Urinary Incontinence: Pathophysiology, Assessment and Treatment Options

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Objectives
• Define urinary incontinence (UI)
• Describe pathophysiology and clinical presentation of common types of UI
• Discuss common medications that affect UI

Objectives
• Discuss pharmaceutical management of various types of UI
• Discuss basic management options for UI symptoms and causes of UI

Urinary Incontinence
• UI is the involuntary leakage of urine
• Two times more common in women than men
• Estimated one - third of women over the age of 60 are incontinent

Micturation
• Complex function
• Continence is voluntary
Causes of Urinary Incontinence

- Problem with nervous system
- Weakness of the muscles
- Blockage of the urethra

Medications Linked to Urinary Incontinence

Medications That Cause Urinary Incontinence

- Medications that may be associated with urinary incontinence include the following:
  - Cholinergic or anticholinergic drugs
  - Alpha - blockers
  - Over - the - counter allergy medications

Medications Linked to Urinary Incontinence

- Alpha blocker anti - hypertensives: Cardura, Minipres, Hytrin
  - While improving symptoms of BPH in men, these medications relax the muscles in the bladder of women causing an increase in severity of incontinence symptoms

Medications That Cause Urinary Incontinence

- Estrogen replacement
- Beta - mimetics
- Sedatives
- Muscle relaxants
- Diuretics
- Angiotensin - converting enzyme (ACE) inhibitors

Medications Linked to Urinary Incontinence

- Antidepressants: Amitriptyline, desipramine, nortripyline
  - Impairs ability of bladder to contract, causing the bladder to not empty completely
- Diuretics: Furosemide and thiazides
  - Increase in amount of urine, worsening incontinence symptoms

Medications Linked to Urinary Incontinence

- Cardura, Minipres, Hytrin
  - While improving symptoms of BPH in men, these medications relax the muscles in the bladder of women causing an increase in severity of incontinence symptoms
Medications Linked to Urinary Incontinence

- Sedatives and Sleeping pills: Patients do not wake up when bladder is full
- Estrogens and progestin combination therapy: Increased risk of developing urinary incontinence in women with history of cardiovascular disease

Medications Linked to Urinary Incontinence

- Angiotensin - converting enzyme (ACE) inhibitors: benazepril, captopril
  - Can cause cough and worsen stress incontinence

Medications Linked to Urinary Incontinence

- Calcium channel blockers: diltiazem, verapamil
  - Interfere with bladder contraction and worsen constipation, causing urine to be retained in the bladder

Medications Linked to Urinary Incontinence

- Antipsychotics: Haloperidol, resperidone, thioridazine, theothixene
  - Slows mobility and causes abrupt urge followed by uncontrollable loss of urine

Medications Linked to Urinary Incontinence

- Opioids: Morphine
  - Interferes with bladder contraction and worsens constipation, causing retention of urine

Medications Linked to Urinary Incontinence

- H-1 antagonists: Diphenhydramine and Chlopheniramine
  - Significant degree of anticholinergic effects
- Alpha agonists: Pseudoephedrine
  - Tightens the urinary spincter causing urine to be retained in the bladder
Medications Linked to Urinary Incontinence

- Cholinergics: Bethanechol
  - Treatment for urinary retention
- Donepezil (Aricept): Reported in clinical trials
  - Cause unknown

Medications Linked to Urinary Incontinence

- Pregabalin (Lyrica): Reported in clinical trials
  - Cause unknown
- Baclofen (Lioresal): With intrathecal use
- Caffeine and alcohol
  - Increase urine production

Types of UI

- Stress
- Urge
- Overflow
- Functional

Stress Incontinence

- Stress Incontinence (SI):
  - Leakage that occurs when laughing, sneezing, coughing, lifting heavy objects, or exerting other pressure on the bladder
  - Urine leaks as result if increased pressure on the bladder and weak muscles in the pelvic floor

Stress Incontinence Causes

- Weak pelvic floor muscles
- Weak urethral sphincter
- Childbirth
- Obesity
- Prostate disease or surgery
- Medications

Stress Incontinence

- Affects both men and women
  - In women, may follow childbirth or menopause
  - In men, may follow prostate cancer treatment, such as radical prostatectomy
Urgency Incontinence

• Urgency Incontinence or Over Active Bladder (OAB):
  – Loss Urgent need to pass urine and the inability to get to a toilet in time

Urgency or OAB

• Bladder spasms resulting in urinary frequency
• Sudden urges to go to the bathroom
• Having to get up at night to go to the bathroom
• Mobility limitations

Overflow Incontinence

• Overflow Incontinence is when the bladder does not empty properly and there is a slow leak, often a constant drip or flow of urine
• Often seen in men with prostate symptoms

Overflow Incontinence

• Causes of overflow incontinence:
  – Weak bladder muscles
  – Blockage of the urethra, such as by prostate enlargement
  – Medical conditions, such as tumors, that cause obstruction of urine flow

Overflow Incontinence

– Constipation
– Pelvic trauma
– Pelvic organ prolapse (women)
– Enlarged prostate (men)
– Spinal Cord injury
– MS

Overflow Incontinence

– Parkinson’s Disease
– Polio
– Other Neurological disorders
**Functional Incontinence**
- The inability to hold urine due to reasons other than neuro-urologic and lower urinary tract dysfunction
- Functional Incontinence is when a person has normal functioning bladder, but is unable to physically or mentally get to the bathroom to urinate

**Causes of Functional Incontinence**
Factors that Can Cause a Person Not to Get to the Bathroom in Time
- Physical
  - Arthritis
  - Muscle weakness
  - Stroke
  - Muscular disease

**Causes of Functional Incontinence**
Factors that Can Cause a Person Not to Get to the Bathroom in Time
- Cognitive
  - Dementia
  - Alzheimer’s Disease
  - Parkinson’s Disease
  - Brain Injury

**Mixed Incontinence**
- Common
- Symptoms of both stress and urgency incontinence are present
- Symptoms of one type of incontinence may be more severe than the other

**Causes of Functional Incontinence**
Factors that Can Cause a Person Not to Get to the Bathroom in Time
- Cognitive
  - Stroke
  - Mentally Challenged

**Mixed Incontinence**
- Treatment may be a combination of the treatments listed for stress or urgency incontinence
- Treatment may be directed to the symptoms which are the most bothersome to the patient
Pharmaceutical Management of Urinary Incontinence

Anti-Cholinergic Agents
Anti-Muscarinic or Muscarinic Receptor Antagonists

- Treatment of urinary incontinence
- First line drug therapy
- Patients with more severe symptoms typically receive greater benefit

Anti-Cholinergic Agents

- May decrease dose or try another medication if patient has inadequate response or intolerable adverse effects

Muscarinic Receptor Antagonists

- Mechanism of action:
  - Depress voluntary and involuntary bladder contractions
  - Decrease in detrusor muscle pressure
  - Targets $M_2$ and $M_3$ receptors in the detrusor muscle

Muscarinic Receptor Antagonists

- $M_3$ receptors are primarily responsible for bladder function and direct contraction of the detrusor muscle

Muscarinic Receptor Antagonists

- Adverse effects:
  - Dry mouth*
  - Blurred vision
  - Constipation*
  - Decreased cognitive function
  - Dry / itchy eyes
  - Dyspepsia
  - Urinary retention
  - *Most common
### Muscarinic Receptor Antagonists

- **Extended release formulations may have lower incidence of dry mouth**
- **Caution in patients with narrow angle glaucoma, impaired gastric emptying or urinary retention**

### Muscarinic Receptor Antagonists

- **Absolute contraindications**
  - include closed angle glaucoma, gastroparesis, GI obstruction, pyloric stenosis, and urinary retention

### Muscarinic Receptor Antagonists

- **Interaction with CYP3A4 inhibitors:**
  - Increased anticholinergic effects with medications such as fluconazole and ketoconazole
  - Constipation, dry eyes, dry mouth

### Muscarinic Receptor Antagonists

- Associated with dose-dependent prolongation of the QT interval
- Avoid in patients at risk for Torsades de pointes
- Dose adjustment recommended with strong CYP34A inhibitors

### Muscarinic Receptor Antagonists

- Darifenacin (Enablex)
- Fesoterodine (Toviaz)
- Flavozate (Urispas)
- Oxybutynin (Ditropan tablets, Oxytrol Transdermal Patch, Gelnique Gel)

### Muscarinic Receptor Antagonists

- Solifenacin succinate (Vesicare, YM905)
- Tolterodine (Detrol, Detrol LA)
- Trospium (Sanctura, Sanctura XR)
**Muscarinic Receptor Antagonists**

- **Fesoterodine (Toviaz)**
  - Indications: Overactive Bladder, Urinary Incontinence, Urinary Urgency
  - Dose: Initially 4 mg by mouth daily
  - May increase to 8 mg if not taking potent CYP3A4 inhibitor

- **Darifenacin (Enablex)**
  - Indications: Overactive Bladder, Urinary Incontinence
  - In theory, has fewer anti-muscarinic side effects than others because of greater affinity for M₃ receptors
  - Dose: Initially 7.5 mg by mouth daily
  - May increase to 15 mg if not taking potent CYP3A4 inhibitor

- **Flavozate (Urispas)**
  - Oral urinary antispasmodic agent with direct actions of smooth muscle, especially of the urinary tract
  - Relaxes detrusor muscle and increases bladder capacity

**Muscarinic Receptor Antagonists**

- **Level 2 drug interaction:** Itraconazole, a potent CYP3A4 inhibitor which increases level of Toviaz, thereby increasing risk of adverse effects
  - Interaction may be exaggerated in patients with renal or hepatic dysfunction

- **Conivaptan (Vaprisol), a CYP34A inhibitor**

**Muscarinic Receptor Antagonists**

- Monitor when less potent CYP34A inhibitors are given: fluconazole, verapamil, diltiazem, grapefruit juice
**Muscarinic Receptor Antagonists**

- Has weak antihistaminic, local anesthetic and analgesic properties
- High doses can produce weak anticholinergic actions

- Contraindications: Achalasia, bladder obstruction, GI Bleeding, GI obstruction, ileus, urethral stricture, urinary retention, urinary tract obstruction
- Level 2 drug interactions: anti-muscarinics, bethanechol

- Adverse reactions: nausea, vomiting, and dry mouth

- Oral immediate release: 5 mg 2-3 times daily with maximum dose of 5 mg 4 times a day
- Oral extended release: 5-10 mg daily
- Transdermal: One patch applied twice weekly
  - Rotate patch site

- Oxybutynin – Ditropan tablets, Oxytrol Transdermal Patch, Gelnique Gel
- Indications: Overactive Bladder, Urinary Incontinence, Neurogenic bladder
- Available as oral and transdermal formulations

- Topical: Apply 3 pumps or one gel packet once daily
  - Rotate sites
- Oxytrol Transdermal is OTC approved for treatment of overactive bladder in women 18 years of age and older
Muscarinic Receptor Antagonists

- Level 2 interactions: Potassium salts and Tegaserod (Zelnorm) due to decreased GI mobility
- GI-related side effects were reported less frequently with the patch and gel formulations

Muscarinic Receptor Antagonists

- Tolterodine (Detrol, Detrol LA)
  - Indications: Overactive Bladder, Urinary Incontinence, Urinary Urgency
  - Preferred in geriatric population
  - QT interval prolongation not observed at dose of 4 mg BID

- Dose immediate release 1-2 mg twice a day, Extended release 4 mg daily
- Level 1 drug interactions: Cisapride, Dofetilide, Dronedarone, Thioridazine, Ziprasidone, Pimozide, Ketoconazole, Voriconazole, Itraconazole

- Ketoconazole requires an acidic pH for oral absorption which is diminished by tolterodine
  - Stagger time of administration by several hours or consider alternative antifungal

- Level 2 interactions: 70+ medications
- Additional adverse effects: dizziness and vertigo
- Most common reason for discontinuation: dry mouth, dizziness and headache

Muscarinic Receptor Antagonists

- Solifenacin Succinate (Vesicare)
  - Indications: Overactive Bladder, Urinary Incontinence
  - Level 1 drug interactions due to potential of QT interval prolongation resulting in torsades de points
**Muscarinic Receptor Antagonists**

- Includes: Cisapride, Dofetilide, Dronedarone, Thioridazine, Ziprasidone, Pimozide, Fluconazole, Ketoconazole, Posaconazole, Voriconazole
- Level 2 drug interactions: 70+ medications

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**Muscarinic Receptor Antagonists**

- Dry mouth most common reason for drug discontinuation
- Dose: 10 mg daily

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**Muscarinic Receptor Antagonists**

- Trospium (Sanctura, Sanctura XR)
  - Indications: Overactive Bladder, Urinary Incontinence, Neurogenic bladder
  - Does not cross blood - brain barrier like oxybutynin

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**Muscarinic Receptor Antagonists**

- Is not a substrate or inhibitor of cytochrome P-450 enzymes
- Dose: Immediate release 20 mg once or twice a day
  - Extended release 60 mg daily in morning

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**Other Medications**

- Mirabegron (Myrbetriq)
- OnabotulinumtoxinA (Botox)
**Other Medications**

- Mirabegron (Myrbetriq)
  - Beta-3 adrenergic receptor agonist
  - First in this class of agents
  - Indications: overactive bladder and urinary incontinence
  - First line drug therapy

- Mirabegron (Myrbetriq)
  - Beta-3 adrenergic receptor agonist
  - First in this class of agents
  - Indications: overactive bladder and urinary incontinence
  - First line drug therapy

- Common adverse reactions:
  - Nausea, headache, hypertension, diarrhea, constipation, dizziness, and sinus tachycardia, UTIs
  - Dose 25 mg daily
  - May increase to 50 mg daily if tolerated

- Monitor blood pressure and heart rate closely
  - Contraindications: Severe uncontrolled hypertension (SBP > 180 and/or DBP > 110)
  - Level 2 drug interactions:
    - Clozapine, digoxin, Doxorubicin, Eliquis, Flecainide, MAOIs, Pimozide, Tamoxifen, Thioridazine

- OnabotulinumtoxinA (Botox)
  - Indications: neurogenic bladder, overactive bladder, urinary incontinence when anti-muscarinic agents are not tolerated or are not providing adequate response

- OnabotulinumtoxinA (Botox)
  - Indications: neurogenic bladder, overactive bladder, urinary incontinence when anti-muscarinic agents are not tolerated or are not providing adequate response

- Boxed Warning: risk of adverse effects if toxin spread beyond injection site (respiratory compromise and death)
  - Requires Risk Evaluation and Mitigation Strategy (REMS) and MedGuide
  - Injected into the detrusor muscle
### Other Medications

- **Dose:** 100 units (10 ml) given as 20 injections of 0.5 ml spaced 1 cm apart
- **Discontinue anti-platelet medications at least 3 days prior to injection**
- **Give antibiotics (excluding aminoglycosides) 1 - 3 days prior to treatment and 1 - 3 days after treatment**

### Other Medications

- **Absolute contraindications:** Infection, urinary retention, urinary tract infection
- **Level 2 drug interactions:** abobotulinumtoxinA, chloroquine, hydroxychloroquine, neuromuscular blockers, rimabotulinumtoxinB

### Over the Counter Medications

- **Azo Bladder Control with Go-Less**
  - Blend of pumpkin seed extract and soy germ
  - Pumpkin seed extract tones the muscles and maintains the strength of the detrusor and sphincter muscles

### Over the Counter Medications

- **Methionine**
  - Oral agent used to control odor, dermatitis and ulceration in incontinent adults
  - Creates an ammonia-free urine by raising pH of urine

- **Soy germ sustains the bladder muscle and pelvic floor**
  - Improvement seen in 2 to 6 weeks
  - **Dose:** One tablet twice daily
  - **$15.86 for 27 days of therapy**
  - Has good consumer reviews
**Over the Counter Medications**
- Take with food or with milk or other liquid
- Contraindications: Liver disease
- No significant drug interactions
- Adverse reactions: Large doses can exaggerate the toxemia of liver disease

**Over the Counter Medications**
- Dose: 200-500 mg by mouth up to 4 times a day after meals

**Off - Label Medications**
- Duloxetine - Do not use in liver failure patients
- Ephedra, Ma Huang
- Bovine collagen implant: for UI due to sphincter deficiency (Reserved for patients who have failed other therapy for at least 12 months)

**Off - Label Medications**
- Contraindications / Precautions: Bovine hypersensitivity (including hypersensitivity to bovine collagen products or dietary beef); history of severe allergies, undergoing desensitization to meat products; cystitis, urethritis, or other infection; autoimmune disease, systemic connective tissue disease; intravenous administration; bladder neck or urethral strictures; pregnancy; children

**Off - Label Medications**
- Drug Interactions: Immunosuppressive therapy, corticosteroids
- Adverse Reactions: Urinary retention, hematuria, injection site reaction, worsening incontinence, erythema, urticaria, abscess formation

**Off - Label Medications**
- Imipramine- reserved for patients with an additional indication such as depression or neuralgia
  - Midodrine
  - Propantheline
  - Pseudoephedrine
**Surgical Interventions**
- Sling procedures
- Bladder neck suspension
- Prolapse surgery
- Artificial urinary sphincter

**Non-Surgical Interventions**
- Urethral insert
- Pessary
- Bulking material injections
- Botulinum toxin type A (Botox)
- Nerve stimulators
- Bladder retraining

**Non-Surgical Interventions**
- Lifestyle changes
- Exercise
- Management of underlying or contributory factors:
  - Constipation
  - Hormone therapy
  - Diabetes
  - Functional

**Bladder Retraining Programs**
- Many studies over the years have supported the success of bladder retraining programs for both women and men experiencing symptoms of urge incontinence and urgency associated with overactive bladder (OAB)

**What Can You Do?**
- Assist patient with
  - Bladder / Void diary, as instructed by the nurse
  - Bladder training, as instructed by the nurse
  - To keep clear the path to the bathroom or bedside commode

**What Can You Do?**
- Following the individualized toileting plan established by their nurse or physician
- Proper application of containment (diapers, pads, condom catheters)
Exercises

- Walking
- Balance exercise
- Abdominal (core) muscle strengthening*
- Pelvic muscle exercise (Kegels)
- Can be done by both men and women


Kegel Exercises

- Kegel Exercises are for men and women
- Stop urination in midstream
- Slow down the flow of urine
- Don’t tense the muscles in your buttocks, legs, or abdomen, and don’t hold your breath

Kegel Exercises

- When you can slow or stop the flow of urine, you’ve successfully located these muscles

Perfect Your Technique

- With the bladder empty, tighten muscles like holding in gas
- Hold for 5 seconds
- Relax for 5 seconds
- Repeat 5 times
- Work up to 10 seconds hold, 10 seconds relax and repeat 10 times

Practice

- Repeat for up to 3 sets per day
- Don’t overdue
- Remember relaxation is as important as tightening!

What Can You Do?

- Encourage patient
  - There are ways to improve their continence the nurse and physician can provide
  - To drink most fluids earlier in the day
What Can You Do?

- Restrict drinking fluids 2 hours prior to bedtime
- To do Kegel exercises as instructed by the nurse

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