

Management of Lower Urinary Tract Symptoms (LUTS) in Older Men

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Conflict of Interest

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Learning Objectives

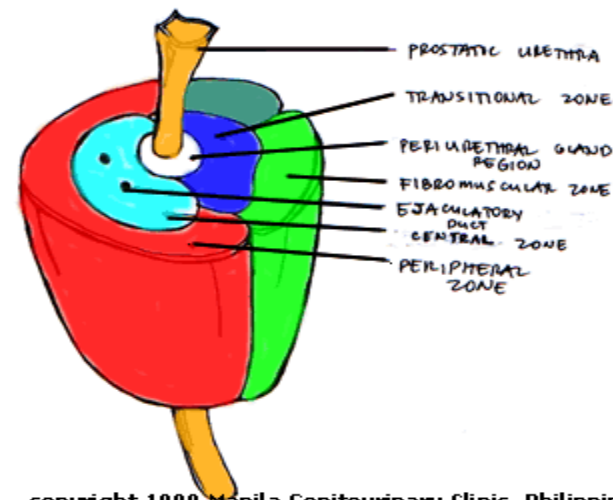
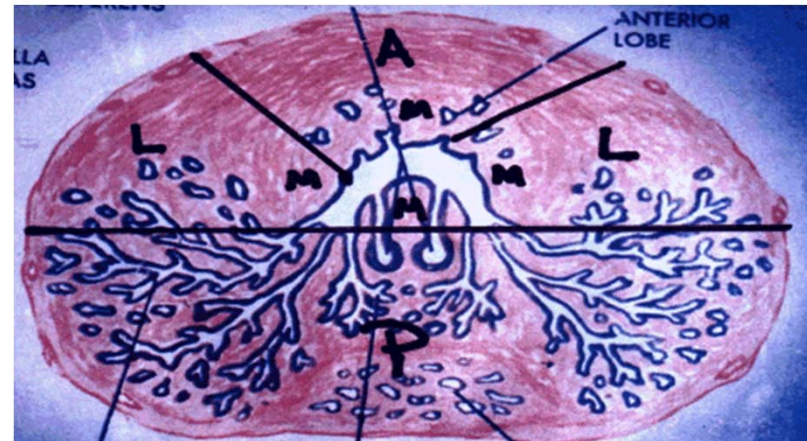
1. Describe the presenting signs and symptoms associated with Lower Urinary Tract Symptoms.
2. Describe the various methods used in the initial evaluation of LUTS.
3. Understand the natural history of LUTS/BPH and complications based on progression.
4. Be aware of the various treatment modalities for LUTS and the appropriate context in which they are used.

Terminology

- Lower urinary tract symptoms (LUTS) secondary to BPH (LUTS/BPH)
- Lower urinary tract symptoms independent of BPH
- Overactive bladder syndrome—urgency w or w/o urge incontinence, usually with frequency and nocturia
- Bladder outlet obstruction (BOO)— generic term for all forms of obstruction
- Benign Prostatic Hyperplasia (BPH)—pathological term
- Detrusor overactivity—urodynamic term
- Benign prostatic obstruction (BPO)— pressure flow studies term

Definition

- ▶ An increase in the numbers of stromal cells in the transition zone of the prostate
- ▶ An increase in the number of alpha-1-receptors

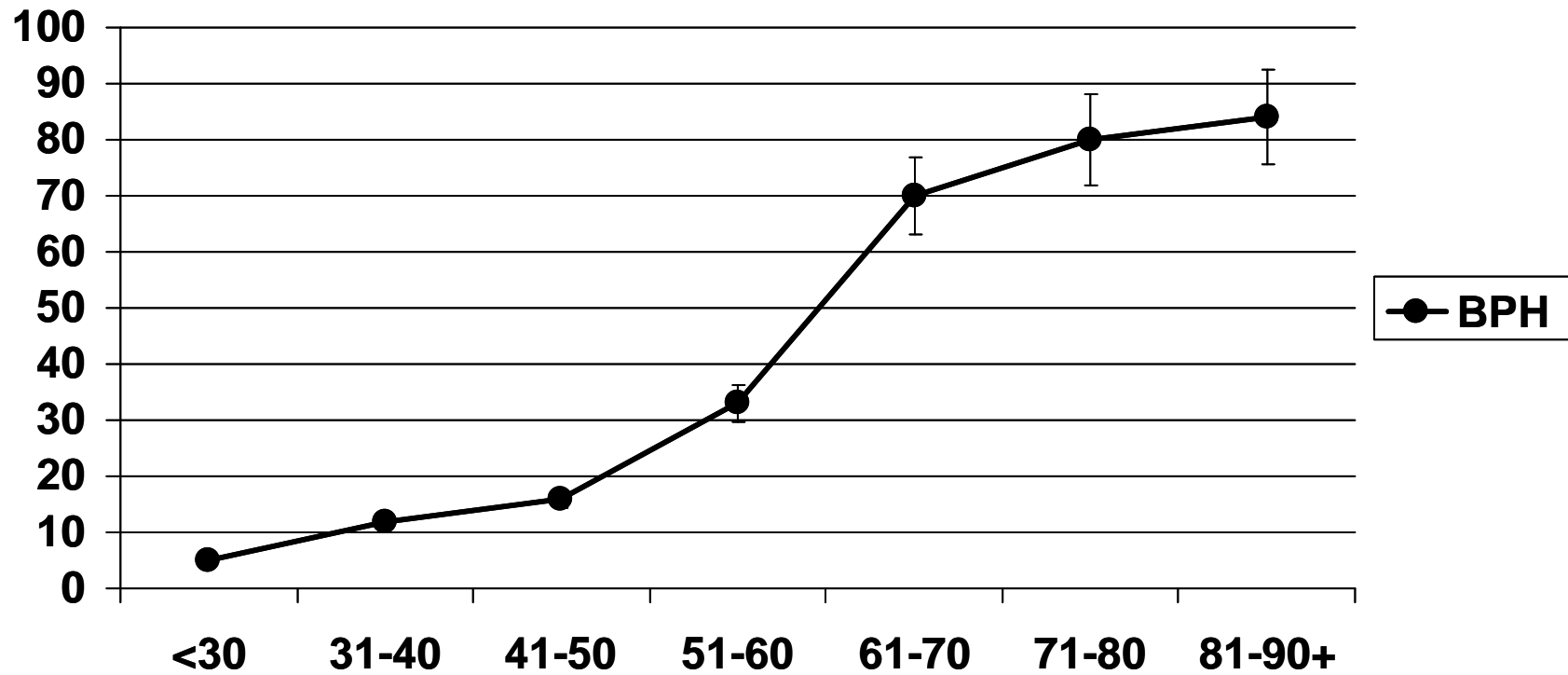


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Can Affect Quality of Life (Bother)

- ▶ Interference with activities of daily living
- ▶ Interference with psychological well being
- ▶ Interference with sleep

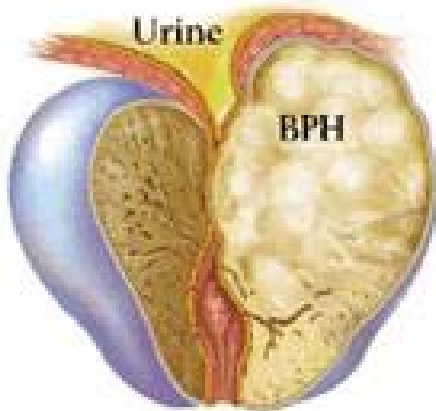
Prevalence (based on age)



Pathophysiology

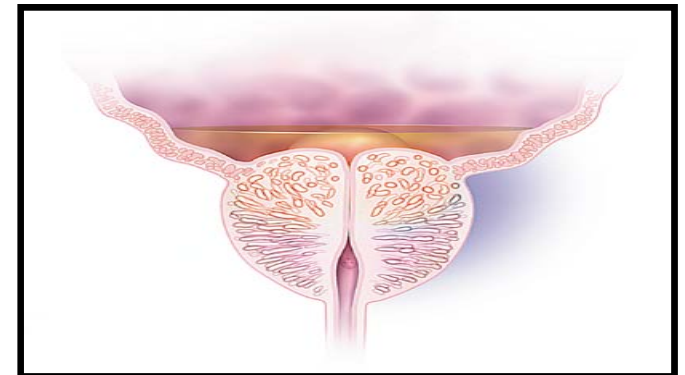
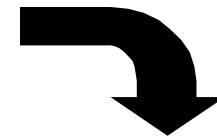
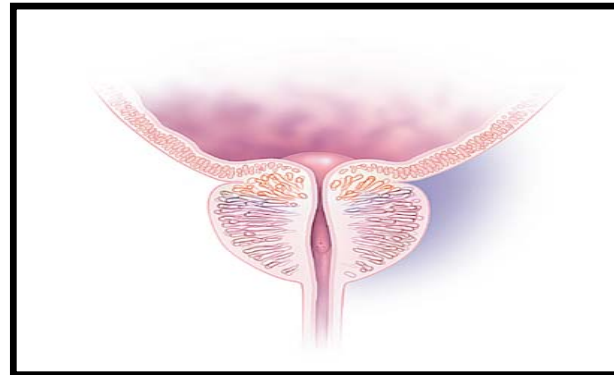
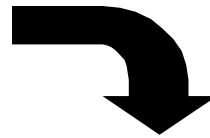
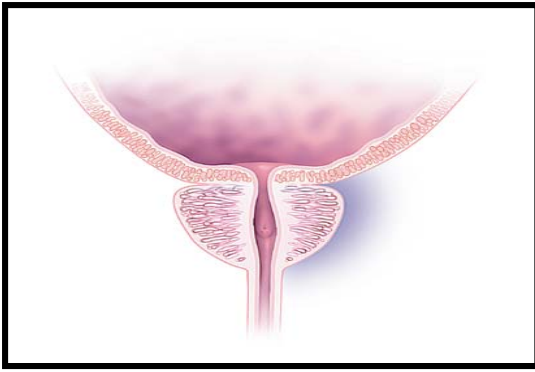


- ▶ **Prostate growth is dependent on:**
 - Time (aging)
 - Presence of androgen (primarily Testosterone)
 - Dihydrotestosterone (DHT) – concentrated intranuclearly primarily in prostatic stromal cells



- ▶ **Resistance is increased by:**
 - Prostate volume
 - Alpha-1 adrenergic stimulation – concentrated in prostatic smooth muscle at bladder neck

Obstruction (Progressive Hyperplasia)



*Degree of bladder outlet obstruction doesn't always correlate with severity of symptoms

Suggestive Symptoms

Obstructive (Voiding)

- Weak stream
- Prolonged micturition
- Straining
- Hesitancy
- Intermittent stream
- Feeling of incomplete bladder emptying

Irritative (Storage)

- Frequency
- Nocturia
- Urgency
- Incontinence

Complications

- ▶ Urinary retention
- ▶ Renal impairment
- ▶ Urinary tract infection
- ▶ Gross hematuria
- ▶ Bladder stones
- ▶ Bladder damage (trabeculations, cellules, diverticula)
- ▶ Urge/overflow incontinence



Initial Evaluation

- ▶ History and AUA symptom score
- ▶ Physical examination
- ▶ Including DRE and neurological evaluation
- ▶ Urinalysis, Urine culture
- ▶ Creatinine, BUN (with high PVR– not routinely recommended)
- ▶ PSA (as appropriate)

AUA Symptom Index (AUA-SI)

Symptom

Scale

- | | |
|--|-----------------------------|
| ▶ Incomplete emptying | 0 – Not at all |
| ▶ Frequency | 1 – Less than 1 time in 5 |
| ▶ Intermittency | 2 – Less than half the time |
| ▶ Urgency | 3 – About half the time |
| ▶ Weak stream | 4 – More than half the time |
| ▶ Straining | 5 – Almost always |
| ▶ Nocturia: number of events per night (0–5) | |

AUA Symptom Index (AUA-SI)

Classification

AUA-SI Score

Mild

0-7

Moderate

8-19

Severe

20-35

PSA Testing

- ▶ Increases detection rate for prostate cancer over DRE alone

<u>Age range</u>	<u>PSA values (ng/ml)</u>
40–49	0.00–2.50
50–59	0.00–3.50
60–69	0.00–4.50
70–79	0.00–6.50

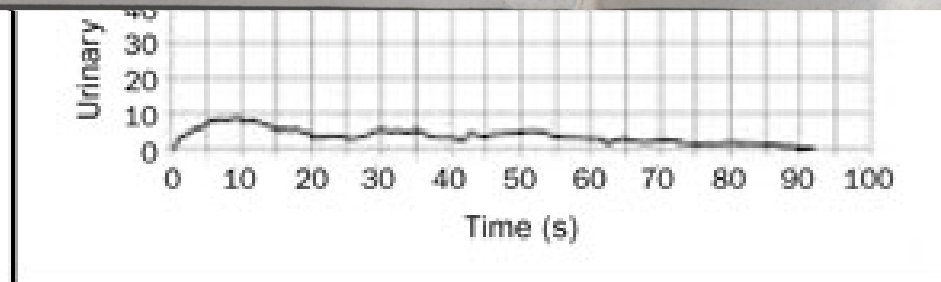
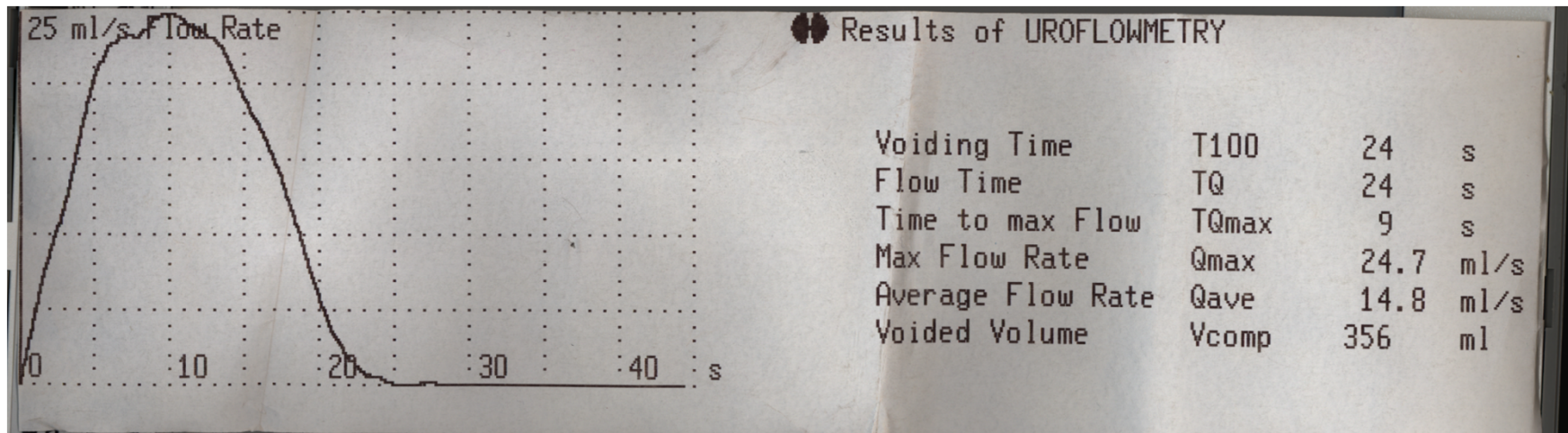
- ▶ Nonspecific for prostate cancer

Evaluation

Objective diagnostic data

- PVR
- Uroflow/BVI (urinary flow/pressure study)
- Cystoscopy
- Urodynamic Studies
- Transrectal ultrasound
- Urine cytology (irritative symptoms)

Uroflow/BVI



Differential Diagnosis of Lower Urinary Tract Symptoms Includes...

- ▶ BPH
- ▶ Overactive bladder
- ▶ Prostate cancer
- ▶ Bladder cancer
- ▶ Urinary tract infection
- ▶ Urethral stricture
- ▶ Neurogenic bladder — neurologic conditions

Summary

- ▶ Patient history, physical exam and appropriate laboratory tests for initial evaluation
- ▶ Differential diagnosis and rule out prostate cancer
- ▶ Assess risk of LUTS/BPH-related outcomes
- ▶ Discuss treatment options

Questions

- ▶ What are the differences in treating men vs women?
- ▶ How common are UTIs in older men?
- ▶ How do you decide to treat if not symptomatic?
- ▶ When and how to use UA/micro/culture?
- ▶ What are the common organisms?
- ▶ Are there new resistant organisms arising that make treatment more difficult?

Goals of Treatment

- Alleviate bothersome symptoms
- Alteration of disease progression
- Prevent complications (AUR, surgery)

General Recommendations

▶ Avoid substances that exacerbate symptoms or cause retention

- A-agonists
 - Decongestants– pseudoephedrine
 - Diet supplement–ephedra
- Anticholinergics
- Caffeine, Alcohol, spicy, acidic foods

▶ Reduce nocturia

- Decrease evening fluid intake
- Avoid diuretics in the evening
- If lower extremity edema, elevate legs one hour before bedtime

Treatment Options

- ▶ Watchful waiting
- ▶ Phytotherapy
- ▶ Medical therapy
- ▶ Minimally invasive procedures
- ▶ Surgery

Watchful Waiting

- ▶ Minimal symptoms
- ▶ Decision not to undergo further treatment now
- ▶ Monitor clinical course

Phytotherapy

- ▶ Saw palmetto (*Serenoa repens*)



African plum (*Pygeum africanum*)

- ▶ Stinging nettle (*Urtica dioica*)



Medical Therapy



- Alpha-adrenergic receptor blockers
- Cardura® (doxazosin mesylate)
- Hytrin® (terazosin hydrochloride)
- Uroxatral® (alfuzosin hydrochloride)
- Flomax® (tamsulosin hydrochloride)*
- Rapaflo® (silodosin hydrochloride)*

*Selective



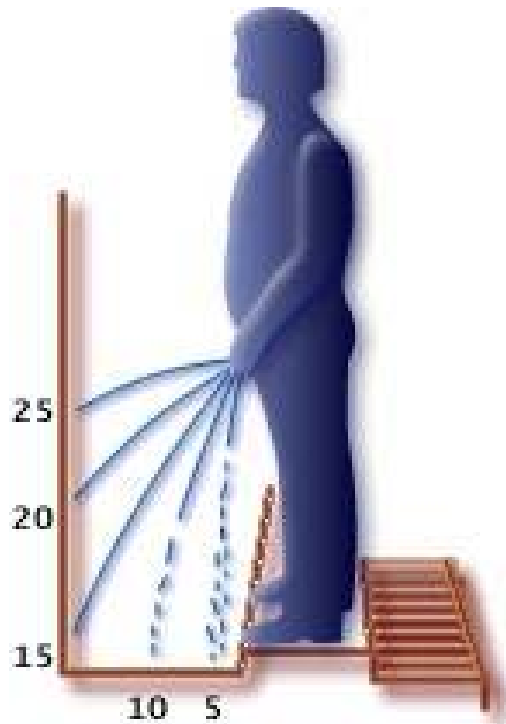
- Type II 5- α reductase inhibitors
- Proscar® (finasteride)
- Avodart® (dutasteride)

Medical Therapy

- **Combination Therapy**
 - Alpha blocker and 5-alpha-reductase inhibitor
 - Jalyn[®] (dutasteride/tamsulosin)
 - Alpha blocker and anticholinergics
- **Anticholinergic Agents**

Alpha-Blockers: Mode of Action and Efficacy

Relaxes prostate and bladder
neck smooth muscle tone



- Significant improvement in symptom scores and flow rate
- Improves symptoms rapidly
- No change in PSA or prostate size
- Not indicated to reduce incidence of AUR or TURP

Alpha blockers

Dose dependent improvement in urinary symptoms score and maximum urinary flow rate

- **Near max improvement in urinary flow rate**
 - Within 8 hours (selective blockers)
 - May take 2–4 weeks (non-selective)
- **Near maximum in voiding symptoms**
 - May take 1–3 months for all

Intraoperative Floppy Iris Syndrome

AUA 2010 Guideline Recommendations

- Men with LUTS/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
- In men with no planned cataract surgery, there are insufficient data to recommend withholding or discontinuing alpha blockers for bothersome LUTS/BPH

*More common with selective alpha blockers

Alpha-Blockers:

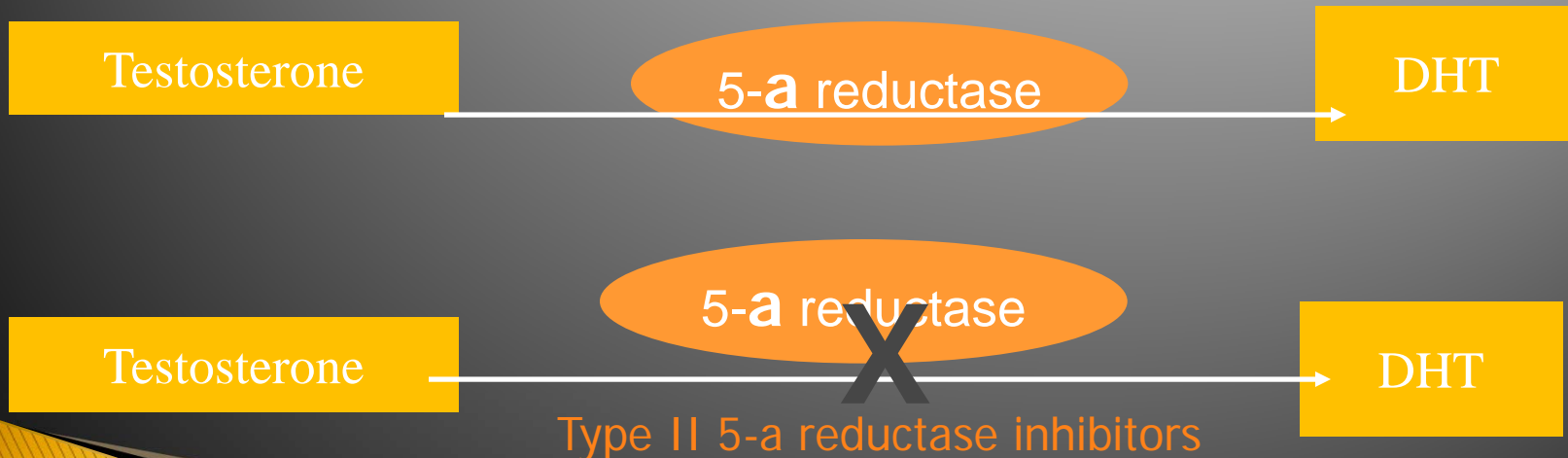
Adverse Reactions



- ▶ Asthenia
- ▶ Postural hypotension
- ▶ Dizziness
- ▶ Nasal congestion/rhinitis
- ▶ Abnormal ejaculation
- ▶ Fatigue
- ▶ Somnolence

Type II 5- α reductase inhibitors: Mode of Action

- Specific inhibitor of the Type II 5- α -reductase enzyme
- Significant decrease in serum and prostatic DHT
- Testosterone remains in normal physiologic range
- PSA and Prostate size decreases



Type II 5- α reductase inhibitors: Efficacy

- ▶ Significantly reduces AUR
- ▶ Significantly reduces BPH-related surgery
- ▶ Significantly improves symptoms and flow rates yearly (>4 years)
- ▶ Achieves and maintains reductions in prostate volumes over 4 years

Type II 5- α reductase inhibitors: Adverse Reactions

- ▶ Impotence
- ▶ Decreased libido
- ▶ Decreased ejaculate
- ▶ Ejaculation disorder
- ▶ Breast enlargement
- ▶ Breast tenderness
- ▶ Rash and hypersensitivity reaction
- ▶ Testicular pain



PSA and Type II 5- α reductase inhibitors

- ▶ Approximate 50% decrease in PSA (may vary in individual patients)
- ▶ *Therefore:* Double PSA value in patients treated 6 months or more for comparison with normal ranges
- ▶ Percent free PSA unaffected
- ▶ Any sustained increase in PSA levels for patients on Type II 5- α reductase inhibitors: should be carefully evaluated

Black Box warning

- ▶ The effects of finasteride on prevention of prostate cancer were evaluated in a large, randomized, placebo controlled study in men considered at increased risk for prostate cancer, and a statistically significant increase in the incidence of higher grade prostate cancer (Gleason score ≥ 7) was found in men who received finasteride (Thompson 2003; Thompson 2013).

MTOPS Study

Combination of finasteride and doxazosin

- ▶ Reduced disease progression by 66% compared to placebo (39% doxazosin alone, 34% finasteride alone)
 - ▶ Greater symptom relief & improvement in urinary flow rate
 - ▶ Reduced risk of invasive therapy by 67% compared (64% finasteride)
- ❖ Especially effective– Prostate >40 ml or PSA >4 ng/ml

Anticholinergic Therapy

Overactive Bladder (OAB) and BPH often coexist

- Generally treat BPH/LUTS first
- Antimuscarinic therapy shown effective in men
 - Tolterodine shown no increased risk of AUR
- Monitor PVR (post void residual) in men at risk for AUR

Overactive Bladder Treatments

- ▶ Oxybutynin (Ditropan, Ditropan XL, Oxytrol patch, Gelnique gel & generic)
- ▶ Darifenacin (Enablex)
- ▶ Fesoterodine (Toviaz)
- ▶ Tolterodine (Detrol, Detrol LA)
- ▶ Trospium (Sanctura, Sanctura XR)
- ▶ Solifenacin (Vesicare)

* Side effects– dry mouth, constipation, dry eyes, blurred vision, dizziness, urinary hesitancy, urinary retention, confusion, falling, drowsiness

- ▶ Mirabegron_(Myrbetriq) beta-3 adrenergic agonist
- ▶ Botox
- ▶ Interstim

Other Non-Surgical Therapy



Clean intermittent catheterization (CIC)

- *Lower* incidence/ risk of urine infection compared to an indwelling urinary catheter
- Prophylactic antibiotics not recommended

Indications for Surgery

- ▶ Acute retention of urine
- ▶ Chronic retention due to prostatic obstruction
- ▶ Recurrent urinary tract infection/hematuria
- ▶ Bladder stones secondary to BPH
- ▶ Renal insufficiency due to BPH
- ▶ Large bladder diverticulum/ diverticula
- ▶ Patient preference

Minimally Invasive Treatments

- ▶ Laser (Nd:YAG, Holmium)
- ▶ Transurethral electrovaporization of the prostate (TUEVP)
- ▶ Microwave thermotherapy (TUMT)
- ▶ Radio frequency applications (TUNA)
- ▶ High-Intensity focused ultrasound (HIFU)
- ▶ Urethral stents (Urolume)

❖ Long-term efficacy unknown in comparison to TURP

Surgery

- Transurethral Resection of the Prostate (TURP)
 - Common form of surgical intervention
 - Highly efficacious
- Transurethral Incision of the Prostate (TUIP)
- Open Prostatectomy

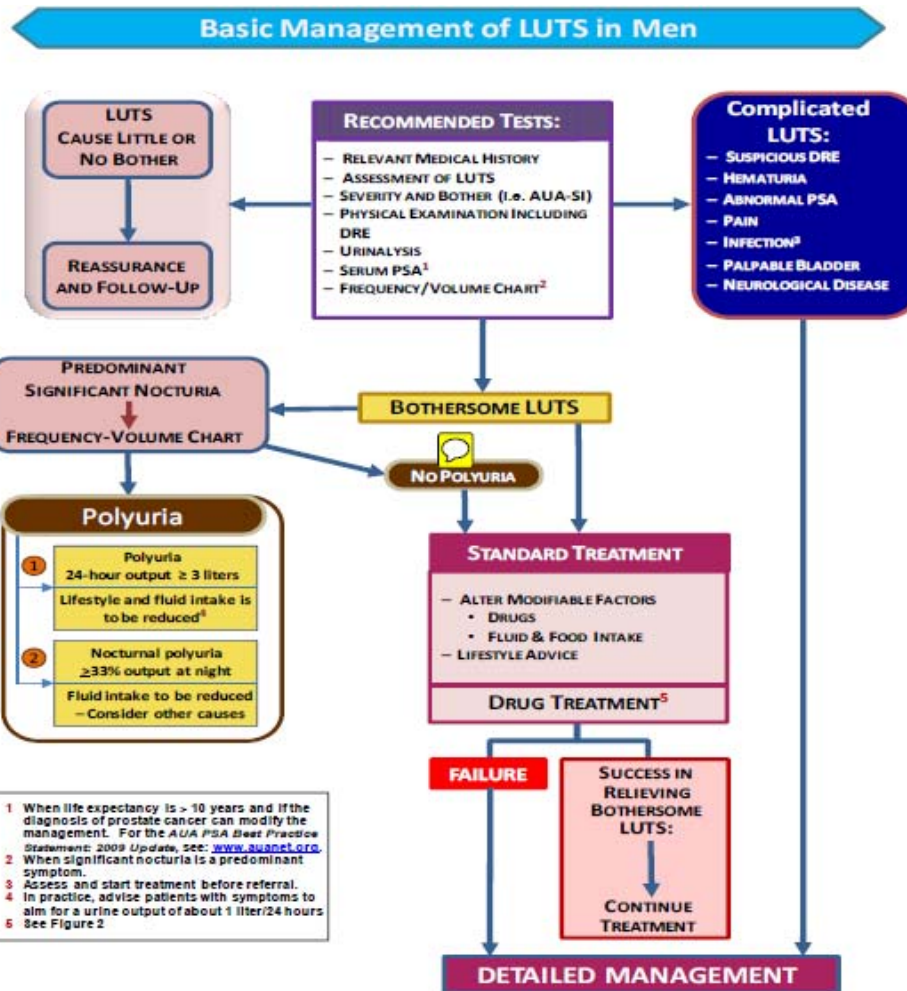


Figure 1.1. Basic management of lower urinary tract symptoms (LUTS) in men (adapted with permission from Abrams 2009). AUA-SI, American Urological Association Symptom Index; DRE, digital rectal exam; PSA, prostate-specific antigen.

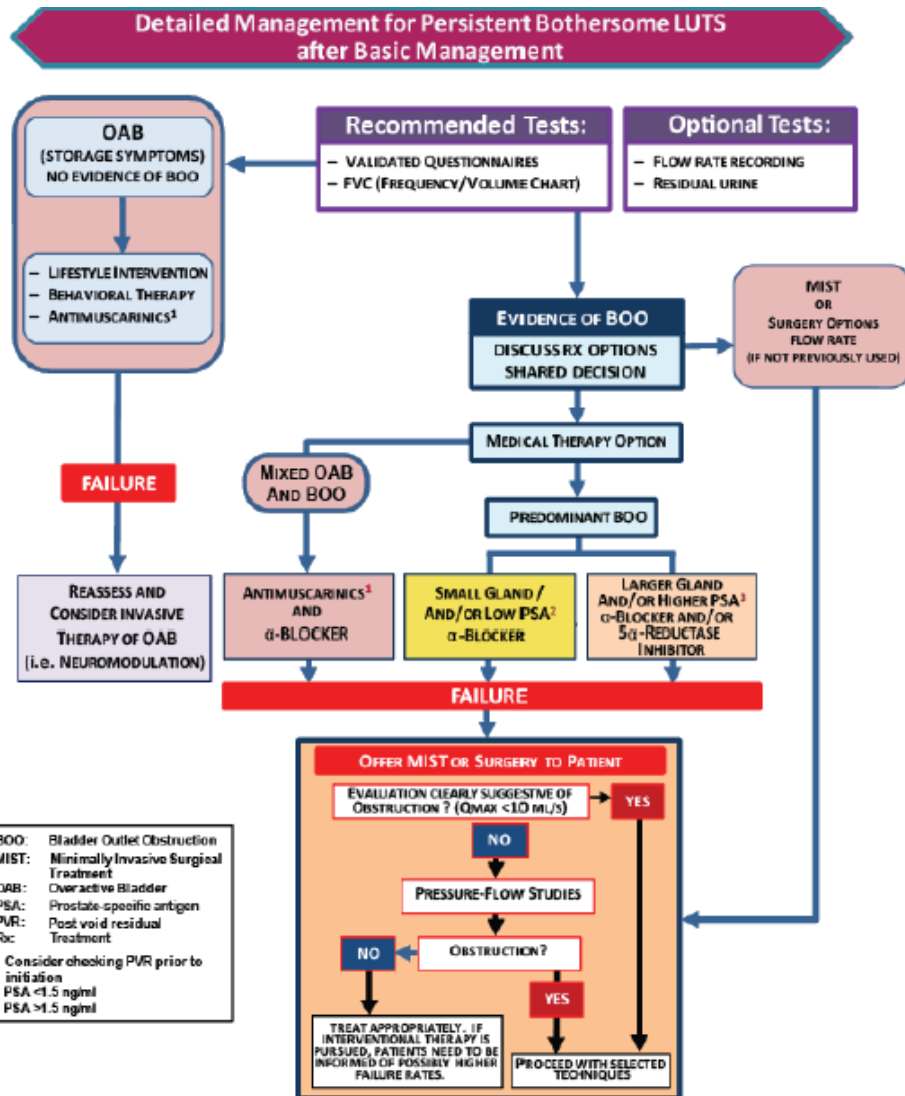


Figure 1.2. Detailed management of persistent, bothersome lower urinary tract symptoms (LUTS) after basic management (adapted with permission from Abrams 2009).

Summary

- ▶ LUTS/BPH is a common disease with potentially serious outcomes
- ▶ As the population ages, LUTS/BPH will be an increasing medical concern for physicians
- ▶ Evaluation of the prostate/urinary symptoms in older men should be part of routine office practice

Questions?



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CLINICAL PRACTICE

Caren G. Solomon, M.D., M.P.H., Editor

Urinary Tract Infections in Older Men

Anthony J. Schaeffer, M.D., and Lindsay E. Nicolle, M.D.

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Article

References

Metrics

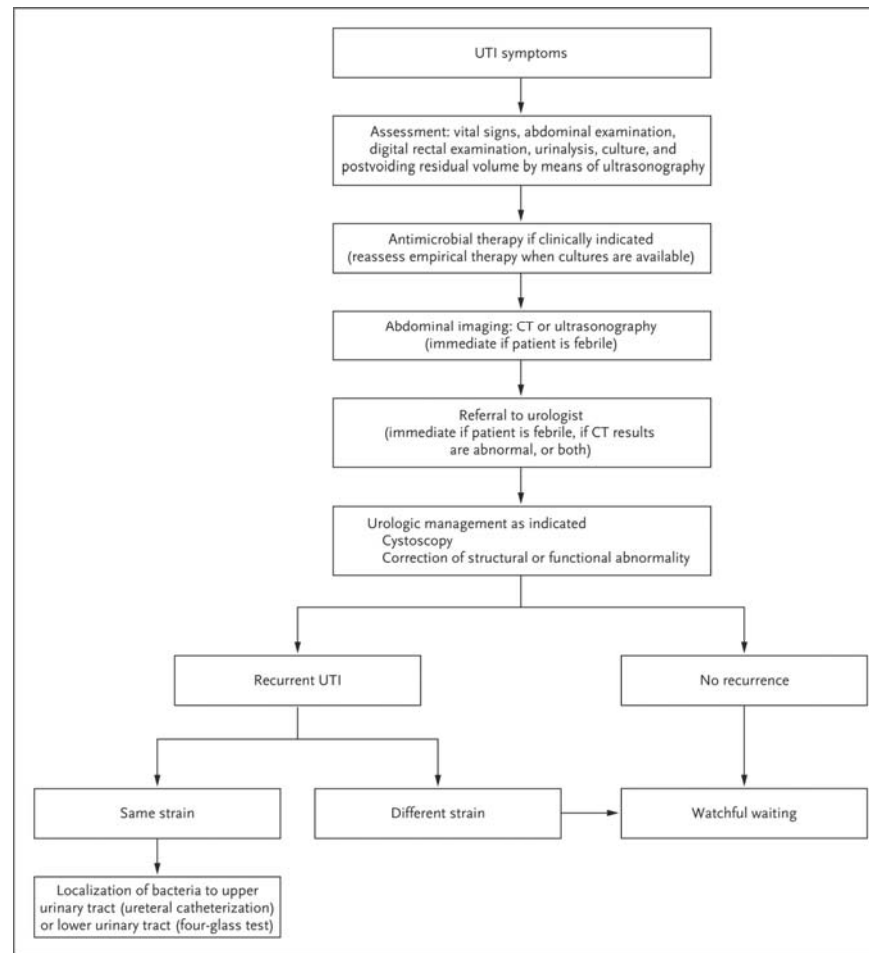
[See Key Clinical Points ▾](#)

This *Journal* feature begins with a case vignette highlighting a common clinical problem. Evidence supporting various strategies is then presented, followed by a review of formal guidelines, when they exist. The article ends with the authors' clinical recommendations.

A 79-year-old community-dwelling man presents with urinary frequency, dysuria, and fever. Culture reveals extended-spectrum beta-lactamase *Escherichia coli*. He had a similar infection several months ago, with the same organism isolated, and he had a response to nitrofurantoin treatment. How would you further evaluate and manage this case?

Evaluation and treatment of Urinary Tract Infections in Older Men

Schaeffer, AJ, Nicolle, LE, N Engl J Med 2016;374:562-571



Antimicrobial Therapy for the Treatment of Urinary Tract Infection and Prostatitis in Men.

Table 1. Antimicrobial Therapy for the Treatment of Urinary Tract Infection and Prostatitis in Men.^a

Antimicrobial Agent	Dose for Normal Renal Function	Clinical Use [†]	Adverse Effects and Contraindications
Oral			
Ciprofloxacin	500 mg twice daily	First-line therapy for cystitis, pyelonephritis, acute prostatitis, or chronic prostatitis	Hypersensitivity; tendinopathy or tendon rupture
Levofloxacin	500 mg or 750 mg daily	First-line therapy for cystitis, pyelonephritis, acute prostatitis, or chronic prostatitis	Hypersensitivity; tendinopathy or tendon rupture
Trimethoprim–sulfamethoxazole	160 mg of trimethoprim and 800 mg of sulfamethoxazole twice daily	First-line therapy for cystitis; second-line therapy for chronic prostatitis	Sulfa hypersensitivity; liver toxic effects
Trimethoprim	100 mg twice daily	First-line therapy for cystitis	
Nitrofurantoin monohydrate macrocrystals	100 mg twice daily	First-line therapy for cystitis only	Lung and liver toxic effects
Fosfomycin [‡]	3 g single dose	Cystitis	
Amoxicillin	500 mg three times daily	Cystitis	Beta-lactam hypersensitivity
Amoxicillin–clavulanate [§]	500 mg three times daily or 875 mg twice daily	Cystitis	Beta-lactam hypersensitivity
Cephalexin	500 mg four times daily	Cystitis	Beta-lactam hypersensitivity
Cefixime	400 mg once daily	For resistant organisms in cystitis or pyelonephritis	Beta-lactam hypersensitivity
Cefpodoxime proxetil	100–200 mg twice daily	Cystitis or pyelonephritis	Beta-lactam hypersensitivity
Parenteral			
Ceftriaxone	1–2 g every 24 hr	First-line therapy for pyelonephritis; use with gentamicin for acute prostatitis	Beta-lactam hypersensitivity
Ciprofloxacin	400 mg every 12 hr	First-line therapy for cystitis, pyelonephritis, acute prostatitis, or chronic prostatitis	Hypersensitivity; tendinopathy or tendon rupture
Levofloxacin	500–750 mg every 24 hr	First-line therapy for cystitis, pyelonephritis, acute prostatitis, or chronic prostatitis	Hypersensitivity; tendinopathy or tendon rupture
Gentamicin or tobramycin	5–7 mg/kg every 24 hr	First-line therapy for pyelonephritis; use with beta-lactam for acute prostatitis	Vestibulocochlear toxic effects; renal failure
Piperacillin–tazobactam [§]	3.375 g every 8 hr	For resistant organisms in cystitis, pyelonephritis, or acute prostatitis	Beta-lactam hypersensitivity
Ceftazidime	1 g every 8 hr	For resistant organisms in cystitis and pyelonephritis	Beta-lactam hypersensitivity
Ceftazidime–avibactam [§]	2.5 g every 8 hr	For resistant organisms in cystitis and pyelonephritis	Beta-lactam hypersensitivity
Cefzolozane–tazobactam [§]	1.5 g every 8 hr	For resistant organisms in cystitis and pyelonephritis	Beta-lactam hypersensitivity
Meropenem	500 mg every 6 hr or 1 g every 8 hr	For resistant organisms in cystitis and pyelonephritis	Hypersensitivity to carbapenems; anaphylactic reaction to beta-lactams
Doripenem	500 mg every 6 hr	For resistant organisms in cystitis and pyelonephritis	Hypersensitivity to carbapenems; anaphylactic reaction to beta-lactams
Ertapenem	1 g once daily	For resistant organisms but not <i>Pseudomonas aeruginosa</i> in cystitis and pyelonephritis	Hypersensitivity to carbapenems; anaphylactic reaction to beta-lactams

^a The data presented here are for commonly used agents and are not comprehensive. First-line therapy is selected on the basis of clinical presentation and the susceptibility of the infecting bacteria. When empirical therapy is initiated, the antimicrobial agent should be reassessed once culture results are available.

[†] The duration of therapy for cystitis is generally 7 days, and the duration of therapy for pyelonephritis is 7 to 14 days; 30 days of therapy is recommended for chronic prostatitis. Treatment for acute prostatitis is usually initiated with parenteral therapy and stepped down to oral therapy when clinically indicated to complete a 30-day course (that includes both the parenteral and oral therapies).

[‡] A single dose of fosfomycin is indicated for the treatment of uncomplicated urinary infection. It may have a role in the treatment of resistant organisms in patients with other presentations of urinary infection, but the effective dose has not yet been determined.

[§] The dose refers to the amount of the first noted agent in the combination.

Schaeffer AJ, Nicolle LE. *N Engl J Med* 2016;374:562-571



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