

Urinary incontinence in the elderly nursing essay

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The International Continence Society defines urinary incontinence (UI) as the involuntary loss of urine. In both men and women, age is a consistently reported risk factor for UI; however, it is not considered a normal consequence of aging. Overall, UI affects up to 30% of community-dwelling older adults and more than 50% of nursing home residents. It is about 2 to 3 times more common in women than in men until the age of 80, after which rates of UI are similar. Despite its high prevalence, up to one-half of cases may not be reported because individuals with UI may not seek medical intervention. Embarrassment and the perception that UI is an expected consequence of aging are common factors in lack of treatment. Urinary incontinence is categorized based on pathophysiology and clinical presentation. The four major categories are: (1) stress urinary incontinence (SUI); (2) urge urinary incontinence (UUI); (3) overflow incontinence; and (4) functional incontinence. Mixed types of incontinence are common and may complicate diagnosis and treatment because of overlapping symptoms. Studies have found that UI has a significant impact on psychological well-being and health care-related quality of life. Urinary incontinence may impair sexual function, restrict activities, interfere with interpersonal relationships, decrease self-esteem, increase caregiver burden, increase financial burden, and cause anxiety or depression. It is a common precipitant of institutionalization in older adults. Because of current demographic trends, UI is an increasingly common medical and socioeconomic problem.

Pathophysiology (B)Continence requires both an appropriately functioning lower urinary tract and the functional ability to use the bathroom. Function of the lower urinary tract is complicated and not completely understood. In

persons with normal physiology, activation of the sympathetic nervous system aids in closing the bladder neck; the bladder fills without leakage while the parasympathetic nervous system is inhibited. As the bladder fills and pressure rises, increased parasympathetic tone causes the detrusor muscle to contract and the bladder to empty. The major neurotransmitter involved in bladder contraction is acetylcholine, which acts at muscarinic receptors. Muscarinic 2 receptors are the most commonly found in the lower urinary tract; however, most UI drug therapy targets the M3 receptors, which are thought to have a larger role in bladder emptying. α -Adrenergic receptors are involved in urethral smooth muscle control. Several classifications of incontinence are based on the underlying problem in the lower urinary tract. Although the terms overactive bladder (OAB) and urge incontinence are used interchangeably, they describe two different conditions. Overactive bladder is a symptom syndrome that includes frequency, urgency, and nocturia. These can all occur with or without urge incontinence. Although the definitions are distinct, these two conditions are treated in the same manner. Table 1-1 outlines the main classifications of incontinence. Age-related changes within the urinary tract contribute to the increased prevalence of UI in the older population. These changes include decreases in bladder compliance, capacity, urethral closing pressure, and ability to postpone voiding; increases in involuntary detrusor contractions, post-void residual (PVR), and frequency of voiding; and weakened pelvic floor musculature (in women) and prostatic enlargement (in men). In addition to age-associated factors, chronic disease burden can contribute to urinary incontinence. Epidemiology/ Functional Impact (B)Prevalence

estimates of UI vary significantly by type of incontinence, definition of UI, and target populations, as well as with variations in study design. Urinary incontinence is reported to affect 30%–60% of women who are middle-aged and older. The National Overactive Bladder Evaluation (NOBLE) program estimated that nearly one-third of women over age 65 suffer from OAB, with about two-thirds of these cases associated with incontinence. Stress urinary incontinence affects about 13% of women age 19–44 years and 22% of women age 45–64 years. In older women, mixed incontinence is most common and accounts for about 50% of all cases. Risk factors for UI in women include age, race/ethnicity, childbirth, hysterectomy, oral hormone therapy, obesity and body mass index, cognitive impairment, mobility impairment, and diabetes. Control of the lower urinary tract system in women is directly affected by loss of pelvic organ support and loss of estrogen at menopause. Up to 70% of women with urinary incontinence relate the onset of symptoms with menopause. Both qualitative and quantitative changes in connective tissue of the urogenital tract are believed to contribute to SUI. Recent investigations suggest a higher prevalence of SUI in women who possess a collagen type I $\alpha 1$ Sp1 polymorphism; this polymorphism is also associated with increased risk of SUI in post-menopausal women. Because UI is more common in women, there are fewer studies evaluating the prevalence and epidemiology of UI in men. In men, UI has a later and more sudden onset than in women. The National Health and Nutrition Examination Study reported an overall UI prevalence in men of 4.5%; this prevalence increased to 16% in men 75 years of age or older. Factors associated with UI in men in this study were age, major depression,

benign prostatic hyperplasia (BPH), and hypertension. In other studies, associated risk factors were found to include lower urinary tract symptoms (LUTS), impaired mobility, and urethral surgery or irradiation. Despite surgical advances, UI remains a common complication for 12%–16% of men undergoing surgery for prostate cancer. Several comorbid conditions are associated with urinary incontinence in both men and women. Urinary incontinence is common after a cerebrovascular accident (CVA), with 40%–60% of patients experiencing UI during hospitalization immediately after CVA. The incidence significantly declines over several months; however, up to one-third of surviving patients continue to have urinary incontinence at 12 months after CVA. A case-controlled analysis noted a higher incidence of UI in community dwelling individuals with CVA (28%) than in those without stroke (20%). Risk factors for UI after stroke include hemiparesis, depression, impaired cognition, age greater than 75 years, dysphagia, visual field defect, and motor weakness. Other conditions resulting in impaired mobility and/or cognition (e. g., Parkinson disease, osteoarthritis, dementia) are associated with urinary incontinence. Urinary frequency and nocturia associated with congestive heart failure or peripheral venous insufficiency can contribute to urinary incontinence. Diabetes is an independent risk factor for the development of urinary incontinence because of polyneuropathy, changes in fluid intake, and diabetes-related functional impairment. Urinary incontinence has a significant socioeconomic impact. Individuals with urinary incontinence may suffer medical and quality of life consequences that compromise overall well-being. Urinary incontinence has been associated with increased risk of urinary tract infections; pressure ulcers; falls;

fractures; and sleep disturbance, which may lead to functional impairment and decline in overall health status. Urinary incontinence is a well-recognized risk factor for nursing home placement. Incontinence after a stroke adversely affects 2-year survival, disability, and functional outcome; it is also associated with a 4-fold increased risk of institutionalization at 1 year.

Psychological and social complications of UI include isolation, depression, anxiety, impaired sexual function, decreased work productivity, increased functional dependency, and increased caregiver burden. The annual direct cost of UI in the United States was about \$20 billion in 2000, with 50%–75% of the cost attributed to routine care such as incontinence pads and diapers, protective items, laundry, odor control, and skin care products. A major contributor to this figure is the cost of institutional care. Clinical Evaluation and Diagnosis (A) As many as 50% of patients with incontinence will not report symptoms to their health care provider. Screening is necessary to identify patients. Screening questions such as: " Do you ever leak urine when you do not want to?" and " Do you ever leak urine when you cough, sneeze, or laugh?" are now part of health care quality assessments through Medicare. Study data show that the degree to which patients are bothered by symptoms varies with the number and type of symptoms. The EPIC study was a population-based survey in Europe that aimed to estimate the prevalence of UI, results were published in 2006. Women older than 65 were more likely to report bothersome symptoms compared with men of the same age; however, men age 65 years or older were more likely to report bothersome symptoms than women of the same age. The reporting of bothersome symptoms increased with age for both men and women. Only

46% of respondents with OAB symptoms had discussed their symptoms with a health care provider, and only 8% were taking a prescription drug for OAB. The Agency for Healthcare Research and Quality recommends a basic diagnostic evaluation for UI. A thorough history should focus on specific symptoms, as well as quality of life and impact on the patient and caregivers. A bladder diary can be used to identify patterns and also to measure efficacy of treatment (Figure 1-1). An abdominal, rectal, and genital physical examination should be performed, and a urinalysis should be used to rule out infection or glucosuria. There is no need to treat asymptomatic bacteriuria; treatment has not been shown to decrease urinary incontinence, especially in patients in nursing homes. Some groups recommend PVRs be measured for all patients; however, this is an area of controversy. Postvoid residuals help determine the amount of urinary retention and should be performed in patients at high risk of urinary retention, including those who have diabetes, are taking anticholinergic drugs, have a neurologic disorder, or with symptoms of voiding difficulty or retention. A PVR of less than 100 mL is normal; greater than 200 mL is considered abnormal. Between those two values, the PVR must be interpreted with other information about the patient. Specialty testing (e. g., urodynamics) is not necessary during initial evaluation and treatment. Another important part of the initial evaluation of UI is to identify any reversible causes or contributors. Several chronic diseases and conditions can contribute to urinary incontinence. These include urinary tract infection, atrophic vaginitis, urinary tract surgeries (prostatectomy), constipation, uncontrolled diabetes, chronic venous insufficiency, delirium, and mobility restraint. Appropriate treatment for each

of these conditions should be implemented and incontinence reassessed. Several drugs can also cause or exacerbate urinary incontinence (Table 1-2). Management of UI (A)Nonpharmacologic Treatment (B)Nonpharmacologic and behavioral strategies are an important part of the comprehensive management of UI. Noninvasive lifestyle and behavioral interventions are the treatment of first choice in the elderly population. Advantages of behavioral interventions include low cost, absence of adverse effects, and ease of implementation. These interventions should be individually tailored; their effectiveness is largely dependent on patient motivation, functional capacity, and cognitive function. Lifestyle Modification (C)Lifestyle modifications for urinary incontinence include smoking cessation, caffeine and alcohol reduction, weight loss, and modified fluid intake. The relationship between caffeine intake and OAB appears to be dose dependent. Patients consuming greater than 400 mg/day of caffeine are 2.4 times more likely to experience detrusor instability. Reduction of caffeine intake should be undertaken gradually to avoid withdrawal symptoms. Data exist to suggest obesity and type 2 diabetes as independent risk factors for UI in women. In the Action for Health in Diabetes (Look AHEAD) trial, moderate weight loss was reported to reduce the incidence but not improve the resolution rate of UI among overweight women with type 2 diabetes (2012). Another recent study of UI in overweight women reported that weight loss decreased the cost of incontinence management by 81% and was independently associated with decreased frequency of incontinence. Modified fluid intake encourages reduction of fluid intake in the evening hours. Many patients will restrict fluid in an attempt to manage incontinence. Patient education regarding the

timing of fluid intake is critical; overall fluid restriction is not recommended because it may lead to dehydration and increased risk of urinary tract infections. Additional supportive measures include education about bladder health, use of absorbent products, and appropriate skin care. Environmental interventions such as toilet proximity, safe path to bathroom, raised toilet seats, grab bars, and toilet substitutes (e. g., urinals, commodes) are particularly useful for patients with functional incontinence. Behavioral Therapy (C) Patient-dependent behavioral therapies require functional capacity, learning ability, and patient motivation. Patients with functional disability or cognitive impairment require systematic toileting assistance, and they are often dependent on caregivers for successful implementation of behavioral interventions. The goal of behavioral interventions is to achieve a satisfactory voiding pattern. Patients with functional and cognitive deficits require toileting assistance and motivated caregivers to effectively implement behavioral strategies. Bladder training is an urge suppression technique that is effective in patients with intact cognition, adequate functional ability to toilet, and motivation to cooperate. The patient gradually increases toileting intervals by resisting or inhibiting the sensation of urgency. Patients learn to urinate according to a scheduled timetable rather than with the symptoms of urge. Distraction and relaxation techniques are employed to help delay voiding and allow development of increased bladder capacity. The goal interval is initially based on the patient's individual voiding habits. Intervals are increased by 15- to 30-minute increments per week until a voiding interval of 3-4 hours is achieved. Bladder diaries can be a useful adjunct to bladder training. The efficacy of bladder training has been

demonstrated in several studies with reduction in incontinence episodes. Regular voiding at timed intervals to avoid a full bladder or prevent involuntary bladder contractions is a useful behavioral strategy for all types of incontinence. Pelvic muscle rehabilitation (PMR), also referred to as Kegel exercises, is commonly used as a treatment strategy for SUI and UUI. Repetitive contraction and relaxation of the pelvic floor muscles is used to improve reflex inhibition of involuntary detrusor contractions and enhance the ability to voluntarily contract the external sphincter. In randomized clinical trials, PMR reduced episodes of UI by 54% to 75% compared with reductions of 6% to 16% in the placebo group. Some patients have difficulty identifying and isolating pelvic floor muscles. Biofeedback and vaginal weights are tools sometimes used to help patients correctly perform the exercises. Studies have failed to demonstrate a benefit of PMR combined with biofeedback or vaginal weights over PMR alone. Referral to a nurse specialist or physical therapist may be of benefit for the patient who is cognitively intact but has difficulty effectively performing the exercises. In summary, PMR is a safe but labor-intensive approach that requires a motivated and cooperative patient. Devices (C) Sacral nerve stimulation (SNS) has U. S. Food and Drug Administration (FDA) approval for use in the treatment of patients with severe refractory urge UI when behavioral management and medications fail or are not tolerated. In SNS, a generator device is inserted subcutaneously in the lower back or buttocks. A lead is attached to the S3 sacral nerve, and electrical stimulation results in decreased contraction of the detrusor muscle. Studies of SNS have shown significant decreases in the number of incontinence episodes and in the

number of incontinence pads used in up to 90% of patients. Efficacy was defined as at least 50% improvement in symptoms and quality of life at 12 months after the procedure. One small study of SNS in older patients reported efficacy in 48% of recipients. Patients with a higher number of daily incontinence episodes (greater than 10) are most likely to benefit. Surgical revision rates range from 3% to 24% and are attributed to lack of efficacy or infection. The extracorporeal magnetic innervation chair has FDA approval for use in the treatment of uncomplicated mild SUI. A low-intensity magnetic field is used to strengthen pelvic floor muscles. Treatments are generally given for 20 minutes twice weekly for a total of 8 weeks. Patients with good manual dexterity are candidates for intravaginal support devices or urethral occlusion inserts. These devices offer the option of temporary or occasional use and are suitable for patients with exercise-induced SUI. Pessaries are often employed in older women who have not responded to behavioral therapies. Insertion is performed by a health care provider, and the pessary can be removed for cleaning and reinserted every 4–6 weeks. Pessaries are suitable for temporary or long-term use. Monitoring for vaginal infection and ulceration are critical to the safe use of these devices. A study conducted in patients with SUI compared pessaries alone, behavioral treatment alone, or a combination of pessary and behavioral treatment. The reported patient satisfaction rate was greater than 50% for all treatment groups at 12 months. Urinary catheters are reserved for patients with chronic bladder emptying difficulty and elevated PVR. Catheters may also be useful as a temporary measure in patients with open skin that must be protected from urine. Severely or terminally ill patients with chronic UI who are bed-bound

may also be appropriate candidates for a urinary catheter. Invasive Treatments (C)Surgical management of SUI is common in the United States with more than 200, 000 procedures performed annually. Surgery is considered the most effective treatment in when SUI is accompanied by uterine prolapse. The Burch colposuspension procedure involves supporting the anterior vaginal wall to the Cooper ligament through a laparoscopic incision. In recent years, the midurethral mesh sling has replaced the Burch procedure as the new gold standard. The midurethral sling procedure employs transvaginal placement of a synthetic mesh below the midurethral area. The Burch procedure and the midurethral sling have comparable rates for cure and complications; however, the midurethral sling procedures offer the advantage of a less-invasive approach, shorter operative times, technical ease, and ability to be performed in the outpatient setting. Reported cure rates are 77% to 96%. Recent data suggest that the overall re-operation rate after SUI surgery is higher for the midurethral sling (13. 0%) compared with the Burch procedure (10. 8%). Periurethral injection of bulking agents (e. g., collagen) improves urethral closure in SUI and may be beneficial in mild cases of postprostatectomy SUI. High short-term cure rates are achieved; however, effectiveness is lost over time, and repeated interventions are often necessary. Reinjection may be associated with inflammatory reactions and scarring, which makes further treatment difficult. The use of bulking agents may be appropriate for patients with refractory SUI who have demonstrated sphincter incompetence based on urodynamic studies. Although not a first-line therapy, artificial urinary sphincters are the most effective treatment for intractable postprostatectomy SUI in men. Subjective

satisfaction rates reach 85%–95%; however, the risk of infection is high (1.8%–10%). Other potential complications include tissue atrophy resulting in worsening incontinence, urethral erosion, and device defects. These complications often necessitate re-operation or removal of the system, with device defects accounting for about one-half of all revision procedures.

Pharmacologic Treatment (B) Nonpharmacologic or behavioral therapy should always be implemented for patients with UI, but pharmacotherapy is often added to help alleviate symptoms. Pharmacotherapy does not cure UI. Drugs should not be implemented without the failure or addition of behavioral

therapies. Interestingly, few data support the combination of drugs and behavioral therapy over each separately. Antimuscarinics (C) The most

commonly prescribed UI drug class is muscarinic receptor blockers. These drugs are primarily used for UUI. Over the last 10 years there have been several additions to this class, with the hope that these new drugs would be more selective for muscarinic receptors in the bladder. This specificity was aimed at reducing the common anticholinergic adverse effects of these

medications. Comparative Efficacy and Tolerability (D) Oxybutynin remains

the gold standard by which other agents are measured. The immediate-release formulation does have significant anticholinergic effects, and it is

thought that the longer-acting formulations, as well as the topical and

transdermal formulations, may have fewer adverse effects. The oxybutynin extended-release formulation may reduce first-pass metabolism, decreasing the active metabolite N-desethyloxybutynin. This metabolite is thought to

cause many of the anticholinergic adverse effects. The oxybutynin

transdermal patch and gel also bypass first-pass metabolism. The only direct

comparison data available are for extended-release oxybutynin, which reduced discontinuation by 20% over oxybutynin immediate release. The oxybutynin transdermal patch must be applied every 3 or 4 days, whereas the gel must be applied daily. As a comparison of anticholinergic adverse effects, the rates of xerostomia with oxybutynin were 71% with immediate release, 29%–61% with extended release, 4%–10% with the transdermal patch, and 2%–12% with gel. The reported adverse event rates for other anticholinergic effects in the package inserts are listed in Table 1-3. In general, extended-release formulations cause dry mouth less often, and many of the anticholinergic adverse effects appear to be dose related. The risk of constipation appears to be greater in the higher dosage forms of some of the newer agents (i. e., solifenacin and darifenacin). There is no evidence that QT prolongation is a major adverse effect of the antimuscarinics when used at normal dosages. There is some evidence these agents may prolong QT intervals in higher dosages or overdose. Clinically it is important to note if a patient is on other QT-prolonging agents when initiating antimuscarinics because there may be a small additive effect. There is insufficient evidence to support other agents (e. g., tolterodine, fesoterodine, trospium) over oxybutynin in terms of better efficacy or tolerability. Solifenacin and darifenacin were believed to be uroselective agents when they were developed. However, the available data do not show that these agents are any better in terms of anticholinergic adverse effects, and they should not be chosen based on being uroselective. A recent systematic review evaluated the efficacy and tolerability of several antimuscarinic agents for UUI in women. This review included literature from 1966-2011 and only randomized

controlled trials were eligible. Of the 94 trials analyzed, antimuscarinics were found to have only a small benefit over placebo in achieving continence and improving UI symptoms. When all drugs were analyzed together, the absolute risk difference in continence was less than 20% (Shamliyan 2012). The drug class was also found to have a significantly higher discontinuation rate because of adverse effects than placebo. The lowest rates of discontinuation were with solifenacin 5 mg daily. More than 50% of patients had stopped treatment with their antimuscarinic at 1 year (Shamliyan 2012). Dry mouth was the most common adverse event reported in the analysis. The review also evaluated the trials that compared antimuscarinics to each other. Fesoterodine was found to be more effective than tolterodine, producing greater rates of continence, but it also had a higher discontinuation rate because of adverse effects. No difference in improvement of UI was found between oxybutynin and tolteridone, although treatment discontinuation rates for oxybutynin were greater. Overall, a small benefit in UI symptoms was seen with antimuscarinic drugs in comparison with placebo. None of the agents had demonstrated superiority on the basis of current evidence. Solifenacin 5 mg had the lowest discontinuation rate because of adverse effects and may be an option if other urge incontinence treatments have failed the patient. One of the major limitations of this analysis was that more than 80% of the patients included were women, reducing the generalizability of the conclusions to men. Because efficacy is similar across the antimuscarinic class, the choice of first-line agent is often influenced by cost, drug interactions, and patient comorbidities. Oxybutynin immediate release costs significantly less than most of the other agents.

Solifenacin and the extended-release and transdermal formulations of other agents may have fewer anticholinergic adverse effects, although this difference is small. These alternatives may be preferred, however, when the patient has comorbidities that make these adverse effects particularly problematic. Discontinuation rates do not typically differ with these formulations. Skin reactions may limit the use of the transdermal products as rates of pruritus and rash can be as high as 15% (Dmochowski 2002). The 2012 American Geriatrics Society Beers criteria lists the oral antimuscarinics as a class that exacerbates constipation and should be avoided unless no alternative is available. Drug interactions may also influence the choice of antimuscarinic. Tolterodine is metabolized by cytochrome P450 (CYP) 2D6 in most patients. Some patients have a genetic polymorphism that hampers metabolism through the 2D6 pathway. These poor metabolizers rely more on the CYP 3A4 pathway for metabolism. In patients that are taking potent CYP 2D6 or 3A4 inhibitors, the dosage of tolterodine should be reduced by 50%. Similarly, darifenacin is metabolized by CYP 2D6 and 3A4, but no formal dosage reductions are recommended for this drug. Fesoterodine and solifenacin are metabolized by CYP 3A4 and their maximum dosages with potent CYP 3A4 inhibitors are 4 mg and 5 mg, respectively. These agents should exert their effect within the first month patients are on the drug.. Follow-up should be done at this time to assess adverse effects and efficacy. Use with Cholinesterase Inhibitors and Patients with Dementia (D)Urinary incontinence is often seen in elderly patients with dementia. The antimuscarinic agents used to treat UUI directly oppose many drugs that treat dementia by increasing cholinergic transmission. Whether

antimuscarinics should be prescribed with cholinesterase inhibitors is controversial. Whether antimuscarinics should be prescribed in general to patients with baseline cognitive impairment has also been controversial. One overlooked issue is that cholinesterase inhibitors have the ability to increase or possibly even precipitate UI episodes. Although only minimal rates of UI are cited in the package inserts for donepezil (1%–3%), rivastigmine (not listed), and galantamine (<1%–2%), clinically this is an important issue to consider. One retrospective study looked at the possible cascade of being prescribed an antimuscarinic agent in response to an adverse effect from a cholinesterase inhibitor. The study looked at 44, 884 older adults, of whom 20, 491 were prescribed a cholinesterase inhibitor (95% donepezil). The results showed that 4. 5% of those prescribed a cholinesterase inhibitor were also prescribed an antimuscarinic agent. Another 3. 1% of those not on a cholinesterase inhibitor were prescribed one (Gill 2005). This increase was statistically significant. An important consideration in patients taking both a cholinesterase inhibitor and an antimuscarinic agent is to take a detailed history on when UI symptoms started or worsened in relationship to the addition of these drugs. A dose reduction or risk-benefit analysis of the cholinesterase inhibitor may be needed to improve UI. Dementia itself can worsen UI; this places an even larger burden on caregivers. Up to one-third of dementia patients are on both cholinesterase inhibitors and antimuscarinics. There is conflicting evidence on the extent to which antimuscarinics affect cognition or potentially reduce efficacy of cholinesterase inhibitors. A prospective cohort study of 3536 nursing home patients who were on a cholinesterase inhibitor found that 10. 6% were prescribed oxybutynin or

tolterodine in the 2-years study period. The authors found that using these two agents together created an additional 0.54 decrease in ADL points (0-28 scale) ($p=0.01$). The MDS-COGS score was used to assess cognitive decline, and this did not differ between groups (Sink 2008). Similarly, another randomized controlled trial in 50 female nursing home patients found no change in cognition when oxybutynin extended release was administered for 4 weeks (Lackner 2008). These two trials cannot be generalized to the community dwelling elderly adult because they were done in the nursing home population. The smaller changes may have more impact in the highly functional community dwelling elderly adult. Several case reports also show cognitive decline with antimuscarinics. There is no definitive evidence to say whether antimuscarinics should be used in patients with cognitive impairment or in patients on a cholinesterase inhibitor. Clinicians should consider the possible interactions carefully. If it is felt an antimuscarinic is necessary in these patients, cognitive function should be monitored after initiation of the drug and on a regular basis thereafter..

Use with Alpha Blockers (D)Men are underrepresented in trials of urinary incontinence drugs, constituting only 10%–25% of study subjects. Drugs used for UI are thought to have similar efficacy and tolerability in the male population. Although lower urinary tract symptoms of UUI and bladder outlet obstruction (BOO) or BPH are similar, the distinction must be made because the use of antimuscarinic agents in BPH can cause significant urinary retention. The use of alpha blockers concomitantly with antimuscarinics has become a subject of interest. In a few trials, this combination has demonstrated improvement in lower urinary tract symptoms and quality of life. For a detailed discussion

of the use of alpha blockers concomitantly with antimuscarinics, see the chapter on benign prostatic hyperplasia in this book. Duloxetine (C) Although duloxetine is approved in the Europe for use in SUI, this remains an off-label use in the United States. The 2012 European Association of Urology Guidelines approve offering duloxetine both men and women who would like symptom relief from SUI, giving this recommendation a Grade A evidence level. Trials in the United States for this indication are ongoing. A phase II trial with 553 women ages 18–65 years with SUI evaluated daily dosages of duloxetine 20–80 mg. The outcome measures, frequency of incontinence episodes, and quality of life were significantly better with duloxetine. There was a dose-dependent effect as well. A 2009 Cochrane review of studies comparing duloxetine versus placebo included 10 randomized controlled trials with 3944 adults with SUI. Trial duration was only 3–12 weeks, but the frequency of incontinence episodes was reduced by up to 50% with duloxetine compared with placebo (Mariappan 2005). It was not known whether this benefit could be sustained, but the available evidence suggested it was a good option for treatment of SUI. Duloxetine has demonstrated improvement in quality of life in several trials, with some patients seeing benefit within 2 weeks of initiation. The typical dose is 40 mg twice daily, and the most common adverse effect reported in most trials was nausea (4%–24%), possibly related to rapid dose escalation. Duloxetine is metabolized by CYP 2D6 and 1A2, and caution must be used with inhibitors of these two enzymes. In the 2012 American Geriatrics Society Beers Criteria, duloxetine is listed with other serotonin-norepinephrine reuptake inhibitors for use with caution in elderly patients because of the risk of

syndrome of inappropriate antidiuretic hormone or hyponatremia. Alpha Agonists (C)The use of alpha agonists for SUI is not as common now that duloxetine is considered a first-line agent. Some guidelines do not even list alpha agonists as an option for treatment anymore. The contraindications to use of these agents (i. e., hypertension, arrhythmia, coronary artery disease, myocardial infarction, hyperthyroidism, kidney failure, and narrow angle glaucoma) make these agents difficult to use. The adverse effects of hypertension, headache, anxiety, and insomnia make these agents even less attractive. Estrogens (C)Oral and topical estrogen therapy was thought to improve symptoms of SUI by increasing alpha receptors and local circulation. Both the Heart and Estrogen/Progestin Replacement Study (HERS) and the Women's Health Initiative Study showed increased urinary incontinence with the use of oral estrogens. In the HERS study, 39% of patients had worsening of incontinence, whereas only 27% in the placebo group had similar outcomes. Oral estrogen also carries risk of cardiovascular adverse events, possible worsening cognition, and increased breast cancer risk. Oral estrogen should not be routinely used for SUI. Topical estrogens can be used and doses for vaginal atrophy are recommended in this case. The 2012 European Association of Urology Guidelines also endorse topical estrogen as an option for SUI, with a Grade A level recommendation. The 2012 Beers Criteria recommend against the use of oral or transdermal patch estrogen in women for any reason. Botulinum Toxin (C)In 2011, the FDA approved labeling of onabotulinumtoxin A for use in patients with detrusor overactivity associated with a neurologic condition (e. g., spinal cord injury, multiple sclerosis) and inadequate response to anticholinergic therapy. The injections

are intradetrusor by cystoscopy. In pre-approval studies, the frequency of incontinence episodes at week 12 was decreased by 19.8% in the botulinumtoxin A group compared with 8.8% in the placebo group. One of the major risks with using botulinumtoxin A is acute urinary retention. Patients must be willing to undergo catheterization as part of this therapy. In the pre-approval trials, catheterization at any time was required by 30.6% of patients in the treatment group versus 6.7% in the placebo group. Prophylactic antibiotics should be given 1–3 days before the injection, again on the day of the injection, and 1–3 days after the injection. Amino glycosides cannot be used. Antiplatelet drugs also must be stopped 3 days before injection. The per-treatment dose is 200 units, and treatments should not be repeated any sooner than 12 weeks. The mean effect of the injection in the initial trials lasted 42–48 weeks. Mirabegron (C) Mirabegron, a new beta 3 adrenergic receptor agonist, was approved in mid 2012 for treatment of overactive bladder with urgency symptoms. Stimulation of the beta 3 receptor causes bladder relaxation during filling. At very high doses (i. e., 200 mg) there was some stimulation of the beta 1 adrenergic receptors, but overall mirabegron has low intrinsic activity for beta 1 or beta 2 receptors. The starting dose is 25 mg and can be titrated up to 50 mg if there is inadequate response at 8 weeks. Patients with a CrCl of 15–29 mL/minute/1.73m² or moderate liver disease should only receive the 25-mg dose. In pre-approval trials, mirabegron at 25 mg and 50 mg significantly decreased the number of incontinence episodes in 24 hours and the number of micturitions in 24 hours over placebo. Decreases were only in the 1 to 2 micturition range but were statistically significant. Mirabegron should be used with caution in

patients taking antimuscarinic therapy or in those who have bladder outlet obstruction because it can cause urinary retention. The most common adverse effect seen in initial trials was hypertension; healthy volunteers had a mean increase in blood pressure in of 3.5 mm Hg systolic and 1.5 mm Hg diastolic. Those patients with uncontrolled hypertension (i. e., greater than 180 mm Hg systolic or 110 mm Hg diastolic) should not take mirabegron. Adverse event rates for the 25 mg-dose were as follows: hypertension (11.3%), nasopharyngitis (3.5%), urinary tract infection (4.2%), and headache (2.1%). Mirabegron inhibits CYP 2D6 metabolism and caution should be used with other drugs that are 2D6 substrates or inhibitors. Mirabegron increases the area under the curve of digoxin by 27% when these are coadministered. The lowest dose of digoxin should be used, and monitoring should be continued regularly. When used concurrently, mirabegron increases warfarin concentrations as much as 9%, and warfarin dose adjustments may be needed. Mirabegron's place in therapy is yet to be determined. Patients with significant cardiovascular issues may not be good candidates for this agent. Cost is also yet to be determined but will likely significantly exceed that of other antimuscarinic agents. Those with cognitive impairment may be a target patient population for this agent if it is not cost prohibitive. Conclusion (A)Urinary incontinence has a large economic and functional impact and will become an even larger issue in the health care system as the population continues to age. Pharmacists can have a large effect on reducing this burden by reviewing the medication profiles of all patients with UI to identify potential reversible causes as well as evaluate for concurrent anticholinergic drugs. Pharmacists are in a prime position to

help guide choice of antimuscarinic in terms of cost, adverse effect profile, patient comorbidities, and administration. Discontinuation rates of antimuscarinics are high because of intolerable adverse effects. It is important for the pharmacist to counsel patients on what to expect from these agents and when they should see results. For patients seeing benefit, adjunctive treatment can be recommended to help with adverse effects such as constipation and dry mouth.

Self-Assessment Questions (A) Questions 1 and 2 pertain to the following case. R. Z. is a 70-year-old woman who presents with increased urinary frequency and a few episodes of urinary incontinence (UI) over the past few weeks. These episodes do not occur during periods of coughing, sneezing, or laughing. R. Z. recently lost her job and is uninsured. She was seen 4 weeks ago as a new patient in your family medicine clinic, and the following drugs were started: amlodipine 5 mg, calcium carbonate 500 mg/vitamin D 200 international units daily, alendronate 70 mg weekly, metformin 500 mg twice daily, and citalopram 10 mg daily. The only medication she was taking 4 weeks ago was hydrochlorothiazide 25 mg daily, which she has been taking for the past 3 years. Her medical history is significant for osteoporosis, diastolic heart failure, hypertension, type 2 diabetes, and depression. Laboratory test results from 4 weeks ago include: hemoglobin A1C 7.3%, SCr 1.1 mg/dL, and potassium 4.0 mEq/L. (Objective 2, 5; Domain 1; Task 1, 2, 3)

1. Which one of the following is the best intervention for R. Z.? A. Start duloxetine 40 mg twice daily. B. Start furosemide 20 mg daily. C. Stop amlodipine 5 mg daily. D. Stop hydrochlorothiazide 25 mg daily.

2. Four weeks later, R. Z. returns and her UI symptoms have not resolved. The symptoms have been

particularly bothersome when she has been out searching for a job. Which one of the following would be best to initiate in R. Z.? (Objective 1, 4; Domain 1; Task 1, 2, 3)A. Oxybutynin immediate release 2. 5 mg twice daily. B. Solifenacin 5 mg daily. C. Vaginal estrogen. D. Tolterodine extended release 2 mg daily. 3. A 62-year-old woman with urge urinary incontinence (UUI) comes to your clinic. She is taking mirtazapine 30 mg for depression, but her depression is not improving and her primary care physician wants to switch her to fluoxetine 10 mg daily. Which one of the following would be the best choice for this patient's UUI? (Objective 3, 4; Domain 1; Task 2, 3)A. Tolterodine. B. Oxybutynin. C. Trospium. D. Darifenacin. 4. In which one of the following patients would a post void residual (PVR) be most important as part of an initial evaluation for lower urinary tract symptoms and UI? (Objective 1, 2; Domain 1; Task 1, 2)A. A 36-year-old woman who has urine leakage with coughing. B. A 51-year-old man with type 2 diabetes who has urine dribbling and increased frequency. C. A 50-year-old woman with epilepsy who has urinary incontinence with seizures. D. A 45-year-old woman with burning upon urination and increased frequency. Questions 5 and 6 pertain to the following case. T. R. is a 67-year-old woman who has been started on mirabegron 25 mg daily for UUI. She has tried nothing else in the past for UI. Her medical history includes: heart failure, deep vein thrombosis (3 episodes), hypertension, hyperlipidemia, and generalized anxiety disorder. Her current home drugs are: carvedilol 6. 25 mg twice daily, lisinopril 10 mg daily, warfarin 3 mg daily, digoxin 0. 125 mg daily, pravastatin 40 mg daily, and escitalopram 10 mg daily. T. R.'s calculated CrCl is 60 mL/minute/1. 73m². Her sitting blood pressure today is 132/80 mm Hg, and her heart rate

is 76 beats per minute. 5. Which of the following would be best to counsel T. R. to monitor for upon initiation of mirabegron? (Objective 3, 4; Domain 1, Task 6) A. Cough, shortness of breath. B. Nausea, vomiting, and diarrhea. C. Swelling, warmth, redness in legs. D. Significant muscle weakness. 6. T. R. does well on the mirabegron. Two months later, she has been titrated to 50 mg daily and returns to the clinic for follow up. She reports a significant decrease in incontinence symptoms. There have been no changes in her medications or medical history. T. R.'s CrCl today is 45 mL/minute/1.73m². Blood pressure and heart rate today are 182/88 mm Hg and 86 beats per minute. Which one of the following is best to recommend regarding T. R.'s mirabegron dosage? (Objective 3, 4; Domain 1; Task 2, 3, 6) A. Continue at 50 mg daily. B. Reduce to 25 mg daily. C. Change to solifenacin 5 mg daily. D. Change to duloxetine 40 mg twice daily. 7. An 80-year-old community dwelling woman describes increased frequency and urgency with urination over the past 2 months. She denies pain with urination and does not have a fever today. Her medical history includes hypertension and constipation with two episodes of bowel obstruction. Her home drugs include: sennosides 8.6 mg three times daily, docusate 100 mg twice daily, lisinopril 5 mg daily, and aspirin 81 mg daily. She gets a rash with sulfa drugs. Her urinalysis is positive for bacteriuria. Which one of the following is best to initiate in this patient? (Objective 1, 2, 5; Domain 1; Task 2, 3) A. Ciprofloxacin 500 mg twice daily for 7 days. B. Oxybutynin extended release 5 mg daily. C. Sulfamethoxazole 800 mg/trimethoprim 160 mg twice daily for 10 days. D. Darifenacin 7.5 mg daily. Questions 8 and 9 pertain to the following case. P. Q. is a 62-year-old woman (height 60", weight 125 lb) who has been using

vaginal estrogen for 1 year for symptoms of stress urinary incontinence (SUI). This has been effective up until a couple of months ago when her symptoms began to return. Her medical history includes coronary artery bypass graft (times 1), hypertension, hyperlipidemia, osteoporosis, peripheral neuropathy, osteoarthritis, and depression. Her other medications include: aspirin 81 mg daily, metoprolol 25 mg twice daily, lisinopril 10 mg daily, rosuvastatin 10 mg daily, alendronate 70 mg weekly, calcium carbonate 500 mg/ vitamin D 200 units twice daily, gabapentin 300 mg twice daily, zolpidem 10 mg daily, ibuprofen 200 mg twice daily, and bupropion SR 150 mg twice daily. Blood pressure is 158/76 mm Hg, heart rate 72 bpm, serum creatinine 1.1 mg/dL. P. Q. would like to try other drug therapy for her UI because she and her husband travel a lot and it is bothersome on these trips. Her symptoms happen throughout the day, usually with coughing and sneezing.

8. Which one of the following would be best to recommend for P. Q.? (Objective 3, 4; Domain 1; Task 2, 3, 6)

A. Duloxetine 20 mg twice daily. B. Oral conjugated estrogens 0.3 mg/medroxyprogesterone 1.5 mg daily. C. Pseudoephedrine 30 mg three times daily. D. Solifenacin 5 mg daily.

9. Which of the following drugs is most likely exacerbating P. Q.'s incontinence? (Objective 5; Domain 1; Task 2, 6)

A. Gabapentin. B. Ibuprofen. C. Lisinopril. D. Zolpidem.

10. An 83-year-old man with Alzheimer disease is being cared for at home. Over the past 2 months, his wife has noticed that he has increased difficulty in making it to the restroom in time to urinate. He has stopped telling her when he needs to use the restroom, and she is not able to direct him to the restroom in the house quick enough. This is causing significant caregiver stress. His wife believes his cognition has started to

worsen over the past 6 months, and she is considering placing him in a nursing home. His home drugs include: terazosin 2 mg at bedtime, aspirin 81 mg daily, donepezil 10 mg at bedtime, lisinopril 5 mg daily, and venlafaxine extended release 75 mg daily. His mini mental status examination score is 15/30, and his geriatric depression scale is 3/15. Standing blood pressure is 110/70 mm Hg. Which one of the following is best to recommend for this patient? (Objective 1, 6; Domain 1; Task 2, 3, 6)A. Change terazosin to tamsulosin 0.4 mg daily. B. Start finasteride 5 mg daily. C. Change venlafaxine to duloxetine 20 mg twice daily. D. Stop donepezil 10 mg daily.

11. Three weeks ago, a 69-year-old man started taking oxybutynin immediate release 5 mg three times daily for UUI. His medical history is significant for severe psoriasis, bipolar disorder, and osteoarthritis. He noticed about 2 weeks ago that he is having significant dry mouth. The patient has tried several nonpharmacologic options recommended by his local pharmacist, but none have worked. The oxybutynin has been effective, and he is happy with the results on his UUI symptoms. Before taking it, he was having to use the bathroom 20 times during the day; he feels this number has been cut in half. However, he does not feel he will be able to take this medication much longer because of the dry mouth. Which one of the following is best to recommend for this patient? (Objective 3, 4; Domain 1; Task 2, 6)A. Oxybutynin extended release. B. Oxybutynin transdermal patch. C. Oxybutynin 10% gel. D. Oxybutynin immediate release 5 mg at bedtime.

12. A 45-year-old man with multiple sclerosis has problems with increased urinary frequency and urgency on a daily basis. He is currently taking no drugs for this problem. In the past he has tried oxybutynin

transdermal patch 3.9 mg/day and tolterodine immediate release 2 mg twice daily; neither resulted in significant improvement. The patient's PVR is 50 cc. Which one of the following is best to recommend for this patient?

(Objective 1, 2, 4; Domain 1; Task 2, 3) A. Darifenacin 7.5 mg daily. B.

Onabotulinumtoxin A 200 units intradetrusor injection. C. Mirabegron 25 mg daily. D. Oxybutynin immediate release 5 mg three times daily.

13. An 86-year-old man presents to the geriatrics clinic with new-onset dribbling and urinary urgency. His medical history includes: osteoporosis, insomnia, depression, and type 2 diabetes. His home drugs include: glipizide 5 mg twice daily, citalopram 20 mg daily, diphenhydramine 50 mg at bedtime, alendronate 70 mg weekly, cholecalciferol 1000 units daily, simvastatin 10 mg daily, aspirin 81 mg daily, and loratadine 10 mg daily. His PVR in clinic today is 310 cc. Recent laboratory test results include hemoglobin A1C 7.5% and SCr 1.2 mg/dL. Which one of the following is best to recommend for this patient? (Objective 1, 5; Domain 1; Task 2, 3) A. Start tamsulosin 0.4 mg

daily. B. Start tolterodine extended release 2 mg daily. C. Increase glipizide to 10 mg twice daily. D. Stop diphenhydramine 50 mg daily.

14. A 69-year-old woman complains of urine loss when she coughs, sneezes, or lifts something heavy. She uses an incontinence pad for protection. She was started on estrogen 0.625 mg daily at menopause, but this was discontinued 5 years ago. Her medical history is significant for six vaginal deliveries, osteoarthritis, and hypertension. Her home drugs include acetaminophen 1000 mg twice daily and lisinopril 10 mg daily. Which one of the following is best to recommend for this patient's UI? A. Pelvic floor rehabilitation. B.

Periurethral injection of a bulking agent. C. Pseudoephedrine 30 mg three

times daily . D. Conjugated estrogen 0. 625 mg daily. Questions 15 and 16 pertain to the following case. B. K. is a 65-year-old woman (height 5'5", weight 142 lbs) who complains of progressive difficulty with bladder control. When she feels like she needs to use the toilet, she is unable to get to the bathroom on time. She gets up two or three times a night to use the rest room. She has experienced a few "accidents" and is deeply embarrassed. When she coughs or sneezes, she loses small amounts of urine. Her home drugs include alendronate 70 mg weekly for osteoporosis, loratadine 10 mg daily for allergies, calcium carbonate 600 mg twice daily, vitamin D 1000 units daily, and ibuprofen 200 mg twice daily for osteoarthritis. She is a lifelong smoker and does not drink alcohol. She consumes one cup of coffee with each meal. Her pain scale rating is 2/10.

15. Which one of the following best explains B. K.'s symptoms of UI? A. Increased diuresis caused by caffeine consumption. B. Functional disability because of osteoarthritis. C. Decreased parasympathetic tone because of the aging process. D. Weakening of the pelvic floor musculature caused by loss of estrogen.

16. Which one of the following is the best intervention to recommend for B. K.? A. Absorbent pads. B. Switch to decaffeinated coffee. C. Weight loss. D. Fluid restriction.

17. A 72-year-old woman (height 5'6", weight 120 lbs) receives a diagnosis of UUI. She lives with her spouse, who is retired. She is mildly cognitively impaired and has mild limitations in performing activities of daily living. Her home drugs include donepezil 10 mg at bedtime and memantine 10 mg twice daily for moderate Alzheimer disease, pravastatin 40 mg in the evening for hyperlipidemia, levothyroxine 75 mcg daily for hypothyroidism, sertraline 50 mg daily for depression, and metoprolol 25 mg twice daily for

hypertension. She does not smoke or drink alcohol. She drinks only decaffeinated coffee. Which of the following is best to recommend for this patient's UUI? A. Discontinue donepezil 10 mg daily. B. Begin trospium 20 mg daily. C. Pelvic floor rehabilitation. D. Prompted toileting on a regular schedule.

18. A 76-year-old woman (height 5'2", weight 132 lbs) with a diagnosis of SUI continues to have frequent episodes despite attempts at pelvic floor rehabilitation with Kegel exercises. A pelvic examination reveals normal genitourinary anatomy. Her medical history is significant for hypertension, hyperlipidemia, insomnia, and chronic kidney insufficiency. Her home drugs include atorvastatin 40 mg daily, amlodipine 10 mg daily, aspirin EC 81 mg daily, and calcium 600 mg/vitamin D 400 units twice daily. Her blood pressure is 152/88 mm Hg and her pulse is 68 beats per minute. Her most recent laboratory results are: TC 182 mg/dL, LDL 111 mg/dL, sodium 135 mEq/L, chloride 101 mEq/L, potassium 3.8 mEq/L, serum glucose 88 mg/dL, and SCr 1.5 mg/dL. Which one of the following is best to recommend for this patient? A. Duloxetine 40 mg twice daily. B. Pessary placement. C. Sacral nerve stimulation. D. Midurethral sling.

19. Two months ago, a 67-year-old man presented to clinic with symptoms of urinary urgency, nocturia, and incontinence. His incontinence episodes are characterized by loss of large amounts of urine. His PVR was 45 mL and his prostate examination was normal. He was started on oxybutynin 5 mg three times daily. Today he returns to clinic for follow-up. He now reports that the symptoms of urgency are improved, but he continues to be incontinent of small amounts of urine both day and night. His PVR today is 315 mL. His medical history is significant for diabetes and congestive heart failure. His

other current drugs include glipizide extended release 10 mg daily, furosemide 20 mg QAM, potassium chloride 20 mEq daily, lisinopril 40 mg daily, metoprolol extended release 50 mg daily, and aspirin EC 81 mg daily. His laboratory results are as follows; A1C 7.6%, sodium 140 mEq/L, potassium 4.1 mEq/L, and SCr 0.9 mg/dL. Which one of the following best explains this patient's current symptoms? A. Increased urine volume secondary to furosemide. B. Increased intraabdominal pressure secondary to ACE inhibitor cough. C. Detrusor underactivity secondary to oxybutynin. D. Urethral relaxation secondary to β -blocker.

20. A 70-year-old man complains of difficulty with bladder control since undergoing radical prostatectomy for prostatic carcinoma 6 months ago. He reports excessive dribbling, and must wear a pad to prevent soiling of his clothing. Cystoscopy shows normal sphincter morphology. His medical history is significant for hypertension, constipation, glaucoma, gastroesophageal reflux disease, and insomnia. His current drugs include losartan 100 mg daily, senna 8.6 mg daily, timolol 0.5% one drop in both eyes twice daily, and pantoprazole 40 mg daily. His blood pressure is 153/82 mm Hg and his SCr is 1.1 mg/dL. Which one of the following is the best initial treatment for this patient? A. Duloxetine 40 mg twice daily. B. Pseudoephedrine 30 mg twice daily. C. Pelvic floor rehabilitation. D. Artificial urethral sphincter.

Explained Answers to Self-Assessment Questions

1. Answer C Both diuretics and dihydropyridine calcium channel blockers can contribute to urinary incontinence or increase frequency of urination. However, after chronic use of hydrochlorothiazide (Answer D) the main mechanism of its antihypertensive effects are no longer fluid loss. The effect of the hydrochlorothiazide on incontinence is

likely minimal after 3 years on the medication and it was started a long time ago. The amlodipine (Answer C) was recently added and can cause increases in urinary frequency because of inhibition of the contraction of smooth muscle resulting in possible urinary retention. The recent initiation and potential effects on urinary frequency make stopping amlodipine (Answer C) the best choice. Answer A is not correct as one should always try to correct potential medication of disease state causes of urinary incontinent before starting drug therapy. While fluid overload from heart failure can contribute to urinary incontinence, there is no evidence of that in this patient and she has diastolic heart failure which less frequently leads to significant fluid retention. 2. Answer ARZ does not have symptoms of SUI so vaginal estrogens (Answer C) would not be the best choice, as it will not address the type of incontinence symptoms she is having. Oxybutynin immediate release, tolterodine extended release, and solifenacin all have similar mechanisms of action and efficacy. They also all have fairly similar tolerability profiles, oxybutynin immediate release may have a higher risk of anticholinergic adverse effects however this patient is uninsured and it is the most affordable medication out of the whole class. Oxybutynin immediate release (Answer A) is the best choice in this case because it has efficacy and the patient will be able to afford to take the medication on a regular basis. Solifenacin (Answer B) and tolterodine extended release (Answer D) are both cost prohibitive in this case. 3. Answer C Fluoxetine inhibits both CYP 2D6 and 3A4. Darifenacin is a substrate of both CYP enzymes and concentrations of darifenacin may increase with fluoxetine use making Answer D not the best choice. Oxybutynin is a substrate of 3A4 and its metabolism may be reduced

leading to higher concentration. The manufacturer recommends oxybutynin be used with caution with fluoxetine making Answer B not the best choice. Tolterodine (Answer A) is a 2D6 and 3A4 substrate and its concentrations can also be increased by as much as 25%. Trospium (Answer C) is not metabolized extensively by the CYP enzymes and will be the least likely to be affected by the addition of fluoxetine. 4. Answer B While there is controversy as to whether everyone should receive a post void residual who reports with symptoms of urinary incontinence it is still prudent to target certain patients that are more at risk for urinary retention. Type 2 diabetes (Answer B) can cause autonomic neuropathy leading to urinary retention and a PVR should be done in all patients with diabetes. Answer A is likely SUI possibly because of recent childbirth and PVR would provide little value. Answer C is a patient with a neurological condition but epilepsy usually does not lead to retention as some other neurological conditions do (multiple sclerosis). In Answer D the patient presents with more symptoms of a urinary tract infection, which should be ruled out before progressing further with a urinary incontinence evaluation. 5. Answer B Mirabegron inhibits CYP 2D6 and has reported drug interactions with both warfarin and digoxin. Mirabegron is believed to increase the concentrations of both R and S isomers of warfarin by 4% and 9% respectively. Given it increase the concentration we would ask the patient to monitor for bleeding, not symptoms of a DVT (Answer C). Answer A is incorrect as mirabegron does not increase lisinopril levels (Answer A). Answer D is also incorrect as mirabegron does not increase pravastatin levels (Answer D). Digoxin levels can be increased by as much as 29% and digoxin toxicity should be monitored for (Answer B). 6. Answer

Mirabegron can increase blood pressure because of its potential beta agonism. In any patient with uncontrolled hypertension (systolic > 180mmHg and/or diastolic > 110mmHg) mirabegron should not be used. Continuing it, even at a reduced dose would not be the best choice (Answers A and B). The patient has symptoms of urge urinary incontinence which duloxetine has not been shown to be effective for (Answer D). In addition the patient is also on another serotonergic agent, escitalopram. Solifenacin (Answer C) would be the best choice as the pt has never been tried on an antimuscarinic agent before which is a reasonable first line choice in urge urinary incontinence. The patient does not have any contraindications to solifenacin therapy. Mirabegron is not first line for urinary incontinence of any type. 7. Answer B This patient has asymptomatic bacteria which should not be treated. Answer C would be incorrect for this reason, in addition she has a sulfa allergy. Answer A would also be incorrect, only if she had a symptomatic urinary tract infection would ciprofloxacin be first line for her lower urinary tract symptoms. Antimuscarinics are an option for this patient, as she seems to have urge urinary incontinence. She has significant constipation, which can be exacerbated by antimuscarinics, however the patient's quality of life is being significantly affected so a trial of one of these agents would be reasonable. Darifenacin 7.5 mg (Answer D) has double the rate of constipation (14%) of oxybutynin extended release 5 mg (7%). Oxybutynin extended release (Answer C) would be the best choice in this patient. 8. Answer A While topical estrogens are an option for stress urinary incontinence in women the oral combined estrogen/progesterone products (Answer B) are not. In several large, well designed trials they have shown to

actually increase incontinence symptoms in women. There are also multiple other risks associated with oral estrogen/progesterone therapy, including high cardiovascular risk as well as increased risk for breast cancer. Alpha agonists have been used in the past for SUI, although in clinical practice are being used less, mainly because of their adverse effect profile. This patient has elevated blood pressure and a significant cardiovascular history.

Pseudoephedrine (Answer C) would not be an appropriate medication in this patient. Solifenacin (Answer D) would be safe to use in this patient but is typically utilized in mixed incontinence (stress with urge) or urge incontinence alone. Duloxetine (Answer A) has been used extensively in Europe for SUI and is seeking FDA approval here with good results. This patient's antidepressant does not interact with the serotonergic actions of duloxetine as bupropion's mechanism of action is with nor epinephrine and dopamine. 9. Answer C All of these medications can make incontinence symptoms worse in some patients. Gabapentin (Answer A) and Ibuprofen (Answer B) can both cause pedal edema that will result in increased nighttime incontinence. This patient is not experiencing incontinence at night, her symptoms are mainly during the day. Zolpidem (Answer D) can contribute to incontinence by increasing sedation and confusion that leads to the inability to recognize needs to use the bathroom or not waking up to use the bathroom. This patient is not experiencing any noted sedation or problems with incontinence while sleeping. Angiotensin converting enzyme inhibitors, such as lisinopril (Answer C), can induce cough. This patient reports coughing is a cause of her incontinence episodes. It would be worthwhile to explore whether lisinopril is a potential cause of her cough. 10.

Answer DTK does not seem to be experiencing symptoms from benign prostatic hypertrophy or overflow incontinence at this time. Terazosin and tamsulosin (Answer A) do not have differences in efficacy so changing from one to the other would not likely provide a change in symptoms for this patient. Tamsulosin may have less incidence of orthostatic hypotension than terazosin but this patient's standing blood pressure is okay and no complaints of orthostatic hypotension. Finasteride (Answer B) is also indicated for incontinence symptoms related to BPH or overflow incontinence. Donepezil (Answer D) can exacerbate or cause incontinence in patients because of its cholinergic effects on the bladder. At this time TK's dementia is worsening significantly on donepezil and its efficacy may be in question. When evaluating patients with new or worsening incontinence one should always try to correct reversible causes of incontinence first. The best choice would be to remove the donepezil and see if symptoms improve before adding an antimuscarinic medication (Answer C solifenacin) that could worsen cognition. 11. Answer A Dry mouth is a common adverse effect of all antimuscarinic medications but there is some evidence the immediate release preparations have a higher incidence. Both extended release oxybutynin and transdermal preparation of oxybutynin bypass the first pass metabolism that creates a metabolite of oxybutynin that may cause more of the dry mouth with the immediate release product. The extended release and transdermal preparations also provide more even concentrations throughout the day lessening dry mouth. LK has severe psoriasis making the transdermal patch (Answer B) or gel (Answer C) not great options for this patient given these products should not be applied to broken skin. LK was

having symptoms throughout the day which have significantly improved with the medication. If his oxybutynin is switched to nighttime only (Answer D) his symptoms are likely to return during the day. This would have been a good option if his symptoms occurred mainly at night. The best option is oxybutynin extended release (Answer A) as this will possibly reduce the dry mouth and still provide him with 24 hour concentrations of oxybutynin in a formulation he can use.

12. Answer B Botulinumtoxin A was recently FDA approved for treatment of detrusor overactivity associated with a neurologic condition with inadequate response to anticholinergic therapy. BC has tried two different anticholinergic medications with minimal results. He would meet criteria to try botulinumtoxin A (Answer B). Mirabegron (Answer C) is a new medication that possibly could provide some benefit given its new mechanism of action. However its place in therapy is yet to be determined and it does not have FDA approval in neurologic conditions or any post marketing surveillance. Darifenacin (Answer A) is a new antimuscarinic agent that the others that the patient has tried. However in meta analyses and reviews of the class the newer agents have not been found to be better in terms of efficacy than the older agents. Oxybutynin immediate release (Answer D) is often considered to be the first line option in urge urinary incontinence because of its cost and comparable efficacy to other agents. However it is not necessary to have the patient fail this medication to use botulinumtoxin A since he has failed two others.

13. Answer D CL's post void residual is significantly elevated suggesting he has urinary retention possibly causing his urinary symptoms. While elevated blood sugars can cause urinary incontinence, CL's hemoglobin A1c is not significantly elevated so

increasing glipizide (Answer C) would not likely provide any impact on his symptoms. Tolterodine extended release (Answer B) could possibly increase his symptoms or make them worse as the antimuscarinic medications can cause urinary retention. CL's post void residual is already high. Tamsulosin (Answer A) may provide some benefit in this patient if his urinary retention is because of benign prostatic hyperplasia or bladder outlet obstruction.

However, meds that could be causing urinary retention should be discontinued before initiating new drug therapy. Diphenhydramine (Answer D) is an anticholinergic medication and CL is taking a high dose of it daily.

The diphenhydramine may be the cause of his urinary retention and should be stopped first. 14. Answer: A Based on her symptoms, this patient has SUI.

Pelvic floor rehabilitation is the best choice because behavioral strategies are the treatment of first choice in the elderly (Answer A is correct). PFR is effective in reducing episodes of incontinence and is inexpensive, non-invasive, and reasonably easy to implement. Periurethral injection of a bulking agent may be effective, but is invasive and effectiveness is lost over time (Answer B is incorrect). It is most useful for refractory SUI with demonstrated sphincter incompetence based on urodynamic studies.

Pharmacologic agents, such as pseudoephedrine would be second line (Answer C is incorrect). Furthermore, pseudoephedrine could interfere with the management of this patient's hypertension. In the WHI study, estrogen was associated with an increased risk of urinary incontinence (Answer D is incorrect). 15. Answer: D Based on this patient's presentation she has mixed SUI and UUI. Weakening of the pelvic floor musculature because of loss of estrogen is the best answer because hormone status directly affects control

of the lower urinary tract in women (Answer D is correct). Her pain scale rating is low and her ibuprofen dose is low as well suggesting low risk of functional impairment because of osteoarthritis (Answer B is incorrect). Aging increases parasympathetic tone (Answer C is incorrect). Excess caffeine consumption may increase diuresis and irritate the bladder, however, this patient has minimal daily caffeine consumption (Answer D is incorrect). 16. Answer: B Caffeine may increase diuresis and irritate the bladder. Eliminating caffeine is a lifestyle modification recommended for the management of urinary incontinence (Answer B is correct). Absorbent pads are useful, but should not supplant lifestyle modifications and behavioral therapies as primary treatment modalities (Answer A is incorrect). This patient is not overweight or diabetic, therefore studies would not support weight loss as a therapeutic intervention (Answer C is incorrect). Fluid restriction may precipitate dehydration or increase risk for urinary tract infections (Answer D is incorrect). Patient should be encouraged to modify fluid intake patterns, but not to restrict overall fluid intake. 17. Answer: D Based on this patient's history, she suffers from moderate cognitive impairment. Behavioral interventions are first line for treatment of UI in the elderly and a patient with moderate cognitive impairment would require caregiver assistance to participate in behavioral methods. Toileting on a regular schedule, prompted by a caregiver represents the simplest behavioral intervention for a cognitively impaired patient (Answer D is correct). Donepezil may precipitate or exacerbate incontinence via cholinergic stimulation of the bladder, however, this patient is living independently and is functional for most of her ADLs and many of her IADLs.

Withdrawal of donepezil may precipitate cognitive step-down which could contribute to her urinary dysfunction (Answer A is incorrect). It is reasonable to leave her on donepezil and use prompted toileting to manage her symptoms. Drug therapy with an antimuscarinic agent, such as trospium, constitutes a second line intervention and would likely increase cognitive impairment (Answer B is incorrect). Pelvic floor rehabilitation requires a relatively cognitively intact and motivated patient and therefore would be inappropriate in this case (Answer C is incorrect). 18. Answer: BCM has failed behavioral interventions for SUI with pelvic floor rehabilitation. Pessary placement is often employed for the treatment of SUI in older patients who fail behavioral therapy since it is less invasive than surgery (Answer B is correct). Duloxetine is not recommended for use in patients with CrCl < 30 mL/minute/1.73m² (Answer A is incorrect). Sacral nerve stimulation is an implantable device beneficial in severe refractory UUI (Answer C is incorrect). This patient has normal genitourinary anatomy and the midurethral sling is a surgical procedure most effective for patients with stress UI caused by uterine prolapse (Answer D is incorrect). 19. Answer: C With a PVR of 315 mL, this patient has significant urinary retention and symptoms are likely caused by overflow. Detrusor underactivity and urinary retention are potential complications associated with antimuscarinic agents such as oxybutynin (Answer C is correct). Increase urine volume with furosemide, increased intraabdominal pressure caused by ACE cough, and urethral relaxation secondary to beta blocker may all contribute to incontinence, but cannot account for high post void residual (Answer A, Answer B, and Answer D are incorrect). 20. Answer: C Based on the patient's

history and presentation he has SUI caused by external sphincter dysfunction after prostatectomy. Urinary incontinence is a common transient problem after prostate surgery. Pelvic floor rehabilitation is the preferred initial treatment because of ease of implementation, non-invasiveness, and low cost (Answer C is correct). The level of evidence to support drug therapy is less than that supporting behavioral interventions or surgery (Answer A and Answer B are incorrect). Duloxetine and pseudoephedrine may exacerbate insomnia. Pseudoephedrine may interfere with blood pressure control. The artificial urethral sphincter is the gold standard for the treatment of SUI in men, however, it is reserved for patients with persistent SUI failing conservative treatment or when the external sphincter denervation or structural damage is present and prognosis for spontaneous recovery is poor (Answer D is incorrect).