#### The Role of the Health Care Provider in Improving Quality of Life for Patients with Overactive Bladder

Association of Reproductive Health Professionals <u>www.arhp.org</u>

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#### **Faculty Disclosure**

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Nothing to disclose.

#### Medical Advisory Committee

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### Learning Objectives

At the conclusion of this program, participants will be able to:

- Demonstrate effective counseling skills in order to facilitate conversations about OAB with appropriate patients
- Recognize the signs of OAB and formulate an appropriate differential diagnosis in order to provide evidence-based care

more...

#### Learning Objectives (continued)

At the conclusion of this program, participants will be able to:

- Provide pharmacological and non-pharmacological treatments, emphasizing adherence
- Develop strategies for patient centered care, including when to refer to a specialist

#### What is urinary incontinence?



#### Is it just about getting old?



# No! Urinary Incontinence is <u>NOT</u> a normal part of getting older!



## **Overactive bladder**

- What is overactive bladder (OAB)?
  - Urinary urgency with or without incontinence
  - Urinary frequency (voiding > 8 times in 24 hours)
  - Nocturia (awakening ≥1 or more times to void)

Urgency: A compelling urge to urinate which is difficult to defer

#### **Urge Incontinence**

 Incontinence associated with urgency



#### Prevalence of OAB

- 17% of adults > 18 y/o
- Increases with age (30% over the age of 65)
- 63% of OAB patients are continent
- 37% of OAB patients are incontinent

Hampel, *Urologe A* 2003;42:776–86; Stewart, *World J Urol* 2003;20:327–36; http://www.census.gov/cgi-bin/ipc/idbrank.pl

#### Prevalence of OAB Compared with Other Chronic Conditions



National Centers for Health Statistics. FastStats. http://www.cdc.gov/nchs/fastats/default.htm. Accessed February 5, 2010; American Diabetes Association. Diabetes Statistics. http://www.diabetes.org/diabetes-basics/diabetes-statistics/. Accessed February 8, 2010; Hu T, et al. Urology. 2004;63(3):461-465.

#### **Prevalence of OAB Comorbidities**



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

#### Falls & Fractures

- In women > 65 years with urge incontinence
  1 or more times per week
  - 19 42% sustain falls
  - Fractures occur in 4–9% of falls
  - Frequent urge incontinence found to be an independent risk factor for falling (OR = 1.26)

#### Why Patients Don't Seek Care

- Embarrassment
- Failure to see symptoms as abnormal
- Belief that symptoms are self-limited
- Perception of lack of treatment efficacy
- Fear of procedure
- Fear of cost of treatment

#### **Clinician Factors**

- Dismisses symptoms as unimportant
- Considers OAB a natural part of aging
- Perceives treatment is ineffective
- Unaware of the differential diagnosis

Milsom I et al. Am J Manag Care. 2000;6(11 suppl):565-573; Milsom I et al. *BJU Int.* 2001;87:760-766; Ricci JA et al. *Clin Ther.* 2001;23:1245-1259.

#### **Clinician Factors**

- Dismisses the impact on Quality of Life
- Does not consider potential complications:
  - Depression
  - Skin infections
  - Falls & fractures

Milsom I et al. Am J Manag Care. 2000;6(11 suppl):565-573; Milsom I et al. *BJU Int.* 2001;87:760-766; Ricci JA et al. *Clin Ther.* 2001;23:1245-1259.

#### Elapsed Time Before Seeking Treatment



Harris Interactive, 2001. Dmochowski RR et al. *Curr Med Res Opin.* 2007;23(1):65-76.

#### Three major types of incontinence

- Stress Incontinence
- Urge Incontinence
- Mixed Incontinence



### OAB, SUI, and UTI

Symptoms	OAB	SUI	UTI
Urgency	Yes	No	Yes
Frequency	Yes	No	Yes
Leaking during physical activity	Sometimes	Yes	No
Amount of leakage	Variable	Variable	Small
Urge incontinence	1/3	No	Sometimes
Nocturia	Usually	sometimes	Usually
Urinalysis & culture	Normal	Normal	Abnormal

#### **Clinical Presentation of OAB**

- "I have OAB" the patient self diagnoses
- The patient complains of lower urinary tract symptoms (LUTS) & the primary health care provider (PHCP) elicits OAB symptoms
- The PHCP probes a reluctant patient who admits she has OAB symptoms

### Differential Diagnosis in Women

#### Uro-gynecologic

- Urinary tract infection
- Stress incontinence
- Pelvic organ prolapse
- Neurogenic bladder
- Postsurgical
- Interstitial cystitis
- Urethral diverticulum
- Bladder cancer

#### Medical

- Polyuria / polydipsia
- Diabetes
- Congestive heart failure
- Medications

### **Diagnostic Evaluation**

- History & questionnaire
- Physical exam
- Urinalysis & culture
- Bladder diary

#### Focused History & Questionnaire

- Lower urinary tract symptoms
- Diabetes
- Neurologic disorders
- Recurrent UTI
- Hematuria
- Kidney stones
- Prior lower abdominal / pelvic surgery
- Women prolapse, vaginitis

### LUTS Symptoms

Storage Symptoms

- Urinary Frequency
- Urgency
- Nocturia
- Incontinence
- Pain

#### Voiding Symptoms

- Hesitancy / Weak
  Stream / Straining
- Incomplete emptying
- Pain
- Post-void dribbling

#### Useful Questions for OAB

- "Are you bothered or worried by your urine control?"
- "Do you have strong, sudden urges to urinate?"
- "Do you go to the bathroom so often that it interferes with your activities?"
- "Do you frequently get up at night to urinate?
- Do you leak urine on the way to the bathroom?"

### **Neurologic Disorders**

- Multiple sclerosis
- Stroke
- Parkinson's disease
- Spinal cord Injury
- Spina bifida

#### **Physical Examination**

- General
- Neurologic
- Urologic / gynecologic
- Neuro-urologic

### **Physical Examination**

Vaginal exam:

- Assess perineal sensation, reflexes
- Assess post-void residual volume
- Atrophic vaginitis
- Pelvic organ prolapse
- Masses
- Tenderness
- Urethral diverticulum

### Pelvic Organ Prolapse

- Grade 0 No descent
- Grade 1 Descent halfway to hymen
- Grade 2 At the hymen
- Grade 3 Halfway past hymen
- Grade 4 > Halfway past hymen



#### Grade1 POP

#### Grade 2 POP



#### Grade 3 POP





#### Grade 4 POP





Urethra

**Bladder Diary** 

- Time of urination
- Voided volume (estimated or measuring cup)
- Description of symptoms

A re-useable, folding measuring container can be purchased at Life-Tech.com

#### OAB BLADDER DIARY Uro-Center of New York Phone (212)772-3900 Fax: (212)772-1919

Name: C		Date:				
Time of Day Diary Started:						
Time you went to bed: Time you got up for the day:						
Time of Urination and/or Incontinence Episode	Why did you urinate at this time? (see question # (a) for responses)	Amount of urination (measure with a cup in cc's, ml's, or ounces)	Incontinence grade (see question # (b) below for responses)			
1)						
2)						
3)						
4)						
5)						
6)						
7)						
8)						
9)						
10)						
11)						
12)						
13)						
14)						
15)						

Another bladder diary is available for download at http://kidney.niddk.nih.gov/kudiseases/pubs/diary/index.htm

Variable	All Patients Mean (Median)	Male Mean (Median)	Female Mean /Median
Volume Day ml		1267 (1105)	1261 (1126)
Volume Night ml		446 (408)	468 (414)
Frequency Day		6.1 (6.0)	6.7 (6.5)
Frequency Night		0.4 (0.3)	0.4 (0.3)
Bladder Capacity day		250 (234)	229 (220)
Bladder capacity night		334 (309)	332 (294)
24hr Volume	1730 (1576)	1713 (1512) *	1729 (1619)*
24hr Frequency	7.1 (7.0)	6.5 (6.3) *	7.1 (6.8) *


### Treatment

- Treatment of remediable condition
- Behavioral therapy
  - Bladder retraining
  - Timed voiding
  - Physiotherapy
- Pharmacotherapy
  - Estrogen
  - Anti-muscarinics (anti-cholinergics)
  - Tricyclic antidepressants

### Remediable Conditions in Women

Uro-gynecologic

- •Pelvic organ prolapse
- •Stress incontinence
- Urethral diverticulum
- •Bladder & ureteral stones

Bladder cancer

**Primary Care** 

•UTI

- •Polyuria / polydipsia
- Diabetes
- •Congestive heart failure
- Medications

Rosenberg et al. Cleve Clin J Med. 2007;74(suppl 3):S21-S29.

#### RD2 Can take out (repetitive) Roxanne Donnelly, 04/16/2010

### **Bladder Retraining**

- Educational and behavioral processes used to reestablish control of urinary incontinence
- Scheduled voiding regimen with gradually progressive voiding intervals
- Urgency control strategies
- Self-monitoring of voiding behavior (diaries)
- Positive reinforcement by clinician

### Bladder Retraining: General Principles

- Patient completes a 24 hour bladder diary
- Health care provider & patient review diary
- Recognize patterns
- Develop Rx strategies
- Usually accomplished in 3 6 weekly visits

# Pattern Recognition

### Pavlovian

- •Garage door
- •Door key
- •Elevator
- •Running water
- Sitting to standing

### Non-Pavlovian

- •Relationship to bladder volume
- •Types of food or fluid consumed
- Preoccupation
- Computer, Reading
- Movie

#### No Pattern

#### RD3 Can take out (repetitive) Roxanne Donnelly, 04/16/2010

### Bladder Retraining: General Principles

- Patient completes a 24 hour bladder diary
- Health care provider & patient review diary
- Recognize patterns
- Develop Rx strategies
- Usually accomplished in 3 6 weekly visits

### **Treatment Strategies**

- Adjust type & amount of fluid Intake consistent with basic fluid requirements
- Fluid restriction may be dangerous, particularly in the elderly
- Adjust inter-voiding interval
- Practice control mechanisms

### The more you drink



### Lifestyle Changes

- Moderate fluid intake
- Avoid dietary bladder irritants (ie, EtOH, caffeine, tomatoes, citrus)
- Improve patient mobility
- Address coexisting health issues
- Improve bowel habits/regularity

## Control Mechanisms (the "Knack")

- Anticipate those activities that bring on symptoms
- Contract pelvic muscles quickly
- Wait until the urge subsides do not rush stop and stay still
- Concentrate on suppressing the urge
- Walk to the bathroom at a normal pace

### What about bladder retraining?

- Incontinence reduced 50%-87%
- Biofeedback helps patient satisfaction but not incontinence response
- Bladder retraining (on protocol) can be as effective as meds for urge incontinence
- Bladder retraining + pelvic muscle rehab probably better than retraining alone
- Better chance to get DRY

### Combination Therapy Reduction in Incontinence



Burgio et al. JAGS. 2000;48:370-374.

### Limitations of Behavioral Therapies

- Requires motivation and compliance
- Require a skilled and trained therapist
- Generally inadequate insurance coverage

## Pelvic Floor Muscle Exercises (PFME)

- Designed to strengthen PFM
- Primarily used in patients with SUI and as part of normal exercise program to maintain "pelvic health"
- Also used to teach the "knack"
- Biofeedback may be useful for teaching & monitoring

### Pharmacologic Treatments

- Estrogen
- Antimuscarinics
  - Non-selective
  - Selective
- Tricyclic antidepressants
- Botulinum toxin



### Estrogen

- Overall subjective improvement in individuals with incontinence<sup>1</sup>
- Improvement more likely with urge incontinence
  - Combined estrogen and progesterone appears to reduce likelihood of cure or improvement
- Estrogen therapy may worsen stress incontinence<sup>2</sup>

Cochrane Database Syst Rev 2003;CD001405.; Hendrix SL. JAMA 2005;293(8):935-48.

### Neurotransmitters

- Acetylcholine
- Main neurotransmitter at nerve endings on detrusor
- Five subtypes of muscarinic receptors
- M1-M5
- M3 receptors = responsible for detrusor contraction



Muscarinic Receptors at a Neuromuscular Junction

# Distribution of Cholinergic and Adrenergic Receptors



# Acetylcholine is neurotransmitter in many other organs



Distribution of muscarinic receptors throughout the body

### Parasympathetic Innervation



Acetylcholine (Ach) stimulates muscarinic receptors that cause detrusor contraction

## Anticholinergics (Antimuscarinics)

- Oxybutynin (Ditropan<sup>®</sup>, Oxytrol<sup>®</sup>)
  - Immediate
  - Extended
  - Patch/gel
- Tolterodine (Detrol<sup>®</sup>)
  - Immediate
  - Extended
- Trospium chloride (Sanctura<sup>®</sup>)
- Darifenacin (Enablex<sup>®</sup>)
- Solifenacin succinate (VESIcare<sup>®</sup>)
- Fesoterodine fumarate (Toviaz<sup>™</sup>)

M3 specific?

### Are There Differences Between Antimuscarinics?

- Efficacy all about the same
- Safety all about the same
- Side effects & tolerability individual variation based on:
  - Receptor selectivity
  - Serum concentration of the active drug

# Efficacy of Anti-muscarinic agents (AMAs)

	% reduction
Urgency	44 - 63%
Urge incontinence	57 – 77%
Frequency	17 – 28%

Sand PK. *Eur Urol* 2007;S6:438–43; Hegde SS. *Br J Phamacol* 2006;147:S80–S87; Hashimoto K *et al. Urol Internationalis* 1999;62:12–164.; Freeman R *et al. Obstet Gynecol* 2003;102:605–11; Chapple CR *et al. Eur Urol* 2005;48:464–70

### Anti-cholinergic trials OBJECT

- Oxybutynin ER 10mg QD vs tolterodine IR 2 mg BID
  - Double-blind RCT at 37 US sites
  - 332 men and women with OAB for 12 wks
- Findings:
  - Oxybutynin ER more effective in reduction of UUI episodes, total incontinence, and frequency
  - Adverse effects and tolerability similar
- Limitations:
  - Different formulations and dosages (extended vs immediate release)
  - No QOL data

Appell RA, et al. Mayo Clin Proc 2001;76:358-63

### Anti-cholinergic trials OPERA

- Oxybutynin ER 10 mg/d (n=391) vs Tolterodine ER 4 mg/d (n=399)
- Randomized, 12-week, double-blind, active-control, multicenter trial
- Adult females with severe OAB
- Avg 37 incontinent episodes/wk
- Avg 10 voids/24 hrs

### **OPERA** Results

### Mean UUI Episodes at Week 12 (End of Study)



- No difference in mean weekly UUI episodes at wk 12
  - 10.8 vs 11.2 (*P*=0.28)

Diokno AC et al. Mayo Clin Proc 2003;78:687-95

### **OPERA** Results

- Oxybutynin more effective at reducing frequency
- More completely dry with oxybutynin
  - 23% oxybutynin vs 16.8% tolterodine
- More dry mouth with oxybutynin

### Oxybutynin vs Tolterodine -Summary

- Equally effective at reducing urgency and urge incontinence
- Oxybutynin may be superior at decreasing frequency but more dry mouth
  - Discontinuation rates similar
- Both have compliance issues due to side effects
- Both improve QOL
  - No head-to-head trials comparing QOL

### Safety

### • CNS

- Cognitive dysfunction (particularly in elderly)
- Memory impairment
- Cardiac
  - Heart Rate
  - QTc interval

# **Cognitive Side Effects**

### • Depend on

- Whether drug crosses blood brain barrier (BBB)
- Premorbid cognitive status
- Receptor subtype (M1, ?M4, ?M5)
- Factors that promote diffusion across BBB:
  - cerebrovascular disease (stroke, aneurysm)
  - multiple sclerosis & spinal cord injury,
  - diabetes mellitus,
  - fever
  - aging

### **Cognitive Side Effects**

- Oxybutynin adversely affects cognition
- Darifenicin, solifenacin & tolterodine do not
- Fesoterodine & trospium probably do not

### Side effects

- Dry eyes
- Dry mouth
- Constipation
- Urinary retention

Narrow (closed) angle glaucoma = contraindication to use
Vast majority of pts discontinue anticholinergics by 1 year!!!

### **Tricyclic Antidepressants**

- Imipramine & amitryptiline
- Inhibit uptake of norepinephrine & serotinin
- Anticholinergic & sympathomimetic effects
- Suppress detrusor contractions
- Increase outlet resistance by urethral contraction
- Not FDA approved for OAB
- Not used as primary treatment
- Effects are additive to anticholinergics
- Usually used in combination with AMA's
## What do I do?

- Start with either tolterodine or oxybutynin
- If pt with cognitive issues, use darifenicin (caution in pts with constipation), tolterodine, or solifenacin
- 2<sup>nd</sup> line: non-generics
- Consider adding tricyclics if OAB sx refractory and pt tolerating anticholinergic side effects

## Specialty Treatments for Refractory OAB

- Botulinum toxin injections into bladder (50 – 80% success, but requires repeated injections)
- Neuromodulation (56 90% success)
- Enterocystoplasty (> 90% success)
- Urinary diversion (>90% success)

## Conclusion

- OAB is a symptom complex with a wide differential diagnosis
- It is common, prevalence about 17%
- Initial Dx & Rx are appropriate for the PCHP
- Behavior modification and AMAs are effective in the majority of patients, but the latter is limited by side effects

## When to Refer to a Specialist

- Hematuria
- Diagnosis unclear
- Voiding symptoms
- Pelvic organ prolapse
- No Rx response
- Elevated PVR
- Prior pelvic surgery
- Bladder pain
- Neurologic disease