolterodine IR at 12 weeks
  - Less side effects than oxybutynin
- **Maximum 7.5 mg/day**
- **Hepatic impairment**
  - Moderate – max 7.5 mg/day
  - Not evaluated in severe

### Mirabegron: β-agonist
- **ER tablet (Myrbetriq®)**
- **Reduces bladder contractions via relaxation of detrusor muscle through β3-agonism**
- **Efficacy in 4-8 weeks, reduction in 0.5 episodes/day at 50 mg dose**
- **Maximum 25 mg/day if CrCl < 30 ml/min**
- **Side effects:** hypertension, nasopharyngitis, UTI, constipation, tachycardia, headache
Other Pharmacologic Treatment

- **Tricyclic Antidepressants** (e.g., imipramine)
  - Increases bladder capacity and outlet resistance, anticholinergic properties
  - Side effects: weakness, fatigue, postural hypotension, hip fractures
- **Botox®** (onabotulinumtoxinA)
  - Muscle paralytic when injected into detrusor muscle
  - Approved January 2013
  - Injected into 20 sites via urethra every 12 weeks
  - Decreases 1.6-1.9 episodes/day

Case BW, cont.

Besides non-pharmacologic options, which treatment for urge UI would be most appropriate for BW?

a) Mirabegron
b) Oxybutynin IR
c) Darifenacin
d) Tolterodine LA

Stress Urinary Incontinence (SUI)

- Involuntary leakage due to increased intra-abdominal pressure that overcomes urethral resistance
- Causes
  - Weak pelvic floor muscles
  - Sphincter incompetence
  - Trauma/damage to urethra
  - Women >>> Men
Stress Urinary Incontinence Triggers

Non-Pharmacologic Treatment for SUI

Pelvic floor muscle training

Pessaries

Pharmacologic Treatment for SUI

- No agent is FDA approved for the treatment of SUI in the United States
- Duloxetine (Cymbalta®)
  - Serotonin and norepinephrine reuptake inhibitor
  - Involved in control of urethral smooth muscle in cats and rats
  - Facilitates pathway between bladder and sympathetic nervous system
  - Increases sphincter tone during storage phase
  - Off-label in US due to suicidal ideation, indicated in UK
  - Side effects (diminish with time): nausea, dry mouth
  - Older adults underrepresented in studies
Pharmacologic Treatment for SUI

- **α-Adrenergic agonists**
  - Pseudoephedrine, phenylephrine
  - Caution in elderly due to side effects
  - Contraindicated in hypertension or obstruction
- **Topical estrogen (creams, vaginal tablets, rings)**
  - SUI + vaginitis or urethritis due to estrogen deficiency
  - NO systemic therapy
  - Used in combination with α-agonists
- **Imipramine**

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Mixed Urinary Incontinence

Treatment of Mixed UI

- Initial therapy depends on predominate symptoms
- Can use combination of treatment strategies for UUI and SUI in the absence of obstruction
  - Pelvic floor muscle training and bladder training
  - Behavioral interventions
  - Medications
Overflow Urinary Incontinence (OUI)

- Volume of urine in bladder overcomes closing pressure
- Symptoms:
  - Diminished stream
  - Straining to void
  - Sense of incomplete emptying
- Causes:
  - Neurogenic bladder
  - Atonic bladder
  - Obstruction (BPH, strictures, neuropathy, impaction)

Treatment of OUI

**Non-pharmacologic**
- Obstruction removal (surgery)
- Bladder training and voiding schedule
- Catheterization
  - Self-catheterization 3-4x/day
  - Surgically placed

**Pharmacologic**
- Bethanechol (Urecholine®)
  - Cholinomimetic
  - SEs: muscle cramping, diarrhea
  - Can cause life threatening ADE in asthma or heart disease
- α₁A-receptor antagonists
  - Located in bladder neck, urethra, and periurethral tissues
  - Treatment of BPH in men
  - Use in women for this reason

Functional Incontinence

- Person is unable or unwilling to reach the toilet
- Causes:
  - Musculoskeletal disorders/weakness
  - Disabilities, vision loss
  - Cognitive impairment
  - Physical restraints
  - Psychological impairments
  - Environment
  - Medications (e.g., sedatives, neuroleptics)
Treatment for Functional UI

- Scheduled or prompted toileting
- Removal of barriers and obstacles
- Physical therapy
- Assistive devices
  - Bedside commode
  - Urinals
  - Elevated toilet seats

Case BW, cont.

After removing the potential acute causes of UI, BW continues to have symptoms. She mentions that she has leakage when she sneezes and often needs to “race to the ladies room” throughout the day.

How would you classify BW’s incontinence?

a) Urge
b) Stress
c) Overflow
d) Mixed

Choosing Pharmacologic Therapy

Most have similar efficacies; New is not always better!!!

Consider symptoms, comorbidities, drug interactions, side effects, etc.

Formulary restriction and insurance coverage
Treatment Approach in Elderly

- Determine if there is another underlying cause
- Anticholinergics are on 2015 Beers Criteria to be avoided in elderly with dementia or cognitive impairment
- Start low and go slow
  - Dose adjust for renal and hepatic impairment
  - Titration based on side effects and tolerability
- Trial of one agent for up to 2 months
- Consider switch to another agent if no improvement and treatment is still necessary

Counseling Tips

- Reduce intake of fluid during the day, especially in the evening (after 6 pm)
- Avoid caffeinated beverages
- Minimize the use of artificial sweeteners, acidic and spicy foods
- Let your pharmacist know about new medications you are taking to see if they contribute to your symptoms

Case BW, cont.

Four weeks after starting darifenacin, BW returns to the clinic because this medication is not working. She has seen commercials for a new medication called “Mybearstricks” and asks if this is a better option. Her blood pressure today is 122/78.

How would you proceed?

a) Check with her insurance first to see if it is covered
b) Counsel her that an effect can take up to 2 months
c) Recommend a switch to solifenacin instead
Take Home Points

- UI is a prevalent condition with the potential to have a significant impact on older adults
- Treatment for UI should include non-pharmacologic approaches before initiating pharmacologic agents
- Efficacy, adverse events, and patient preference need to be considered when developing a treatment plan
- Pharmacists can monitor for efficacy and help mitigate adverse effects for patients with UI

References

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