

Prostate Diseases Update: Prostate Potpourri

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Learning Objectives

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

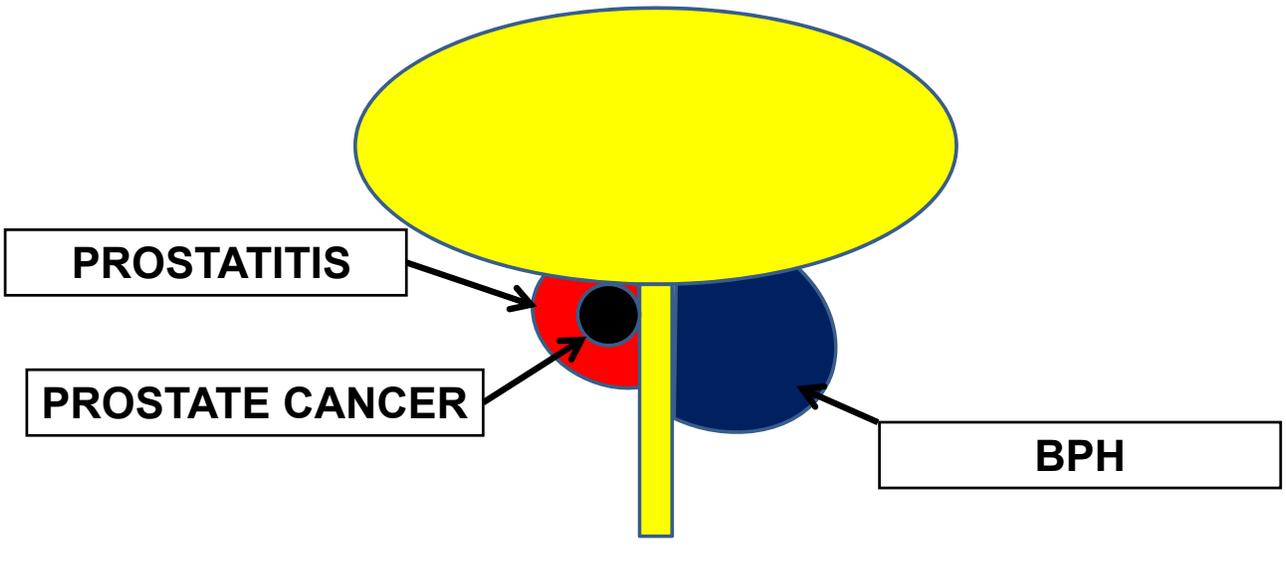
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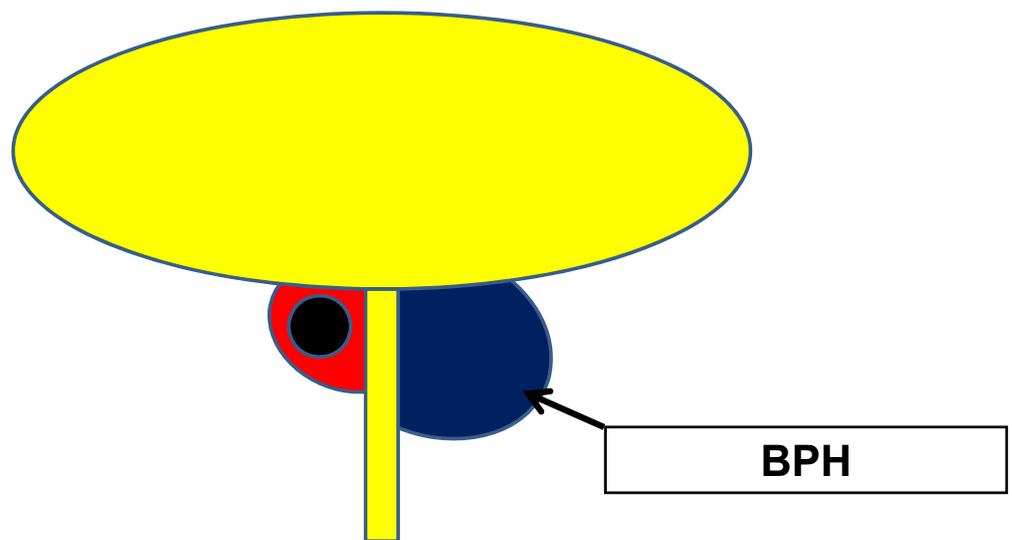


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Learning Objectives



BENIGN PROSTATIC HYPERPLASIA



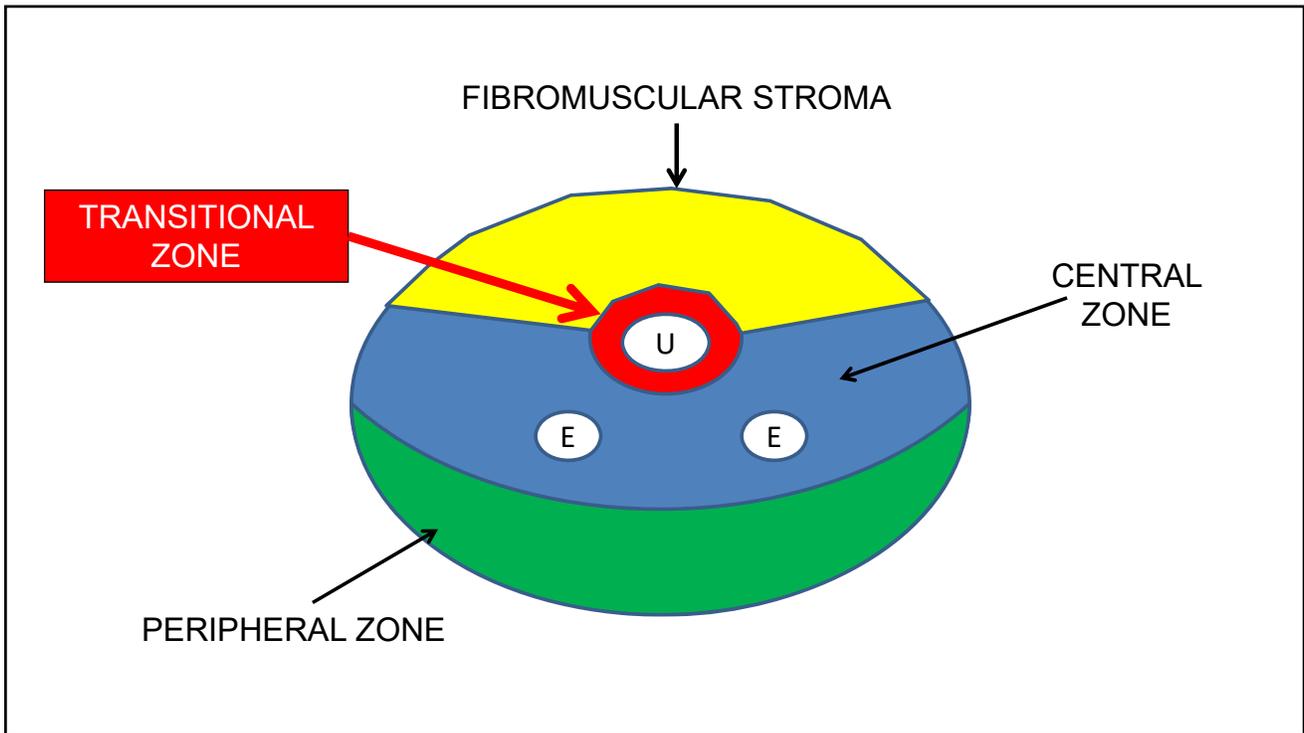
Poll Question 1

Which of the following is MOST accurate about the American Urological Association (AUA) Symptom Index?

1. It is administered by a physician.
2. A 10 point change in symptoms is considered significant.
3. It can be used to guide initial therapy.
4. It has not been validated.
5. It only assesses obstructive symptoms.

Pathophysiology

- Pathophysiology is incompletely understood
 - Anatomic obstruction
 - Disruption of neural mediators of smooth muscle (α -adrenergic (1A, 1B, 1D), muscarinic (M2, M3), phosphodiesterase enzymes (type 5))
- Gland size on physical exam or ultrasound does NOT correlate with symptoms
- BPH may be asymptomatic, produce troublesome symptoms (50%), or cause impaired voiding, hydronephrosis and acute renal insufficiency (<1%)



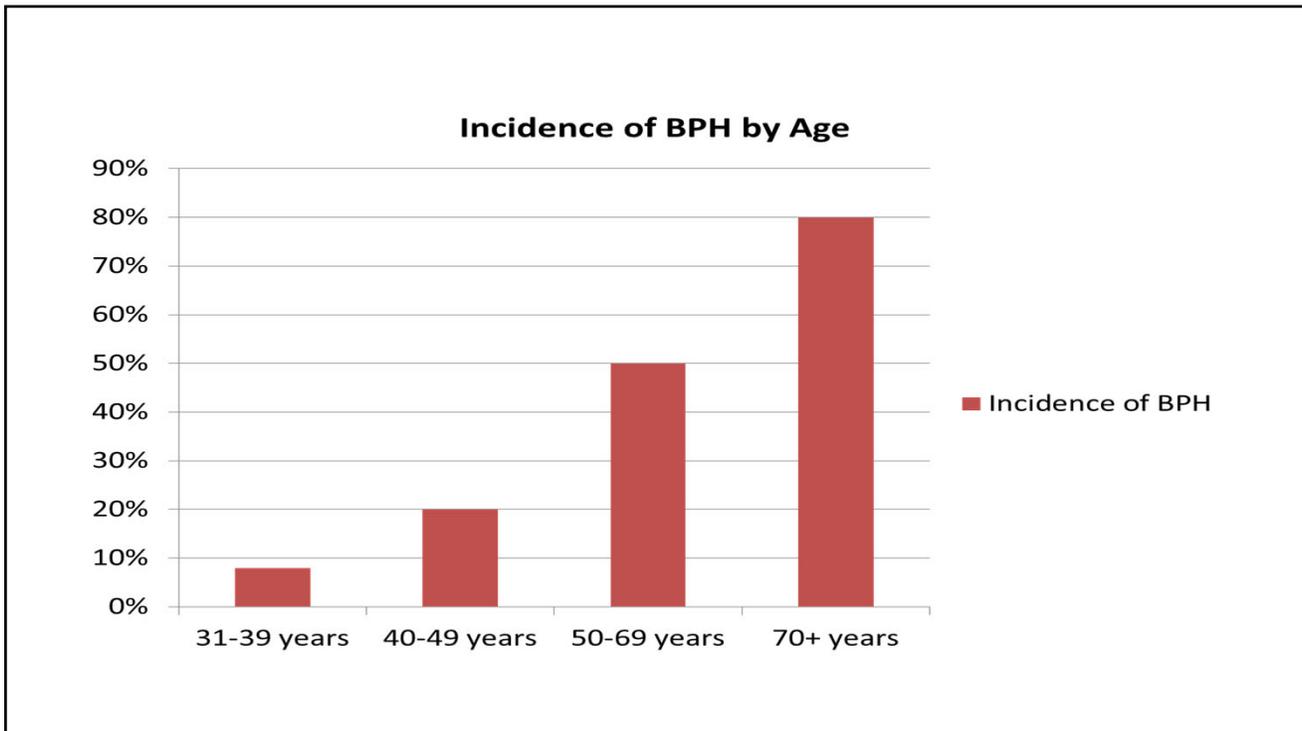
Risk Factors

Proven

- Increasing Age
- Genetics

Unproven

- Race (African American)
- Physical Inactivity
- Obesity
- Tobacco Use
- Excessive Alcohol Use
- Post Vasectomy
- Metabolic Syndrome/DM



History

- PMHX:
 - Conditions that can lead to neurogenic bladder (Parkinson's Disease, stroke)
 - Conditions that can lead to urethral stricture (STI, trauma, urinary tract instrumentation)
 - Cystitis, prostatitis, bladder tumor
 - Diabetes mellitus

History Continued

- MEDICATIONS
 - Antihistamines (\downarrow parasympathetic tone)
 - Decongestants (\uparrow α -adrenergic stimulation)
 - Diuretics (\uparrow urine production)
 - Opiates (impaired autonomic function)
 - Tricyclic antidepressants (anticholinergic effects)

American Urological Association (AUA) Symptom Index

- 7 question, validated tool to objectively assess the severity of LUTS in men
- Can be self-administered and scored by nurse or physician
- Score ranges from 0 to 35
- A 3 point change in symptoms is considered clinically significant

AUA Symptom Index

- In the past month, how often have you experienced the following symptoms*:
 - Sensation of not completely emptying your bladder
 - Need to urinate <2 hours after urinating
 - Stopped and started again while urinating
 - Found it difficult to postpone urination
 - Had a weak urinary stream
 - Had to push or strain to begin urination
 - How many times do you get up at night to urinate?

*0: Not at all	1: Less than 20% of the time	2: Less than 50% of the time
3: 50%	4: More than 50% of the time	5: All the time

AUA Symptom Index Score

SCORE	CATEGORY	TREATMENT
0-7	MILD	WATCHFUL WAITING
8-19	MODERATE	WATCHFUL WAITING OR MEDICAL THERAPY
20-35	SEVERE	MEDICAL THERAPY*

*Surgical therapy should be considered if complications are present and/or patient failed medical therapy.

International Prostate Symptom Score (I-PSS)

- First 7 questions are identical to the AUA Symptoms Index; scoring is also identical
- Eighth question:
 - *If you were to spend the rest of your life with your urinary condition just the way it is now, how would you feel about that?*
 - Score ranges from 0 (delighted) to 6 (terrible)

Physical Examination

- Mental status
- Palpation of flanks/abdomen
- Inspection of external genitalia
- Digital rectal examination
 - Sphincter tone
 - Anal/rectal masses
 - Size, symmetry, nodules of prostate

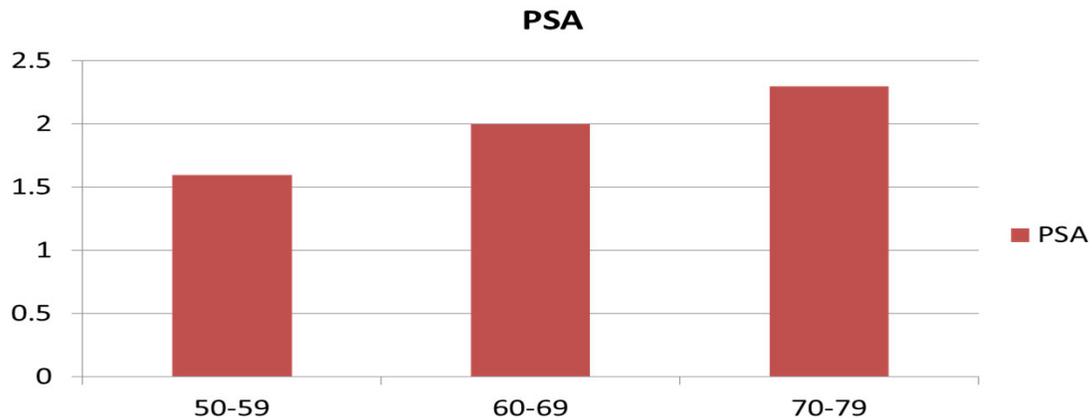
Laboratory Evaluation

- Urinalysis
 - Evaluate for UTI, hematuria
- Serum creatinine
 - Exclude obstructive uropathy

Should I obtain a PSA on a man with BPH?

- European Association of Urology (2017)
 - PSA if diagnosis of prostate cancer will change management
- Canadian Urological Association (2018)
 - PSA if life expectancy >10 years
- American Urological Association (2018)
 - PSA recommended if life expectancy >10 years

PSA and Prostate Volume



PPV: 78% for predicting a prostate volume of >30 mL

Other Evaluation

- Not routinely recommended:
 - Upper urinary tract imaging
 - Postvoid residual urine volume
- Cystourethroscopy is recommended only in patients with additional risk factors
 - Hematuria, urethral injury/stricture, bladder cancer, previous lower urinary tract surgery

AUA Symptom Index Score

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Evidence for Watchful Waiting

- Medical Therapy of Prostatic Symptoms (MTOPS) trial
- Median follow up of 4.5 years
- Annual progression rate 4.5% (defined as increase in AUA score of >4 points, acute urinary retention, or recurrent UTI)
- No renal failure noted

Watchful Waiting Continued

- Watchful waiting \neq no intervention
- Moderate the use of alcohol
- Moderate the use of caffeine
- Limit salt
- Maintain time-voiding schedule
- Decrease total fluid intake
- Reassess symptoms annually

Pharmacotherapy

- α -Adrenergic blockers
 - Nonselective
 - α 1, short-acting
 - α 1, long acting
 - α 1A selective
- 5 α -Reductase inhibitors
- Others

α -Adrenergic blockers

- Obstructive symptoms of BPH may be caused by increased smooth muscle tension in the prostate stroma, urethra, and bladder neck
- α -Adrenergic blockers relax the smooth muscle and may also influence sympathetic/ parasympathetic outflows to the bladder

α -Adrenergic blockers

- Partial relief in 48 hours
- Maximum effect in 4 weeks
- Improve symptoms scores by 30-40%
- Lower BP but less effective than thiazides, ACE-I
 - Increased mortality (ALLHAT)
- Do not combine with PDE-5 inhibitors (\downarrow BP)

α -Adrenergic blockers

NONSELECTIVE (α -1, α -2)

Phenoxybenzamine

SELECTIVE (α -1)

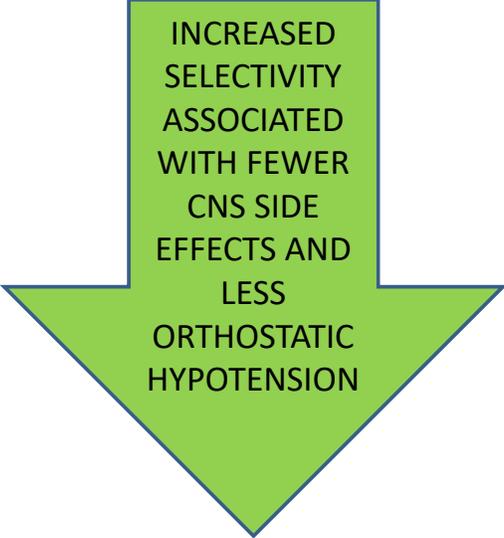
Prazosin

LONG-ACTING SELECTIVE (α -1)

Terazosin, Doxazosin

α 1A-BLOCKERS

Tamsulosin, Silodosin, Alfuzosin

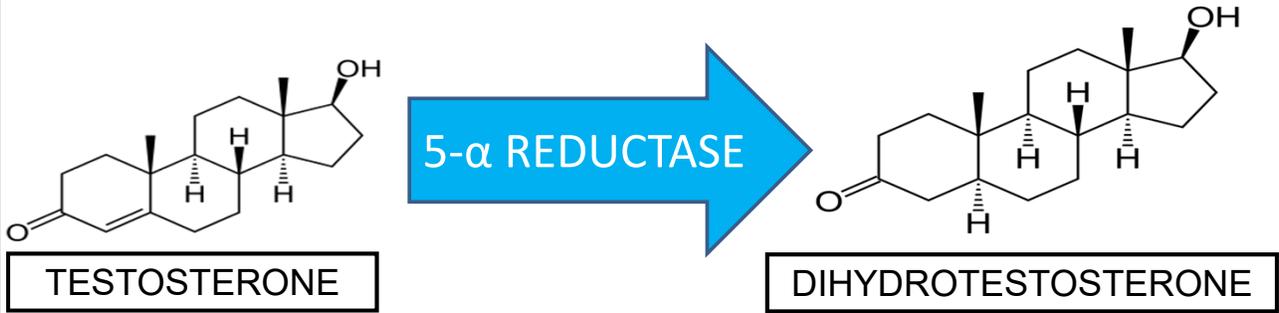


INCREASED
SELECTIVITY
ASSOCIATED
WITH FEWER
CNS SIDE
EFFECTS AND
LESS
ORTHOSTATIC
HYPOTENSION

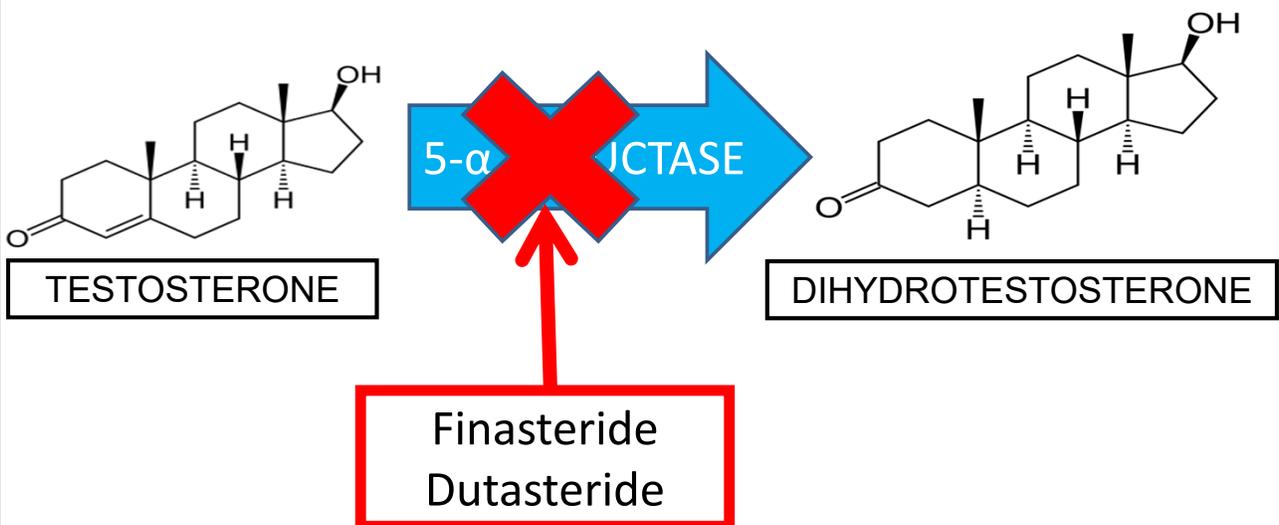
α -Adrenergic blockers

- Intraoperative Floppy Iris Syndrome
 - Described in 2005 as progressive intraoperative miosis, billowing of a flaccid iris, and iris prolapse towards the incision site during cataract surgery in men who recently started α -blockers
 - α -blockers should not be started prior to planned cataract surgery; insufficient evidence about withholding or discontinuing current therapy
 - Highest risk with tamsulosin

5- α REDUCTASE INHIBITORS



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5 α -Reductase Inhibitors

- Most beneficial when prostate >40 mL
- Degree of symptomatic improvement similar to that achieved with α -blockers (4-5 points)
- May reduce prostate size and prevent progression of BPH, reducing the risk of acute urinary retention (NNT: 26) and surgical intervention (NNT: 18) after 4 years
- Patients may not notice a change in symptoms for 3-6 months

5 α -Reductase Inhibitors

- Finasteride results in 80-90% reduction of prostatic type 2 5 α -reductase
- Gland volume decreases by 20-30%
- Decreases PSA levels by 40-50% after 6 months
- If PSA is used, patients taking finasteride should have their PSA levels doubled and then compared to age-related norms
- Similar results with dutasteride (reduces types 1 and 2 5 α -reductase)

5 α -Reductase Inhibitors and Cancer Risk

- Prostate Cancer Prevention Trial (PCPT) enrolled men >55, PSA <3, to receive finasteride or placebo for 5 years
- Finasteride arm had:
 - Lower incidence of prostate cancer (NNT: 17)
 - Increased incidence of moderate/high grade prostate cancer (NNH: 77)
- Survival the same in both groups after 18 years
- More recent studies show no increase in risk of high grade prostate cancer after 8 years of follow up
- NOT recommended for chemoprophylaxis

Combination Therapy

- MTOPS Trial (2003)
 - Doxazosin/finasteride combination superior to either agent alone in reducing LUTS
- CombAT Trial (2007)
 - Tamsulosin/dutasteride combination superior to either agent alone in reducing LUTS
- Conduct Trial (2013)
 - Tamsulosin/dutasteride (fixed dose) combination superior to either agent alone in reducing LUTS

Combination Therapy Recommendations

AUA (2014)

- Combination therapy is appropriate and effective **option** for patients BPH and demonstrable prostatic enlargement.

CUA (2018)

- Combination therapy is **recommended** treatment for patients with BPH and prostatic enlargement.

Consider discontinuing the alpha-blocker if symptoms improve after 6 to 9 months of therapy.

Other Pharmacotherapies

- Saw palmetto
 - Most studied phytotherapy; no evidence of efficacy
- Other phytotherapy (lack of evidence):
 - African plum bark, purple cone flower roots, stinging nettle, South African star grass, rye pollen extract, pumpkin seeds
- Tadalafil (PDE-5 inhibitor)
 - 5 mg daily; FDA approved; small trial over 6 months showed 2-3 point improvement

Prostatic Urethral Lift (PUL)

- Permanent device that compresses prostatic tissue
- AUA: Use if prostate is <80 mL and middle lobe is enlarged
- Does not affect PSA
- Approximately 30-40% improvement in symptoms compared to sham
- May be less effective than TURP
- May be reasonable if there are concerns over ED



Surgical Therapy

Indications for surgical therapy:

1. Failure of medical therapy
2. Refractory urinary retention
3. Recurrent UTI
4. Persistent hematuria
5. Bladder stones
6. Renal insufficiency

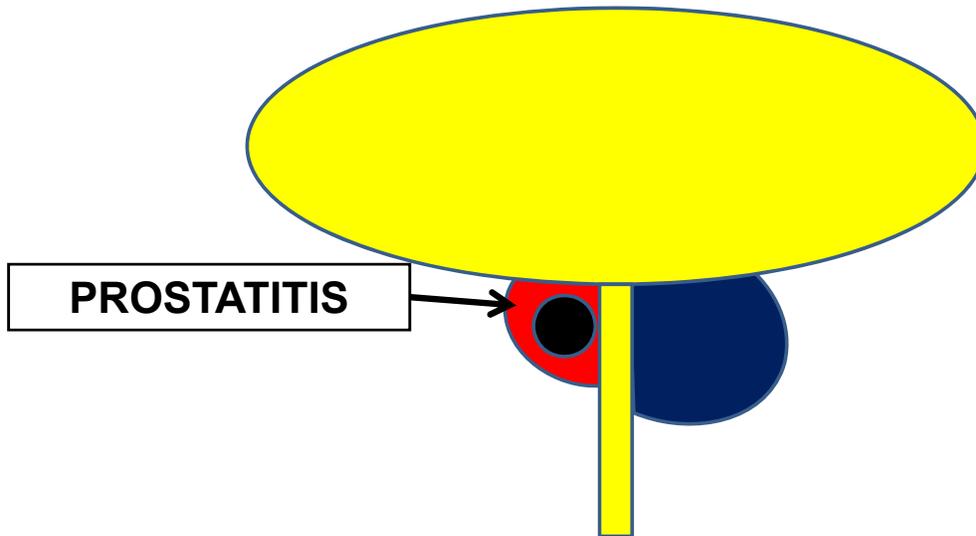
Transurethral Resection of the Prostate (TURP)

- Most common surgical procedure for BPH
- Reduces symptoms in 88% of patients
- Primary procedure if prostate 30-80 cc
- Complications: bleeding (2-9%), retrograde ejaculation (65%), ED (7%), incontinence (<1%)
- Retreatment rate is 2%/year

Other Surgical Therapies

- In general, less invasive strategies have fewer complications than TURP, a faster recovery time, and a higher recurrence rate
- Should be performed by a surgeon who is trained in these procedures

PROSTATITIS



Poll Question 2

Which of the following is TRUE concerning chronic bacterial prostatitis?

1. A single pathogen must be isolated.
2. Symptoms must be present for at least 6 months.
3. Constitutional symptoms are common.
4. Finasteride is recommended as add on therapy.
5. NIH Chronic Prostatitis Symptom Index is a validated tool for diagnosing chronic prostatitis.

NIH Consensus Classification of Prostatitis (1999)

CATEGORY	TYPE	DESCRIPTION
I	Acute Bacterial	Severe prostatitis symptoms, systemic infection, and acute bacterial urinary tract infection (UTI)
II	Chronic Bacterial	Chronic bacterial infection, ± prostatitis symptoms, usually represents recurrent UTI caused by same organism
III	Chronic Pelvic Pain Syndrome	Chronic pelvic pain symptoms, ± voiding symptoms, in the absence of UTI
IV	Asymptomatic	Inflammatory prostatitis in the absence of urinary tract symptoms

Acute Bacterial Prostatitis (NIH Category I)

- True prevalence and incidence are unknown
- Organism must be identified on culture
 - Coliform bacteria (*E. coli*, *Klebsiella* sp., *Proteus* sp.)
 - *N. gonorrhoea* and *C. trachomatis* in at-risk men
- Untreated may lead to sepsis
- Presents with irritative or obstructive LUTS
- Pain may be pelvic, suprapubic
- Systemic symptoms common (fever, chills, malaise, nausea, vomiting)

Acute Bacterial Prostatitis (NIH Category I)

- DRE should be done but prostatic massage avoided
- Bladder can be palpated if >300 mL urine present
- Focused evaluation:
 - Midstream UA and culture (all), CBC/BMP/blood culture (ill)
 - Imaging not typically required
- Treatment:
 - 4-6 weeks of treatment recommended
 - Sulfa drugs, fluoroquinolones have the best penetration into prostate tissue

Chronic Bacterial Prostatitis (NIH Category II)

- Pelvic pain for >3 months, but systemic symptoms are uncommon
- Urine culture consistently grows the same bacteria
- *E. coli* is the most common pathogen
- Less than 10% of all cases of chronic prostatitis
- Risk Factors: BPH, history of STI, retrograde ejaculation, recent instrumentation

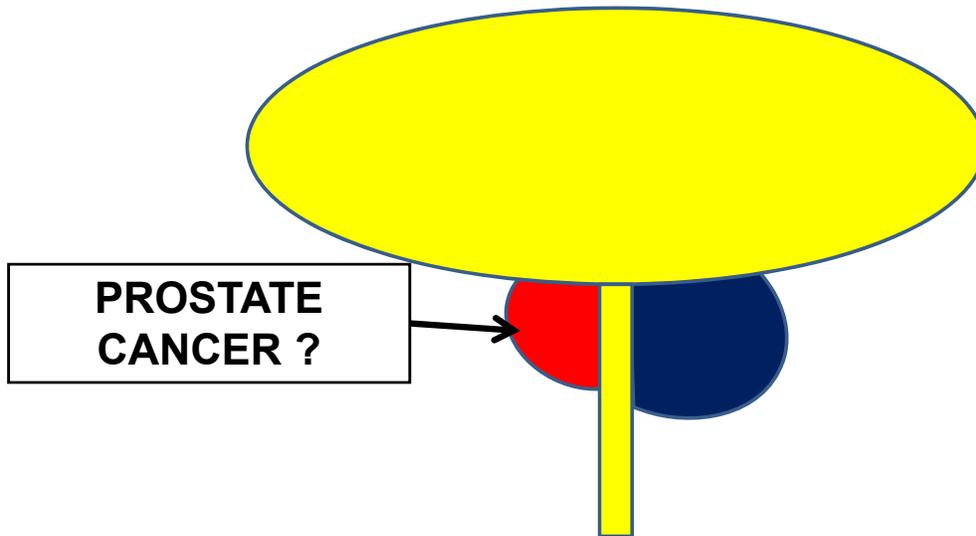
Chronic Bacterial Prostatitis (NIH Category II)

- NIH Chronic Prostatitis Symptom Index
 - validated tool for assessing pain, voiding symptoms, and impact on quality of life.
 - [Http://www.prostatitis.org/symptomindex.html](http://www.prostatitis.org/symptomindex.html)
- Treatment (4-6 weeks):
 - FIRST LINE: fluoroquinolone
 - SECOND LINE: macrolide (if *Chlamydia* is suspected)
trimethoprim
 - Consider tamsulosin, alfuzosin, or silodosin as add on therapy if significant LUTS are present

Chronic Nonbacterial Prostatitis /Chronic Pelvic Pain Syndrome (CNP/CPPS)

- NIH Type IIIA (inflammatory; + leukocytes, - culture)
 - Trial of antimicrobial therapy; α -blockers or suppressive antibiotics for persistence/relapse
- NIH Type IIIB (noninflammatory; - leukocytes/culture)
 - No clearly superior/recommended therapy
 - Questionable role of antimicrobials, α -blockers, anti-inflammatory agents
 - Complex syndrome that often requires urology consultation and multimodal therapy

Prostate Cancer Screening



Should I Screen My Male Patients with a PSA test?

- The “easy” groups are average risk men who are:
 - Younger than 55 years of age
 - Older than 70 years of age
 - Life expectancy less than 10 years
- **AUA, USPSTF, AAFP do not recommend screening with PSA in these groups**



Should I Screen My Male Patients with a PSA test?

- The “hard” groups:
 - High risk men (family history of prostate cancer, African American race)
 - 55-69 year old men at average risk



Average Risk Men age 55-69 years

- AUA, USPSTF recommend shared decision making in average risk men age 55-69 years
- AAFP does NOT recommend PSA testing

Comparison of PSA Screening Recommendations

GROUP	<40 YEARS	40-54 YEARS	55-69 YEARS	>70 YEARS
USPSTF	NO	NO	SHARED DECISION MAKING	NO
AUA	NO	NO (AVERAGE RISK)	SHARED DECISION MAKING	NO
AAFP	NO	NO	NO	NO

USPSTF: Risks versus Benefits for PSA Screening

POSSIBLE BENEFITS

- Die of prostate cancer with no screening: 5 in 1000
- Die of prostate cancer with screening: 4-5 in 1000
- Do not die of prostate cancer because of screening: 0-1 in 1000

POSSIBLE HARMS

- At least 1 false positive screening PSA test: 100-120 in 1000
- Prostate cancer diagnosis: 110 in 1000
- MI due to tx: 2 in 1000
- DVT/PE to tx: 1 in 1000
- ED due to tx: 29 in 1000
- Incontinence: 18 in 1000
- Death due to tx: <1 in 1000

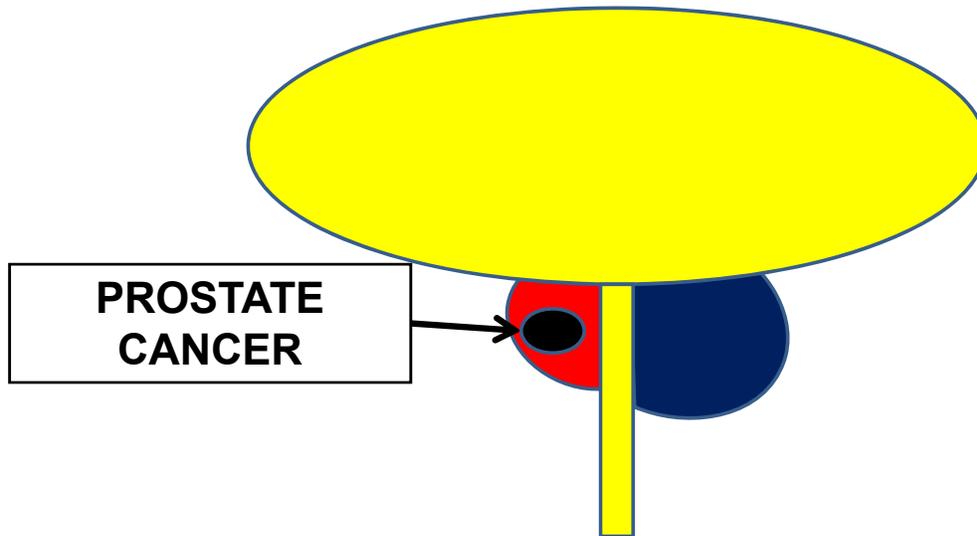
High risk men (family history of prostate cancer, African American race)

- AUA (2018):
 - There is a great deal of uncertainty about screening high risk men for prostate cancer
 - Decisions should be individualized based on personal preferences and an informed discussion regarding the uncertainty of benefit and the associated harms of screening
 - The risk of prostate cancer increases directly with the number of affected first degree relatives, and is higher if the disease occurred in multiple generations and/or was diagnosed at an early age (below age 55 years)
 - Unknown when to start, how frequently to screen, when to stop

Are There Other Ways to Screen for Prostate Cancer?

- Although DRE is widely used, there is no evidence to support it as a first line test
- Unknown benefit to PSA density, PSA kinetics, free PSA, or urine PCA3 levels as primary screening tests
- Ideal interval between PSA unknown
- Cutoff of 4 ng/mL usually used for biopsy

Localized Prostate Cancer Treatment



Poll Question 3

Which of the following is TRUE concerning active surveillance of localized prostate cancer?

1. It is identical to watchful waiting
2. It is no longer recommended
3. It can be used for men with a Gleason score of greater than 8
4. Reassessment is recommended if the PSA doubles
5. Compared to prostatectomy, it is associated with a higher 10 year mortality

Gleason Score

SCORE	DESCRIPTION
1	Well differentiated cancer with small, well formed, closely packed glands
2	Moderately differentiated cancer with larger, more spread out glands
3	Moderately differentiated cancer with infiltrative pattern
4	Poorly differentiated cancer with few recognizable glands
5	Anaplastic cancer with few to no recognizable glands

Gleason Score = the sum of the 2 most frequent patterns seen in the biopsy

-4 + 3 = Gleason Score of 7

-Order is important; 4 + 3 is worse than 3 + 4

Are Watchful Waiting and Active Surveillance the Same Thing?

- Watchful Waiting
 - Simple observation with no monitoring
 - Recommended with limited life expectancy
- Active Surveillance (ASCO)
 - PSA every 3-6 months, annual DRE, follow up biopsy at 12 months, then every 2 years
 - Recommended for localized disease, Gleason score ≤ 6
 - Reassessment recommended for doubling of PSA

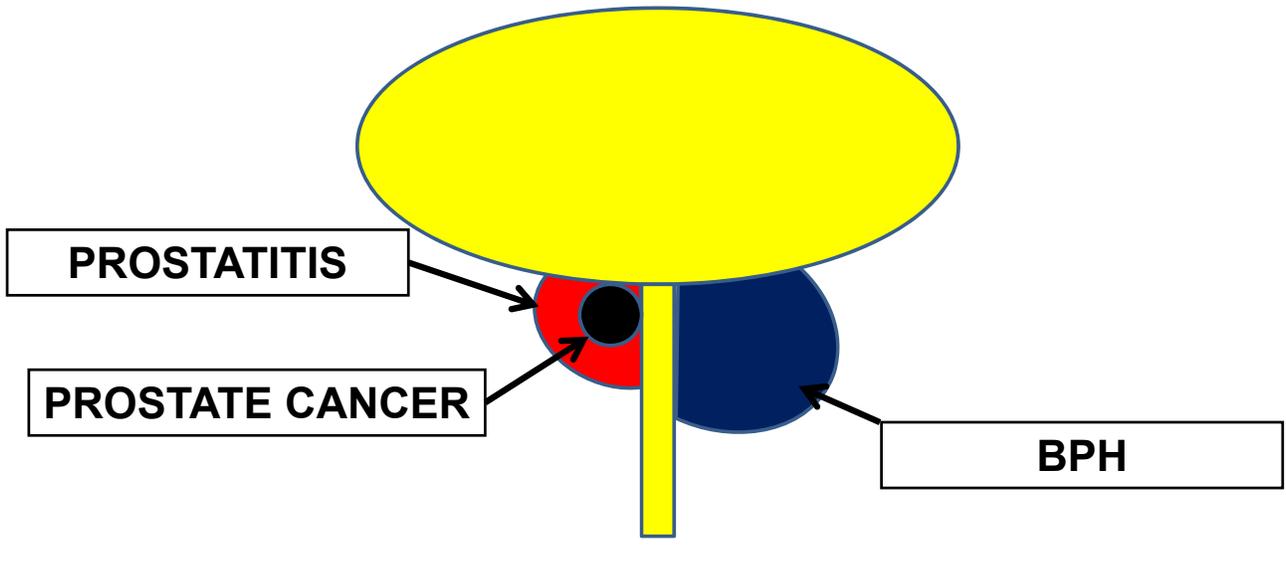
What Does the Data Say?

- 1643 men, age 50-69 years, PSA-detected cancer
- Mean PSA 4.8, 77% had Gleason score of 6
- Compared to prostatectomy or XRT + antiandrogen therapy, active surveillance had
 - Similar cancer-related mortality at 10 years (1%)
 - Similar overall mortality at 10 years (10%)
 - Less incontinence, sexual dysfunction, bowel problems

Practice Recommendations

- α -blockers are an effective treatment for moderate to severe LUTS due to BPH (SORT A)
- Avoid prostatic massage in acute bacterial prostatitis (SORT C)
- Men with localized, low grade prostate cancer may be offered active surveillance (SORT B)

Summary



Contact Information

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Questions



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