Benign Prostatic Hyperplasia (BPH)

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Learning Objectives

1. Perform a differential diagnosis to distinguish between prostatitis, BPH, and other urologic conditions in male patients.
2. Coordinate referral and follow-up care with other specialists (e.g. urologist, surgical) when red flags identified during diagnosis and evaluation indicate necessity.
3. Use current evidence-based recommendations to determine appropriate pharmacologic, surgical, CAM, or watchful waiting treatment strategy.
4. Develop collaborative care plans with patients, emphasizing adherence to prescribed pharmacotherapies.

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Audience Engagement System

Step 1 Step 2 Step 3

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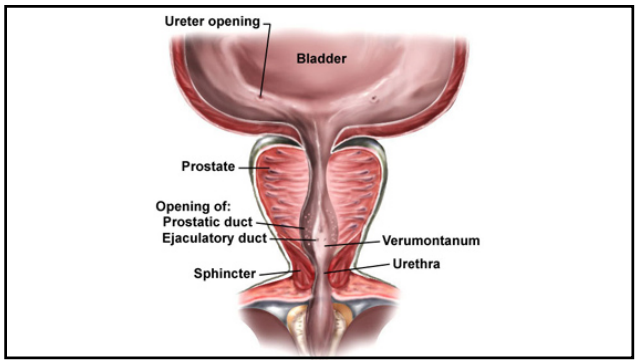

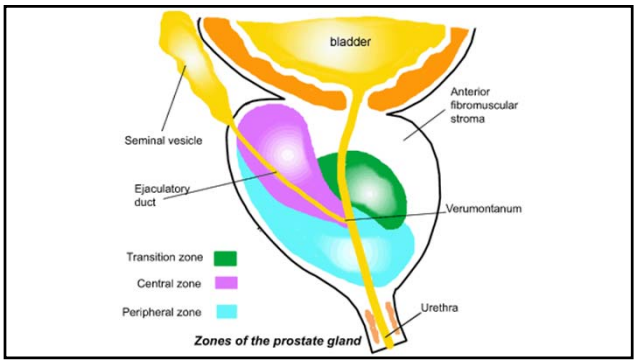

Prostate Disease

- BPH - Microscopic Hyperplasia
  Proliferation of the stroma and epithelium
- BPE - Palpable enlargement of the prostate
  Detected by DRE or ultrasound
- Collection of urinary symptoms associated with prostatic hyperplasia
  LUTS – Lower Urinary Tract Symptoms
  BOO – Bladder Outlet Obstruction

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Benign Prostatic Hyperplasia

- Size correlates poorly with symptoms
- 50% of men with microscopic hyperplasia develop clinical prostate enlargement
- 30% to 50% of men with gland enlargement manifest symptoms

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Prevalence of Histological BPH

Age	Prevalence
31-40	8%
51-60	40-50%
>80	80%

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Prevalence of LUTS

Age	Prevalence
50-59	26%
60-69	33%
70-79	41%
80-89	46%

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Static and Dynamic Factors

- Static Obstruction
  Due to the bulk of the enlarged prostate encroaching upon the prostatic urethra
- Dynamic Obstruction
  Related to the tension of the prostate smooth muscle

LUTS/BPH

- Storage Symptoms
  Frequency, Nocturia, Urgency, Incontinence
- Voiding Symptoms
  Weak stream, Splitting or Spraying, Intermittent Stream, Hesitancy, Straining, Terminal Dribbling

Other causes of LUTS

- Urethral stricture
- Bladder neck contracture
- Carcinoma of the prostate
- Carcinoma of the bladder
- Bladder calculi
- Urinary tract infection
- Prostatitis
- Neurogenic bladder

Prostatitis
NIH Classification

I. Acute bacterial prostatitis
II. Chronic bacterial prostatitis (Sx > 3 mos.)
III. Chronic Pelvic Pain Syndrome
   A. Inflammatory
   B. Noninflammatory
IV. Asymptomatic prostatitis

Acute Bacterial Prostatitis
Clinical Presentation

- Systemic Symptoms
  Fever, Chills, Malaise, Myalgia
- Irritative Symptoms
  Frequency, Urgency, Dysuria
- Obstructive Symptoms
  Dribbling, Hesitancy, AUR
- Pelvic/Perineal Pain

AES Question 1

Which of the following statements is true regarding the evaluation of patients presenting with symptoms of acute bacterial prostatitis?

A. U/A should be obtained following vigorous prostatic massage.
B. Rectal Exam is contraindicated.
C. Mid stream urine culture should be obtained to identify the causative organism.
D. PSA should be drawn to R/O prostate Ca.

Acute Bacterial Prostatitis Evaluation

DRE – Prostate enlarged, boggy, tender
Suprapubic Tenderness?
Scrotal Tenderness?
U/A/C&S
CBC, ESR, CRP if needed
Defer PSA for one month

Acute Bacterial Prostatitis

- E. coli – 67%
- Pseudomonas – 13%
- Klebsiella sp. – 6%
- Gram (+) – 5%
- Other – 9%

World J Urol 2013;31:711-716

Acute Bacterial Prostatitis Treatment

- Empiric Antibiotic Therapy
  Fluroquinolones (Good tissue penetration)
  - Ciprofloxacin 500 mg BID
  - Levofloxacin 500 mg Daily
  Trimethoprim/sulfamethoxasole 160mg/800mg BID
- Duration of treatment 4-6 wks

Evaluation of BPH – AUA Guidelines

- History (AUA-SI, IPSS)
- Focused physical – Size of bladder
  - Prostate exam
- U/A
- PSA
  (In men with at least a 10 year life expectancy who want to know.)

AUA Symptom Index

Over the past month, how often have you?	Not at all	Less than 1 time in 5	Less than half the time	About half the time	More than half the time	Almost always
Had a sensation of not completely emptying your bladder after you finish urinating?	0	1	2	3	4	5
Had to urinate again less than 2 hrs after you finished urinating?	0	1	2	3	4	5
Stopped and started again several times when you urinated?	0	1	2	3	4	5
Found it difficult to postpone urination?	0	1	2	3	4	5
Had a weak urinary stream?	0	1	2	3	4	5
Had to push or strain to begin urination?	0	1	2	3	4	5
How many times do you typically get up to urinate at night?	None 0	1 time 1	2 times 2	3 times 3	4 times 4	≥5 times 5

AUA Symptom Index

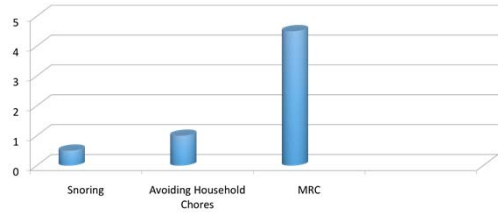
- Score = 0-7 Mild Symptoms
- Score = 8-19 Moderate Symptoms
- Score = 20-35 Severe Symptoms

International Prostate Symptom Score (Bother Score)

If you were to spend the rest of your life with your urinary condition the way it is now, how would you feel about that?

0=Delighted
1=Pleased
2=Mostly Satisfied
3=Mixed – About equally satisfied and dissatisfied
4=Mostly Dissatisfied
5=Unhappy
6=Terrible

Marital Bother Score



AES Question 2

Which of the following statements about BPH is true?

A. Acute urinary retention is a common complication of BPH.
B. Patients with minimal symptom scores do not require treatment.
C. Early treatment of BPH reduces the incidence of renal insufficiency.
D. Prostate size correlates closely with symptoms.

BPH

- Acute urinary retention – uncommon (annual risk < 1%)
- Irreversible renal insufficiency is rare
- Management decisions should be based on the presence and severity of symptoms

N Engl J Med. 2003;349(25)

Treatment

- Goals of treatment – Quality of Life
  - Symptom Control
- Watchful Waiting
  -Option for patients with minimal bother (Even with high IPSS ratings)
  - Minimize alcohol, caffeine, evening fluids
  - Minimize alpha agonists, anticholinergics, antihistamines, Ca channel blockers

Medical Therapy

- Alpha Adrenergic Blockers
  - Decrease prostatic and urethral smooth muscle tone
  - Increase detrusor muscle vascular supply
- 5 Alpha Reductase Inhibitors
  - Block conversion of testosterone to dihydrotestosterone
  - Reduce prostate volume

Alpha Adrenergic Blockers

- Nonselective - alpha-1_B
  Terazosin (Hytrin)
  Doxazosin (Cardura)
- Selective - alpha -1_A
  Tamsulosin (Flomax)
  Alfuzosin (Uroxatral)
  Silodosin (Rapaflo)

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AUA Treatment Guidelines

- STANDARD
  (1)Health outcomes of the interventions are sufficiently well known to permit meaningful decisions and
  (2) there is virtual unanimity about which intervention is preferred.

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AUA Treatment Guidelines

- RECOMMENDATION
  (1) the health outcomes of the intervention are sufficiently well known to permit meaningful decisions, and
  (2) an appreciable but not unanimous majority agrees on which intervention is preferred.

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AUA Treatment Guidelines

- OPTION
  (1) the health outcomes of the interventions are not sufficiently well known to permit meaningful decisions, or
  (2) preferences are unknown or equivocal.

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AUA Treatment Guidelines

- Patients with mild symptoms of LUTS secondary to BPH (AUA-SI score <8) and patients with moderate or severe symptoms (AUA-SI score ≥8) who are not bothered by their LUTS should be managed using a strategy of watchful waiting.

  (Standard)

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AUA Treatment Guidelines

- Alfuzosin, doxazosin, tamsulosin, terazosin are appropriate and effective treatment alternatives for patients with bothersome, moderate to severe LUTS secondary to BPH (AUA Symptom Index score ≥8).

  (Option)

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AUA Treatment Guidelines

- Although there are slight differences in the adverse events profiles of these agents, all four appear to have equal clinical effectiveness.

(Option)

AUA Treatment Guidelines

- 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.

(Recommendation)

AES Question 3
True or False?

All alpha blockers approved for the treatment of BPH have similar effects on ejaculatory function.

A. True
B. False

Alpha Adrenergic Blockers

- Terazosin, Doxazosin
  Hypotension, Dizziness
  No impact on ejaculatory function
- Tamsulosin, Alfuzosin
  Rhinitis
  Ejaculatory Dysfunction

Ejaculatory Dysfunction

- Tamsulosin 0.4 mg daily – 6%
- Tamsulosin 0.8 mg daily – 18%
- Silodusin – 22-28%
- Afluzosin – No impact on ejaculatory function

5 Alpha-Reductace Inhibitors

- Finasteride (Proscar)
  Reduces circulating DHT levels by 70%
- Dutasteride (Avodart)
  Reduces circulating DHT levels by >90%

5 Alpha-Reductase Inhibitors

- Comparable in efficacy
- Decrease prostate volume 20% to 30%
- Lower IPSS ratings 3 to 4 points
- Increase urine flow rates
- Decrease urinary retention & need for surgery
- Gradual clinical effect (6 to 12 months)
- Most benefit with prostate volume > 40 mL

Eur Urol 2004;46:547-554

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Prostate Volume & PSA

- 5 alpha reductace inhibitors – more effective if prostate volume > 40 mL
- PSA levels correlate with prostate volume
  PSA > 1.6 for men in 50's
  > 2.0 for men in 60's
  > 2.3 for men in 70's
- 70% sensitive & 70% specific for a prostate volume > 40 mL

Urology 1999;53(3)

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5 Alpha-Reductase Inhibitors

- Decreased libido – 6%
- Erectile dysfunction – 8%
- Ejaculatory disorders – 4%

- Lower PSA levels approximately 50%

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Prostate Cancer Prevention Trial

- 18,882 men with risk of prostate CA
- Normal DRE & PSA $\leq$ 3
- Finasteride 5 mg./d or placebo
- After 7 years
  - 25% decrease in the incidence of CA
  - Aggressive CA (Gleason score $\geq$ 7) significantly increased in treatment group

N Engl J Med 2003;349:215-224

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AES Question 4

Which of the following statements is false?

A. The combination of an alpha blocker and a 5-ARI is more effective than either agent alone for slowing progression of symptoms in men with large prostates.
B. 5 Phosphodieterase inhibitors have been shown to lower IPSS scores.
C. Anticholinergic agents are contraindicated in men with BPH
D. The AUA does not recommend alternative therapies such as Saw Palmetto for the treatment of BPH

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MTOPS Study

- 3047 men with BPH
- Doxazosin
- Finasteride
- Combination
- Placebo

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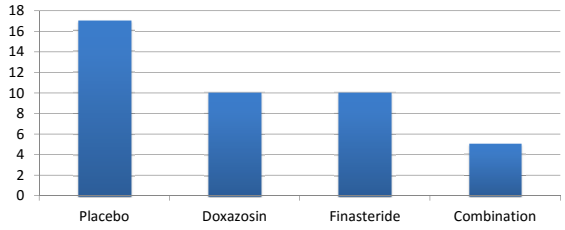
MTOPS
Progression of Symptoms



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CombAT

- 4844 men with BPH
- Tamsulosin
- Dutasteride
- Combination

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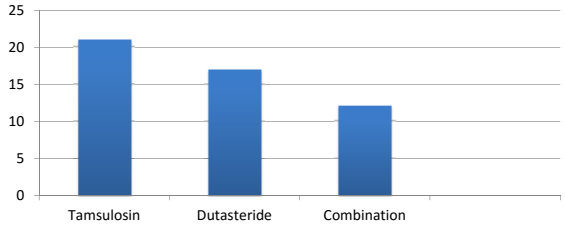
CombAT
Progression of Symptoms



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MTOPS/CombAT

- Combination therapy superior to monotherapy in preventing progression of symptoms, AUR, Surg.
- Combination therapy most effective for:
- PSA > 4.0
- Prostate volume > 40 mL

Eur Urol 2010: 57:123-131

N Engl J Med 2003;349:2387-2398

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AUA Treatment Guidelines

- The combination of an alpha-blocker and a 5-ARIs (combination therapy) is an appropriate and effective treatment for patients with LUTS associated with demonstrable prostatic enlargement based on volume measurement, PSA level as a proxy for volume, and/or enlargement on DRE.

  (Option)

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Anticholinergic Medications

- Detrusor overactivity – identified in 45-50% of men with BPH
- Incidence increases with the severity of obstruction
- OAB symptoms increase in the aging male in the same proportion as women

EUR UROL 2011;59:377-386

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Anticholinergic Medications

- Useful for treatment of overactive bladder
- Combined with alpha blockers
  -Improve symptoms scores
  -Decrease urgency and frequency
- No significant increase in episodes of acute urinary retention

JAMA 2006;296:2319-2328

AUA Treatment Guidelines

- Anticholinergic agents are appropriate and effective treatment alternatives for the management of LUTS secondary to BPH in men without an elevated post-void residual and when LUTS are predominantly irritative.

(Option)

5-Phosphodiesterase Inhibitors

- Reduce smooth muscle tone of the detrusor, prostate and urethra
- Use of PDE5i alone is associated with improvement of IPSS score (-2.8)
- Combination of PDE5i and alpha-blockers is superior to alpha-blockers alone

Eur Urol 2012;61:994-1003

5-Phosphodiesterase Inhibitors

- AUA treatment guidelines – not mentioned
- Tadalafil approved by FDA for Tx of BPH 5 mg daily
- May potentiate hypotensive effects of alpha blockers

Beta3 Adrenoceptor Agonists

- Principal Beta receptor in the bladder
- Stimulation increases bladder capacity
- No interference in micturation pressure, PVR or voiding contraction
- Mirabegron – Beta3 agonist

Alternative Therapies

- Saw Palmetto
  Limited data to support efficacy
- 2012 systematic review of 32 RCCTs
- Saw Palmetto vs. Placebo
- No difference in urinary symptom scores, urinary flow or prostate size

Cochrane Database Syst Rev 2012;12:CD001423

Alternative Therapies

- Beta-sitosterol
- Cernilton (rye grass pollen extract)
- Pygeum
- Substantial placebo effect
- Data is conflicting
- Not approved by the FDA
- Not recommended by the AUA

AUA Treatment Guidelines

- No dietary supplement, combination phytotherapeutic agent or other nonconventional therapy is recommended for the management of LUTS secondary to BPH.

  (Recommendation)

Practice Recommendations

- Use the AUA Symptom Index or IPSS to evaluate and monitor the severity of lower urinary tract symptoms in men with BPH.
- Use an alpha adrenergic blocker as first line therapy for men with BPH/LUTS.
- Add a 5 alpha reductase inhibitor for those patients with large prostates who's symptoms are not controlled with monotherapy.

Surgical Therapy

- TURP is the benchmark
- Symptoms improve in 80% to 90%
- 1% annual risk of repeat surgery
- IPSS scores decrease 15-20 points
- Quality of life is enhanced only with severe LUTS
- Ejaculatory dysfunction 65% to 70%
- 1% to 2% perioperative mortality

Surgical Therapy

- Monopolar TURP
  Resectoscope – monopolar diathermy loop
  Continuous irrigation – nonconductive sol'n
  Risk of post operative hyponatremia
- Bipolar TURP
  Bipolar electrocautery
  Saline used as irrigant
  Eliminates risk of hyponatremia

Plasma Vaporization ("Button" procedure)

- Bipolar electrocautery
- High-frequency electric current passes between two electrodes
- Vaporizes prostate tissue
- Minimal blood loss
- No tissue available for pathology

Laser Techniques

- Photoselective Vaporization (PVP)
- Holmium laser enucleation of the prostate (HoLEP)
- Thulium laser enucleation of the prostate (ThuLEP)

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Other Surgical Therapies

- Open Prostatectomy (glands > 80 mL)
- Transurethral incision of the prostate (glands < 30 mL)
  Less ejaculatory dysfunction, Less bleeding, Higher rate of reoperation
- Stents (high risk patients)

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Minimally Invasive Procedures

- TUNA – Transurethral needle ablation
  Radiofrequency waves – heats tissue
  Low failure rate (25% after 5 years)
  Irritative symptoms, Urinary retention
- TUMT – Transurethral microwave thermo-therapy
  Heat destroys tissue
  Failure rate 10% to 16% annually
  Requires indwelling catheter for 4-6 weeks

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New Technologies

- Prostatic Urethral Lift
- Convective Water Vapor
- Prostate Artery Embolization
- Waterjet Ablation
- Histotripsy
- PRX302 (Genetically modified protein)

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Questions

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Associated Session

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