

**Urinary Incontinence:
Pathophysiology,
Assessment and
Treatment Options**

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Faculty

**Jacqueline Giddens, MSN, RN
Nurse Consultant
Bureau of Home & Community Services**

**Nancy Bishop, RPh
Assistant State Pharmacy Director
Alabama Department of Public Health**

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 That Cause Urinary Incontinence

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

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 Linked to Urinary Incontinence

- **Antidepressants: Amitriptyline, desipramine, nortriptyline**
 - **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

- **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, risperidone, 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 Chlorpheniramine
 - Significant degree of anticholinergic effects
- **Alpha agonists:** Pseudoephedrine
 - Tightens the urinary sphincter 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

Causes of Functional Incontinence Factors that Can Cause a Person Not to Get to the Bathroom in Time

- Cognitive
 - Stroke
 - Mentally Challenged

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

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 Anti - Muscarinic or Muscarinic Receptor Antagonists

- 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 / itchy eyes
 - Dry mouth*
 - Blurred vision
 - Constipation*
 - Decreased cognitive function
 - *Most common
 - Dyspepsia
 - Urinary retention

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 CYP3A4 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**

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**

Muscarinic Receptor Antagonists

- **Darifenacin (Enablex)**
 - **Indications: Overactive Bladder, Urinary Incontinence**
 - **In theory, has fewer anti - muscarinic side effects than others because of greater affinity for M₃ receptors**

Muscarinic Receptor Antagonists

- **Dose: Initially 7.5 mg by mouth daily**
 - **May increase to 15 mg if not taking potent CYP3A4 inhibitor**
- **Level 2 drug interaction: Conivaptan (Vaprisol), a CYP3A4 inhibitor**

Muscarinic Receptor Antagonists

- **Monitor when less potent CYP3A4 inhibitors are given: fluconazole, verapamil, diltiazem, grapefruit juice**

Muscarinic Receptor Antagonists

- **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

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

Muscarinic Receptor Antagonists

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

Muscarinic Receptor Antagonists

- **Adverse reactions:** nausea, vomiting, and dry mouth

Muscarinic Receptor Antagonists

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

Muscarinic Receptor Antagonists

- 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

Muscarinic Receptor Antagonists

- **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

Muscarinic Receptor Antagonists

- 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

Muscarinic Receptor Antagonists

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

Muscarinic Receptor Antagonists

- 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

Muscarinic Receptor Antagonists

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

Muscarinic Receptor Antagonists

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

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

Muscarinic Receptor Antagonists

- No level 1 drug interactions
- Severity of dry mouth less than oxybutynin

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

Other Medications

- Relaxes detrusor muscle via beta-3 AR activation, increasing bladder capacity during the urine storage phase
- Can be alternative to anti - muscarinics

Other Medications

- 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

Other Medications

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

Other Medications

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

Other Medications

- **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

Other Medications

- Adverse reactions: Urinary retention, UTI, hematuria, dysuria, injection site reaction, weakness in muscles adjacent to the injected muscle

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

- 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

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

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**

***Resource:**

<http://eldergym.com/lower-back-exercise.html>

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 overdo**
- **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**

Contact Information

**Jacqueline Giddens, MSN, RN
Nurse Consultant
Bureau of Home and Community Services
Jacqueline.Giddens@adph.state.al.us
(334) 206-5685**

**Nancy Bishop, RPh
Assistant State Pharmacy Director
Nancy.Bishop@adph.state.al.us
(334) 206-3014**

Alabama Department of Public Health