OBJECTIVES

- Discuss the pathophysiology and clinical presentation of urgency and urge incontinence
- Discuss the evaluation and management for urgency and urge incontinence
- Understand treatment options available for refractory urgency and urge incontinence

IMPORTANT DEFINITIONS

- Incontinence = involuntary loss of urine
- Urgency = abrupt and strong desire to void
- Urgency Incontinence = loss of urine accompanied by or immediately preceded by urgency
- OAB = overactive bladder, urgency with or without incontinence, based on symptoms and not diagnostic findings
- Stress Incontinence = leakage of urine associated with coughing, sneezing, or anything else that increases the intra abdominal pressure
TYPES OF INCONTINENCE

- Urgency Incontinence (aka OAB, urgency)
- Stress Incontinence
- Mixed Incontinence
- Unconscious (unaware) incontinence
- Functional Incontinence
- Continuous urinary incontinence
- Nocturnal enuresis
- Postmicturition dribble
- Overflow incontinence
- Extra-urethral incontinence (fistula)

OAB Symptoms

- Urgency: Sudden, strong desire to urinate
- Frequency: 8+ visits to the toilet per 24 hours
  - 2+ visits to the toilet during sleeping hours (nocturia)

SPECTRUM OF URINARY INCONTINENCE AND OAB

- SUI
- Mixed (UUI+SUI)
- UUI
  - Urgency
  - Frequency
  - Nocturia
- OAB

HOW IMPORTANT IS INCONTINENCE?

INCONTINENCE IS PREVALENT

NATIONAL OVERACTIVE BLADDER EVALUATION (NOBLE) PROGRAM

- Large US prevalence study for OAB
  - November 2000–January 2001
  - 17,231 households contacted
  - 5,204 completed interviews
  - 4,160 controls, 1,044 cases

- Conclusions
  - Over 33 million OAB sufferers (16.6% of population)
  - 63% OAB dry; 37% OAB wet
  - OAB significantly impairs health related quality of life, even in those without urge incontinence

PREVALENCE OF OAB IN THE US

- Overall, 16.6% had symptoms of OAB
- Prevalence of OAB increased with age


NOBLE: US Prevalence of Overactive Bladder

16.6% of adults
51.9 million adults

US Population = 313 million adults


PREVALENCE OF OVERACTIVE BLADDER: INCONTINENT VERSUS CONTINENT

19.2 million (6.1% of the population)
37% Incontinent
63% Continent
32.7 million (10.5% of the adult population)

**Prevalence of Chronic Conditions in the US**

†Stewart W et al. Prevalence of OAB in the US: results from the NOBLE program.

**INCONTINENCE IS MORBID**

Incontinence has the magical power of transforming a healthy laugh into a polite smile.

**IMPACT OF OAB ON QUALITY OF LIFE**

- **Physical**
  - Limitations or cessation of physical activities

- **Psychological**
  - Guilt/depression
  - Loss of self-esteem
  - Fear of:
    - being a burden
    - lack of bladder control
    - urine odor

- **Social**
  - Reduction in social interaction
  - Limiting and planning travel around toilet accessibility

- **Domestic**
  - Requirements for specialized underwear, bedding
  - Special precautions with clothing

- **Occupational**
  - Absence from work
  - Decreased productivity
THE COST OF URINARY INCONTINENCE

- The total direct and indirect cost of incontinence in the United States in 2000 was estimated to be $19.5 BILLION!
  - Drugs
  - Surgical procedures
  - Office visits
  - Supplies (diapers, pads, clothes, etc)

SO HOW ARE THINGS SUPPOSED TO WORK???

NORMAL MICTURITION

- The sympathetic nervous system (SNS) promotes bladder filling, parasympathetic nervous system (PNS) promotes voiding
- As urine fills the bladder, the detrusor stretches allowing the bladder to expand and maintain nearly constant detrusor pressure
- On average, there is about 300ml of urine in the bladder before the brain is triggered to recognize fullness
NORMAL MICTURITION

- Spinal reflex mechanisms activate SNS and somatic pathways to the bladder outlet both promoting bladder filling and tightening bladder outlet (sphincter) while the brain suppresses PNS outflow to the bladder.
- When intravesical pressure >> resistance in urethra...urine flows
- The Pudendal nerve innervates the external sphincter
RISK FACTORS FOR OAB

- Bladder inflammation (cystitis, stones)
- Chronic bladder outlet obstruction (detrusor over-activity)
- Post-menopausal status
- Aging
- Central nervous system disorders
  - MS, CVA, Parkinson's Disease
- Idiopathic (most common cause)

EVALUATION OF THE PATIENT WITH OAB (AND INCONTINENCE IN GENERAL)

- History
- Physical Exam
- Labs
- Imaging ???
- Additional Testing ???

HISTORY OF PRESENT ILLNESS

- Precipitating factors = cough, sneeze, lift, strain, change in body position, sudden urge, locations (key in door, entering bathroom)
- Severity = pads per day, wetness of pad when changed, number of accidents, altering diet/en? Leak at night?
- Other voiding symptoms = dysuria, hematuria, urgency, frequency, nocturia, intermittent stream, weak stream, empty bladder?
- What happens if they can't get to a bathroom? (leakage, increased pain, urge subsides)
- Consider a questionnaire (AUA, MESA, IPSS)
INCONTINENCE QUESTIONNAIRES
- Incontinence Impact Questionnaire (IIQ and IIQ-7)
- Urinary Incontinence-specific Quality of Life Instrument (I-QOL)
- King’s Health Questionnaire (KHQ)
- Urgent/Urinary Distress Inventory (UDI)
- Urgent/Urinary Distress Inventory Short Form (UDI-6)
- Leicester Impact Scale (LIS)
- Overactive Bladder Symptom and Health–related Quality of Life (OAB-Q)
- Bristol Female Lower Urinary Tract Symptoms (BFUTS)
- International Continence Society—Male (ICSMALE)
- Danish Prostate Symptoms Score—Male (DANPSS)
- Medical, Epidemiological, and Social Aspects of Aging Questionnaire (MESA)

MEDICAL, EPIDEMIOLOGICAL, AND SOCIAL ASPECTS OF AGING QUESTIONNAIRE (MESA)

<table>
<thead>
<tr>
<th>Urge Symptoms</th>
<th>Never</th>
<th>Rarely</th>
<th>Sometimes</th>
<th>Often</th>
</tr>
</thead>
<tbody>
<tr>
<td>Some women receive very little warning and suddenly find that they are losing, or are about to lose urine beyond their control. How often does that happen to you?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>If you can’t find a toilet or find that the toilet is occupied, and you have an urge to urinate, how often do you end up losing urine or wetting yourself?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Do you lose urine when you suddenly have the feeling that your bladder is very full?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Does washing your hands cause you to lose urine?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Does cold weather cause you to lose urine?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Does drinking cold beverages cause you to lose urine?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Total</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
</tbody>
</table>

PAST MEDICAL/SURGICAL HISTORY
- Obstetrical history = gravida, para, delivery type, traumatic, episiotomy
- Prior GU conditions = stricture, STD, UTI, BPH
- Prior pelvic surgery (abdominal, vaginal, urethral)
- Neurologic disease = MS, CVA, back injury/surgery, weakness, numbness
- Active Medical Conditions = CHF, DM, closed angle glaucoma
SOCIAL HISTORY

- Fluid consumption: what they drink and how much they drink and when they drink it
- Alcohol intake
- Tobacco use

DIFFERENTIAL DIAGNOSIS: OAB AND STRESS INCONTINENCE

Medical History

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Overactive Bladder</th>
<th>Stress Incontinence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urgency (strong, sudden desire to void)</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Frequency with urgency (&gt;8 times/24 hours)</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Leaking during physical activity (e.g., coughing, sneezing, lifting)</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Amount of urinary leakage with each episode of incontinence (if present)</td>
<td>Large</td>
<td>Small</td>
</tr>
<tr>
<td>Ability to reach the toilet in time following an urge to void</td>
<td>Often no</td>
<td>Yes</td>
</tr>
<tr>
<td>Waking to pass urine at night</td>
<td>Usually</td>
<td>Seldom</td>
</tr>
</tbody>
</table>


SPECTRUM OF URINARY INCONTINENCE AND OAB

- OAB
- Mixed (UUI+SUI)
- UUI
  - Urgency
  - Frequency
  - Nocturia

- SUI
PHYSICAL EXAM

- Neurologic
  - Reflexes
  - Sensation
  - “get up and go test”
- Abdomen
- Pelvic

THE PELVIC EXAM

In the Male
- Position/size of meatus
- Palpate urethra
- Bulbocavernous reflex (BCR) = absence of BCR is almost always associated with a neurologic abnormality
- Rectal exam
  - Prostate size
  - Anal sphincter tone
  - BCR
- BCR

In the Female
- Position/size of meatus
- Vaginal epithelium
- Use a hemi-speculum
- Urethral hypermobility
- Cystocele
- Enterocele
- Rectocele
- Check for leak with cough
- Check with cough and valsava

PELVIC ORGAN PROLAPSE (POP)
GRADE IV CYSTOCELE

COMPLETE VAULT EVERSION

DIAGNOSTIC TESTING
- U/A and Urine Culture
  - Rule out infection
  - Hematuria needs further evaluation (CT, cystoscopy, urology referral)
- Post Void Residual
  - Check for retention
  - Bladder scan or cath
- Voiding Diary??
ADDITIONAL TESTING FOR INCONTINENCE

- Urodynamics
- Cystoscopy
- Bladder x-ray = voiding cystourethrogram (VCUG)
- CT scan
- Pelvic ultrasound
- Pelvic MRI
- Spinal imaging
- Brain imaging

- Only necessary for urge incontinence when the picture is unclear or if initial treatments fail

TREATMENT OF URGE URINARY INCONTINENCE AND OVERACTIVE BLADDER

- Behavioral Modifications/Bladder Training
- Biofeedback
- Estrogen
- Pharmacologic
- Surgical Procedures

Treatment strategies

- Surgical Intervention
  - Sacral Neuromodulation
  - OnabotulinumtoxinA
  - Tibial Nerve stimulation
  - Intravesical therapy
- Pharmacotherapy
- Acupuncture
- Behavioral modification
- Patient education

- Efficacy
Nonpharmacologic Treatments

- Behavioral Modification
  - Education
  - Timed voiding
  - Delayed voiding
  - Diet
  - Pelvic floor exercises

BEHAVIORAL THERAPY

- Avoid bladder irritants
- Timed Voiding
- Bladder Training
  - Void by a strict schedule
  - Suppress the urge to void
    - Keep body still, deep breaths, mental distraction, kegels
    - When urge subsides, so not void until next scheduled void
  - May decrease SUI and UUI episodes by 50%, but need a motivated patient!
- Modest Fluid restriction (esp at night)
- Voiding diary

BLADDER IRRITANTS

- Apples
- Mayonnaise
- Bananas
- Apple Juice
- NutraSweet
- Sweet and Low
- Cantaloupes
- Peaches
- Soy Sauce
- Carbonation
- Pineapple
- Alcohol
- Chilies/Spicy Foods
- Plums
- Processed meats and fish
- Chocolate
- Strawberries
- Tofu
- Citrus Fruits
- Tea
- Yogurt
- Coffee (including Decaffeinated)
- Tomatoes
- Cranberries
- Vinegar
- Grapes
- Vitamin B Complex
- Guava
KEGEL EXERCISES

- Also called Pelvic Floor Muscle Training (PFMT)
- If done correctly, can decrease SUI and UUI episodes by up to 80%
- Must know which muscles to isolate and contract
  - Patients can initially learn which muscles to contract by starting and stopping their urinary stream
  - Some muscles you used if trying not to pass gas
  - Women can place a finger in the vagina and should feel their vaginal muscles contracting around their finger
  - Abdominal muscles should be relaxed
- 10 contractions, 3x daily, hold for 6-8 secs (also do prior to cough, sneeze, lift)
- Continence improves 6-12 weeks after starting

BIOFEEDBACK

- Teaching tool to help patient locate, learn to control, and strengthen the pelvic floor muscles (does not actually do anything to the muscles)
- Sensors are applied to the patient’s body (vaginal, rectal, or skin probes)
- Sensors are connected to a monitor/graph that show the degree of pelvic floor muscle activity and provides auditory or visual feedback to the patient.
ESTROGEN IN POSTMENOPAUSAL WOMEN

• Vaginal estrogen
  • Proven efficacy in reducing recurrent UTI’s in postmenopausal females
  • Appropriate for symptoms related to atrophic vaginitis
  • NOT consistently shown to have benefit for OAB (may worsen LUTS)
  • CONTRAINDICATIONS: DVT or PE, recent CVA or MI, estrogen dependent cancer, abnormal uterine bleeding, liver dysfunction

ANTICHOLINERGICS

• Inhibit the binding of acetylcholine to the cholinergic (muscarinic) receptor
• Goal is to suppress involuntary detrusor contractions
• Indicated for frequency, nocturia, urgency, and urge incontinence
• 6 main drugs on the market
  • All have about equal efficacy and side effects
• Achieve their maximal effect in 2-3 months

MUSCARINIC RECEPTORS (M1-M5)

Muscarinic receptors are also located throughout the CNS

- Dizziness
- Somnolence
- Impaired Memory & Cognition

- Iris/Ciliary Body = Blurred Vision
- Lacrimal Gland = Dry Eyes
- Salivary Glands = Dry Mouth
- Heart = Tachycardia
- Gall Bladder
- Stomach = Dyspepsia
- Colon = Constipation
- Bladder (detrusor muscle)
MUSCARINIC RECEPTOR SUBTYPES

- M1: bladder and brain
- M2: bladder and heart
- M3: bladder, smooth muscle (GI), brain, eyes, salivary, detrusor contraction

OAB meds have an M3 selectivity, but binding to other M subtypes still occurs

Antimuscarinics

<table>
<thead>
<tr>
<th>Generic Name</th>
<th>Trade Name</th>
<th>Available Doses</th>
<th>Mode of Delivery</th>
<th>Year Approved</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oxybutynin</td>
<td>Ditropan</td>
<td>IR: 2.5 mg; 5 mg Oral (tds)</td>
<td>1975</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Ditropan XL</td>
<td>ER: 5 mg; 10 mg Oral (qd)</td>
<td>1999</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Oxytrol</td>
<td>36 mg/patch (3.9 mg/ft²) Transdermal</td>
<td>2008</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Gelnique</td>
<td>10% gel Transdermal</td>
<td>2009</td>
<td></td>
</tr>
<tr>
<td>Tolterodine</td>
<td>Detrol</td>
<td>IR: 1 mg; 2 mg Oral (qd)</td>
<td>1998</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Detrol LA</td>
<td>ER: 2 mg; 4 mg Oral (qd)</td>
<td>2001</td>
<td></td>
</tr>
<tr>
<td>Propiverine</td>
<td>Detrunorm</td>
<td>15 mg Oral (qd)</td>
<td>2006</td>
<td></td>
</tr>
<tr>
<td>Solifenacin</td>
<td>Vesicare</td>
<td>5 mg; 10 mg Oral (qd)</td>
<td>2005</td>
<td></td>
</tr>
<tr>
<td>Darifenacin</td>
<td>Enablex</td>
<td>7.5 mg; 15 mg Oral (qd)</td>
<td>2005</td>
<td></td>
</tr>
<tr>
<td>Fesoterodine</td>
<td>Toviaz</td>
<td>4 mg; 8 mg Oral (qd)</td>
<td>2009</td>
<td></td>
</tr>
</tbody>
</table>

Antimuscarinics: Tolerability

- In a meta-analysis:
  - Dry mouth is the most commonly reported adverse event (29.6% on treatment vs 7.9% on placebo), followed by pruritus (15.4% on treatment vs 5.2% on placebo), constipation, headache and abnormal vision.

- Tolerability may limit persistence
  - Recent study showed that 6-month cumulative discontinuation rate for anticholinergics in women is high at 59%
  - The median time to discontinuation of anticholinergics in that study was 4.76 months

ANTICHOLINERGICS
- Oxybutinin (Ditropan, Ditropan XL, oxytrol)
  - Oldest of its class
  - Multiple dosing options
    - 5mg – 30mg PO q daily
  - Oxytrol is a patch form and now available OTC
    - Theoretically less systemic side effects
  - Metabolized by cytochrome P450 system
  - Confusion in elderly

ANTICHOLINERGICS
- Tolterodine (Detrol, Detrol LA)
  - Lipophillic (unlikely to cross BBB)
  - Metabolized by cytochrome P450 system
- Darifenacin (Enablex)
  - M3 receptor selective
  - Metabolized by cytochrome P450 system
  - Originally developed as IBS medication
  - Fesoterodine (Toviaz)
    - Structurally related to tolterodine
    - Parent compound has no affinity to muscarinic receptor
    - Metabolized immediately by serum esterases
    - Serum levels predictable (more so than oxybutinin), allowing dose increases. No “poor metabolizers”.
    - Dose adjustments for severe renal/liver impairment.

ANTICHOLINERGICS
- Solifenacin (Vesicare)
  - Long Half-life
  - Metabolized by cytochrome P450 system
- Trospium (Sanctura)
  - Not metabolized by cytochrome P450. 60% is excreted unchanged in urine
  - Only DAB med that could exert a direct therapeutic effect on urothelium
  - Quaternary amine = less likely to cross BBB
  - No clear data showing it is more effective
ANTICHOLINERGICS

- Side Effects
  - Dry mouth **
  - Dry eyes
  - Constipation
  - Blurred vision
  - Dyspnea
  - Urinary retention **
- Contraindications: urinary retention, narrow angle glaucoma, gastric retention, intestinal obstruction, myasthenia gravis

MIRABEGRON
MYRBETRIQ

- Beta-3 agonist
- Once daily dosing – 25, 50 mg
- Minimal anticholinergic type side effects
- HTN closely assessed, minimal impact seen
- Avoid in those with poorly controlled HTN
- Efficacy similar to anti-muscarinic agents
- May be preferable in patients with heavy anti-cholinergic load

TREATMENT OPTIONS FOR REFRACTORY UI/OAB

- Botox injections
  - Inhibits muscle contraction by blocking the release of acetylcholine at the neuromuscular junction
  - Injected through a cystoscope in 10-30 sites
  - Effects wear off in 3-12 months
  - 100 units for idiopathic, 200 units for neurologic

- Neuromodulation
  - Sacral nerve stimulator (Interstim)
  - Uses direct electrical stimulation of the S3 afferent nerve
  - Not effective if S3 nerve is damaged
  - 2 stage procedure
  - Indicated for patients who fail or cannot tolerate conservative treatments

PTNS

- Percutaneous Tibial Nerve Stimulation (PTNS)
  - Has been shown to decrease urgency, frequency, and pelvic pain in up to 60% of patients
  - 30 minutes weekly for 12 weeks
  - Research ongoing
SURGICAL OPTIONS FOR UUI/OAB

- Augmentation cystoplasty
  - Piece of bowel added to dome of bladder
  - 80% dry, 10-40% need catheter
  - Lower success in patients with XRT
- Urinary diversion
  - Rarely indicated

WHEN TO REFER TO UROLOGY

- Continuous leakage
- Conservative measures are ineffective
- Not responding to medications
- Prior GU procedures
- Hematuria
- Recurrent UTI
- Neurologic disorder/SCI

REMEMBER

- Urinary incontinence is common, bothersome, and embarrassing…but it is treatable!
- Ask your patients if leakage is a problem
- Try behavioral modifications…they work!
- You can try medications for OAB without invasive testing
- Know when to refer
QUESTIONS??

- Feel free to email me anytime

brooke.zilinskas@utsouthwestern.edu