

EPISODE 1 – THE NURSE PRACTITIONER PERSPECTIVE

Let's Talk Overactive Bladder
OVERCOMING BARRIERS TO ATTAINING PATIENT-SPECIFIC GOALS

Identified by the Center for Independent Professionals' Qualifications and Services (CIPQS)

Supported by an educational grant from Adelson Scientific and Medical Affairs, Inc.

Screening, Diagnostic Techniques and Nonpharmacologic Management

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What Is Overactive Bladder Syndrome?

International Continence Society definition

- A symptom syndrome suggestive of lower urinary tract dysfunction
- Urgency, with or without urgency incontinence, usually with frequency and nocturia
- No proven infection or other obvious pathology

Abrams P, et al. *NeuroUrol Urodyn.* 2002;21:167-178.
Wein A.J, et al. *Urology.* 2002;60(suppl 5A):7-12.

What Distinguishes OAB From Other Common Urinary Disorders?

ICS Definition of Overactive Bladder (OAB)^{1,2}

- A symptom syndrome suggestive of lower urinary tract dysfunction
- Urgency, with or without urgency incontinence, usually with frequency and nocturia
- In absence of metabolic or pathologic conditions

ICS: International Continence Society
SUI: stress urinary incontinence
UUI: urgency urinary incontinence

1. Abrams P, et al. *NeuroUrol Urodyn.* 2002;21:167-178.
2. Wein A.J, et al. *Urology.* 2002;60(suppl 5A):7-12.
3. Adapted from Wein A.J. *J Urol.* 2006;175(3 pt 2):S5-S10.

Overactive Bladder Is Very Prevalent

OAB is equally prevalent in men and women and increases with age
OAB is a more prevalent condition than chronic sinusitis or heart disease

Age (years)	Men (%)	Women (%)
< 25	10	5
25-34	6	6
35-44	12	11
45-54	18	24
55-64	25	24
65-74	30	32
≥ 75	35	30

Overall prevalence, with and without urgency incontinence
N = 5204, P = NS women vs. men

Adapted from Stewart WF, et al. *World J Urol.* 2003;20:327-336; Plets JR, et al. *Summary Health Statistics for U.S. Adults: National Health Interview Survey, 1998.* National Center for Health Statistics. *Vital Health Stat.* 2002;10(209).

Urgency Urinary Incontinence in OAB Is More Prevalent in Women

Gender	With UUI (%)	Without UUI (%)
Women (n = 463)	55%	45%
Men (n = 401)	16%	84%

- OAB is not life-threatening, but a serious medical concern
- OAB is not only a “woman’s disease”

Stewart WF, et al. *World J Urol.* 2003;20:327-336.
Chapple CR. *Expert Opin Pharmacother.* 2006;7:2421-2434.

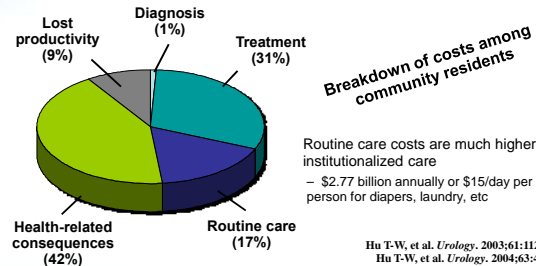
Types of Patients

- Patients with or without comorbidities
- Men (with LUTS/OAB/BPH/BOO)
- Women (with SUI, mixed urinary symptoms, OAB wet or dry)
- Older patients
- Patients with new symptoms
- Patients with severe symptoms
- Previously treated patients that are unsatisfied or treatment refractory

LUTS: lower urinary tract symptoms
BPH: benign prostatic hyperplasia
BOO: bladder outlet obstruction

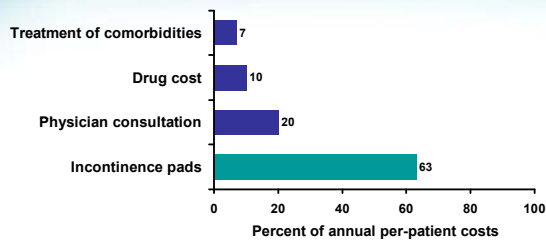
Estimated Costs of OAB in the United States

- Total annual costs of OAB are ≈ \$12 billion
– 70% among community residents, 30% institutionalized residents



Hu T-W, et al. *Urology*. 2003;61:1123-1128.
Hu T-W, et al. *Urology*. 2004;63:461-465.
Mullins CD, et al. *Am J Manag Care*. 2005;11(4 suppl):S101-S102.

Incontinence Pad Use Is the Cost Driver in OAB Management

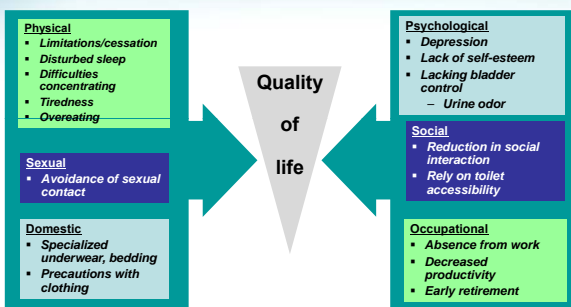


The cost of managing the subpopulation with UII was estimated to be 70% of the total

N = 16,776 European men and women aged >40 years

Reeves P, et al. *Eur Urol*. 2006;50:1050-1057.

OAB Negatively Impacts Many Quality-of-Life Aspects



Adapted from Tuharo A. *Urology*. 2004;64(suppl 6A):2-6.
Irwin DE, et al. *BJU Int*. 2005;97:96-100. Muller N. *Urol Nurs*. 2005;25:109-115.

Physicians' and Patients' Perceptions Differ

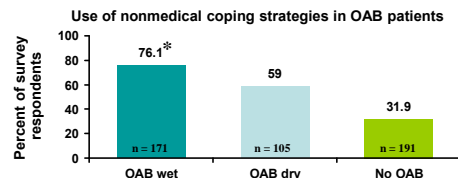
- In 85% of cases of women discussing their incontinence symptoms with their physician, the patient had to raise the issue
- Only 34% of patients with diagnosed OAB receive treatment
- More than 50% of women who discussed OAB with a healthcare provider waited more than a year to seek treatment

Dmochowski RR. *Int Urogynecol J Pelvic Floor Dysfunct*. 2006;17:650-658.
Dmochowski RR, et al. *Curr Med Res Opin*. 2007;23:65-76.

Why Patients Would Rather Cope With OAB Than Seek Help

Barriers to Communication

- Fear of embarrassment
- Fear resulting from misconceptions about OAB
- Differences in perception of symptom severity, degree of bother, willingness to seek treatment



*P < 0.001 vs. control

Ricci JA, et al. *Clin Ther*. 2001;23:1245-1259.
Dmochowski RR. *Int Urogynecol J Pelvic Floor Dysfunct*. 2006;17:650-658.

OAB Diagnosis Has a Positive Impact on Knowledge, Communication, and Management

	Diagnosed	Not diagnosed but having symptoms
Quality of life has improved	47%	32%
Higher sense of self-esteem	40%	21%
Likely to discuss condition with spouse/partner	62%	27%
Likely to discuss condition with doctor/nurse	95%	31%
Seeking information	24%	3%
Managing the symptoms	97%	44%

N = 1420 online interviews

Muller N. *Urol Nurs.* 2005;25:109-115.

Effective Questioning to Detect OAB

The first complaint may not be the chief complaint

- What brings you here today? What are your concerns?
- What is your most distressing symptom?
- How are you handling your urinary symptoms?
 - What do you mean you urinate frequently?
 - How long have you experienced these symptoms?
- What have you tried to solve your problems?
- When asking these questions:
 - Respect the patient's situation
 - Consider a treatment plan
 - Aim for patient-centered medicine

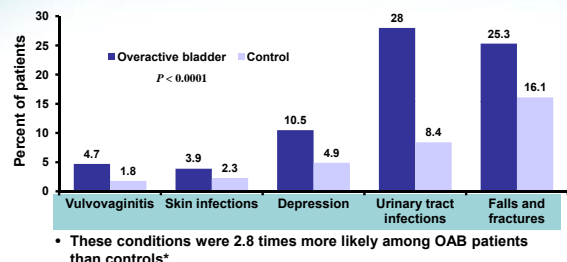
Marshall-Kehrel D, et al. *Urology.* 2006;68(suppl 2A):29-37.

Useful Questions to Direct the Diagnosis of OAB

Do you have to rush to go to the toilet? Do you do this because of a sudden intense feeling so you have to urinate IMMEDIATELY?	Urgency
Do you feel that you urinate too often during the day?	Frequency
Do you have to get up during the night to urinate? Does the urge to urinate wake you?	Nocturia
When you feel the urge to go to the bathroom, do you have leaks or wetting accidents?	Urgency urinary incontinence

Rosenberg MT, et al. *Cleve Clin J Med.* 2005;72:149-156.
Irwin DE, et al. *Eur Urol.* 2006;50:1306-1315.

Look for Comorbidities of OAB



11,556 adult patients with OAB, 11,556 controls, matched on propensity score
*95% CI, 2.6-2.9

Adapted from Darkow T, et al. *Pharmacotherapy.* 2005;25:511-519.

Risk Factors for Incontinence That Also May Influence OAB

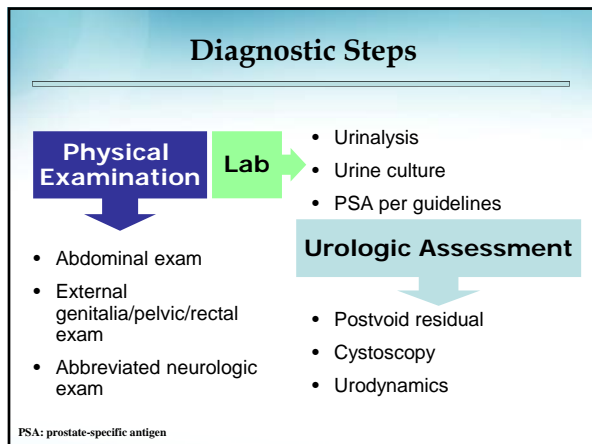
- Immobility
- Diminished cognitive status or delirium
- Stroke
- Diabetes
- Lumbar disk disease
- Fecal impaction
- Urinary tract infections
- Use of diuretics and hypnotics
- Multiple vaginal deliveries
- Hysterectomy, vaginal or bladder surgery
- Obesity (female)

Rosenberg MT, et al. *Cleve Clin J Med.* 2005;72:149-156.

OAB Symptoms May Be Worsened by Medication

Sedatives	Confusion, secondary incontinence
Alcohol, caffeine, diuretics	Diuresis
Anticholinergics other than antimuscarinics (eg, antipsychotics)	Impair detrusor contractility, voiding difficulty, overflow incontinence
α-Agonists	Increase outlet resistance, voiding difficulty
β-Blockers	Decrease urethral closure, stress incontinence
Calcium-channel blockers	Reduce bladder smooth muscle contractility
ACE inhibitors	Induce cough, stress urinary incontinence
Cholinesterase inhibitors	Can precipitate urgency incontinence

Lavelle JP, et al. *Am J Med.* 2006;119(3 suppl):37S-40S.
DuBeau CE. *J Urol.* 2006;175(3 pt 2):S11-S15.
Gill S, et al. *Arch Intern Med.* 2005;165:808-813.



Patients Requiring Urologic Workup

- Hematuria
 - UTI, bladder cancer?
- Vaginal prolapse
- Neurologic disease or injury
- Postsurgical problems
- Sterile pyuria
- Recurrent urinary tract infections
- Pelvic pain, interstitial cystitis

- Elevated levels of postvoid residual
 - May be sign of retention
- Abnormalities of the prostate
- Refractory symptoms
 - eg, antimuscarinic treatment failure
- Patient preference

Wein AJ. *Urology*. 2003;62(suppl 5B):20-27.
 Erdem N, et al. *Am J Med*. 2006;119(3 suppl 1):S38-S44.
 Imam, KA. *Rev Urol*. 2004;6(suppl 1):S38-S44.
 Nitli V, et al. *Int J Clin Pract*. 2005;59:825-830.

UTI: urinary tract infection

Question

A 62-year-old woman complains of urgency, frequency and urgency urinary incontinence. UA is negative. The next step is:

1. Urodynamics
2. Dietary modification
3. Behavioral therapy
4. Antimuscarinics

Question

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1. Urodynamics
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3. Behavioral therapy
4. Antimuscarinics

Behavioral and Lifestyle Modifications for OAB Symptoms

Lifestyle Changes

- Alter fluid intake
- Quit smoking
- Modify diet
- Reduce weight
- Regulate bowel function

Behavioral Approaches

- Pelvic floor (Kegel) exercises
- Scheduled voiding

Newman DK, et al. *Curr Opin Obstet Gynecol*. 2013;25:388-394.
 Newman DK, Wein AJ. *Urol Clin North Am*. 2013;40:613-635.
 Wyman JF. *J Wound Ostomy Continence Nurs*. 2005;32(suppl 1):S11-S15.

Lifestyle Changes Affect OAB Symptoms

- Alter fluid intake**
 - Reduce in patients with high fluid intake (>2400 mL/day)
 - May lessen episodes of incontinence and voiding frequency
 - Increase in patients with a low fluid intake (<1500 mL/day)
 - May improve urine concentration, lessening irritation of the bladder lining
- Quit smoking**
 - Nicotine irritates detrusor muscle causing bladder contraction and urgency
 - Repeated coughing may cause urinary leakage
- Modify diet**
 - Reduce caffeine
- Reduce weight**
 - Lessen stress on the bladder
- Regulate bowel function**
 - Constipation and straining increase pressure on the bladder

Newman DK, et al. *Curr Opin Obstet Gynecol*. 2013;25:388-394.
 Newman DK, Wein AJ. *Urol Clin North Am*. 2013;40:613-635.

Limitations of Behavioral and Lifestyle Modifications for OAB

- Proper execution is labor-extensive and time-consuming, costly if physical therapy is needed
- Gradual results, dry rate 25%–35%
 - No long-term performance data of behavioral modifications
 - Antimuscarinics are often preferred over bladder training
- Diet/weight/exercise: OAB patients are statistically less likely to exercise regularly or go for long walks
 - Contributor to already-compromised health status

Active patient participation required

Borello-France D, et al. *Clin Obstet Gynecol*. 2004;47:70-82.
 Alhasso AA, et al. *Cochrane Database Syst Rev*. 2006;4.
 Milne JL, et al. *Urol Nurs*. 2006;26:41-51.

Management Expectations for Uncomplicated OAB

Most patients with OAB may require long-term treatment for continued benefit

- Pharmacotherapy:
 - Patients may feel benefits within days
 - Maximal benefit after 4 to 6 weeks
 - Long-term treatment is often needed to maintain effects
- Behavioral modifications:
 - Treatment likely requires long-term compliance, but trial data are sparse
- Younger women with less severe OAB:
 - During treatment for 4 to 6 months, patients might be able to retrain bladder
- Initial health education interventions can
 - Improve compliance with medication and
 - Increase the use of behavioral modification therapy

Chapple CR. *Expert Opin Pharmacother*. 2006;7:2421-2434.
 Rovner ES. *Expert Opin Pharmacother*. 2005;6:653-666.
 Alhasso AA, et al. *Cochrane Database Syst Rev*. 2006;4.
 Choo M-S, et al. *J Urol*. 2005;174:201-204.
 Herschorn S, et al. *Can J Urol*. 2004;11:2430-2437.

Case 1: Donna Complaint and Evaluation

- Donna, 57-year-old woman, urinary frequency every 1 to 2 hours, nocturia at least 1–2 times per night
- Worst symptom is strong urinary urgency, often with incontinence episodes
- Past antimuscarinic medication 2 years ago
 - She experienced dry mouth and discontinued medication
- Medical history
 - Hypertension treated with diuretic and calcium channel blocker
 - Vaginal hysterectomy 15 years ago for uncontrolled bleeding
- Physical exam and labs
 - No abnormalities
 - Atrophic vaginitis
 - Urinalysis normal
- Patient expectation: she wants immediate symptom relief

Case 1: Donna Treatment and Follow-up

- **Treatment plan**
 - Take diuretic in the morning to improve nocturia
 - Clinician starts Donna on 5 mg solifenacin QD
 - Fluid modification and reduction or elimination of bladder irritants
 - eg, caffeine and alcohol
 - Pelvic floor exercises and urge control technique to decrease urgency and delay voiding
- **Follow-up at 4 weeks**
 - Urgency improved, less UUI episodes, no adverse events
 - Nocturia and frequency still present
 - Patient reduced caffeine intake
 - Change in treatment
 - Increase dose to 10 mg solifenacin QD
 - Switch hypertensive to nondiuretic
 - Reinforce behavioral modifications
- **Follow-up at 6 weeks**
 - Decreased daytime frequency, no nocturia and only rare UUI episodes
 - Sleep is improved
 - Some dry mouth improved with sugar-free candy
 - Uses urge control techniques
 - No compliance with pelvic floor exercises

EPISODE 2 – THE PRIMARY CARE PERSPECTIVE

Let's Talk Overactive Bladder
OVERCOMING BARRIERS TO ATTAINING PATIENT-SPECIFIC GOALS

Partly provided by the Center for Independent Professionals' Education and Services (CIPES)

Supported by an educational grant from Allergan Scientific and Medical Affairs, Inc.

Early Recognition, Diagnosis, and Management of Overactive Bladder

Matt T. Rosenberg, MD
Director
Mid Michigan Health Centers
Department of Family Medicine
Allegiance Health Systems
Jackson, MI

What is the Diagnosis?

Mr. Jones
60-year-old male
No medical problems
No medications
Urgency, frequency and nocturia

Mrs. Jones
59-year-old female
No medical problems
No medications
Urgency, frequency and nocturia

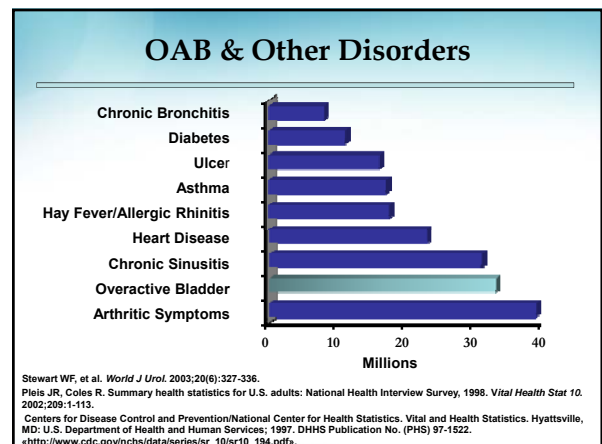
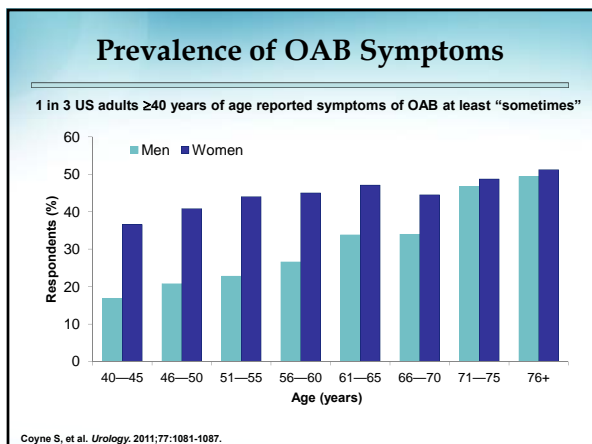
Definition of OAB

OAB is a syndrome or symptom complex defined as: **“Urgency, with or without urgency incontinence, usually with frequency and nocturia”**

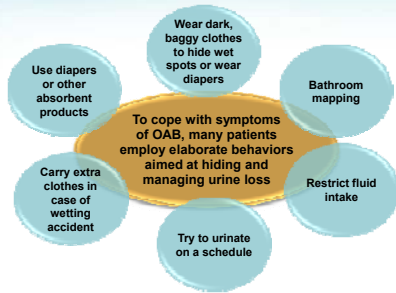
Urgency is the key symptom of OAB

Urgency is defined as “a sudden compelling desire to void, which is difficult to defer”

Abrams P, et al. Urology. 2003;61:37-49.
Rosenberg MT, et al. Int J Clin Pract. 2007;61:1535-1546.



Coping Strategies



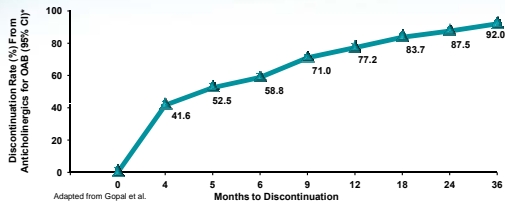
Rosenberg MT. *Curr Urol Rep.* 2008.
 Abrams P, et al. *Am J Manag Care.* 2000;6(11 Suppl):S580-S590.
 Ricci JA, et al. *Clin Ther.* 2001;23:1245-1259.

OAB is Prevalent, Undiagnosed and Undertreated

- 33.3 million US adults are said to have OAB
- Less than 50% will discuss with healthcare provider
- Only a minority will be diagnosed and offered treatment
- A smaller proportion will stay on therapy

Stewart WF, et al. *World J Urol.* 2003;20:327-336.
 Rovner E, Wein A. *Curr Urol Rep.* 2002;3:434-438.
 Milsom I, et al. *BJU Int.* 2001;87:760-766.
 Benner J, et al. *J Urol.* 2009;181:2591-2598.
 Rosenberg M, et al. *Cleve Clinic J Med.* 2007;74:S21-S29.
 Goepel M, et al. *Eur Urol.* 2002;41:234-239.
 Dmochowski RR, et al. *Curr Med Res Opin.* 2007;23:65-76.

High Discontinuation Rate for Patients on OAB Therapy



Adapted from Gopal et al.
Study Design: UK study. Overall drug discontinuation for all women prescribed anticholinergic medications (N=29,369). Unadjusted cumulative incidence of discontinuation (95% CI).

*Cumulative incidence of discontinuation was determined using the Kaplan-Meier method.
 Gopal M, et al. *Obstet Gynecol.* 2008;112:1311-1318.

The Reality is We Can Do Better in the Identification and Treatment of OAB

Why is OAB Underdiagnosed and Undertreated?

The answer is education and communication

Unfortunately, if we don't understand the disease, we may not identify it even to refer, let alone treat!!!!!!

Diagnosing of OAB Takes a Village



Rosenberg MT. *Curr Urol Rep.* 2008;9:428-432.
 Yu YF, et al. *Value Health.* 2005;8:495-505.

Patients Don't Discuss Bladder Issues with the Provider

- Embarrassment
- Fear of invasive procedures or need for surgery
- Perception of lack of available and effective treatment

Ricci JA, et al. *Clin Ther* 2001;23:1245-1259.
Milsom I, et al. *BJU Int* 2001;87:760-766.

What Do Patients Say?

- I have had this problem and did not know who to talk to
- My previous doctor told me it was part of aging
- It became a problem only when my diaper overflowed
- I thought it was normal as my sister and mother had this
- You mean going to the bathroom every hour is not normal?
- I am too embarrassed

MacDiarmid S, Rosenberg, M. *Curr Med Res Opin.* 2005; 21:1413-1421.

The Urologist and the Urogynecologist Role in the Partnership

- Identification and initial evaluation of OAB starts in the office of the PCP
- There is a significant amount of medically related LUTS
- The diagnosis of OAB does not require an extensive or complicated evaluation

Stewart WF, et al. *World J Urol.* 2003;20:327-336.
Darkov T, et al. *Pharmacotherapy.* 2005;25:511-519.
Allinger RL, et al. *J Comm Health Nurs.* 2005;22:135-142.
Rosenberg M, et al. *Cleve Clinic J Med.* 2007;74:S21-S29.

Potential Misconceptions In OAB

- OAB is a natural part of aging
- Diagnosis and treatment of genitourinary disease is to be determined by a specialist
- Diagnosis and treatment is outside the realm of the PCP setting

MacDiarmid S, Rosenberg, M. *Curr Med Res Opin.* 2005;21(9):1413-1421.

What Do Doctors Say?

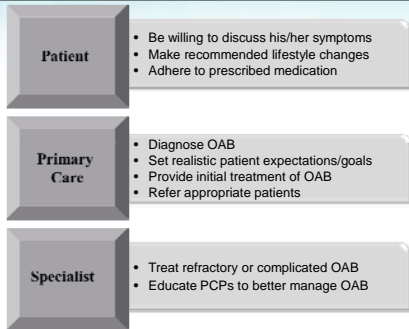
- No time
- Treatments are not all that effective
- If it was a problem for the patient, he or she would bring it up
- Your bladder/penis/kidney won't kill you, your heart will, so I need to focus

MacDiarmid S, Rosenberg, M. *Curr Med Res Opin.* 2005;21(9):1413-1421.

Realities of OAB Management

- The PCP is the first line of contact
- Diagnosis and treatment **is within** the realm of the PCP setting
- Current treatments offer **significant improvement** of patient symptoms and patient quality of life

Treating OAB Takes a Village



Rosenberg MT. *Curr Urol Rep.* 2006;9:428-432.
Yu YF, et al. *Value Health.* 2005;8:495-505.

What Does the PCP Need?

Keep It Simple
Keep It Effective
Keep Us From Harming Our Patients

It All Comes Down to "Normal"

- How many times a day does a **normal** person need to urinate
- What is the **normal** volume of urine voided per micturition?
- Is it **normal** for older people to get up during the night to use the bathroom?

Function of the Bladder

Normal Function

- Storage capacity (300 – 500 mL of fluid)
 - Adequate low pressure urinary storage (bladder)
 - Adequate outlet resistance (sphincter)
- Empty to completion (minimal residual)
 - Adequate bladder contraction
 - Absence of outlet obstruction

Abnormal Function (**failure to store or empty**)

- Voiding frequently small amounts
- Uncontrollable urge (urgency)
- Incomplete emptying
- Hesitancy, poor stream

Wein AJ. Pathophysiology and categorization of voiding dysfunction. In: Wein AJ, Kavoussi LR, Novick AC, et al, eds. *Campbell-Walsh Urology*. 9th ed. Philadelphia, PA: W. B. Saunders/Elsevier; 2007:1973-1985.

Function of the Prostate

- Normal Function
 - Does not grow (enlarge) into the urethra thereby allowing unobstructed flow
 - It is intimately associated with the continence mechanism
 - Produces fluid for seminal emission
- Abnormal Function (**failure of flow**)
 - Obstruction of urinary flow ("obstruction" "retention")
 - Sphincteric damage /usually surgical - ("stress incontinence")

Wein AJ. Pathophysiology and categorization of voiding dysfunction. In: Wein AJ, Kavoussi LR, Novick AC, et al, eds. *Campbell-Walsh Urology*. 9th ed. Philadelphia, PA: W. B. Saunders/Elsevier; 2007:1973-1985.

Lower Urinary Tract Symptoms (LUTS): Bladder or Prostate?

Storage (bladder)	Voiding (prostate)
Urgency	Hesitancy
Frequency	Poor flow/weak stream
Nocturia	Intermittency
Urge incontinence	Straining to void
Stress incontinence	Terminal dribble
Mixed incontinence	Prolonged urination
Overflow incontinence	Urinary retention

Chapple CR, et al. *Eur Urol.* 2006;49:651-658.

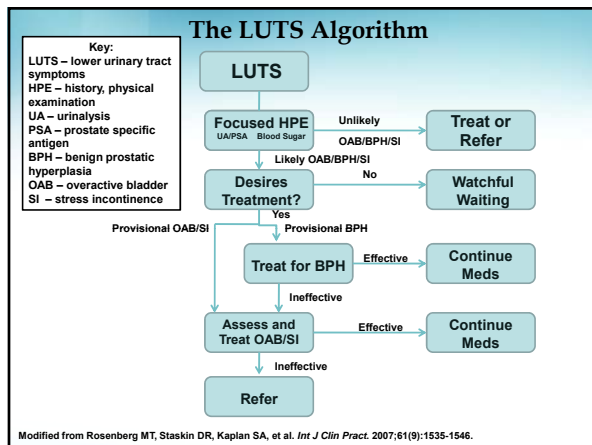
It is all about VOLUME VOIDED and FLOW



Rosenberg MT, et al. *Int J Clin Pract.* 2010; 64(4):488-496.

Guess What Happens When You Understand What is Normal?

- Your patients will understand what is normal, and subsequently, what is abnormal
- You recognize when you have something to fix



Defining LUTS

Frequency	<ul style="list-style-type: none"> • Patient considers that he/she voids too often by day • Normal is <8 times per 24 hours
Nocturia	<ul style="list-style-type: none"> • Waking to urinate during sleep hours • Considered a clinical problem if frequency is greater than twice a night
Urgency	<ul style="list-style-type: none"> • Sudden compelling desire to pass urine that is difficult to defer
UII	<ul style="list-style-type: none"> • Involuntary leakage accompanied by, or immediately preceded by, urgency
OAB "Wet"	<ul style="list-style-type: none"> • OAB with UII
OAB "Dry"	<ul style="list-style-type: none"> • OAB without UII
Warning Time	<ul style="list-style-type: none"> • Time from first sensation of urgency to voiding

Abrams P, et al. *NeuroUrol Urodyn.* 2002;21:167-78.
 Wein A, et al. *J Urol.* 2006;175:55-10.
 Zinner N, et al. *Int J Clin Pract.* 2006;60:119-26.
 Wein AJ. *Am J Manag Care.* 2000;6:5559-64.

Simple Questions the PCP Can Ask

- Do you have a sudden urge to void and can barely make it to the bathroom?
- Do you wear a pad or diaper?
- Can you sit through a movie without going to the bathroom?
- Do you leak urine?
- Do you get up at night?

The Evaluation of LUTS

- Medical and surgical history
- Medications
- Focused physical examination
- Voiding diary
- Labs
- Urodynamics, cystoscopy, and diagnostic renal and bladder ultrasound **not necessary** in initial workup of uncomplicated patients

American Urological Association (AUA) Guideline. AUA Web site. 2012.
http://www.auanet.org/content/media/OAB_guideline.pdf. Accessed March 21, 2014.

Examples in the Medical and Surgical History that May Cause LUTS

- Diabetes (new onset or poorly controlled)
 - Causing polyuria/polydipsia
- Congestive heart failure
 - Nighttime fluid mobilization
- Recent Surgery
 - Catheterization during surgery, immobilization, constipation from pain medications

A recent onset of the symptoms may provide a clue to the etiology

Rosenberg MT, Newman DK, Tallman CT, et al. *Cleve Clin J Med*. 2007;74(suppl 3):S21-S29.

Medications as a Cause of LUTS

Sedatives	Confusion, secondary incontinence
Alcohol, Caffeine, Diuretics	Diuresis
Anticholinergics	Impair contractility, voiding difficulty, overflow incontinence
α-Agonists	Increased outlet resistance, voiding difficulty
β-Blockers	Decreased urethral closure, stress incontinence
Calcium Channel Blockers	Reduce bladder smooth muscle contractility
ACE Inhibitors	Induce cough, stress urinary incontinence
First-generation antihistamines	Increase outlet resistance
Cholinesterase inhibitors	Precipitate urge incontinence
Opioids	Direct effect, constipation

Wyman JF, et al. *Int J Clin Pract*. 2009;63:1177-1191.
Newman DK. *Nurse Pract*. 2009;34:33-45.

The Focused Physical Examination

- Abdominal
 - Tenderness, masses, distension
- Neurological
 - Mental and ambulatory status, neuromuscular function
- Genitourinary
 - Meatus and testis
 - Vaginal mucosal integrity, urethral mobility, bladder prolapse
- Rectal
 - Tone
 - Prostate size, shape, nodules and consistency

Rosenberg MT, Newman DK, Tallman CT, et al. *Cleve Clin J Med*. 2007;74(suppl 3):S21-S29.

Laboratory Tests

- Urinalysis
 - Infection, blood
 - The urine is not an adequate screener for diabetes since the blood sugar must be above 180 mg/dL before it spills into the urine
- A random or fasting blood sugar
 - Diabetes
- Prostate specific antigen
 - Prostate specific not cancer specific but can be used in screening
 - Excellent as a surrogate marker for prostate size
 - PSA is more accurate than a DRE when estimating prostate size
 - A PSA of 1.5 ng/mL equates to a prostate volume of at least 30 grams(mL)

Rosenberg MT, Staskin DR, Kaplan SA, et al. *Int J Clin Pract*. 2007;61,9:1535-1546.
Bosch J, et al. *Eur Urol*. 2004;46:753-759.
Roerborn CG, et al. *Urology*. 1989;33:381-9.

The Purpose of the Voiding Diary

- Identifies voiding frequency and voided volume
- Differentiates behavioral vs. LUTS pathology
 - Voiding frequently
 - excessive volume (**behavioral**)
 - small amounts as a result of always being in a rush (**behavioral**)
 - small amounts (**OAB**)
- Alerts patients to habits /opportunities to modify
- Can monitor effect of treatment

Wyman JF, et al. *Int J Clin Pract*. 2009; 63(8):1177-91.

The Post Void Residual (PVR) is Only Needed in Select Patients

- The fear of patients going into retention when treated for OAB leaves many patients untreated
- If PVR residual is less than 50 mL, causing retention when treating OAB is extremely unlikely
 - **FACT**: most PCPs will not have bladder scanner and will not want to catheterize a patient
 - **FACT**: most PCPs will have access to an ultrasound unit and can order a post void residual
- Use common sense, if you are treating the patient for voiding too frequently (OAB) and they have not voided in 6–8 hours or have a sense to void but cannot, have them contact you

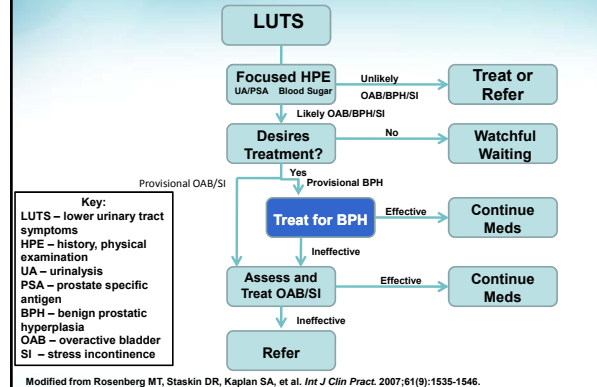
Rosenberg MT. *Curr Opin Urol*. 2008;9(6):428-32.
Rosenberg MT, Staskin DR, Kaplan SA, et al. *Int J Clin Pract*. 2007;61(9):1535-1546.

Indications for Referral

- History of recurrent urinary tract infections or other infection
- Pelvic irradiation
- Microscopic or gross hematuria
- Prior genitourinary surgery
- Elevated prostate-specific antigen
- Abnormal genital exam
- Suspicion of neurological cause of symptoms
- Meatal stenosis
- History of genitourinary trauma
- Pelvic pain
- Uncertain diagnosis or patient choice

Rosenberg MT, Staskin DR, Kaplan SA, et al. *Int J Clin Pract.* 2007;61(9):1535-1546.

The Male (or Prostate) Dilemma



Treatment Now Can Be Empiric

- No identifiable etiology
- No reversible causes
- Is patient bothered enough for treatment?
 - No, watchful waiting
 - Yes, consider algorithm
 - Weak flow – think Prostate
 - Poor voiding volumes – think Bladder
 - Incontinence – think Bladder/Outlet

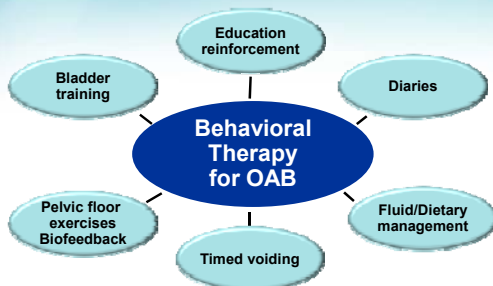
Rosenberg MT. *Curr Urol Rep.* 2008;9:428-432.

Treatment Guidelines for OAB

- Behavioral treatment
- Pharmacologic management
- Referral for specialist management/surgery

Kirby M, et al. *Int J Clin Pract.* 2006;60:1263-1271.
 Burigo K, et al. *J Am Geriatr Soc.* 2000;48:370-374.
 Gormley EA, et al. American Urological Association (AUA) Guideline. Available at: <https://www.auanet.org/education/guidelines/overactive-bladder.cfm>. Amended 2014.

Behavioral Therapy for OAB



No matter what the treatment course, behavioral modification should be offered to every patient

Soda T, et al. *J Urol.* 2010; 184: 1000-1004.

Habit Changes: Managing Bladder Health

Technique	
Lifestyle Modification	Diet, fluid, bowel, and weight management Smoking cessation
Timed/Prompted Voiding	Urination at a fixed interval that avoids the symptom Useful for urgency and urinary incontinence not associated with frequency Good option in patients with cognitive impairment

Wyman JF, et al. *Int J Clin Pract.* 2009;63:1177-91.
 Wigg AS, et al. *BJU Int.* 2007;99:502-9.
 Lucas MG, et al. *Eur Urol* 2012;62(6):1130-42.

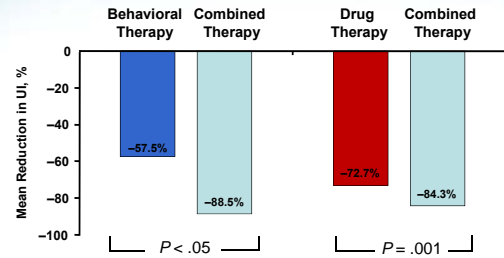
How to Perform Pelvic Floor Muscle Exercises

- Explain location of perineal muscles (anal area)
- Contract perineal muscles, squeezing upward through the pelvis
- Sit or stand with your legs apart, don't hold your breath
- Hold the contraction for 10 seconds, then gradually relax
- Repeat at least 5 times, increase to 30-40 per day in groups of 10
- Relaxation is as important as contraction for muscle rehabilitation
- Use exercises to control symptoms
 - eg, during urge episode, not during urination

The exercises can be performed anywhere

Harv Womens Health Watch, www.health.harvard.edu/newsletters/Harvard_Womens_Health_Watch/2011/January/how-to-perform-kegel-exercises.

Additive Effect of Combining Behavioral And Drug Therapy



Burgio KL, et al. J Am Geriatr Soc. 2000;48:370-374.

EPISODE 3 – THE UROLOGIST PERSPECTIVE

Let's Talk Overactive Bladder
OVERCOMING BARRIERS TO ATTAINING PATIENT-SPECIFIC GOALS

Jointly provided by
Center for Independent
Professional Development
and Research (CIPDR)

Supported by an educational grant from
Astellas Scientific and Medical Affairs, Inc.

Utilizing Current Pharmacologic Options to Attain Treatment Goals

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Los Angeles, CA
Chief of Urology
Rancho Los Amigos National Rehabilitation Center
Downey, CA

Question

A 67-year-old woman with OAB has inadequate results with behavioral therapy for 1 month and desires further therapy. The next step is:

1. Urodynamics
2. Antimuscarinics
3. Beta3-agonist
4. Botulinum toxin A injection
5. Neuromodulation

Diagnosis and Treatment of Overactive Bladder (Non-Neurogenic) in Adults: AUA/SUFU Guideline

AUA. Available at <https://www.auanet.org/common/pdf/education/clinical-guidance/Overactive-Bladder-Algorithm.pdf>. Amended 2014.

Treatment of Overactive Bladder (Non-Neurogenic) in Adults: AUA/SUFU Guideline

First-Line Treatments

Clinicians should offer behavioral therapies as first-line therapy to all patients with OAB

- Bladder training
- Bladder control strategies
- Pelvic floor muscle training
- Fluid management

Behavioral therapies may be combined with pharmacologic management

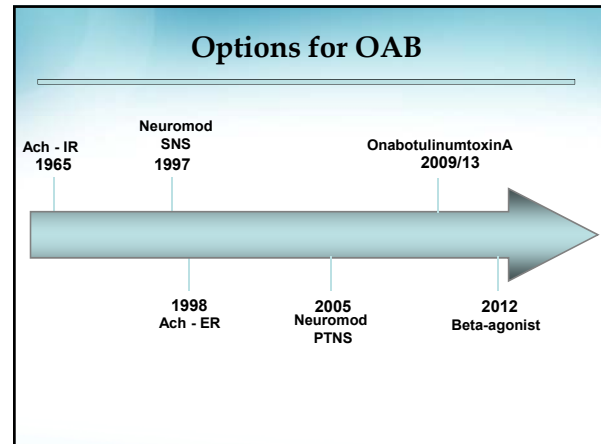
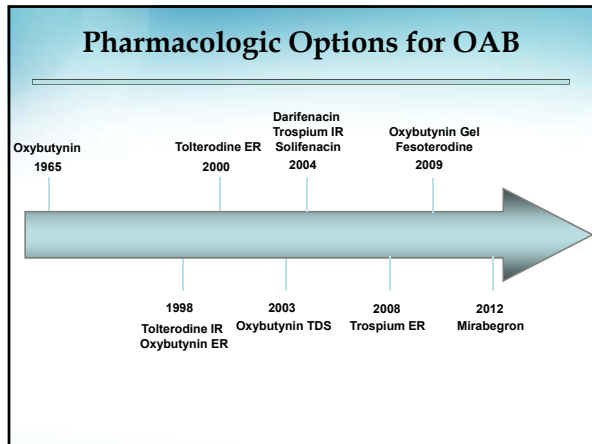
AUA/SUFU. Available at: <https://www.auanet.org/education/guidelines/overactive-bladder.cfm>. Amended 2014.

2014 ACP Guidelines: Nonsurgical Management of Urinary Incontinence (UI) in Women

ACP recommends:

- Pelvic floor muscle training
 - for first-line treatment of stress UI
 - with bladder training for mixed UI
- Bladder training in women with urgency UI
- Pharmacologic therapy
 - women with urgency UI if bladder training unsuccessful
 - selection should be based on tolerability, AE profile, ease of use, and cost
 - Against treatment with systemic pharmacologic therapy for stress UI
- Weight loss and exercise for obese women with UI

ACP, American College of Physicians
Qaseem A, et al. *Ann Intern Med.* 2014;161:429-440.



Treatment of Overactive Bladder (Non-Neurogenic) in Adults: AUA/SUFU Guideline

Second-Line Treatments

- Clinicians should offer oral antimuscarinics* or beta3 (β 3)-adrenoceptor agonists
- If an immediate-release (IR) and extended-release (ER) formulations are available, ER formulations preferential (lower dry mouth rate)
- Transdermal (TDS) oxybutynin may be offered
- If a patient experiences inadequate symptom control and/or unacceptable adverse drug events with one antimuscarinic:
 - Dose modification
 - Different antimuscarinic medication
 - β 3-agonist

* Listed in alphabetical order: darifenacin, fesoterodine, oxybutynin, solifenacin, tolterodine & trospium

AUA/SUFU. Available at: <https://www.auanet.org/education/guidelines/overactive-bladder.cfm>. Amended 2014.

Antimuscarinics - Leader of the Pack?

- Review of randomized trials revealed no compelling evidence for differential efficacy across medications
- The choice of medication for a particular patient depends on the patient's history of:
 - Prior antimuscarinic use
 - Information regarding adverse events experienced in the past
 - Impact on the patient of adverse events
 - Patient preferences
 - Comorbidities
 - Use of other medications
 - Availability of and resources to acquire specific medications

A scatter plot with 'UUA_reduction_per_Dose_Treatment' on the y-axis (ranging from 0.00 to 0.80) and 'UUA_side_effects_per_Dose_Treatment' on the x-axis (ranging from 0.0 to 0.5). Data points are categorized by medication: Darifenacin (open circle), Oxybutynin (filled circle), Solifenacin (open square), Tolterodine (filled square), and Trospium (filled triangle). The plot shows a general negative correlation between side effects and efficacy.

AUA/SUFU. Available at: <https://www.auanet.org/education/guidelines/overactive-bladder.cfm>. Amended 2014.

Antimuscarinics How to Decide?

Immediate-release	Extended-release
<ul style="list-style-type: none"> Oxybutynin Tolterodine Trospium 	<ul style="list-style-type: none"> Oxybutynin (oral and transdermal) Tolterodine Solifenacin Darifenacin Trospium Fesoterodine

Antimuscarinics How to Decide?

Marketing or Reality???

Muscarinic selectivity

- M2/M3 primarily in bladder (M3 primary)
- All antimuscarinics block M3
- But may see less blockade of:
 - M1/M4 - cognition
 - M2 - cardiac

Antimuscarinics How to Decide?

Marketing or Reality???

Minimization of cognitive impact

- M3 selective (no M1/M5) – darifenacin
- Quaternary amine (can't cross BBB) - trospium

Antimuscarinics How to Decide?

Marketing or Reality???

Less drug-drug interaction or If hepatic impairment

- Renal excretion (no CYP 3A4) – trospium
- Not metabolized by liver (serum esterases) - fesoterodine

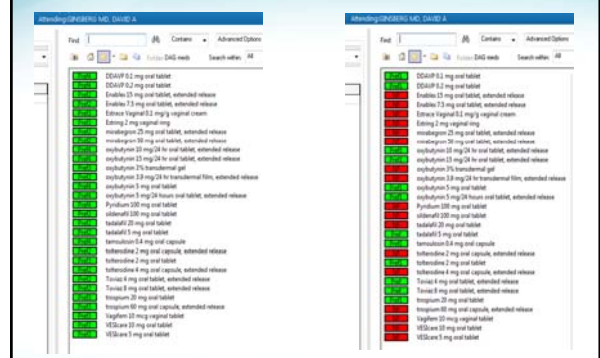
Antimuscarinics How to Decide?

Marketing or Reality???

Baseline constipation

- Avoid M3 selective blockade – darifenacin

...Or, How We Really Decide?



Question

Common adverse events associated with antimuscarinics include:

1. Dry mouth
2. Hypertension
3. Arrhythmia
4. Urinary retention

Treatment of Overactive Bladder (Non-Neurogenic) in Adults: AUA/SUFU Guideline

Second-Line Treatments

- Do not use antimuscarinics in patients with narrow-angle glaucoma unless approved by the treating ophthalmologist
- Use antimuscarinics with extreme caution in patients with impaired gastric emptying or a history of urinary retention
- Manage constipation and dry mouth before abandoning effective antimuscarinic therapy.
- Use caution in prescribing antimuscarinics in patients who are using other medications with anticholinergic properties
- Use caution in prescribing antimuscarinics or β 3-agonists in the frail OAB patient
- Patients who are refractory to therapy should be evaluated by an appropriate specialist if they desire additional therapy

AUA/SUFU. Available at: <https://www.auanet.org/education/guidelines/overactive-bladder.cfm>. Amended 2014.

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AUA/SUFU. Available at: <https://www.auanet.org/education/guidelines/overactive-bladder.cfm>. Amended 2014.

Minimizing Impact of Adverse Effects

- Majority of patients discontinue after a few weeks or months
- Adverse effects commonly cited as reason for discontinuation

Constipation

- Education
- Dietary fiber
- Fluid
- Psyllium-based fiber supplements

Dry mouth

- Oral lubricants
- Avoid EtOH-based mouthwash
- Small sips of water
- Sugar-free candies/gum

Kelleher CJ, et al. *Br J Obstet Gynaecol.* 1997; 104: 988.
Benner JS, et al. *BJU Intl.* 2010; 105: 1276.
D'Souza AO, et al. *J Manag Care Pharm.* 2008; 14: 291.

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AUA/SUFU. Available at: <https://www.auanet.org/education/guidelines/overactive-bladder.cfm>. Amended 2014.

OAB Symptoms May Be Worsened by ...

Sedatives	Confusion, secondary incontinence
Alcohol, caffeine	Diuresis
Anticholinergics other than antimuscarinics	Impair detrusor contractility Voiding difficulty Overflow incontinence
α-Agonists	Increase outlet resistance, voiding difficulty
β-Blockers	Decrease urethral closure Stress incontinence
Calcium-channel blockers	Reduce bladder smooth muscle contractility
ACE inhibitors	Induce cough, stress urinary incontinence

Lavelle JP, et al. *Am J Med.* 2006;119:375-408.
DuBeau CE. *J Urol.* 2006;175:S11-S15. Gill S, et al. *Arch Intern Med.* 2005;165:808-813.

Question

A 72-year-old woman with OAB has improvement with oxybutynin IR 5 mg TID but complains of dry mouth. The next step is:

1. Oxybutynin ER 10 mg
2. Solifenacin 5 mg
3. Mirabegron 50 mg
4. Botulinum toxin A

Antimuscarinic Alternative

- Non-antimuscarinic option an advance in treatment of OAB
- β 3-agonist (i.e., mirabegron) approved by the FDA June 2012
- Only medication with FDA-indication for OAB that is not an antimuscarinic

Beta Receptors & The Bladder

- Human bladder and urothelium contain β_1 , β_2 , and β_3 ARs¹
- 95% of β receptors in human bladder are β_3 ²
- Selective β_3 agonism – significant relaxation of human bladder muscle strips compared to β_1 and β_2 agonism³

AR, adrenergic receptor

1. Tyagi P, et al. *Internat Braz J Urol.* 2009;35:76-83.
2. Yamaguchi O. *Urology.* 2002;59:25-9.
3. Igawa Y, et al. *J Urol.* 2001;165:240-4.

Question

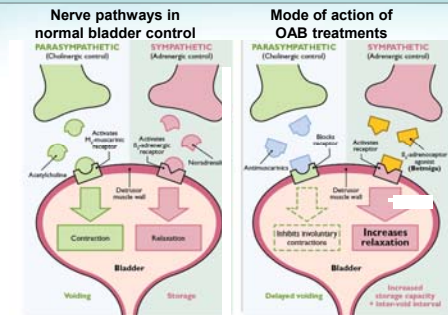
Common adverse events associated with beta3- agonists include:

1. Dry mouth
2. Hypertension
3. Arrythmia
4. Urinary retention

Beta Agonists

- Development of selective β_3 -agonists for OAB
 - Avoid activation of the β_1 and β_2 -AR (and undesirable adverse effects such as increased heart rate and muscle tremors)
- Mirabegron
 - Approved for OAB in Japan, US, Europe & Canada
 - In US: once daily, two doses (25 and 50 mg)
 - No dry mouth or constipation
 - Hypertension

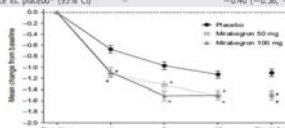
Antimuscarinics vs. β_3 -Agonists



Adapted from Chu FM, Dmochowski R. *Am J Med* 2006;119(3 Suppl 1):3-8.

Mirabegron Pooled Analysis of 3 Phase III Studies

	Placebo	Mirabegron 50 mg
Co-primary end-points		
Change from baseline to Final Visit in the mean number of incontinence episodes/24 h (IAS-I)		
Baseline	2.73 (0.09)	2.71 (0.09)
Final Visit	1.64 (0.09)	1.23 (0.08)
Change from baseline	-1.09 (0.09)	-1.48 (0.08)
Adjusted change from baseline* (95% CI)	-1.10 (-1.23, -0.97)	-1.49 (-1.63, -1.36)
Adjusted difference vs. placebo* (95% CI)	-	-0.40 (-0.58, -0.21) [†]



Nitti VW, et al. *IJCP*. 2013; 67: 619-32.

Mirabegron Pooled Analysis of 3 Phase III Studies

	Placebo	Mirabegron 50 mg
Co-primary end-points		
Change from baseline to Final Visit in the mean number of micturitions/24 h (IAS)		
Baseline	11.58 (0.09)	11.70 (0.09)
Final Visit	10.29 (0.09)	9.93 (0.09)
Change from baseline	-1.18 (0.08)	-1.77 (0.08)
Adjusted change from baseline* (95% CI)	-1.20 (-1.34, -1.06)	-1.75 (-1.89, -1.61)
Adjusted difference vs. placebo* (95% CI)	-	-0.55 (-0.75, -0.36) [†]



Nitti VW, et al. *IJCP*. 2013; 67: 619-32.

Mirabegron Pooled Analysis of 3 Phase III Studies

Number of patients (%)	Mirabegron				Tolterodine ER 4 mg (n = 495)
	Placebo (n = 1380)	25 mg (n = 432)	50 mg (n = 1375)	100 mg (n = 928)	
Any TEAE	658 (47.7)	210 (48.4)	647 (47.1)	402 (43.1)	1259 (64.0)
Drug-related TEAE	232 (16.8)	87 (20.1)	256 (18.4)	172 (18.5)	515 (18.8)
TEAE leading to discontinuation	46 (3.2)	17 (3.9)	53 (3.9)	34 (3.7)	104 (3.8)
Drug-related TEAE leading to discontinuation	27 (2.0)	11 (2.5)	35 (2.5)	25 (2.7)	71 (2.4)
SAE	29 (2.1)	7 (1.6)	29 (2.1)	26 (2.8)	62 (2.3)
Drug-related SAE	6 (0.4)	3 (0.7)	7 (0.5)	3 (0.3)	13 (0.5)
Common TEAEs by preferred term (reported by ≥ 3% in total mirabegron group)					
Hypertension	105 (7.6)	49 (11.3)	103 (7.5)	48 (5.2)	200 (7.3)
Neuropharyngitis	35 (2.5)	15 (3.5)	54 (3.9)	25 (2.7)	94 (3.4)
Urinary tract infection	25 (1.8)	18 (4.2)	40 (2.9)	25 (2.7)	83 (3.0)
Antimuscarinic AEs of interest by preferred term (reported by ≥ 2% in any group)					
Headache	43 (3.1)	10 (2.3)	47 (3.4)	23 (2.5)	80 (2.8)
Dry mouth	29 (2.1)	8 (1.9)	23 (1.7)	23 (2.5)	50 (1.9)
Constipation	20 (1.4)	7 (1.6)	22 (1.6)	15 (1.6)	44 (1.6)
Drug-related* TEAEs by preferred term (reported by ≥ 2% in any group)					
Hypertension	43 (4.4)	30 (6.9)	65 (4.7)	32 (3.4)	127 (4.0)
Headache	18 (1.3)	4 (0.9)	28 (2.0)	12 (1.3)	44 (1.4)
Dry mouth	22 (1.6)	7 (1.6)	13 (0.9)	20 (2.2)	40 (1.5)

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Nitti VM, et al. *IJCP*. 2013; 67: 619-32.

Maximizing Oral OAB Agents? Combo Antimuscarinic & β3-Agonist

Symphony Trial

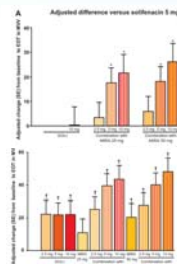
- Phase 2
- 1306 patients with OAB
- Anticholinergic – solifenacin
- Beta3-agonist – mirabegron
- 12 treatment groups
 - Placebo
 - 6 combo (soli 2.5, 5 or 10 mg + mirabegron 25 or 50 mg)
 - 5 monotherapy (solifenacin 2.5, 5 or 10 mg or mirabegron 25 or 50 mg)

Abrams P, et al. *Eur Urol*. 2014; [Epub ahead of print]

Results

MVV (primary end point)

- Four combo groups superior to solifenacin 5 mg
 - solifenacin 5 + mirabegron 25
 - solifenacin 10 + mirabegron 25
 - solifenacin 10 + mirabegron 50
 - solifenacin 10 + mirabegron 50
- All arms except mirabegron 25 mg superior to placebo



MVV, mean volume voided
Abrams P, et al. *Eur Urol*. 2014; [Epub ahead of print]

Results

Adverse events

- No significant impact on PVR (one retention pt*)
- Two most common – dry mouth & hypertension
- Anticholinergic side effect (dry mouth, constipation, etc.) – dose relationship with solifenacin monotherapy
 - No increase with combo therapy
- Hypertension – negligible, decreased in some groups

*Patient taking solifenacin 2.5 mg plus mirabegron 25 mg
Abrams P, et al. *Eur Urol*. 2014; [Epub ahead of print]

Behavioral Therapy (BT) plus Antimuscarinics

1. BT + meds (oxybutynin) in elderly women
 - BT alone 58% UI reduction → 89% reduction with BT + oxy
 - Oxy alone 73% UI reduction → 84% reduction with BT + oxy

1. Burgio KL, et al. *J Am Geriatr Soc.* 2000;48:370.
2. Burgio KL, et al. *Ann Intern Med.* 2008;149:161.
3. Rai BP, et al. *Cochrane Database Syst Rev.* 2012;12 (CD003193).
4. Borello-France D, et al. *Phys Ther.* 2010;90:1493.

Behavioral Therapy



BT + Antimuscarinics

1. BT + meds (oxybutynin) in elderly women
 - BT alone 58% UI reduction → 89% reduction with BT + oxy
 - Oxy alone 73% UI reduction → 84% reduction with BT + oxy
2. Tolterodine alone vs. tolterodine + BT
 - Combo – greater decrease in UI and patient satisfaction
 - Use of BT does not improve ability to come off meds
3. Cochrane Review
 - Antimuscarinics > BT alone
 - Antimuscarinics + BT > BT alone
 - Antimuscarinics + BT vs. antimuscarinics alone unclear
4. Adherence – 10 weeks of meds +/- BT
 - Week 10 – 81% pelvic floor exercises 5-6 days/week
 - 12 months – 32% pelvic floor exercises 5-6 days/week



1. Burgio KL, et al. *J Am Geriatr Soc.* 2000;48:370-4.
2. Burgio KL, et al. *Ann Intern Med.* 2008;149:161-9.
3. Rai BP, et al. *Cochrane Database Syst Rev.* 2012;12.
4. Borello-France D, et al. *Phys Ther.* 2010;90:1493-505.

Treatment of Overactive Bladder (Non-Neurogenic) in Adults: AUA/SUFU Guideline

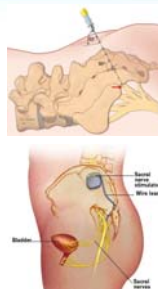
Third-line Treatments – clinician may offer if failed second tier therapies (oral meds)

- Sacral neuromodulation (SNS)
 - In office testing
 - Willing to undergo a surgical procedure for permanent implant
- Peripheral tibial nerve stimulation (PTNS)
 - Done in office
 - Able and willing to undergo treatments weekly X 12 weeks
- Intradetrusor onabotulinumtoxinA
 - Done in office
 - Able and willing to perform self-catheterization if necessary

AUA/SUFU. Available at: <https://www.auanet.org/education/guidelines/overactive-bladder.cfm>. Amended 2014.

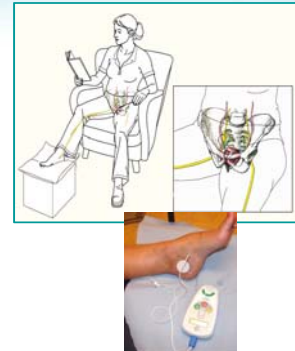
Sacral Nerve Stimulation

- Stimulation of S3
- “Modulate” inappropriate reflexes
- Initial stimulation
- Permanent implant if ≥50% improvement
- Multiple indications
- Change battery ~5 years



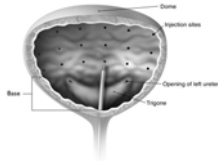
Percutaneous Tibial Nerve Stimulation

- Urgent® PC minimally invasive neuro-modulation system
- Retrograde stimulation of sacral nerve plexus
- Treat weekly for 12 weeks
- If successful – monthly stimulation



OnabotulinumtoxinA

- Injections done in office
- OAB and NGB refractory to antimuscarinics
- Treatment effect 6–9 months
- Repeat treatments durable
- Temporary retention risk



Assessment of Outcomes

- Voiding diary
- Patient-related global response scales
 - Urgency
 - Urgency incontinence
 - Frequency
 - Nocturia
- Validated OAB-specific questionnaires
- Query of adverse events