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AN OVERVIEW OF OAB

Including evaluation of and management approaches for overactive bladder (OAB)

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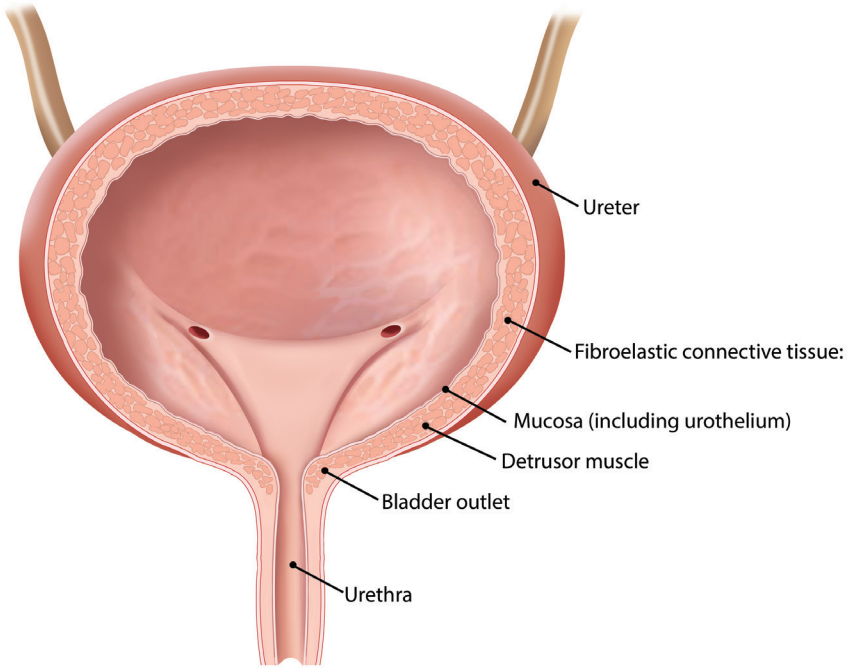
THE BLADDER:
Anatomy and Normal Function

BLADDER ANATOMY: A REFRESHER

The bladder wall has 3 layers[1]

- Internal layer (*mucosa*)—the epithelium, which appears smooth when the bladder is full, but contracts into folds when the bladder empties
- Middle layer (*detrusor muscle*)—the detrusor muscle, which is responsible for emptying the bladder
- External layer (*fibroelastic connective tissue*)—this layer expands with the distention of the bladder



The detrusor is the muscular layer of the bladder[1,2]

- It also has 3 layers, with intermingled smooth muscle fibers arranged into inner and outer longitudinal layers and a middle circular layer
- The changes in the thickness and organization of the detrusor layer may contribute to the bladder's ability to accommodate increasing volumes of urine
- Micturition depends on the contraction of the neurally mediated detrusor

Adequate storage depends on a relaxed bladder and a closed outlet, while efficient voiding depends on an adequate bladder contraction coordinated with relaxation of the bladder outlet[3]

References: 1. Chung BI, Sommer G, Brooks JD. Anatomy of the lower urinary tract and male genitalia. In: Wein AJ, Kavoussi LR, Novick AC, Partin AW, Peters CA, eds. *Campbell-Walsh Urology.* 10th ed. Philadelphia, PA: Elsevier Saunders; 2012:33-70. **2.** Yoshimura N, Chancellor MB. Physiology and pharmacology of the bladder and urethra. In: Wein AJ, Kavoussi LR, Novick AC, Partin AW, Peters CA, eds. *Campbell-Walsh Urology.* 10th ed. Philadelphia, PA: Elsevier Saunders; 2012:1786-1833. **3.** Wein AJ. Pathophysiology and classification of lower urinary tract dysfunction: overview. In: Wein AJ, Kavoussi LR, Novick AC, Partin AW, Peters CA, eds. *Campbell-Walsh Urology.* 10th ed. Philadelphia, PA: Elsevier Saunders; 2012:1834-1846.

BLADDER ANATOMY: A REFRESHER (CONT'D)

The bladder serves 2 main functions[1]

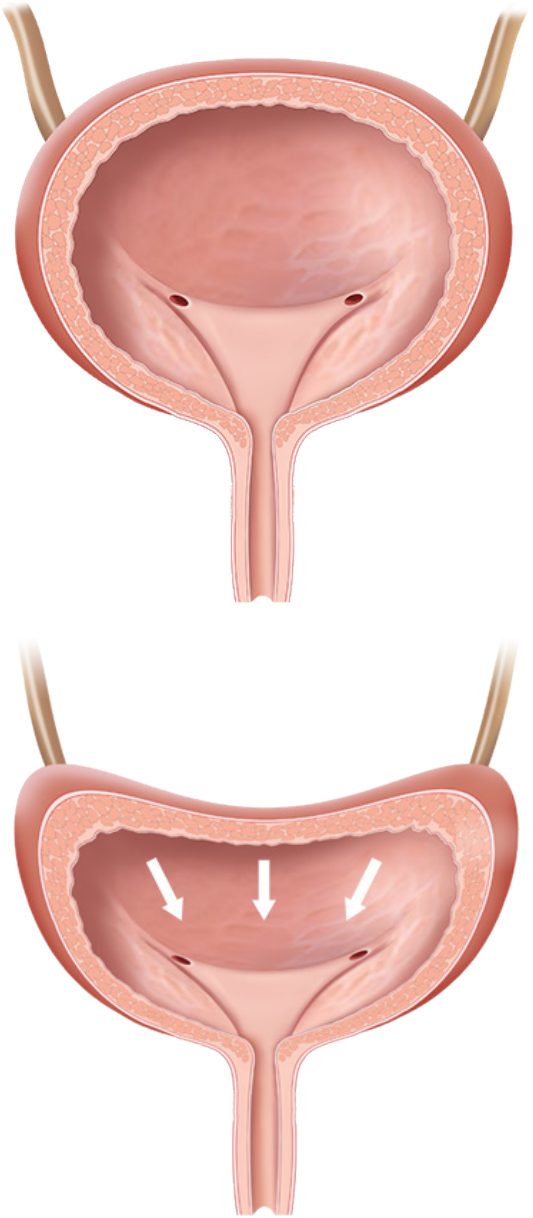
- To **store** urine
- To **void** urine

Filling/storage phase[1]

- This phase makes up the majority of the micturition cycle
- The bladder relaxes to store urine
- The urinary sphincter closes with high resistance to stop urinary flow

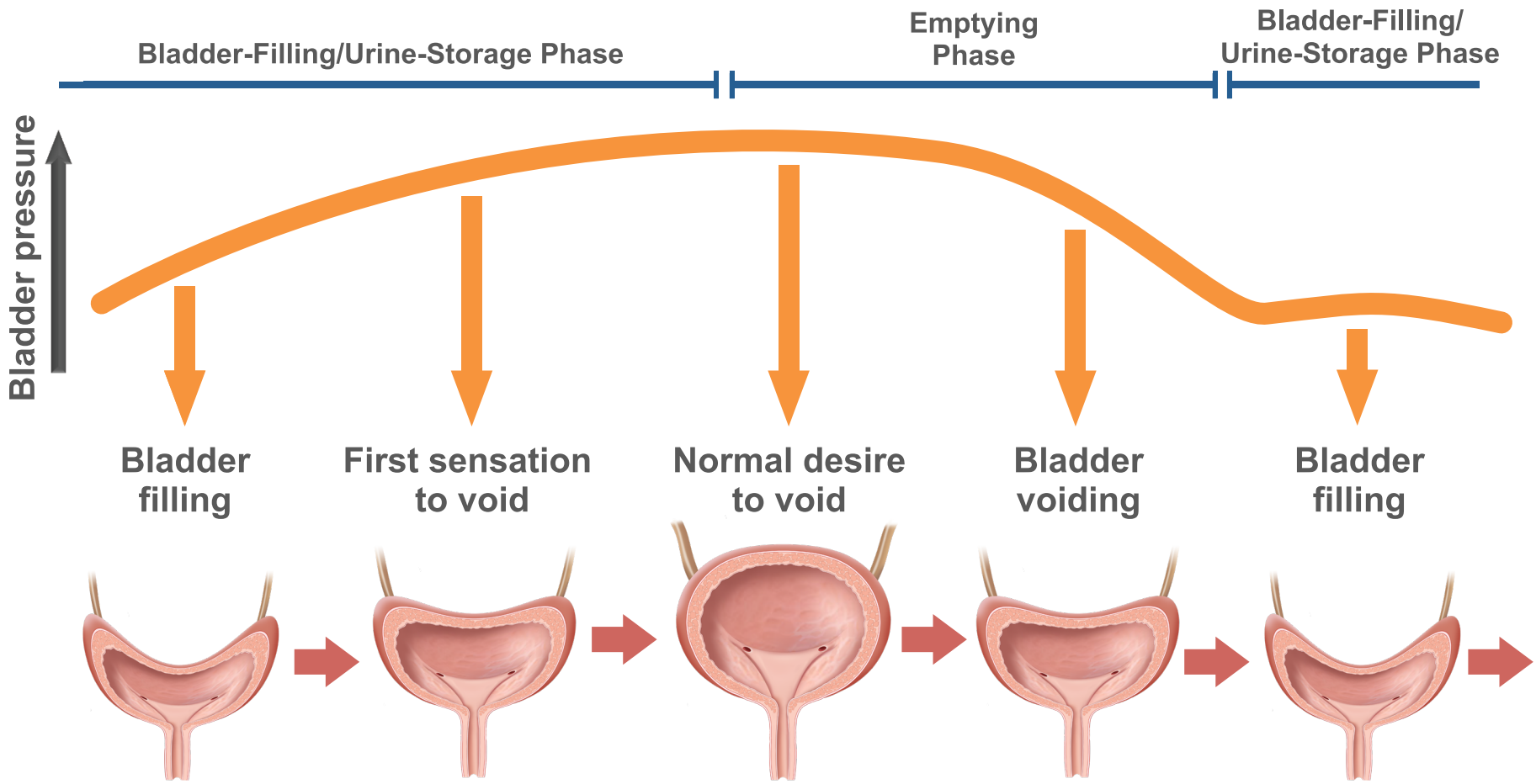
Emptying/voiding phase[1]

- The bladder contracts to void urine
- The urinary sphincter opens to allow urinary flow



Reference: 1. Chu FM, Dmochowski R. Pathophysiology of overactive bladder. *Am J Med.* 2006;119(3):3S-8S.

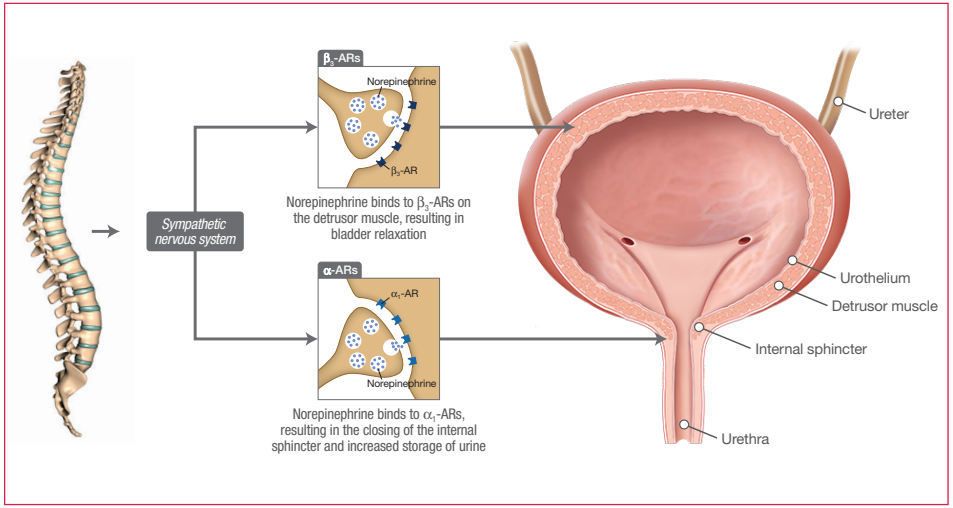
BLADDER FUNCTION: STORAGE AND VOIDING[1]

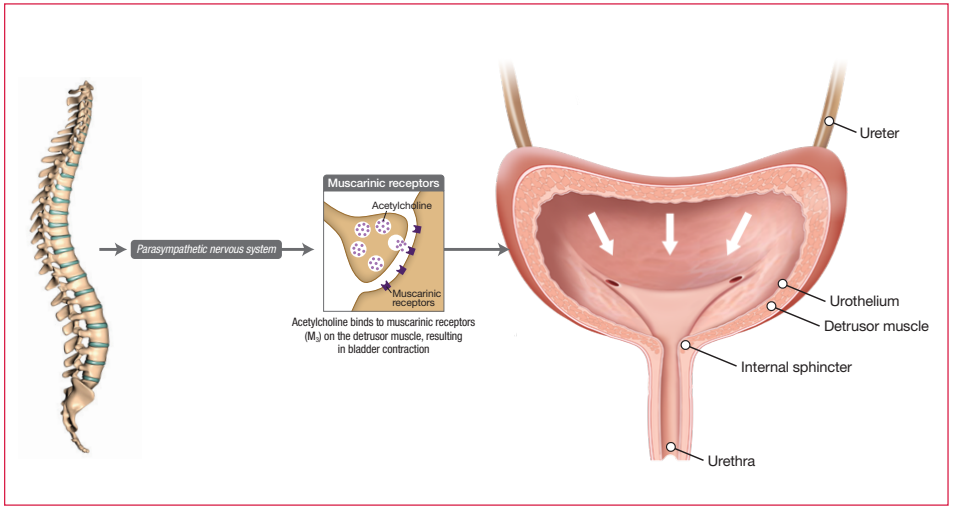


Reference: 1. Chu FM, Dmochowski R. Pathophysiology of overactive bladder. *Am J Med.* 2006;119(3):3S-8S.

NEUROLOGIC CONTROL OF THE BLADDER: THE AUTONOMIC NERVOUS SYSTEM[1]

- Regulation of bladder storage and voiding involves both sympathetic and parasympathetic control[1]
- Storage and voiding of the bladder are primarily regulated by 2 neurotransmitters—norepinephrine and acetylcholine—respectively[1-4]
- Norepinephrine, released from the sympathetic nerves, activates certain adrenergic receptors—β_3-ARs and α_1-ARs—in the bladder to relax the detrusor muscle and close the internal sphincter[1,4-6]
- Muscarinic receptor function is mediated by acetylcholine which controls the contraction of the detrusor muscle and relaxation of the internal sphincter muscle to facilitate voiding[1,4,7]





References: 1. Fowler CJ, Griffiths D, de Groat WC. The neural control of micturition. *Nat Rev Neurosci.* 2008;9(6):453-466. **2.** Andersson KE. Advances in the pharmacological control of the bladder. *Exp Physiol.* 1999;84(1):195-213. **3.** Mansfield KJ, Liu L, Mitchelson FJ, Moore KH, Millard RJ, Burcher E. Muscarinic receptor subtypes in human bladder detrusor and mucosa, studied by radioligand binding and quantitative competitive RT–PCR: changes in ageing. *Br J Pharmacol.* 2005;144(8):1089-1099. **4.** Andersson KE. Pharmacology of lower urinary tract smooth muscles and penile erectile tissues. *Pharmacol Rev.* 1993;45(3):253-308. **5.** Chancellor MB, Yoshimura N. Neurophysiology of stress urinary incontinence. *Rev Urol.* 2004;6(Suppl 3):S19-S28. **6.** Yamaguchi O. β_3-adrenoceptors in human detrusor muscle. *Urology.* 2002;59(5 Suppl 1):25-29. **7.** Chess-Williams R. Muscarinic receptors of the urinary bladder: detrusor, urothelial and prejunctional. *Auton Autacoid Pharmacol.* 2002;22(3):133-145.

AUTONOMIC NERVOUS SYSTEM: THE SYMPATHETIC DIVISION

The *sympathetic* division facilitates storage via activation of β-receptors on the bladder body and via activation of α-receptors in the bladder base and outlet[1]

- Bladder *storage* makes up the majority of the micturition cycle[2]

Norepinephrine, released from the sympathetic nerves, activates β_3-ARs and α_1-ARs in the bladder to relax the detrusor muscle and close the internal sphincter[1,3-5]

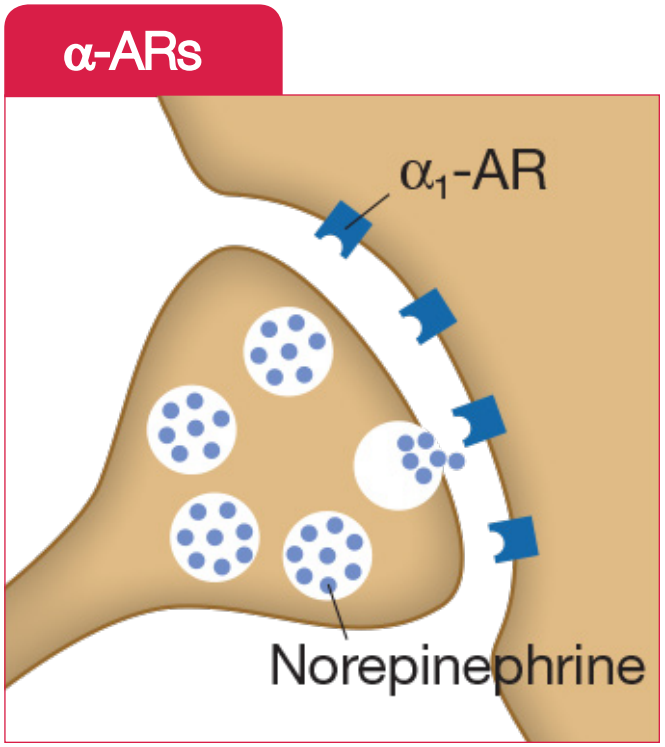
- Three different types of β-ARs are expressed in the human bladder: β_1-AR, β_2-AR, and β_3-AR. In an experiment to determine β-AR subtype expression, β_3-AR was found to make up 97% of the total β-AR messenger RNA (mRNA) in bladder tissues. The β_1-AR and β_2-AR subtypes make up 1.5% and 1.4% of the total β-AR mRNA, respectively[1,3-5]
- Both α_1-ARs and α_2-ARs are expressed in the lower urinary tract in humans.[4] Activation of noradrenergic pathways contracts the urethra to maintain continence at the onset of the storage phase of micturition.[6] Although expressed in the bladder to a lesser degree than β-receptors, α_1 predominates in the bladder neck[7]

References: 1. Fowler CJ, Griffiths D, de Groat WC. The neural control of micturition. *Nat Rev Neurosci.* 2008;9(6):453-466. **2.** Chu FM, Dmochowski R. Pathophysiology of overactive bladder. *Am J Med.* 2006;119(3):3S-8S. **3.** Yamaguchi O. β_3-adrenoceptors in human detrusor muscle. *Urology.* 2002;59(5 Suppl 1):25-29. **4.** Andersson KE. Pharmacology of lower urinary tract smooth muscles and penile erectile tissues. *Pharmacol Rev.* 1993;45(3):253-308. **5.** Chancellor MB, Yoshimura N. Neurophysiology of stress urinary incontinence. *Rev Urol.* 2004;6(Suppl 3):S19-S28. **6.** Conley RK, Williams TJ, Ford APDW, Ramage AG. The role of α_1-adrenoceptors and 5-HT_{1A} receptors in the control of the micturition reflex in male anaesthetized rats. *Br J Pharmacol.* 2001;133(1):61-72. **7.** Andersson KE. Advances in the pharmacological control of the bladder. *Exp Physiol.* 1999;84(1):195-213.

AUTONOMIC NERVOUS SYSTEM: THE SYMPATHETIC DIVISION (CONT'D)

Expression of α-ARs in the bladder

- Both α_1-ARs and α_2-ARs are expressed in the lower urinary tract in humans[1]
  - Activation of noradrenergic pathways contracts the urethra to maintain continence during the storage phase of micturition[2]
  - α_1 predominates in the bladder neck[3]
- Norepinephrine binds to α_1-ARs, which are expressed in the urethra, resulting in the closing of the internal sphincter and an increase in urine volume[4]
  - Contraction of the internal sphincter is mediated by both the sympathetic and pudendal nerves

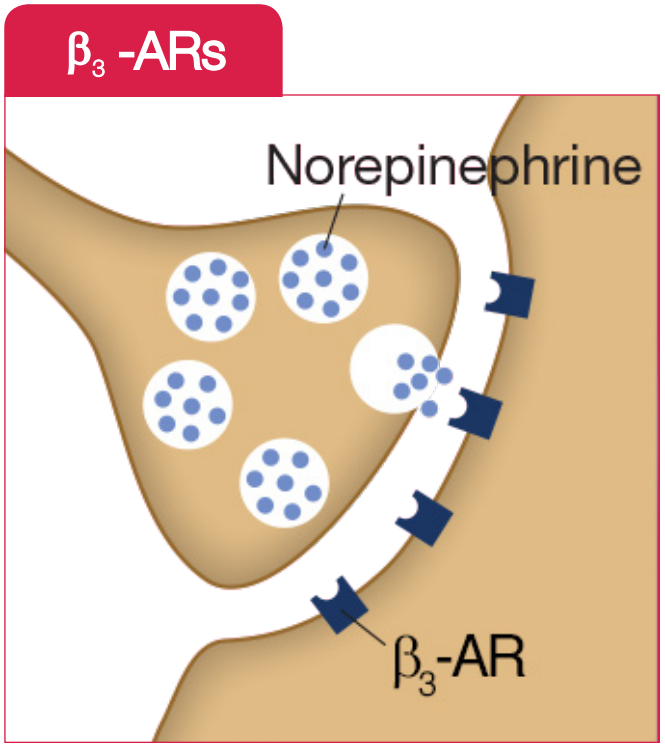


References: 1. Andersson KE. Pharmacology of lower urinary tract smooth muscles and penile erectile tissues. *Pharmacol Rev.* 1993;45(3):253-308. **2.** Conley RK, Williams TJ, Ford APDW, Ramage AG. The role of α_1-adrenoceptors and 5-HT_{1A} receptors in the control of the micturition reflex in male anaesthetized rats. *Br J Pharmacol.* 2001;133(1):61-72. **3.** Andersson KE. Advances in the pharmacological control of the bladder. *Exp Physiol.* 1999;84(1):195-213. **4.** Fowler CJ, Griffiths D, de Groat WC. The neural control of micturition. *Nat Rev Neurosci.* 2008;9(6):453-466.

AUTONOMIC NERVOUS SYSTEM: THE SYMPATHETIC DIVISION (CONT'D)

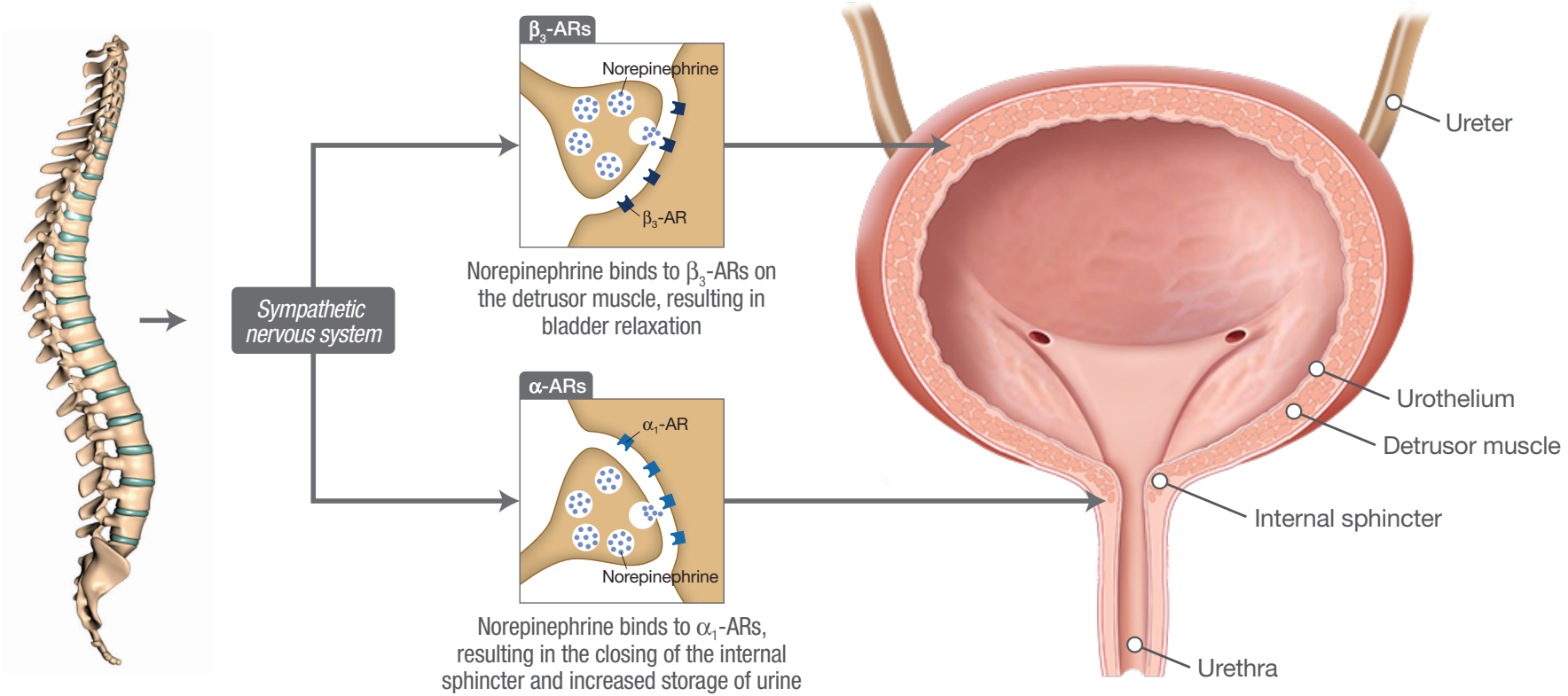
Expression of β-ARs in the bladder

- Sympathetic nerves determine the duration of the urine storage phase during the micturition cycle[1]
  - Norepinephrine released from sympathetic nerves activates β_3-AR in the human detrusor muscle to relax the bladder
- All 3 β-ARs are expressed in the human bladder, but β_3-messenger RNA (mRNA) predominates[2]
  - The β_1-AR and β_2-AR subtypes make up 1.5% and 1.4% of the total β-AR mRNA, respectively
- While β-ARs are expressed in the detrusor muscle, they are also found in the urothelium, which contributes to the regulation of bladder function[3,4]
  - During the storage phase, the urothelium stretches in tandem with the bladder wall when the bladder starts filling with urine



References: 1. Chu FM, Dmochowski R. Pathophysiology of overactive bladder. *Am J Med.* 2006;119(3):3S-8S. **2.** Yamaguchi O. β_3-adrenoceptors in human detrusor muscle. *Urology.* 2002;59(5 Suppl 1):25-29. **3.** Otsuka A, Shinbo H, Matsumoto R, Kurita Y, Ozono S. Expression and functional role of β-adrenoceptors in the human urinary bladder urothelium. *Naunyn Schmiedebergs Arch Pharmacol.* 2008;377(4-6):473-481. **4.** De Groat WC. The urothelium in overactive bladder: passive bystander or active participant? *Urology.* 2004;64:7S-11S.

AUTONOMIC NERVOUS SYSTEM: THE SYMPATHETIC DIVISION[1] (CONT'D)



Reference: 1. Fowler CJ, Griffiths D, de Groat WC. The neural control of micturition. *Nat Rev Neurosci.* 2008;9(6):453-466.

AUTONOMIC NERVOUS SYSTEM: THE PARASYMPATHETIC DIVISION

The *parasympathetic* division primarily mediates bladder contraction[1]

- Bladder *voiding* is primarily regulated by this division

Muscarinic receptors, a component of the parasympathetic nervous system, are activated by acetylcholine[2-7]

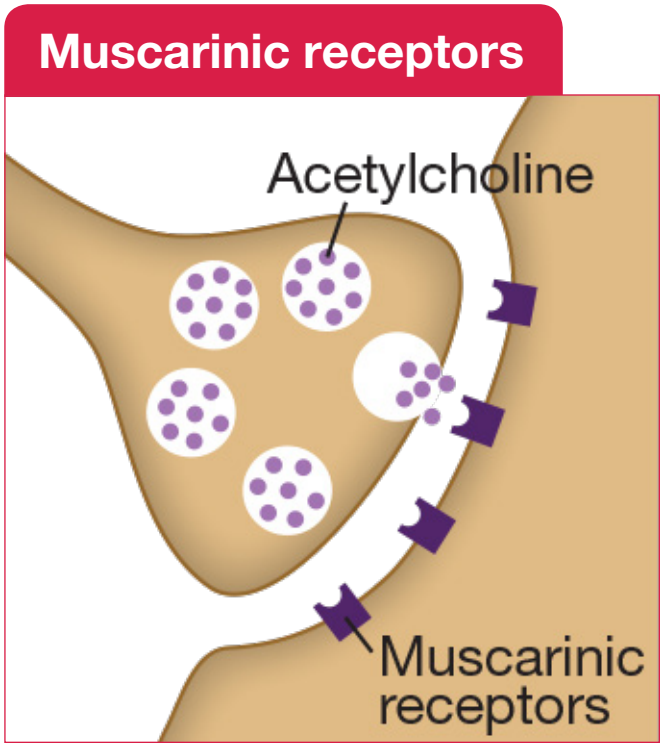
- There are 5 subclasses of muscarinic receptors: M_1, M_2, M_3, M_4, and M_5[2]
- The muscarinic receptors can be found in urothelial cells[3-4]
  - M_2 and M_3 are the predominant muscarinic receptors found in the bladder[5]
  - M_3-receptors are important for normal bladder contraction, while M_2-receptors may play a more prominent role in certain disease states (demonstrated *in vitro*)[6]
  - Binding of acetylcholine to M_3-receptors on the detrusor muscle activates a signaling pathway that leads to bladder contraction and voiding[7]

References: 1. Fowler CJ, Griffiths D, de Groat WC. The neural control of micturition. *Nat Rev Neurosci*. 2008;9(6):453-466. **2.** Andersson KE. Advances in the pharmacological control of the bladder. *Exp Physiol.* 1999;84(1):195-213. **3.** Otsuka A, Shinbo H, Matsumoto R, Kurita Y, Ozono S. Expression and functional role of β-adrenoceptors in the human urinary bladder urothelium. *Naunyn Schmiedebergs Arch Pharmacol.* 2008;377(4-6):473-481. **4.** Mansfield KJ, Liu L, Mitchelson FJ, Moore KH, Millard RJ, Burcher E. Muscarinic receptor subtypes in human bladder detrusor and mucosa, studied by radioligand binding and quantitative competitive RT-PCR: changes in ageing. *Br J Pharmacol.* 2005;144(8):1089-1099. **5.** Yamaguchi O, Shishido K, Tamura K, Ogawa T, Fujimura T, Ohtsuka M. Evaluation of mRNAs encoding muscarinic receptor subtypes in human detrusor muscle. *J Urol.* 1996;156(3):1208-1213. **6.** Chess-Williams R, Chapple CR, Yamanishi T, Yasuda K, Sellers DJ. The minor population of M_3-receptors mediate contraction of human detrusor muscle *in vitro. J Auton Pharmacol.* 2001;21(5-6):243-248. **7.** Andersson KE. Pharmacology of lower urinary tract smooth muscles and penile erectile tissues. *Pharmacol Rev.* 1993;45(3):253-308.

AUTONOMIC NERVOUS SYSTEM: THE PARASYMPATHETIC DIVISION (CONT'D)

Muscarinic receptors play an important role in bladder contraction

- Muscarinic receptors can be found on urothelial cells[1,2]
- M_2- and M_3-receptors are the predominant muscarinic receptors found in the bladder[3-5]
  - Binding of acetylcholine to M_3-receptors on the detrusor muscle activates a signaling pathway that leads to bladder contraction and voiding
  - M_3-receptors appear to be important for normal bladder contraction, with M_2-receptor activation serving a more prominent role in certain disease states (demonstrated *in vitro*)



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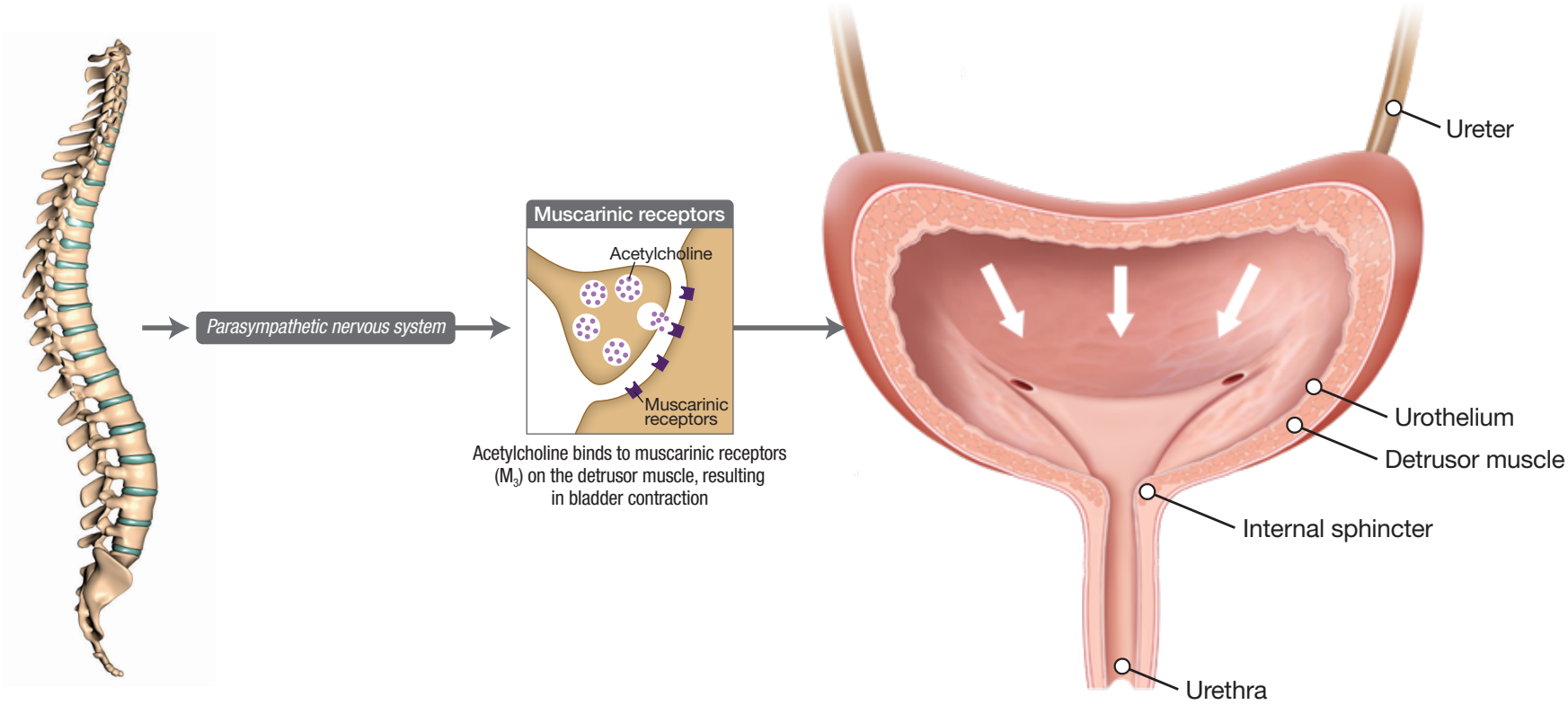
AUTONOMIC NERVOUS SYSTEM: THE PARASYMPATHETIC DIVISION[1,2] (CONT'D)



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AN INTRODUCTION TO OAB:
Definition, Prevalence, and Impact

OAB DEFINED

OAB is a clinical diagnosis characterized by a sudden, urgent need to urinate, with or without urine leakage, usually with daytime and nighttime frequency, in the absence of a urinary tract infection (UTI) or other obvious pathology[1]

The 4 key OAB symptoms are[1,2]

- **Urgency,** the hallmark symptom of OAB, which can be described as a sudden, compelling desire to pass urine that is difficult to defer
- **Frequency,** which is defined as having to void too often during waking hours
- **Nocturia,** or the experience of waking at least once during the night to void
- **Urge urinary incontinence,** which is the involuntary leakage or loss of urine accompanied by, or immediately preceded by, urgency

References: 1. Gormley EA, Lightner DJ, Burgio KL, et al. *Diagnosis and Treatment of Overactive Bladder (Non-Neurogenic) in Adults: AUA/SUFU Guideline.* Linthicum, MD: American Urological Association Education and Research, Inc.; 2014:1-57. **2.** Abrams P, Cardozo L, Fall M, et al. The standardisation of terminology of lower urinary tract function: report from the Standardisation Sub-committee of the International Continence Society. *Am J Obstet Gynecol*. 2002;187(1):116-126.

PREVALENCE OF OAB

OAB is a common condition that affects millions of people[1]

According to a 2005 Internet-based, cross-sectional, population-representative survey

- An estimated **46 million adults (36%)** aged ≥40 years of age in the United States report OAB symptoms at least "sometimes"*
  - **In men,** prevalence of OAB symptoms at least "sometimes" and at least "often" was **27.2%** and **15.8%,** respectively
  - **In women,** prevalence of OAB symptoms at least "sometimes" and at least "often" was **43.1%** and **32.6%,** respectively

*129.3 million (2005 US Census: adults ≥40 years of age) x 35.6% (in the total sample, prevalence of OAB symptoms at least "sometimes" was 35.6%) = 46.02 million US adults ≥40 years of age reported symptoms of OAB at least "sometimes."[1]

Study Design: An Internet-based, cross-sectional, population-representative survey of 10,584 women and 9416 men ≥40 years.[1]

A separate study predicts that, in North America overall, the prevalence of OAB will increase by 18.4% from 2008 to 2018[2†]

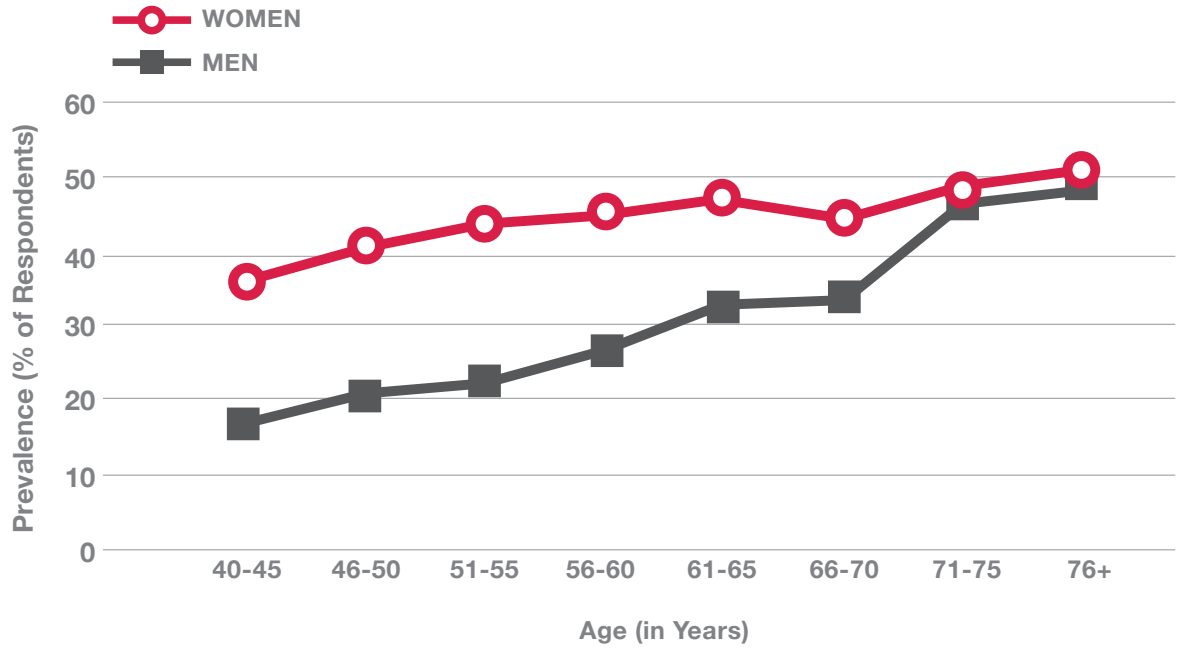
†Calculated with an estimation model using gender- and age-stratified prevalence data from the EPIC study along with gender- and age-stratified worldwide and regional population estimates from the US Census Bureau International Data Base. EPIC is a large, population-based, cross-sectional telephone survey that assessed the prevalence of lower urinary tract symptoms (LUTS), OAB, urinary incontinence, and LUTS/bladder outlet obstruction in 19,165 men and women in 5 countries.[2]

References: 1. Coyne KS, Sexton CC, Vats V, Thompson C, Kopp ZS, Milsom I. National community prevalence of overactive bladder in the United States stratified by sex and age. *Urology.* 2011;77(5):1081-1087. **2.** Irwin DE, Kopp ZS, Agatep B, Milsom I, Abrams P. Worldwide prevalence estimates of lower urinary tract symptoms, overactive bladder, urinary incontinence and bladder outlet obstruction. *BJU Int.* 2011;108(7):1132-1138.

PREVALENCE OF OAB: UNITED STATES[1]*

According to EpiLUTS, a 2005 internet-based, cross-sectional, population-representative survey, the prevalence of OAB symptoms increases with age in both men and women†*

Adults reporting urgency or urge urinary incontinence and frequency of OAB symptoms at least "sometimes"



*EpiLUTS is Epidemiology of Lower Urinary Tract Symptoms.

†In this study, prevalence of OAB symptoms at least "sometimes" was 35.6%, which is approximately 1/3 of the total sample. From a 2005 Internet-based, cross-sectional, population-representative survey of 10,584 women and 9416 men ≥40 years of age.

Reference: 1. Coyne KS, Sexton CC, Vats V, Thompson C, Kopp ZS, Milsom I. National community prevalence of overactive bladder in the United States stratified by sex and age. *Urology.* 2011;77(5):1081-1087.

BURDEN OF OAB: ECONOMIC

OAB comes with a significant financial cost[1]

- Data from epidemiologic studies indicate significant increases in
  - **Diagnostic tests**
  - **Medical and surgical therapy**
  - **Hospitalizations**
  - **Skin irritations**
  - **Infections**

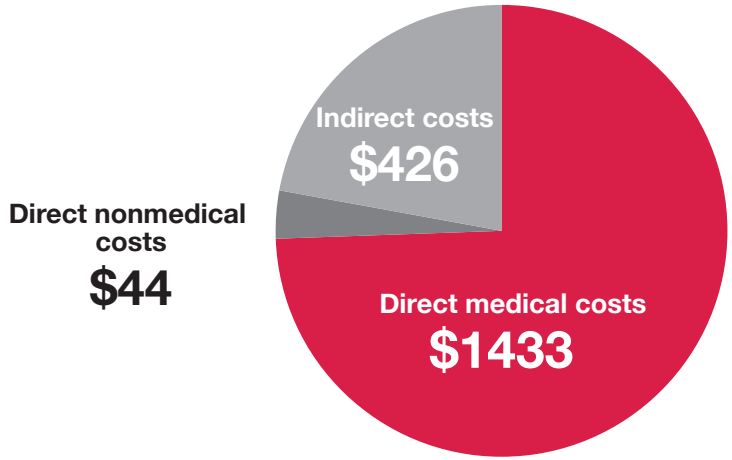
Employers experience a cost in the form of employee absenteeism and reduced work productivity[2,3]

References: 1. Ganz ML, Smalarz AM, Krupski TL, et al. Economic costs of overactive bladder in the United States. *Urology*. 2010;75(3):526-532. **2.** Wu EQ, Birnbaum H, Marynchenko M, Mareva M, Williamson T, Mallet D. Employees with overactive bladder: work loss burden. *J Occup Environ Med*. 2005;47(5):439-446. **3.** Coyne KS, Sexton CC, Irwin DE, Kopp ZS, Kelleher CJ, Milsom I. The impact of overactive bladder, incontinence and other lower urinary tract symptoms on quality of life, work productivity, sexuality and emotional well-being in men and women: results from the EPIC study. *BJU Int.* 2008;101(11):1388-1395.

BURDEN OF OAB: ECONOMIC[1] (CONT'D)

Annual total OAB costs in 2007 in the US: $66 billion

Average Per Capita Costs, 2007: $1925



Estimated Per Capita Costs vs National Costs,* 2007-2020†

2007
$1925‡
$65.9 billion*

2015
$1944‡
$76.2 billion*

2020
$1970‡
$82.6 billion*

*Total OAB population.
†77% of the projected annual total costs of OAB from 2007 to 2020 could be attributed to the direct medical costs incurred by an increasingly elderly population.
‡Average per patient.
Findings are based on a review of the medical literature, practice guidelines, and Medicare and managed care fee schedules from 2005 to 2010.
Direct medical costs included primary care and specialist physician visits, prescriptions (Rx) and over-the-counter (OTC) medications, physical therapy, surgery, and emergency departments.
Direct nonmedical costs included pantiliners, disposable pads, and skin protection.
Indirect costs included lost productivity.

Reference: 1. Ganz ML, Smalarz AM, Krupski TL, et al. Economic costs of overactive bladder in the United States. *Urology.* 2010;75(3):526-532.

BURDEN OF OAB: DAILY LIVING

OAB can intrude into many aspects of a person's life

- Patients with OAB typically restrict their activities and may experience[1,2]
  - **Sleep disruption**
  - **Depression**
  - **Work disruption**
  - **Decreased ability to carry out daily activities**
  - **Negative impact on intimacy**

References: 1. Coyne KS, Sexton CC, Irwin DE, Kopp ZS, Kelleher CJ, Milsom I. The impact of overactive bladder, incontinence and other lower urinary tract symptoms on quality of life, work productivity, sexuality and emotional well-being in men and women: results from the EPIC study. *BJU Int.* 2008;101(11):1388-1395. **2.** Payne CK. Conservative management of urinary incontinence: behavioral and pelvic floor therapy, urethral and pelvic devices. In: Wein AJ, Kavoussi LR, Novick AC, Partin AW, Peters CA, eds. *Campbell-Walsh Urology.* 10th ed. Philadelphia, PA: Elsevier Saunders; 2012:2003-2025.

BURDEN OF OAB: COPING BEHAVIORS

To cope with symptoms of OAB, many patients employ elaborate behaviors aimed at hiding and managing urine loss[1,2]

- It is important that the healthcare provider (HCP) assesses the presence of OAB symptoms, as most patients are reluctant to discuss their symptoms with HCPs[1]

References: 1. Milsom I, Abrams P, Cardozo L, Robert RG, Thüroff J, Wein AJ. How widespread are the symptoms of an overactive bladder and how are they managed? A population-based prevalence study. *BJU Int.* 2001;87(9):760-766. **2.** Ricci JA, Baggish JS, Hunt TL, et al. Coping strategies and health care-seeking behavior in a US national sample of adults with symptoms suggestive of overactive bladder. *Clin Ther.* 2001;23(8):1245-1259.

OAB:
Evaluation and Diagnosis

DIAGNOSING OAB: PATIENT HISTORY

Which urinary symptoms does the patient have?[1]

- Clinician should carefully assess duration of bladder symptoms and baseline symptom levels to ensure that symptoms are not the consequence of some other condition
- Assess bladder storage symptoms associated with OAB (e.g., urgency, urgency incontinence, frequency, and nocturia)
- Assess other bladder storage problems (e.g., stress incontinence episodes)
- Assess bladder emptying (e.g., hesitancy, straining to void, prior history of urinary retention, force of stream, and intermittency of stream)

Diary to determine number of voids, frequency of incontinence episodes, volume of each void, associated urgency, and pad use[1]

Quality of life[1]

- Is it affecting daily activities (sleep, work)?
- Is it interfering with sexual and social activities?

Reference: 1. Gormley EA, Lightner DJ, Burgio KL, et al. *Diagnosis and Treatment of Overactive Bladder (Non-Neurogenic) in Adults: AUA/SUFU Guideline*. Linthicum, MD: American Urological Association Education and Research, Inc.; 2014:1-57.

DIAGNOSING OAB: PATIENT HISTORY (CONT'D)

Factors that may lead to a complicated OAB condition[1]

- Neurologic diseases (i.e., stroke, multiple sclerosis, and spinal cord injury)
- Mobility deficits
- Medically complicated/uncontrolled diabetes
- Chronic pelvic pain
- History of recurrent urinary tract infections (UTIs)
- Pelvic prolapse or pelvic surgery
- Pelvic cancer (bladder, colon, cervix, uterus, prostate) and pelvic radiation
- Patients with urgency incontinence, particularly younger patients or patients with extremely severe symptoms, could represent an occult neurologic condition
- Patients who have failed multiple antimuscarinics to control OAB symptoms

Diagnosing OAB can be complicated by hurdles within the HCP/patient dialogue[2]

- Patients may be experiencing OAB symptoms, but do not initiate the conversation with their HCP
- Miscommunications may occur due to lack of a clear, in-depth discussion of OAB symptoms, comorbidities, and medical history

References: 1. Gormley EA, Lightner DJ, Burgio KL, et al. *Diagnosis and Treatment of Overactive Bladder (Non-Neurogenic) in Adults: AUA/SUFU Guideline.* Linthicum, MD: American Urological Association Education and Research, Inc.; 2014:1-57. **2.** Milsom I, Kaplan SA, Coyne KS, Sexton CC, Kopp ZS. Effect of bothersome overactive bladder symptoms on health-related quality of life, anxiety, depression, and treatment seeking in the United States: results from EpiLUTS. *Urology.* 2012;80(1):90-96.

DIAGNOSING OAB: ASSESSMENT[1,2]

Most cases of OAB can be diagnosed based on a patient history and symptom assessment (including degree of bother and effect on daily activities), a physical examination, and a urinalysis.[1]

Initial workup of uncomplicated OAB is symptom-based and does not require invasive testing[1]

As per AUA guidelines, the following assessments may be performed:

Physical Examination[1,2]

- Neurologic
- Mental status
- Weight/Body mass index (BMI)
- Abdomen
- Genitalia

Urinalysis[1,2]

- Rule out urinary tract infections (UTIs), glucosuria, hematuria, proteinuria, etc.

Post-void residual (PVR) measurement[1]*

- PVR should be measured with an ultrasound bladder scanner or a catheter immediately after the patient voids
- PVR is not necessary for patients who are receiving first-line behavioral interventions or for uncomplicated patients (i.e., patients without a history of or risk factors for urinary retention) receiving antimuscarinic medications

***Not recommended for uncomplicated OAB.**

References: 1. Gormley EA, Lightner DJ, Burgio KL, et al. *Diagnosis and Treatment of Overactive Bladder (Non-Neurogenic) in Adults: AUA/SUFU Guideline*. Linthicum, MD: American Urological Association Education and Research, Inc.; 2014:1-57. **2.** Gomelsky A, Dmochowski RR. Diagnosis of overactive bladder syndrome and stress urinary incontinence. In: Hashim H, Abrams P, eds. *Overactive Bladder Syndrome and Urinary Incontinence*. New York, NY: Oxford University Press Inc.; 2012:21-33.

CONSIDERATIONS FOR DIAGNOSING COMPLICATED OAB[1]

- Urodynamic testing
- Cystoscopy
- Diagnostic renal ultrasound
- Diagnostic bladder ultrasound

Reference: 1. Gormley EA, Lightner DJ, Burgio KL, et al. *Diagnosis and Treatment of Overactive Bladder (Non-Neurogenic) in Adults: AUA/SUFU Guideline*. Linthicum, MD: American Urological Association Education and Research, Inc.; 2014:1-57.

DIAGNOSING OAB: RULE OUT OTHER CAUSES OF SYMPTOMS

Local pathology[1,2]

- Infection
- Bladder stones
- Bladder tumors
- Interstitial cystitis
- Outlet obstruction

Medications[2]

- Diuretics
- Antidepressants
- Antihypertensives

Metabolic factors[1]

- Diabetes
  - Polydipsia
  - Polyuria

Review of Systems[2]

- Sexual and bowel function
- Recent weight gain or loss
- Lower extremity edema
- Depression and anxiety

References: 1. Gormley EA, Lightner DJ, Burgio KL, et al. *Diagnosis and Treatment of Overactive Bladder (Non-Neurogenic) in Adults: AUA/SUFU Guideline.* Linthicum, MD: American Urological Association Education and Research, Inc.; 2014:1-57. **2.** Gomelsky A, Dmochowski RR. Diagnosis of overactive bladder syndrome and stress urinary incontinence. In: Hashim H, Abrams P, eds. *Overactive Bladder Syndrome and Urinary Incontinence.* New York, NY: Oxford University Press Inc.; 2012:21-34.

OAB:
Treatment Approaches

AUA/SUFU: OAB TREATMENT GUIDELINES[1]

FIRST LINE

- **Behavioral therapies for all patients**
- **May be combined with oral agents**

SECOND LINE

- **Oral agents and transdermal preparations**
- **Dose modification or switch to a different oral agent if inadequate efficacy or poor tolerability**

THIRD LINE

- **IntradetrusorOnabotulinumtoxinA**
- **Peripheral tibial nerve stimulation (PTNS)**
- **Sacral neuromodulation (SNS)**
- **Other surgical options**

AUA/SUFU, American Urological Association/Society of Urodynamics Female Pelvic Medicine and Urogenital Reconstruction.
Adapted from the AUA/SUFU treatment guidelines.

Reference: 1. American Urological Foundation. Diagnosis & Treatment Algorithm: AUA/SUFU Guideline on Non-Neurogenic Overactive Bladder in Adults [Web page]. American Urological Foundation website. http://www.auanet.org/common/pdf/education/clinical-guidance/overactive-bladder-algorithm.pdf. Accessed May 12, 2016.

BEHAVIORAL THERAPY OPTIONS

Bladder Training[1]

- Self-monitoring with a bladder diary for 3-7 days is a helpful first step in behavioral therapy
- Helps the patient document the time of each void and incontinence episode to help pinpoint the circumstances at the time of incontinence
- Symptom questionnaires are also useful to quantitate and follow patients' responses to bladder symptom and bother changes with OAB therapies, as well as document baseline and post-treatment results

Pelvic Muscle Exercises[1,2]

- Focuses on the bladder outlet and the pelvic floor muscle to increase strength, control, and urge suppression
- Pelvic floor muscle training and exercise includes pelvic floor relaxation, active use of pelvic floor muscles for urethral occlusion and urge suppression (urge strategies), urge control techniques (distraction, self-assertions), and normal voiding techniques

Biofeedback[1-3]

- Patients learn how to properly perform pelvic floor muscle contraction and how to strengthen the urinary sphincter
- A vaginal or perineal pressure sensor worn by the patient relays information about when a muscular contraction has occurred and the strength of the contraction

Fluid/Dietary Management[1]

- Fluid management (i.e., reduction in fluid intake) can reduce frequency and urgency
- Caffeine reduction, dietary adjustments (avoiding bladder irritants), weight loss, and other lifestyle changes are also recommended

References: 1. Gormley EA, Lightner DJ, Burgio KL, et al. *Diagnosis and Treatment of Overactive Bladder (Non-Neurogenic) in Adults: AUA/SUFU Guideline.* Linthicum, MD: American Urological Association Education and Research, Inc.; 2014:1-57. **2.** Burgio KL, Borello-France DF. Pelvic floor muscle exercises and behavioral therapy. In: Kreder K, Dmochowski R, eds. *The Overactive Bladder: Evaluation and Management.* London, England: Informa Healthcare; 2007:87-94. **3.** Blaivas JG, Purohit RS. *Diagnosis and Treatment of Overactive Bladder.* New York, NY: Oxford University Press, Inc.; 2011:1-61.

PHARMACOLOGIC THERAPY FOR OAB[1]

- Oral agents and transdermal preparations
- Dose modification or change to a different oral agent, if inadequate efficacy or poor tolerability

Reference: 1. Gormley EA, Lightner DJ, Burgio KL, et al. *Diagnosis and Treatment of Overactive Bladder (Non-Neurogenic) in Adults: AUA/SUFU Guideline*. Linthicum, MD: American Urological Association Education and Research, Inc.; 2014:1-57.

INVASIVE PROCEDURES

Neuromodulation involves 2 different procedures[1,2]

- Sacral nerve stimulation (SNS)
- Peripheral tibial nerve stimulation (PTNS)

BotulinumtoxinA (BTX-A)

- May require frequent post-void residual evaluation and patient may have to self-catheterize[1]

Bladder Augmentation/Augmentation Cystoplasty

- A surgical procedure to increase bladder capacity[3]

Bladder Diversion/Urinary Diversion

- A surgical procedure that may be used in rare cases for severe, refractory, or complicated OAB patients[1]
- Substantial risks are involved, including malignancy, and patients may need long-term intermittent self-catheterization[1]

Invasive procedures should only be considered for carefully selected and thoroughly counseled patients who have been refractory to first- and second-line OAB treatments and are willing to undergo a surgical procedure[1]

References: 1. Gormley EA, Lightner DJ, Burgio KL, et al. *Diagnosis and Treatment of Overactive Bladder (Non-Neurogenic) in Adults: AUA/SUFU Guideline.* Linthicum, MD: American Urological Association Education and Research, Inc.; 2014:1-57. **2.** Hashim H, Abrams P. Treatment of overactive bladder syndrome and stress urinary incontinence. In: Hashim H, Abrams P, eds. *Overactive Bladder Syndrome and Urinary Incontinence.* New York, NY: Oxford University Press, Inc.; 2012:35-54. **3.** Cespedes RD, Gerboc JL. Other therapies for storage and emptying failure. In: Wein AJ, Kavoussi LR, Novick AC, Partin AW, Peters CA, eds. *Campbell-Walsh Urology.* 10th ed. Philadelphia, PA: Elsevier-Saunders; 2012:2186-2203.

MEDICARE HEALTH OUTCOMES SURVEY (HOS)

- **The Medicare HOS is the first patient-reported outcomes measure used in Medicare managed care (Part C)[1]**
  - —HOS is used by the Centers for Medicare & Medicaid Services (CMS) to develop its 5-Star Quality Rating System, which evaluates quality and performance in Medicare Advantage (Part C) Health Plans
- **The HOS assessment occurs over a 2-year period of time[1]**
  - —As of 2014, 17 rounds of data have been collected
- **Improving bladder control is part of the Medicare HOS**
  - —HOS contains 4 questions for patients relating to bladder control[2]
  - —These questions are currently under revision and were tested in 2015 to assess quality of care and impact on quality of life[3]

References: 1. Medicare Health Outcomes Survey [homepage]. http://www.hosonline.org. Accessed May 12, 2016. **2.** Medicare 2015 Part C & D Star Rating Technical Notes [downloadable document]. http://www.cms.gov/ Medicare/Prescription-Drug-Coverage/PrescriptionDrugCovGenIn/PerformanceData.html. Accessed May 12, 2016. **3.** Medicare Request for Comments [Web page]. http://www.cms.gov/ Medicare/Prescription-Drug-Coverage/PrescriptionDrugCovGenIn/Downloads/2016-Request-for-Comments-v-11_25_2014.pdf. Accessed May 12, 2016.

2016 IMPROVING BLADDER CONTROL HOS QUESTIONS

Questions regarding urinary incontinence, some of which may be relevant for patients with overactive bladder, in the HOS[1]

Many people experience leakage of urine, also called urinary incontinence. In the **past six months**, have you experienced leaking of urine?

During the past six months, how much did leaking of urine make you change your daily activities or interfere with your sleep?

Have you **ever** talked with a doctor, nurse, or other health care provider about leaking of urine?

There are many ways to control or manage the leaking of urine, including bladder training exercises, medication and surgery. Have you ever talked with a doctor, nurse, or other health care provider about any of these approaches?

Reference: 1. Medicare 2015 Part C & D Star Rating Technical Notes [downloadable document]. http://www.cms.gov/Medicare/Prescription-Drug-Coverage/PrescriptionDrugCovGenIn/PerformanceData.html. Accessed May 12, 2016.

SUMMARY

The bladder serves 2 main functions—the **storage** and the **voiding** of urine—and is controlled by the **autonomic nervous system (ANS)**

OAB involves the following key symptoms

- Urgency, with or without incontinence, often involving frequency and nocturia

OAB is a condition that affects millions of people and comes with economic, health, and quality-of-life burdens

OAB can be diagnosed, in most cases, based on

- Patient history and symptom assessment
- Physical examination
- Urinalysis

OAB can be treated in a variety of ways, including

- Behavioral therapy
- Pharmacologic therapy
- Surgical procedures

080-0917-PM July 2016