The Prostate and Its Challenges
“LUTS in the Aging Male”

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Instructor, Harvard Medical School
No financial disclosures.
Dr. Webber

- 60 yoM healthy
- 2010 presented to Urology with post-void residual of 500cc.
- Started on Tamsulosin (PVR 280cc)
- Added Finasteride (PVR 450cc)
- TURP recommended and declined
- Changed to Dutasteride
- Tamsulosin increased to 0.8mg -> nasal congestion. Then 0.4 BID.
- TURP recommended, self-referred to my clinic.
• Urinates every 2hrs during day and 3 times per night. Has to Valsalva to void.
• Started self-treating for recurrent UTIs 2-3x per year
• Very bothered by retrograde ejaculation on Tamsulosin
• I recommended TURP:
  – Significant PVR
  – Recurrent Infections
• He is concerned with TURP and risk of retrograde ejaculation or permanent ED
• He asks to start Tadalafil
• We discussed that Tadalafil improves SUBJECTIVE symptoms, but not OBJECTIVE symptoms.
• Starts Tadalafil 5mg daily.
• PVR remains ~300cc through 2015
• 2016 Preplace foleys before elective surgeries
• 2017 – hasn’t required surgery, remains on active duty.
Take Homes

• BPH is common in the aging male
• Primary Care Doctors can feel comfortable with initiating medical management:
  – Alpha-1-blocker (Floppy Iris Syndrome, Blood Pressure, Retrograde Ejaculation)
  – 5-alpha Reductase Inhibitors (Changes the PSA interpretation)
  – PDE-5 Inhibitors
  – Anticholinergics
  – Combination
• LUTS is not always due to BPH: Young Patient, Isolated nocturia
• When to see Urology: Recurrent UTIs, hematuria, Episodes of Retention
Overview

• Etiology and Pathophysiology of BPH
• Diagnostic Evaluation
• Non-Invasive Therapies
  – Lifestyle Modifications
  – Phytotherapy
  – Alpha-Blockers
  – 5α-Reductase Inhibitors
  – Phosphodiesterase Inhibitors (Cialis)
  – Anticholinergics
• Surgical Interventions
Prevalence of LUTS

• In 2003, the Multinational Survey of the Aging Male (MSAM-7) surveyed the prevalence of moderate-to-severe LUTS:

  Men aged 50–59 years          22%
  Men aged 70–80 years          45.3%
  \( p < 0.0001 \)

Prior to 1990: TURP
(Transurethral Resection of the Prostate)
History of Medical Therapy for BPH

• In 1970’s non-selective $\alpha$-blockers were studied
  – phenoxybenzamine & prazosin
• 1980’s “selective $\alpha_1$-blockers ” were introduced
  – Terazosin, doxazosin, and alfuzosin
• 1990’s 5-alpha reductase inhibitors & $\alpha_{1a}$-subtype-selective agents
  – Finasteride & dutasteride
  – Tamsulosin and silodosin

• In 1990 results of PRCT showed that COMBINATION of finasteride and terazosin significantly improved LUTS and increased flow rates.
TRANSURETHRAL RESECTION OF THE PROSTATE AMONG MEDICARE BENEFICIARIES: 1984 TO 1997


The Journal of Urology
Volume 164, Issue 4, Pages 1212-1215 (October 2000)
DOI: 10.1016/S0022-5347(05)67143-1
Pathophysiology of BPH
Pathophysiology of Aortic Stenosis

Normal

Aortic Stenosis

Dilated Cardiomyopathy

Dilated ventricle
Pathophysiology of BPH
“Normal”

- Generally urinates about 3-4x per day
- Wakes 0-1x per night
BPH

- **Daytime Frequency:**
  - Every 1-3 hrs

- **Nocturia:**
  - 1-4x per night

- **Urgency:**
  - Often accompanied by a detrusor contraction

- **Weakened Stream**

- **Post-void Dribble**
End-Stage BPH

- “I have no problems Doc”
- “I go 1 or 2 times a day”
- Recurrent UTIs
- Diapers may indicate overflow incontinence
- Hydronephrosis – renal failure
- Volume Overload – may mimic CHF
Presentation of BPH

• The severity of urinary symptoms do NOT correlate with the degree of obstruction

• The severity of urinary symptoms do NOT correlate with the size of prostate (either by DRE or on imaging)
Workup of BPH

**Recommended Tests:**
- Relevant Medical History
- Assessment of LUTS
- Severity and Bother (i.e. AUA-SI)
- Physical Examination Including DRE
- Urinalysis
- Serum PSA<sup>1</sup>
- Frequency/Volume Chart<sup>2</sup>

- AUA Guidelines 2011
- AAFP Recommendations for Practice
- Canadian Urologic Guidelines
- European Association of Urology
Differential Diagnosis for LUTS

• Increased Urine Output

• Decreased Bladder Storage Capacity (myopathy or neuropathy)

• Bladder Irritation

• Bladder Outlet Obstruction
Increased Urine Output

• Glucosuria - Diabetes
• New Diuretic Medicine
• CHF with LE edema

• Polyuria: >3L per 24 hours
  – Goal UOP for pts with urinary sx is <1L / 24 hrs
  – Consider fluid intake, SIADH

• Nocturnal Polyuria: >33% UOP during night
  – Normally produce <25% while sleeping
  – Lying Prone -> ADH release -> decreased UOP
    • Elderly have disruption in this endocrine loop
    • Pillows and La-Z-Boys

• Obstructive Sleep Apnea –
  – OSA -> ANP release -> increased UOP
# SIMPLE DAILY VOIDING DIARY

**NAME**

**DATE**

<table>
<thead>
<tr>
<th>Time of Day</th>
<th>Amount Voided CC or MLS (example 100 or 200)</th>
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<td>4:00</td>
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<td>5:00</td>
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</table>
Decreased Bladder Storage Capacity (myopathy or neuropathy)

- Diabetes
- Cerebrovascular Accident or Upper Motor Neuron compromise
- Multiple Sclerosis
- Parkinson’s Disease
- Spinal Cord
  - Degenerative Disk Disease
Bladder Irritation

- Bladder Infection
- Hematuria
- Bladder Cancer
- Distal ureteral stone
- *Schistosomiasis haemotobium*
Bladder Outlet Obstruction

• Urethral Stricture
  – Prior Urologic procedures, Gonorrhea
• Meatal Stenosis
• Significant Phimosis (especially in elderly)
• Penile Cancer
**Intact Penis:** The foreskin protects the sensitive meatus from an irritating environment. The meatus is normally a wide slit. Finger applies pressure to show how wide the meatus opens.

**Circumcised Penis:** With no protective foreskin in infancy, the glans is exposed to urine and diapers that irritate the meatus, causing it to stenose (narrow) and restrict urine flow.
Medical History

• Medications – can account for 10% of LUTS\textsuperscript{1}
  – Antidepressants 4 %
  – Diuretics 3 %
  – Bronchodilators 2 %
  – Antihistamines 1%

\textsuperscript{1}Wuerstle MC, et al. Arch Intern Med. 2011
Workup of BPH

- RECOMMENDED TESTS:
  - RELEVANT MEDICAL HISTORY
  - ASSESSMENT OF LUTS
  - SEVERITY AND BOTHER (i.e. AUA-SI)
  - PHYSICAL EXAMINATION INCLUDING DRE
  - URINALYSIS
  - SERUM PSA
  - FREQUENCY/VOLUME CHART

- AUA Guidelines 2011
- AAFP Recommendations for Practice
- Canadian Urologic Guidelines
- European Association of Urology
Lower Urinary Tract Symptoms (LUTS) (formerly “Prostatism”)

- Urinary Frequency:
  - How many times do they wake to urinate
  - How frequently do they urinate during the day
- Urinary Urgency
- Strength of Flow
- Do they push (Valsalva)
- Double Voiding
- Post-void dribbling
- Sense of incomplete emptying
# International Prostate Symptom Score (AUA Symptom Score)

<table>
<thead>
<tr>
<th>Question</th>
<th>Not at all</th>
<th>Less than 1 time in 5</th>
<th>Less than half the time</th>
<th>About half the time</th>
<th>More than half the time</th>
<th>Almost always</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Over the past month, how often have you had a sensation of not emptying your bladder completely after you finished urinating?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>2. Over the past month, how often have you had to urinate again less than two hours after you finished urinating?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>3. Over the past month, how often have you found you stopped and started again several times when you urinated?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>4. Over the past month, how often have you found it difficult to postpone urination?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>5. Over the past month, how often have you had a weak urinary stream?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>6. Over the past month, how often have you had to push or strain to begin urination?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>7. Over the past month, how many times did you most typically get up to urinate from the time you went to bed at night until the time you got up in the morning?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
</tbody>
</table>

**Total Symptom Score**
Workup of BPH
(AUA Guidelines 2011)

Score <8
Not Bothersome
Reassure & Follow

Complicated:
- Recurrent Retention
- Recurrent UTI
- Recurrent Hematuria
- Bladder stones
- CRI
Surgery
(Option Chronic Foley)

Score ≥8
Bothersome (+/- Further Tests)
Lifestyle Advice
Pharmacologic Therapy

Failure (~10%)
Exam and Labs

• UA
  – Glucose, Protein, UTI
  – Hematuria (Formal UA with 3 or more RBC/HPF)

• PSA
  – Most guidelines for PSA screening refer to “asymptomatic” patient
  – Men with a PSA level of ≥3 and LUTS were more likely to be diagnosed with benign disease than prostate cancer

• DRE
  – Low Sensitivity (59%) and PPV (28%) for prostate cancer

Collin SM, et al. BJU Int. 2008
Exam and Labs

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Tests that Suggest Bladder Outlet Obstruction

• **Post-Void Residual**
  – Either by bladder scan or “Renal Ultrasound”
  – “Normal” PVR can be up to 100mls

• **Uroflow** (In Urology Office) – flow rate

• **Urodynamic study (UDS)** - determines not only the flow rate, but most importantly, whether the bladder is able to contract
Uroflow

RATE (cc/sec)

TIME
Urodymanics
Urodymanics
Therapies for BPH
Non-Invasive Therapies
Lifestyle Modifications

- Weight loss
- Change HTN med from diuretic to alternative if possible, limit diuretics to morning.
- Diet: Avoid caffeine, alcohol, spicy foods, acidic foods
- Decrease fluid intake in the evening
- Avoid α-agonists (decongestants)
- Limit fluid intake to <1.5-2.0L per day
Non-Invasive Therapies
Phytotherapies

• Phytotherapies are not recommended as the standard for treatment of BPH at this time
  
  – Saw Palmetto (*Serenoa repens*)
  – African Plum (*Pygeum africanum*)
Non-Invasive Therapies
Medical Approach

• What medications work and why?
Benign Prostatic Hyperplasia

Obstruction Results from:

- Prostatic growth into the urethral lumen due to increased # of Epithelial and Stromal Cells

- Increase in Urethral Resistance due to:
  - Increase # of prostate smooth muscle cells
  - Increased number of α-1 adrenergic receptors on the SMC.
Medical Approach

• $\alpha$ -1 receptors on SMC of prostate
  – Relax the smooth muscle of prostate and bladder neck
    • Terazosin, Doxazosin
    • Tamsulosin, Alfuzosin, Silodosin

• $5\alpha$ -Reductase Inhibitors Prostate Stroma
  – Shrink the Prostate Stroma
    • Finasteride
    • Dutasteride
### α-1A Receptor Subtypes

<table>
<thead>
<tr>
<th></th>
<th>Prostate α-1A</th>
<th>Bladder / Spinal Cord α-1D</th>
<th>Vasculature α-1B (1A)</th>
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<tbody>
<tr>
<td>Terazosin</td>
<td>X</td>
<td>X</td>
<td>X</td>
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<tr>
<td>(Hytrin®)</td>
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<td></td>
<td></td>
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<tr>
<td>Doxazosin</td>
<td>X</td>
<td>X</td>
<td>X</td>
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<tr>
<td>(Cardura®)</td>
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<tr>
<td>Alfuzosin</td>
<td>X</td>
<td>X</td>
<td>X</td>
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<tr>
<td>(Uraxatral®)</td>
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<td></td>
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<tr>
<td>Tamsulosin</td>
<td>X</td>
<td>X</td>
<td></td>
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<tr>
<td>(Flomax®)</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Silodosin</td>
<td>X</td>
<td>X</td>
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<tr>
<td>(Rapaflo™)</td>
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</table>
Nonselective α-1 Blockers

Terazosin, Doxazosin, Alfuzosin

- Effects vasculature
- Side Effects: dizziness, orthostatic hypotension (uncommon), syncope (rare)
- Require titration, Take at Bedtime – REASSURE patient that symptoms subside
  - Terazosin/Hytrin: 2mg -> 5mg -> 10mg
  - Doxazosin/Cardura: 2mg -> 4mg -> 8mg
    (Start at 1mg if older, frail, low BP)
- 2-4 weeks for near maximal improvement
- Need to space at least 4 hours from Viagra. Cannot use with Cialis.
Selective α-1A Blockers
Tamsulosin, Silodosin

• Near maximal improvement within 8 hours
• Cause less (if any) dizziness

• Highest rate of retrograde ejaculation
• Nasal Congestion

• Do not need to space 4 hours from Viagra.
• OK to use with Cialis
• Sulfa allergy – minimal cross-reactivity
Efficacy of the $\alpha$-1A Blockers

Tamsulosin, Silodosin

• Efficacy of the following are comparable:
  – Doxazosin, terazosin, alfuzosin, Tamsulosin
  – No clinical comparisons with silodosin

• Silodosin is the only one which has been shown to improve UDS outcomes
Meta-Analysis of Blood Pressure Effects for α-1 Blockers

- 25 Studies
- OR of developing:
  - Dizziness
  - Hypotension
  - Syncope

α-1 Blockers and Cardiovascular Effects

- Patients with HTN and CHF have chronic activation of sympathetic nervous system
- Thus at higher risk for increased cardiovascular side effects of blocking the α-1B receptors
  - Doxazosin, Terazosin, Alfuzosin all had higher adverse events in these patients (Doxazosin was withdrawn from ALLHAT due to increased risk of cardiovascular disease, esp CHF)
  - Tamsulosin has not been shown to adversely effect these patients compared to placebo

- Do not use these medicines for Blood Pressure control
- Use Tamsulosin or Silodosin preferentially in patients with HTN/CHF

Barenderecht MM, et al. BJU International. 2005
Intraoperative Floppy Iris Syndrome

- Severe complication during cataract surgery with patients on alpha-1 blocker
  - Intraoperative miosis causes iris prolapse toward incision, which can result in capsule rupture

- Incidence of IFIS on Tamsulosin is 43-90% (less on Doxazosin or Terazosin)

- Whether stopping medicine prior to surgery mitigates risk is unknown
Intraoperative Floppy Iris Syndrome

New Recommendations:

• Men with LUTS secondary to BPH for whom alpha-blocker therapy is offered should be asked about planned cataract surgery.

• Men with planned cataract surgery should avoid the initiation of alpha-blockers until their cataract surgery is completed.
5α-Reductase Inhibitors (Finasteride and Dutasteride)

• Finasteride inhibits type II 5ARI
• Dutasteride inhibits type I&II 5ARI

• Reduces prostate volume by 20-25%
• Takes 6-9 months to achieve noticeable change in symptoms (improvement continues with time)
• Takes 12-18 mo to obtain same flow rate as α-blocker

• REDUCES PSA by HALF! (Includes Finasteride 1mg / Propecia)
  – Consider checking a PSA before starting
• Side effect: Impotence (5%), decreased libido (<4%)
5α-Reductase Inhibitors

- **DHT**
- **5-AR (↑ Prostate Growth, ↑ PSA, ↓ Apoptosis (↓ Hair Growth))**

**5-AI:**
- Finasteride
- Dutasteride
5α-Reductase Variability

- ~25-30% of patients do not show improvement on 5α-Reductase Inhibitors
- 5-7% show worsening of symptoms
- 5α-Reductase Type II is variably expressed
- 30% of adult prostates do not express 5α-Reductase Type II

5α-Reductase Inhibitors

- Reductase Inhibitors

- T (Testosterone)
- DHT (Dihydrotestosterone)

- 5-AR (1,2)
- ↑ Prostate Growth
- ↑ PSA
- ↓ Apoptosis
- (↓ Hair Growth)
5α-Reductase Variability

• Longitudinal studies have shown that 30% of men have prostate sizes that do not increase with time.

• Current research suggests that this is a somatic epigenetic event (rather than underlying chromosomal variability)

5α-Reductase Variability

- Age and Obesity independently promote methylation and suppression of 5α-Reductase protein expression.
  - Obesity is known to increase the risk of BPH patients requiring surgery
  - Obesity is a factory associated with decreased clinical benefit of 5α-Reductase inhibitors

5α-Reductase Inhibitors

Prostate Cancer Risk

• There is a proven benefit of using both Finasteride (PCPT) and Dutasteride (REDUCE Trial) for prostate cancer risk reductions.

• (REDEEM TRIAL)

• In the PCPT there was a slight INCREASE in HIGH GRADE prostate cancer with Finasteride.
  – Most experts believe this was statistical artifact due to reduced volume of Finasteride-treated gland

• In the REDUCE trial, there was NOT a difference in High Grade prostate cancer.
Tadalafil
FDA-approved for BPH

- Tadalafil improves the IPSS scores, the IPSS Quality of Life (QoL) and the BPH Impact Index (BII).
- Onset of efficacy is ~1-4 weeks
- Its efficacy is irrelevant to the erectile function status of the patients.

- In studies thus far, tadalafil is not associated with improvement in Flow Rate or PVR.
## Combination – MTOPS & ComBAT Trials

<table>
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<th>Comparison</th>
<th>MTOPS (NIH Funded)</th>
<th>CombAT (GlaxoSmithKline Funded)</th>
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<td></td>
<td>Placebo</td>
<td>Tamsulosin</td>
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<tr>
<td>MTOPS Trial, NEJM, 2003</td>
<td>36g</td>
<td>Dutasteride Combination</td>
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<td>Table adapted from Lebor. Reviews in Urology 2011.</td>
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<table>
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<th>Mean Prostate Size</th>
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<th>Tamsulosin</th>
<th>55g</th>
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<tr>
<td></td>
<td>Doxazosin</td>
<td>14%</td>
<td>Dutasteride</td>
<td>14%</td>
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<td></td>
<td>Finasteride</td>
<td>7%</td>
<td>Combination</td>
<td>13%</td>
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<td></td>
<td>Combination</td>
<td>9%</td>
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<th>Worsening Symptom Score (4 points)</th>
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<th>Tamsulosin</th>
<th>14%</th>
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<tr>
<td></td>
<td>Doxazosin</td>
<td>7%</td>
<td>Dutasteride</td>
<td>13%</td>
</tr>
<tr>
<td></td>
<td>Finasteride</td>
<td>9%</td>
<td>Combination</td>
<td>8%</td>
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<tr>
<td></td>
<td>Combination</td>
<td>5%</td>
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<th>Risk of: Retention, Surgery</th>
<th>Placebo</th>
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<th>Tamsulosin</th>
<th>13%</th>
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<tbody>
<tr>
<td></td>
<td>Doxazosin</td>
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<td>Dutasteride</td>
<td>6%</td>
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<td></td>
<td>Finasteride</td>
<td>3%</td>
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<td></td>
<td>Combination</td>
<td>2%</td>
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Combination

• MTOPS: In Glands <40g, α1-blocker outperformed 5-ARI with regards to LUTS

• CombAT: In Glands >50g, 5-ARI outperformed α-blocker at reducing the risk of retention or need for surgery

Combination

In Practice, the $\alpha_1$-blocker are generally started before 5-ARI:

- $\alpha_1$-blocker reach effect much faster (2 weeks vs 1-1.5 years)
- $\alpha_1$-blocker are efficacious in all prostate sizes, whereas 5-ARI do not work as well in small glands
- 30% of patients won’t respond to 5-ARI (which you may not know for 1-1.5 years)

Combination
Withdrawing the α-1 Blocker

• Studies suggest that the α-1 blocker can be stopped after 6-12 months without worsening voiding symptoms

Baseline Voiding Sxs | When can α-blocker be withdrawn?
---|---
IPSS <20 | >6 Months
IPSS >20 | >9 Months

(Such that 80% will not have worse sxs)

(Remember: 12-18 months to get best 5ARI flow-rate)
Adding an Anticholinergic  
(Oxybutynin, Tolterodine, Darifenacin, Trospium, Solifenacin)

• Anticholinergics put bladder in the “storage” phase:
  – Relax detrusor
  – Contract Sphincter (increasing outlet obstruction)

• Helpful in relieving urgency/frequency associated with hypertrophic/overactive bladder.
  – Specifically in those patients already treated with α-blocker
Adding an Anticholinergic

- Theoretic concern that these could put patients into retention
- In patients with PVR<200 cc, risk of requiring catheter is <1%

- Perhaps best used temporarily while waiting for bladder hypertrophy to resolve
  - Can be used “prn” – when they need a good nights sleep or have a movie date.
Long-Term Patterns of Use and Treatment Failure With Anticholinergic Agents for Overactive Bladder

Michael B. Chancellor, MD, Kristen Migliaccio-Walle, BS, Thomas J. Bramley, PhD, Sham L. Chaudhari, MS, Catherine Corbell, PhD, Denise Globe, PhD

Clinical Therapeutics
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DOI: 10.1016/j.clinthera.2013.08.017

• Retrospective cohort study of data from the IMS LifeLink Health Plans Claims Database

• 103,250 Patients followed from January 2005 to June 2010

• 24 months of follow-up from the index prescription.
Figure 2

Proportion of Patients on Anticholinergics (%)

Time (days)
Anticholinergic Warnings

• 25 studies have found significant association of anticholinergic use with:
  – Cognitive decline
  – Delirium
  – Dementia

• Avoid in patients with Narrow-angle Glaucoma.
Surgical Interventions
Surgical Interventions

• TURP (Transurethral Resection of Prostate)
• Laser Ablation or Enucleation
• Suprapubic (Open)Prostatectomy
• TUMT (Transurethral Microwave Therapy)
• TUNA (Transurethral Needle Ablation)
• Prostatic Stent
• UroLift
TransUrethral Resection of Prostate
HoLAP (Holmium Laser Ablation Prostate)
PVP (Photoselective Vaporization – Greenlight)
HoLEP
(Holmium Laser Enucleation of Prostate)
Suprapubic “Open” Prostatectomy
TUMT and TUNA

(Microwave Therapy and Needle Ablation)

European Association for Urology Patient Website
Prostatic Stent and UroLift

European Association for Urology Patient Website
Surgical Interventions

- **TURP (Transurethral Resection of Prostate)**
  - Remains Gold Standard
- **Laser Ablation or Enucleation**
  - Option which has more post-operative “bother” and less durability with time. Less bleeding.
- **Suprapubic Prostatectomy**
  - Best option for VERY large (>100g) glands
- **TUMT (Transurethral Microwave Therapy)**
- **TUNA (Transurethral Needle Ablation)**
  - Fallen out of favor
- **Prostatic Stent** - Fallen out of favor
- **UroLift** - ??
Questions on Medical Management of BPH?
Myrbetriq/Vesicare Combo


Combination treatment with mirabegron and solifenacin in patients with overactive bladder: efficacy and safety results from a randomised, double-blind, dose-ranging, phase 2 study (Symphony).

Abrams P¹, Kelleher C², Staskin D³, Rechberger T⁴, Kay R⁵, Martina R⁶, Newgreen D⁶, Paireddy A⁶, van Maanen R⁶, Ridder A⁶.

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**Fig. 2 Neurogenic Innervation and Control of Bladder Musculature – receptor sites**
*(from the FDA meeting slide show)*

- Acetylcholine
- Antimuscarinics
- M3 muscarinic receptor
- (contraction) detrusor smooth muscle (relaxation)
- B3 Agonist
- Norepinephrine
- β3 adrenergic receptor
Overall treatment outcomes after initial choice of anticholinergic agent at 24 months (N = 103,250).
Improvement in Mean Volume Voided (Improvement in Bladder Capacity)
Improvement in Urge Episodes during 24 hrs
α-1 Blockers and Cardiovascular Effects

• To compensate for standing, the sympathetic nervous system increases venous tone to maintain cardiac return

• The α-1 Blockers interfere with this, resulting in orthostatic hypotension

• However, with time (weeks) the body activates compensatory mechanisms to maintain BP
BPH Pathogenesis
### Subtypes of $\alpha_1$-adrenergic Receptors

<table>
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