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AN OVERVIEW OF OAB

Including evaluation of and management approaches for overactive bladder

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THE BLADDER:
Anatomy and Normal Function

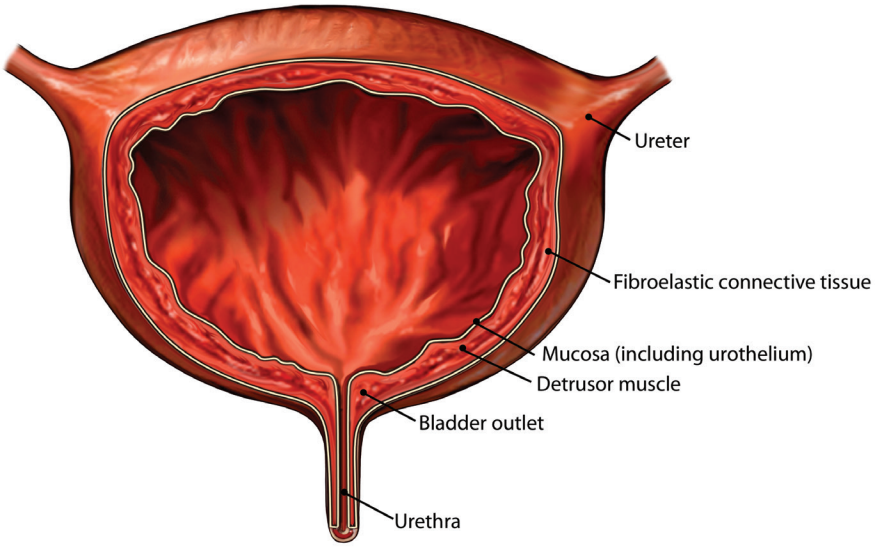
BLADDER ANATOMY: A REFRESHER

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;2:33-70. **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;60:1786-1833. **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;61:1834-1846.

BLADDER ANATOMY: A REFRESHER

The bladder serves 2 main functions[1]:

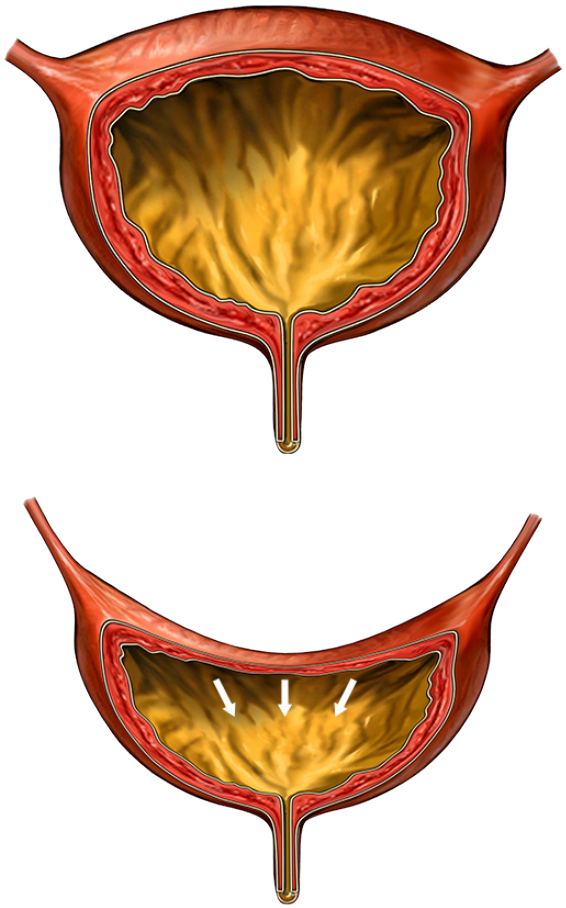
- To **store** urine
- To **void** urine

Filling/storage phase[1,2]

- 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
- A moderately full bladder holds approximately 500 mL (1 pint) of urine, but can hold nearly double that if necessary, with a maximum capacity of 800-1000 mL

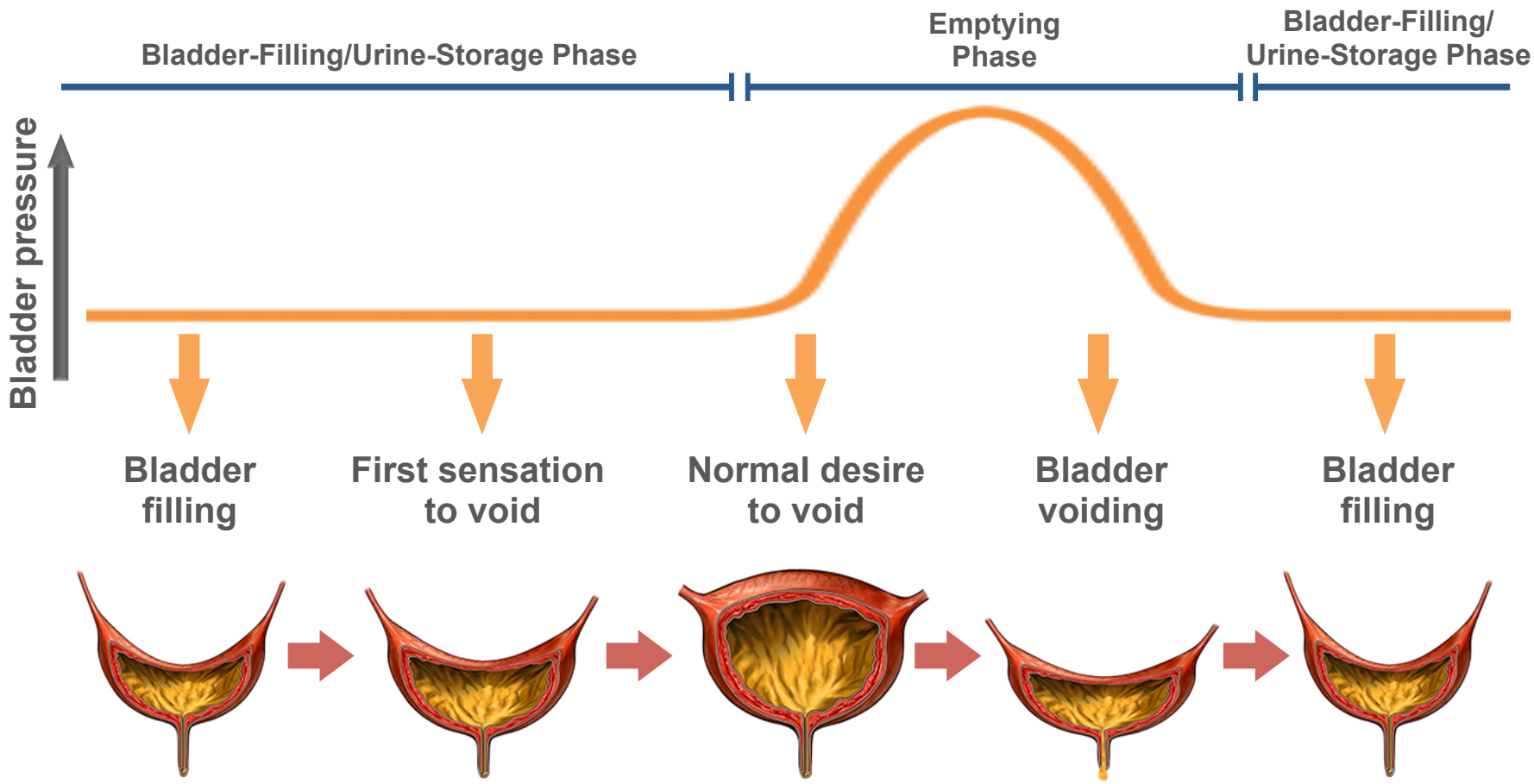
Emptying/voiding phase[1]

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



References: 1. Chu FM, Dmochowski R. Pathophysiology of overactive bladder. *Am J Med.* 2006;119:3S-8S. **2.** Marieb EN, Hoehn K. The autonomic nervous system. The urinary system. In: Marieb EN, Hoehn K, eds. *Human Anatomy & Physiology.* 9th ed. San Francisco, CA: Pearson Education, Inc.; 2012;9:524-543,954-989.

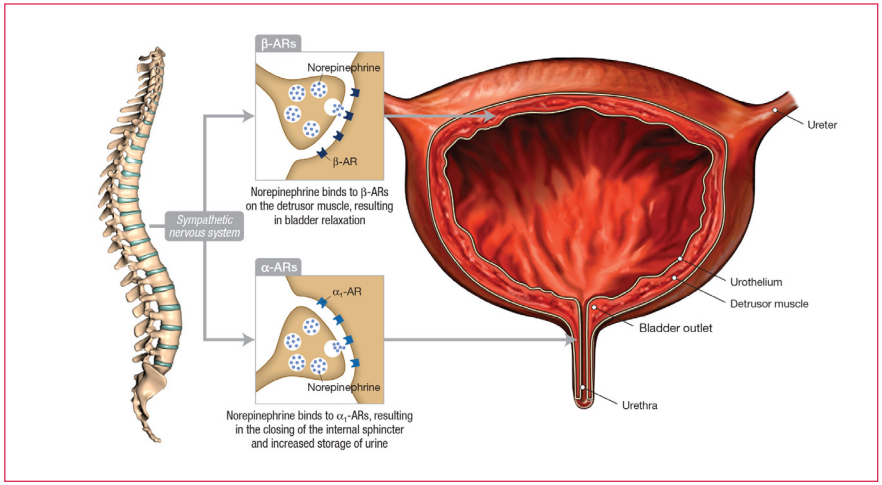
BLADDER FUNCTION: STORAGE AND VOIDING[1]

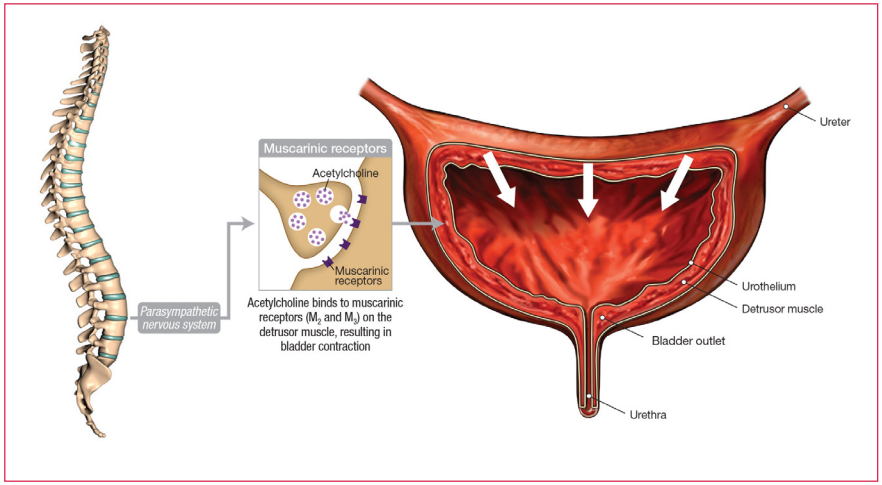


Reference: 1. Chu FM, Dmochowski R. Pathophysiology of overactive bladder. *Am J Med.* 2006;119:3S-8S.

NEUROLOGIC CONTROL OF THE BLADDER: THE AUTONOMIC NERVOUS SYSTEM

- Regulation of bladder storage and voiding involves both sympathetic and parasympathetic control[1]
- Storage and voiding of the bladder are primarily regulated by two neurotransmitters–norepinephrine and acetylcholine–respectively[1-4]
- Norepinephrine, released from the sympathetic nerves, activates the adrenergic receptors (ARs), α-ARs and β-ARs, in the bladder to relax the detrusor muscle and close the internal sphincter, respectively[1]
- The muscarinic receptors (M1 to M5) are mediated by acetylcholine and control the contraction of the detrusor muscle and relaxation of the internal sphincter muscle to facilitate voiding[1,4,5]





References: 1. Fowler CJ, Griffiths D, de Groat WC. The neural control of micturition. *Nat Rev Neurosci.* 2008;9:453-466. **2.** Andersson K-E. Physiological Society symposium: the physiology and pathophysiology of the lower urinary tract. Advances in the pharmacological control of the bladder. *Exp Physiol.* 1999;84:195-213. **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;144:1089-1099. **4.** Andersson K-E. Pharmacology of lower urinary tract smooth muscles and penile erectile tissues. *Pharmacol Rev.* 1993;45:253-308. **5.** Chess-Williams R. Muscarinic receptors of the urinary bladder: detrusor, urothelial and prejunctional. *Auton Autacoid Pharmacol.* 2002;22:133-145.

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 the ARs—β-AR and α-AR—in the bladder to, respectively, relax the detrusor muscle and close the internal sphincter[1]

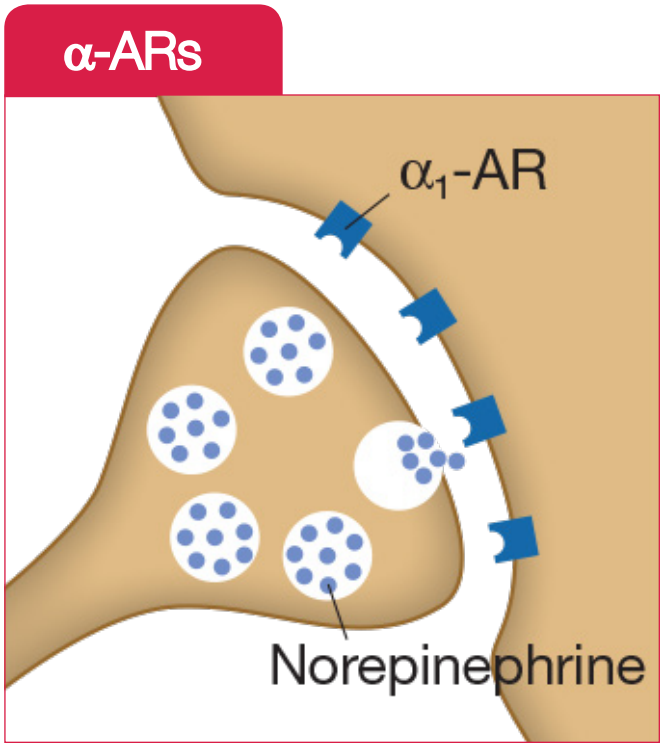
- Three different types of β-ARs are expressed in the human bladder: β_1-AR, β_2-AR, and β_3-AR. The β_3-AR made up 97% of the total β-AR messenger RNA (mRNA) in bladder tissue samples in an experiment to determine β-AR subtype expression, making it predominantly responsible for detrusor muscle relaxation. The β_1-AR and β_2-AR subtypes made up 1.5% and 1.4% of the total β-AR mRNA, respectively[3]
- 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.[5] Although expressed in the bladder to a lesser degree than β-receptors, α_1 predominates in the bladder neck[6]

References: 1. Fowler CJ, Griffiths D, de Groat WC. The neural control of micturition. *Nat Rev Neurosci.* 2008;9:453-466. **2.** Chu FM, Dmochowski R. Pathophysiology of overactive bladder. *Am J Med.* 2006;119:3S-8S. **3.** Yamaguchi O. β_3-adrenoceptors in human detrusor muscle. *Urology.* 2002;59:25S-29S. **4.** 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;133:61-72. **5.** Andersson K-E. Pharmacology of lower urinary tract smooth muscles and penile erectile tissues. *Pharmacol Rev.* 1993;45:253-308. **6.** Andersson K-E. Physiological Society symposium: the physiology and pathophysiology of the lower urinary tract. Advances in the pharmacological control of the bladder. *Exp Physiol.* 1999;84:195-213.

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

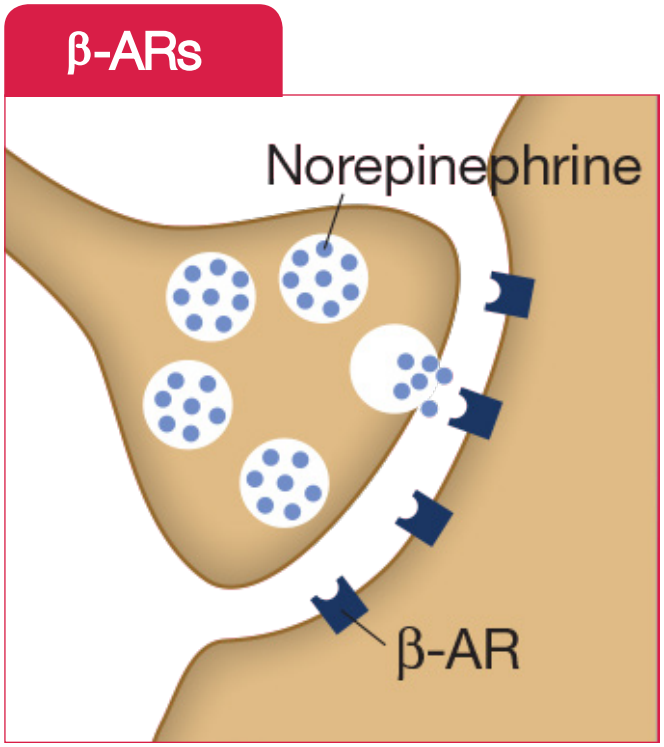


References: 1. Andersson K-E. Pharmacology of lower urinary tract smooth muscles and penile erectile tissues. *Pharmacol Rev.* 1993;45:253-308. **2.** Conley RK, Williams TJ, Ford APDW, Ramage AG. The role of α_1-adrenoceptors and 5-HT1A receptors in the control of the micturition reflex in male anaesthetized rats. *Br J Pharmacol.* 2001;133:61-72. **3.** Andersson K-E. Physiological Society symposium: the physiology and pathophysiology of the lower urinary tract. Advances in the pharmacological control of the bladder. *Exp Physiol.* 1999;84:195-213 **4.** Fowler CJ, Griffiths D, de Groat WC. The neural control of micturition. *Nat Rev Neurosci.* 2008;9:453-466.

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

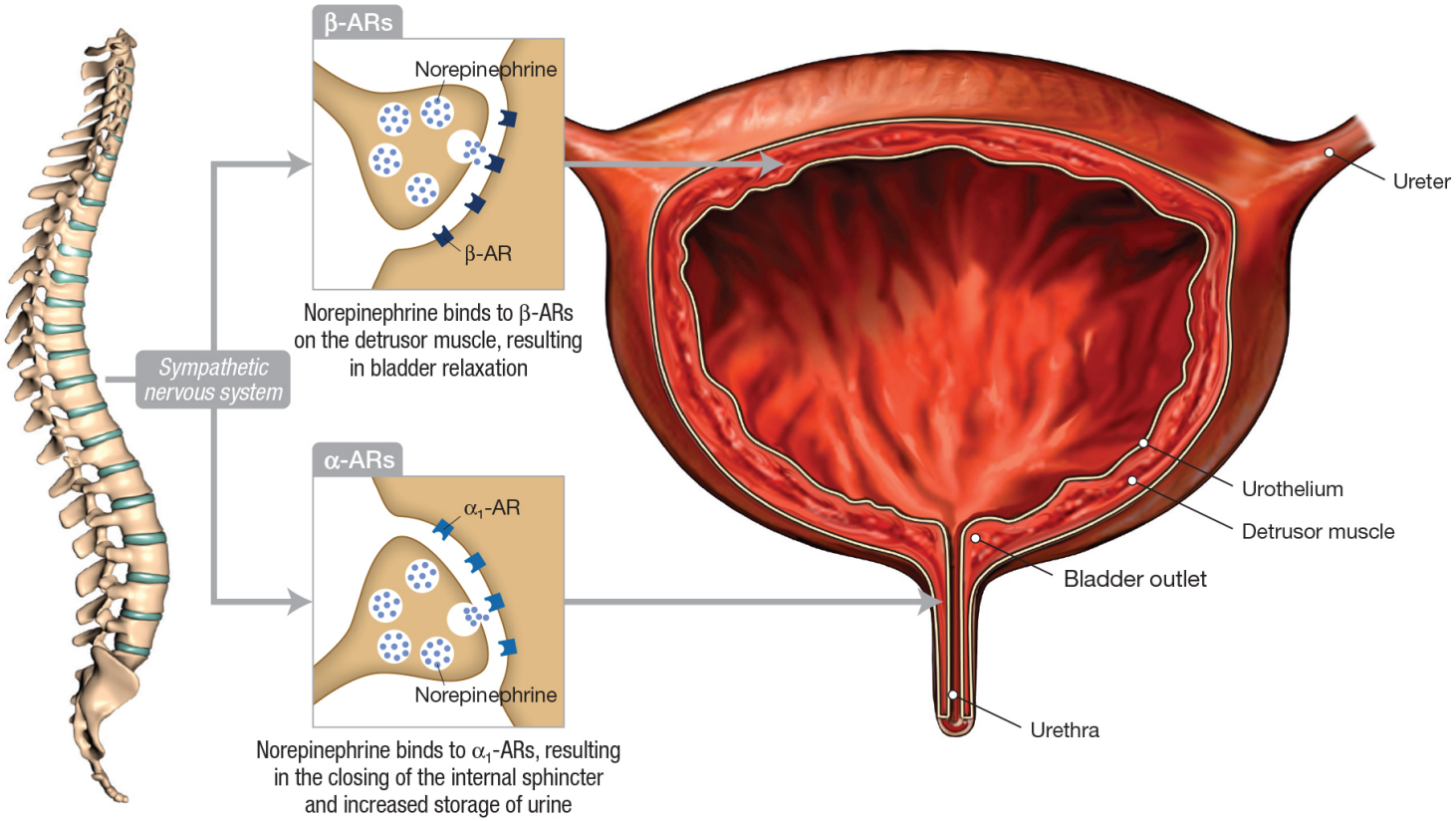
Expression of β-ARs in the bladder

- Sympathetic nerves determine the duration of the urine-storage phase during the micturition cycle[1]
  - Norepinephrine released from sympathetic nerves activates β-ARs in the 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;119:3S-8S. **2.** Yamaguchi O. β_3-adrenoceptors in human detrusor muscle. *Urology.* 2002;59:25S-29S. **3.** Otsuka A, Shinbo H, Matsumoto R, Kurita Y, Ozono S. Expression and functional role of β_3-adrenoceptors in the human urinary bladder urothelium. *Naunyn Schmiedebergs Arch Pharmacol.* 2008;377:473-481. **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;9:453-466.

AUTONOMIC NERVOUS SYSTEM: THE PARASYMPATHETIC DIVISION

The *parasympathetic* division primarily mediates bladder contraction[1,2]

- Bladder *voiding* is primarily regulated by this division

***Muscarinic receptors,* a component of the parasympathetic nervous system, are activated by acetylcholine[3-8]**

- There are 5 subclasses of muscarinic receptors: M_1, M_2, M_3, M_4, and M_5[3]
- The muscarinic receptors can be found in urothelial cells[4,5]
  - M_2 and M_3 are the predominant muscarinic receptors found in the bladder[6]
  - 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*)[7]
  - Binding of acetylcholine to M_2- and M_3-receptors on the detrusor muscle signals the bladder to contract so voiding can occur[8]

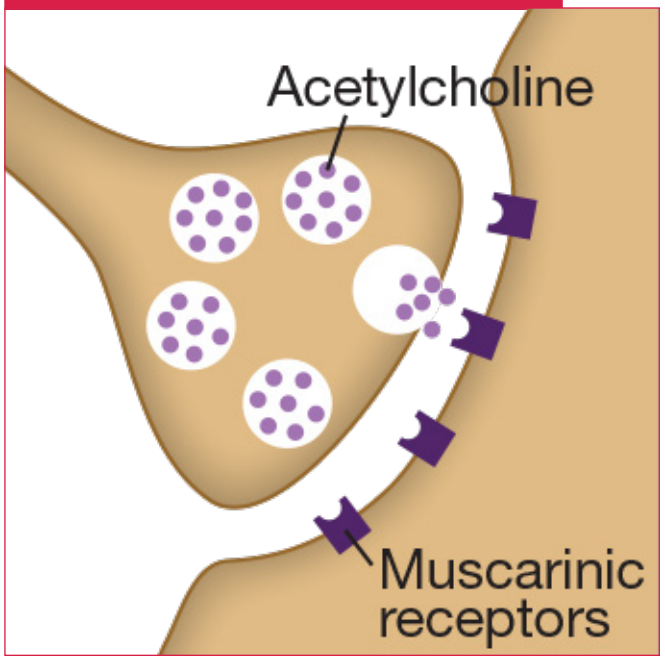
References: 1. Fowler CJ, Griffiths D, de Groat WC. The neural control of micturition. *Nat Rev Neurosci.* 2008;9:453-466. **2.** Marieb EN, Hoehn K. The autonomic nervous system. The urinary system. In: Marieb EN, Hoehn K. *Human Anatomy & Physiology.* 9th ed. San Francisco, CA: Pearson Education, Inc. 2012;9:524-543,954-989. **3.** Andersson K-E. Physiological Society symposium: the physiology and pathophysiology of the lower urinary tract. Advances in the pharmacological control of the bladder. *Exp Physiol.* 1999;84:195-213. **4.** Otsuka A, Shinbo H, Matsumoto R, Kurita Y, Ozono S. Expression and functional role of β_3-adrenoceptors in the human urinary bladder urothelium. *Naunyn Schmiedebergs Arch Pharmacol.* 2008;377:473-481. **5.** 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;144:1089-1099. **6.** 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;156:1208-1213. **7.** 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;21:243-248. **8.** Andersson K-E. 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

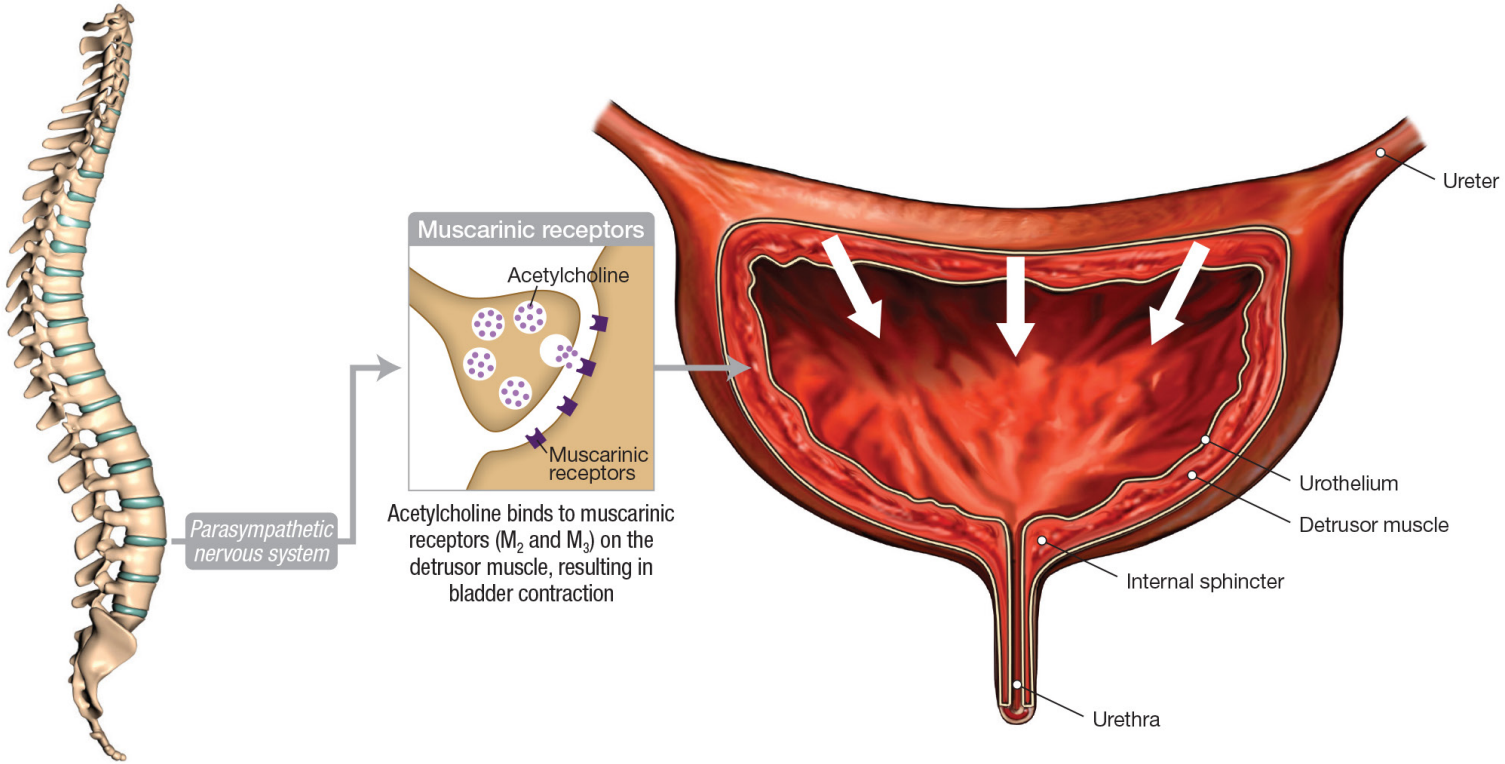
- Muscarinic receptors can be found on urothelial cells[1,2]
- M_2- and M_3-receptors are the predominant muscarinic receptors found in the bladder[3-5]
  - Binding of acetylcholine to M_2- and M_3-receptors on the detrusor muscle signals the bladder to contract so voiding can occur
  - M_3-receptors 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*)

Muscarinic receptors



References: 1. 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;377:473-481. **2.** 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;144:1089-1099. **3.** 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;156:1208-1213. **4.** Andersson K-E. Pharmacology of lower urinary tract smooth muscles and penile erectile tissues. *Pharmacol Rev.* 1993;45:253-308. **5.** 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;21:243-248.

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



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AN INTRODUCTION TO OAB:
Definition, Prevalence, and Impact

OVERACTIVE BLADDER (OAB) DEFINED

Overactive bladder (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. American Urological Association Guideline. Diagnosis and treatment of overactive bladder (non-neurogenic) in adults: AUA/SUFU Guideline. May 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[1,2]

According to an Internet-based, cross-sectional, population-representative survey

- An estimated **46 million adults (36%)** ≥40 years of age in the US 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 of age.[1]

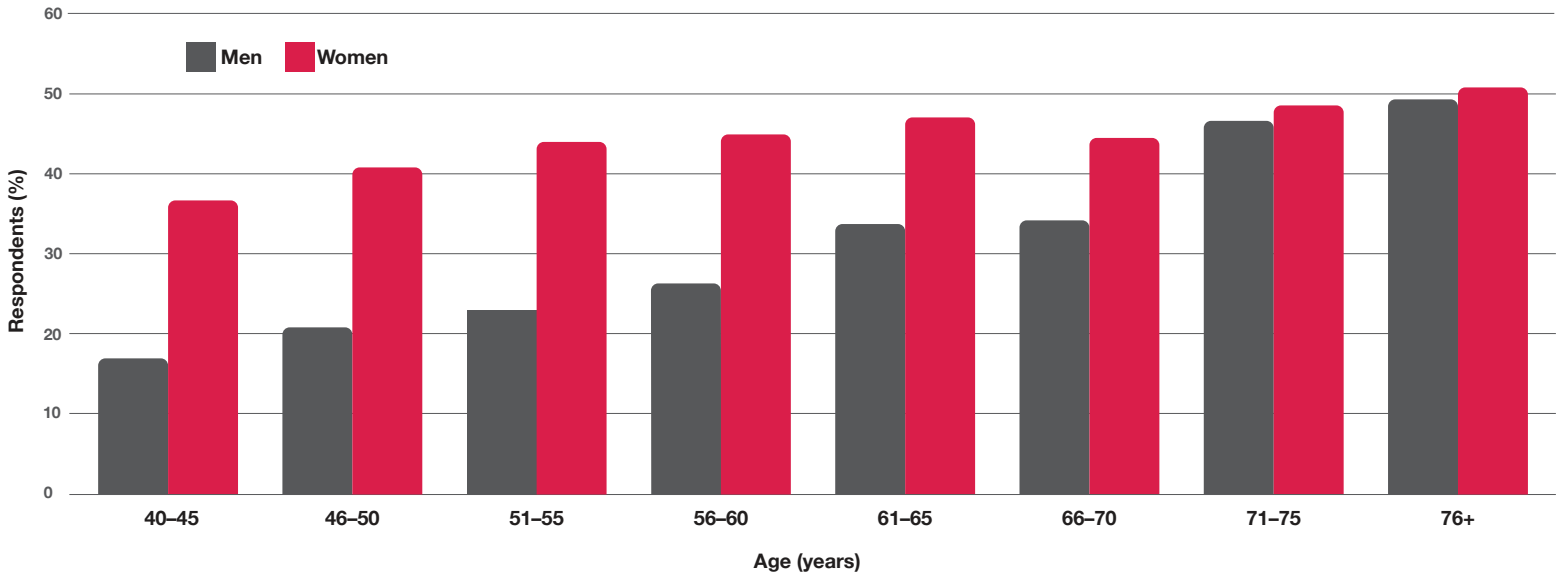
A separate study predicts that, in North America overall, the prevalence of OAB will increase by 18.4% from 2008 to 2018[2†]

†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 LUTS, OAB, UI, and LUTS/BOO in 19,165 men and women in 5 countries.[2]

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

1 in 3 US adults ≥40 years of age reported symptoms of OAB at least "sometimes"



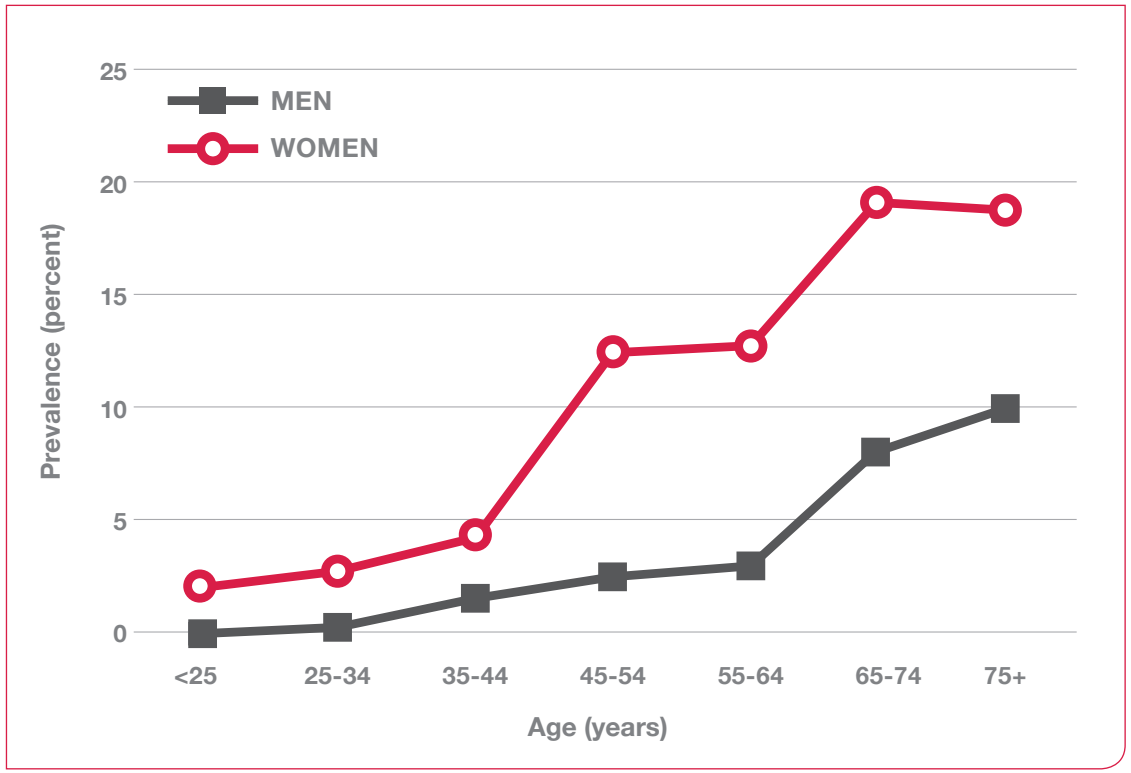
*Adults who had experienced urgency or urge incontinence in the last 4 weeks and defined occurrence as at least "sometimes."

Data were gathered in the Epidemiology of Lower Urinary Tract Symptoms (EpiLUTS), a population-based, cross-sectional survey conducted in the United States, United Kingdom, and Sweden. In the US, 20,000 men and women aged 40 years or older were recruited from Internet-based panels developed from consumer and voter databases. All respondents were asked to complete a series of questions about their symptoms.[1]

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

PREVALENCE OF OAB: WITH INCONTINENCE, BY AGE[1]

- Data from the NOBLE Program show that the prevalence of OAB symptoms **without incontinence increases with age in both men and women**
- However, OAB **with incontinence is more common in women** than in men at all ages, especially in **the elderly** (see chart)



Reference: 1. Stewart WF, Van Rooyen JB, Cundiff GW, et al. Prevalence and burden of overactive bladder in the United States. *World J Urol.* 2003;20:327-336.

BURDEN OF OAB: ECONOMIC

OAB comes with a significant financial cost[1-3]

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

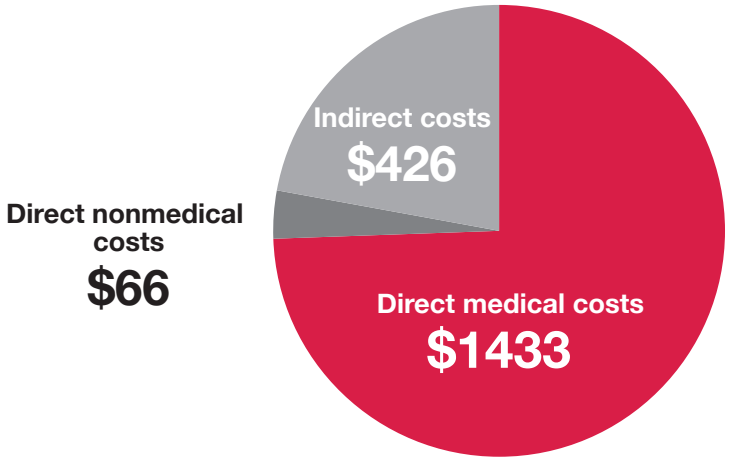
Employers experience a cost in the form of **employee absenteeism** and **reduced work productivity**[4,5]

References: 1. Ganz ML, Smalarz AM, Krupski TL, et al. Economic costs of overactive bladder in the United States. *Urology.* 2010;75:526-532. **2.** Tubaro A. Defining overactive bladder: epidemiology and burden of disease. *Urology.* 2004;64(suppl 6A):2-6. **3.** Wagner TH, Hu T, Bentkover J, et al. Health-related consequences of overactive bladder. *Am J Manag Care.* 2002;8(19):S598-S607. **4.** 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. **5.** 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;101:1388-1395.

BURDEN OF OAB: ECONOMIC (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 5 most recent years of the medical literature, practice guidelines, and Medicare and managed care fee schedules.
Direct medical costs included primary care and specialist physician visits, Rx and OTC medications, physical therapy, surgery, 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;75:526-532.

BURDEN OF OAB: DAILY LIVING

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

- Patients with incontinence 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;101:1388-1395. **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;3:2003-2025.

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 HCP assess the presence of OAB symptoms, as, according to one study, ~55% of patients did not mention their OAB symptoms to their HCP.[3] In another study conducted in Europe, 40% of patients did not discuss their symptoms with their HCP[2]
  - This was due either to embarrassment or the misperception that such urologic symptoms are a normal aspect of aging

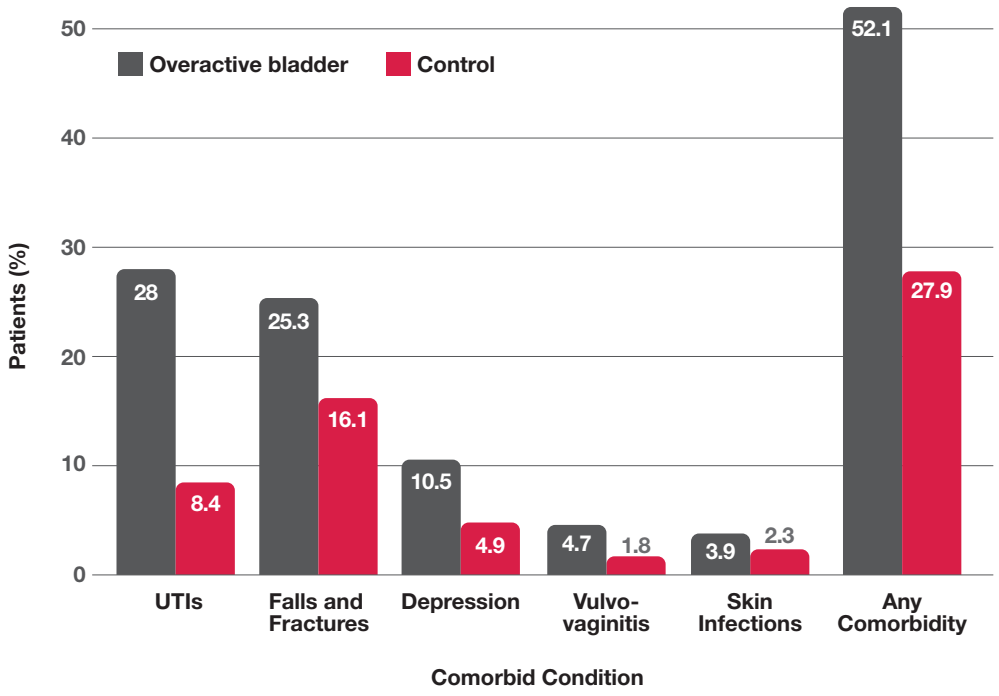
References: 1. Abrams P, Kelleher CJ, Kerr LA, Rogers RG. Overactive bladder significantly affects quality of life. *Am J Manag Care*. 2000;6(suppl):S580-S590. **2.** Milsom I, Abrams P, Cardozo L, Robert RG, Thüroff J, Wein AJ. How widespread are the symptoms of an overactive bladder and how are they managed? A population-based prevalence study. *BJU Int.* 2001;87:760-766. **3.** Benner JS, Becker R, Fanning K, Jumadilova Z, Bavendam T, Brubaker L; for the OAB Medication Use Study Steering Committee. Bother related to bladder control and health care seeking behavior in adults in the United States. *J Urol.* 2009;181:2591-2598.

BURDEN OF OAB: PATIENT COMORBIDITIES

Patients with OAB were significantly more likely to suffer from[1,2]*

- Urinary tract infections (UTIs)
- Falls and fractures
- Depression
- Vulvovaginitis
- Skin infections

* Findings are based on a retrospective cohort study using electronic pharmacy and medical claims data from a regional pharmacy benefits and medical management organization.



- More than half of the patients with OAB had at least 1 of these comorbidities[1]
- In a survey with 919 respondents, patients with OAB incurred 20% more physician visits than people without OAB[2]

References: 1. Darkow T, Fontes CL, Williamson TE. Costs associated with the management of overactive bladder and related comorbidities. *Pharmacotherapy.* 2005;25(4):511-519. **2.** Wagner TH, Hu T, Bentkover J, et al. Health-related consequences of overactive bladder. *Am J Manag Care.* 2002;8(19):S598-S607.

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 (eg, urgency, urgency incontinence, frequency, nocturia)
- Assess other bladder storage problems (eg, stress incontinence episodes)
- Assess bladder emptying (eg, 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?

Factors that may aggravate OAB symptoms include[1]

- Neurologic diseases (ie, stroke, multiple sclerosis, 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 suffering with 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. American Urological Association Guideline. Diagnosis and treatment of overactive bladder (non-neurogenic) in adults: AUA/SUFU Guideline. May 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. *Urol.* 2012;80:90-96.

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]

Physical Examination[1]

- Neurologic
- Mental status
- Weight/BMI
- Abdomen
- Genitalia

Urinalysis[1,2]

- Rule out urinary tract infections, glucosuria, hematuria, proteinuria, etc

Post-void residual 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 (ie, 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. American Urological Association Guideline. Diagnosis and treatment of overactive bladder (non-neurogenic) in adults: AUA/SUFU Guideline. May 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.

DIAGNOSING COMPLICATED OAB: URODYNAMIC TESTING CONSIDERATIONS

- Uroflowmetry[1]
- Cystometry[1,2]
- Leak Point Pressure Measurement[1]
- Pressure Flow Study[1]
- Electromyography[1]
- Video Urodynamic Tests[1]
- Post-Void Residual Measurement[1]

References: 1. National Kidney and Urologic Diseases Information Clearinghouse (NKUDIC). Urodynamic testing. http://kidney.niddk.nih.gov/kudiseases/pubs/urodynamic/. Accessed July 25, 2013.
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.

DIAGNOSING OAB: RULE OUT OTHER CAUSES OF SYMPTOMS

Local pathology[1-3]

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

Medications[3,4]

- Diuretics
- Antidepressants
- Antihypertensives
- Sedatives
- Opioids

Metabolic factors[1,2]

- Diabetes
  - Polydipsia
  - Polyuria

Review of Systems[3]

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

References: 1. Wein AJ. Diagnosis and treatment of the overactive bladder. *Urology.* 2003;62(suppl 5B):20–27. **2.** Gormley EA, Lightner DJ, Burgio KL, et al. American Urological Association Guideline. Diagnosis and treatment of overactive bladder (non-neurogenic) in adults: AUA/SUFU Guideline. May 2014:1-57. **3.** 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. **4.** Ellsworth PI. Overactive bladder—etiology, diagnosis, and impact. *Medscape Reference.* http://emedicine.medscape.com/article/459502-overview#aw2aab6b5. Accessed July 26, 2013.

OAB:
Treatment Approaches

AUA: 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

- **SNS**
- **PTNS**
- **Intradetrusor onabotulinumtoxinA**
- **Other surgical options**

SNS=sacral neuromodulation; PTNS=peripheral tibial nerve stimulation.
Adapted from the AUA OAB treatment guidelines.

Reference: 1. Gormley EA, Lightner DJ, Burgio KL, et al. American Urological Association Guideline. Diagnosis and treatment of overactive bladder (non-neurogenic) in adults: AUA/SUFU Guideline. May 2014:1-57.

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 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[1,3]

- Focuses on the bladder outlet and the pelvic floor muscle to increase strength and 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 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. American Urological Association Guideline. Diagnosis and treatment of overactive bladder (non-neruogenic) in adults: AUAS/SUFU Guideline. May 2014:1-57. **2.** Blaivas JG, Purohit RS. *Diagnosis and Treatment of Overactive Bladder.* New York, NY: Oxford University Press, Inc.; 2011:1-61. **3.** 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.

PHARMACOLOGIC THERAPY[1]

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

Reference: 1. Gormley EA, Lightner DJ, Burgio KL, et al. American Urological Association Guideline. Diagnosis and treatment of overactive bladder (non-neurogenic) in adults: AUA/SUFU Guideline. May 2014:1-57.

INVASIVE PROCEDURES[1]

Neuromodulation involves 2 different procedures[1,2]

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

BotulinumtoxinA (BTX-A)

- Is known to block the release of acetylcholine and paralyzes any muscle into which it is injected[1,3]
- Precise mechanism of action when injected into the detrusor muscle is unknown[3]

Bladder Augmentation/Augmentation Cystoplasty

- A major operation that increases bladder capacity[1,4]

Bladder Diversion/Urinary Diversion

- A surgical procedure that creates an opening in the skin of the lower abdomen to access an artificial urine reservoir created from the bowel[1,5]
  - This reservoir is connected to the bladder and holds the diverted urine until it can be drained into a urostomy bag

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. American Urological Association Guideline. Diagnosis and treatment of overactive bladder (non-neurogenic) in adults: AUA/SUFU Guideline. May 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.** National Collaborating Centre for Women's and Children's Health. *Urinary Incontinence: The Management of Urinary Incontinence in Women*. London, UK: RCOG Press; 2006:1-249. **4.** Cespedes RD, Gerboc JL. Other therapies for storage and emptying bladder. In: Wein AJ, ed. *Campbell-Walsh Urology*. 10th ed. Philadelphia, PA: Elsevier-Saunders; 2012:2186-2203. **5.** Costa JA, Schwartz BF. Urinary diversions and neobladders. *Medscape Reference*. http://emedicine.medscape.com/article/451882-overview#a0103. Accessed July 26, 2013.

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 with frequency and nocturia

OAB is a common 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
- Invasive procedures

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