



# PROSTATE DISEASE AND CANCER

Know and understand:

- How to establish a diagnosis of BPH
- Lifestyle modification, pharmacologic therapy, and surgical treatment options for BPH
- What to tell healthy men about prostate-specific antigen (PSA) screening for prostate cancer
- Which patients with prostate cancer are candidates for watchful waiting
- How to recognize and treat prostatitis

- Benign Prostatic Hyperplasia (BPH)
- Prostate Cancer
- Prostatitis

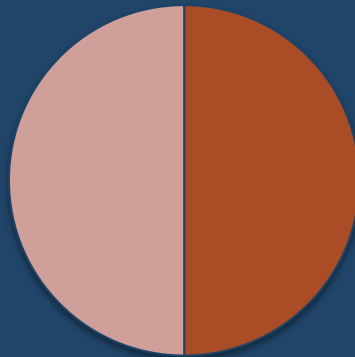
# OVERVIEW OF PROSTATE DISEASE

- **BPH** develops in over half of men  $\geq 65$  years and an overwhelming majority of men after age 85
- **Prostate cancer** is the second leading cause of cancer death in men, but many patients have asymptomatic or low-grade tumors
- The prevalence of **prostatitis** is similar to that of ischemic heart disease or diabetes mellitus

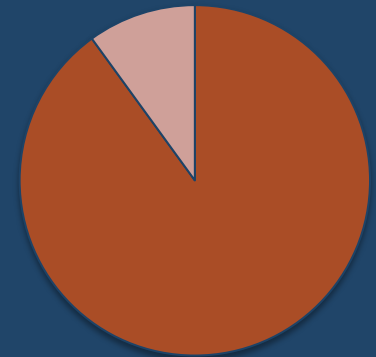
# DEFINITION & EPIDEMIOLOGY OF BPH

Noncancerous enlargement of the epithelial and fibromuscular components of the prostate gland

Microscopic BPH is present in 50% of men by age 60



Microscopic BPH is present in 90% of men by age 85



Half of men with microscopic BPH develop palpable macroscopic BPH  
Of those with macroscopic BPH, only half develop clinically significant disease brought to medical attention

# PROSTATISM (LOWER URINARY TRACT SYMPTOMS)

- **Irritative**
  - Frequency
  - Urgency
  - Nocturia
- **Obstructive**
  - Hesitancy
  - Intermittency
  - Weak stream
  - Incomplete emptying

# INTERNATIONAL PROSTATE SYMPTOM SCORE

- Quantitative index developed by the American Urological Association **for assessing symptom severity and monitoring treatment response**
- Adopted by the World Health Organization
- Assessing symptom severity is useful for long-term patient management but has not been found to correlate with prostate size, urine flow rates, or postvoid residual volume

# DIAGNOSIS OF LOWER URINARY TRACT SYMPTOMS

- **Digital rectal examination (DRE)** may be unremarkable or reveal an enlarged, smooth, rubbery, symmetrical gland
- **Urinalysis** is routinely performed to evaluate for UTI, hematuria, and glycosuria
- Additional subsequent tests include postvoid residual urine volume (often done by office or bedside bladder scan), urine flow rates, and pressure flow studies.
  - Consider when the diagnosis is uncertain or an invasive treatment is being planned



- Depends on the patient and is driven by the impact of symptoms on the patient's quality of life
- Medical and surgical treatments are available, with medication the usual first approach
- Indications for surgical treatment include:
  - Patient preference
  - Dissatisfaction with medication
  - Refractory urinary retention
  - Renal dysfunction, bladder stones, recurrent UTIs, or hematuria if these are clearly due to prostatic obstruction

# LIFESTYLE MANAGEMENT OF BPH

Interventions	Rationale	Comments
<ul style="list-style-type: none"> <li>• Reduce night-time fluids to manage nocturia</li> <li>• Eliminate bladder irritants (eg, caffeine, alcohol, nicotine)</li> <li>• Avoid drugs (especially anticholinergics) that aggravate symptoms</li> </ul>	<p>Factors outside the urinary tract contribute to urinary symptoms</p>	<ul style="list-style-type: none"> <li>• Often sufficient management for mild symptoms</li> <li>• Complements management for moderate to severe symptoms</li> </ul>

# ALPHA-ADRENERGIC ANTAGONISTS FOR BPH

Agents	Rationale	Comments
<ul style="list-style-type: none"><li>• Selective for <math>\alpha_1</math>: prazosin (off-label)</li><li>• Long-acting, selective for <math>\alpha_1</math>: terazosin, doxazosin</li><li>• Slow-release, long-acting, selective for <math>\alpha_1</math>: tamsulosin, silodosin, alfuzosin</li></ul>	Relaxation of the smooth muscle in hyperplastic prostate tissue, prostate capsule, and bladder neck decreases resistance to urinary flow	Adverse effects: dizziness, mild asthenia, headaches, postural hypotension (reduced with careful dose titration, not present with slow release $\alpha_1$ agents), abnormal ejaculation, rhinitis

# CAUTION WITH USE OF ALPHA-ADRENERGIC ANTAGONISTS

- For patients undergoing cataract surgery, intraoperative floppy iris syndrome (IFIS), characterized by sudden intraoperative iris prolapse and pupil constriction, is a **potential risk of all  $\alpha$ -blockers, with the greatest frequency and severity of IFIS among those using tamsulosin**

# 5 $\alpha$ -REDUCTASE INHIBITORS FOR BPH

Agents	Rationale	Comments
<ul style="list-style-type: none"><li>• Finasteride</li><li>• Dutasteride</li></ul>	Reduced tissue levels of dihydrotestosterone result in prostate gland size reduction	<ul style="list-style-type: none"><li>• Most effective for men with larger prostates (&gt;40 g)</li><li>• Improvement in symptoms and urine flow rates may not be evident for up to 6 months</li></ul>

# ANTICHOLINERGIC MEDICATIONS FOR BPH

- Anticholinergic agents have a role in managing lower urinary tract storage symptoms in men with BPH
- Used alone, or in combination with  $\alpha$ -blockers, they do not seem to significantly increase postvoid residual urine volumes or provoke acute urinary retention

# PHOSPHODIESTERASE-5 (PDE-5) INHIBITORS FOR BPH

Agents	Rationale	Comments
<ul style="list-style-type: none"> <li>Tadalafil</li> </ul>	<p>PDE-5 activity in bladder neck, prostatic urethra, and prostate musculature contributes to urinary symptoms</p>	<ul style="list-style-type: none"> <li>Effective for men with or without erectile dysfunction</li> <li>Only drug that can treat both BPH and ED</li> <li>Use caution when using with <math>\alpha</math>-blockers due to possible additive effects of hypotension</li> </ul>

# SURGICAL MANAGEMENT OF BPH

<b>Interventions</b>	<b>Rationale</b>	<b>Indications</b>
<ul style="list-style-type: none"> <li>• Transurethral resection of the prostate</li> <li>• Open prostatectomy</li> <li>• Transurethral vaporization of the prostate</li> <li>• Transurethral incision of the prostate</li> <li>• Stent placement</li> </ul>	<p>Removal or expansion of peri-urethral prostate tissue reduces obstruction to urinary flow</p>	<ul style="list-style-type: none"> <li>• Recurrent urinary tract infection induced by benign prostatic hypertrophy</li> <li>• Recurrent or persistent gross hematuria</li> <li>• Bladder stones</li> <li>• Renal insufficiency</li> </ul>



# MANAGEMENT OF ACUTE URINARY RETENTION

- Sudden and painful inability to pass urine
- Urologic emergency
- Occurs in up to a third of men undergoing TURP
- May be the result of natural progression of BPH, or it may be precipitated by surgical procedures, infection, or medications
- Immediate management consists of bladder decompression, usually with a urethral catheter

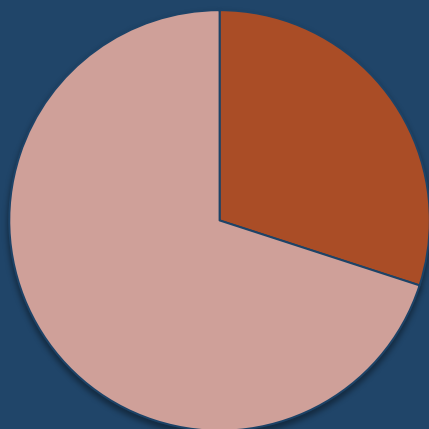
# EPIDEMIOLOGY OF PROSTATE CANCER (1 of 3)

- Most common noncutaneous cancer among men in the US
- Incidence increases with age; rare in men <40
- Incidence varies according to race; **black Americans have the highest risk in the world**
  - Among black American men, prostate cancer occurs at an earlier age, has a higher mortality rate, and tends to be at a more advanced stage of disease at diagnosis

- Family history is also a contributing factor
  - Men with one first-degree relative affected have more than a 2-fold increased risk
- History of sexually transmitted infection can be associated with an increased risk

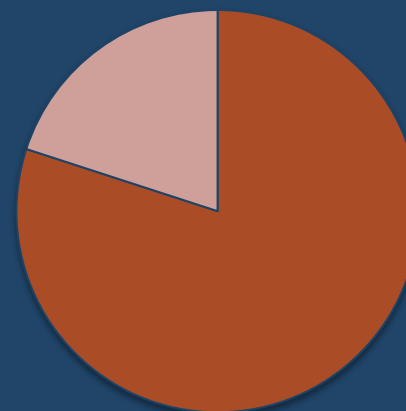
# EPIDEMIOLOGY OF PROSTATE CANCER (3 of 3 )

Histologic evidence of prostate cancer in autopsy studies



Men older than 50

■ Found  
■ Not found



Men older than 80

# SYMPTOMS OF PROSTATE CANCER (1 of 2)

- Most patients, especially those with early-stage, potentially curable disease, are asymptomatic
- Direct invasion of the urethra and bladder can lead to:
  - Irritative voiding symptoms
  - Urinary incontinence
  - Hematuria
- Extension of disease to adjacent nerves may cause:
  - Impotence
  - Pelvic pain

# SYMPTOMS OF PROSTATE CANCER (2 of 2)

- Nodal metastasis may cause **extrinsic ureteral obstruction**
- Lymphatic obstruction may result in **leg edema**
- Hematogenous metastasis to bone may cause:
  - **Severe local pain**
  - **Normochromic, normocytic anemia**
  - **Pathologic fractures**
  - **Spinal cord compression**
  - **Less commonly, hematogenous metastasis involves the lung, liver, and adrenal glands**

# PROSTATE CANCER SCREENING CONTROVERSY

- The benefit of early detection and the best approach to treatment of prostate cancer are controversial
- Most men with prostate cancer die with the disease, not from it
- Guidelines agree that the controversy about screening should be discussed with patients, using a shared-decision making approach

- Allows palpation of the posterior surfaces of the lateral lobes, where cancer most often begins
- Can often detect local extension of prostate cancer into the seminal vesicles
- Parts of the prostate gland cannot be reached
- About half of cancers thought to be confined to the prostate on the basis of DRE are found during surgery to have spread
- Biopsy confirms only about 1/3 of positive DRE



- **Not specific for prostate cancer**
  - PSA elevations occur in benign conditions of the prostate
  - False-negative rate 30%–40%
  - Positive predictive value 28%–35%
- **Novel measurements may improve accuracy:**
  - PSA density
  - PSA rate of change or velocity
  - Age-adjusted PSA reference ranges
  - Ratio of free to complexed PSA

# BIOPSY FOR DIAGNOSIS OF PROSTATE CANCER

- Abnormal DRE or PSA test suggests the need for transrectal ultrasound–guided biopsy of the prostate
- Spring-loaded core needle biopsies are routinely taken from the base, middle, and apex of each lobe (6 samples total)
- Biopsies may be taken from suspicious areas on ultrasound in addition to palpable nodules

# GLEASON GRADING SYSTEM FOR PROSTATE CANCER

- **Gleason grade** ranges from 1 (well differentiated) to 5 (poorly differentiated)
- **Gleason score**: sum of the most common Gleason grade seen + the next most common Gleason grade seen (ranges from 2–10)
- Scores are sometimes grouped as:
  - 2–4 = well differentiated (favorable prognosis)
  - 5–7 = moderately differentiated
  - 8–10 = poorly differentiated (unfavorable prognosis)

# STAGING OF PROSTATE CANCER

<b>TNM Stage</b>	<b>Jewett-Whitmore stage</b>	<b>Description</b>
T1	A1, A2	Tumor is an incidental finding
T1c		Tumor is identified by needle biopsy as a follow-up to screening that detected increased PSA
T2	B1, B2	Tumor is palpable, confined to prostate
T3	C1, C2	Tumor extends beyond the prostate capsule, may involve seminal vesicles
T4	C2	Tumor invades adjacent structures (eg, bladder neck, rectum, pelvic wall)
N	D1	Lymph node metastasis present
M	D2	Distant metastasis present

# STAGING EVALUATION OF PROSTATE CANCER

- Initial evaluation includes:
  - PSA level
  - DRE findings
  - Transrectal ultrasonography results and Gleason score
  - Bone scans on patients with bone pain or PSA values >10 ng/mL
- For patients electing active treatment:
  - Surgical assessment of lymph node involvement ± prostate surgery or implantation of radioactive seeds
  - CT is often employed

# MANAGEMENT OF LOCALIZED PROSTATE CANCER (1 of 3)

Management	Description	Comments
Watchful waiting	Prostate cancer is not treated until symptoms develop	<ul style="list-style-type: none"> <li>• Offered to men with less than a 10-year life expectancy; significant medical comorbidities; small, well-differentiated tumors; or unwillingness to bear treatment burdens</li> <li>• Awaiting symptoms sacrifices opportunity for cure</li> </ul>
Active Surveillance	Prostate cancer treatment is delayed until evidence of disease progression	<ul style="list-style-type: none"> <li>• Offered to men with cancer detected by PSA screening, Gleason score &lt;7, small volume involvement</li> </ul>

# MANAGEMENT OF LOCALIZED PROSTATE CANCER (2 of 3)

Management	Description	Comments
Radical prostatectomy	Surgical removal of the entire prostate gland and seminal vesicles	<ul style="list-style-type: none"><li>• Offered to men with an absence of surgical contraindications</li><li>• Adverse effects realized immediately</li></ul>

# MANAGEMENT OF LOCALIZED PROSTATE CANCER (3 of 3)

Management	Description	Comments
External beam radiation therapy	Standard regimen delivers 6000–7000 rads of pelvic radiation over a 5- to 8-week period	<ul style="list-style-type: none"> <li>• Radiation reaches tissues outside the prostate including pelvic lymph nodes</li> <li>• Adverse effects occur initially from radiation-induced inflammation, then develop over time as scar tissue develops</li> </ul>
Brachytherapy	Radioactive seeds (eg, iridium, palladium) are implanted into the prostate gland using computed tomography scan guidance	<ul style="list-style-type: none"> <li>• Improvements in prostate imaging allow uniform distribution of seed, overcoming past limitations</li> <li>• Adverse effects occur initially from radiation-induced inflammation, then develop over time as scar tissue develops</li> </ul>



# MANAGEMENT OF LOCALLY ADVANCED PROSTATE CANCER

- **Radiation therapy** is the recommended treatment
- **Neoadjuvant androgen deprivation** increases the chance of survival and freedom from metastases
- **Timing of androgen deprivation is controversial**
  - Patients may have a prolonged asymptomatic period
  - Long-term androgen deprivation can have substantial negative effects on quality of life including loss of stamina, increased fatigue, hot flashes, diminished muscle mass, and premature osteoporosis
- **Patients should be given the choice of early vs. delayed androgen deprivation**

# ANDROGEN ABLATION FOR ADVANCED PROSTATE CANCER

Orchiectomy and luteinizing hormone–releasing hormone (LHRH) agonists are equally effective at reducing androgens to castration levels

- LHRH agonists (eg, **leuprolide** and **goserelin**) produce castration levels about a month after an initial increase in serum testosterone levels
- Antiandrogens (eg, **flutamide**) are often given before LHRH agonists to blunt the effects of the testosterone increase
- **Complete androgen ablation** (adding chemical or surgical castration to antiandrogens) slightly improves survival

# RADIATION THERAPY FOR ADVANCED PROSTATE CANCER

- Useful for:
  - Relieving the pain of isolated bone metastasis
  - Reducing the risk of fracture
- Diffuse bone metastases require alternative approaches
  - Bone-seeking radiopharmaceuticals such as strontium or radium can be beneficial for pain control
  - Androgen deprivation and bisphosphonates can decrease bone pain

- May have acute bacterial, chronic bacterial, or nonbacterial cause
- Sources of infection:
  - **Most common:** ascending urethral infection and/or reflux of infected urine into the prostatic ducts
  - Direct extension or lymphatic spread from the rectum
  - Hematogenous spread
- **More than 80% of patients with prostatitis have no identifiable infectious agent**

# DIAGNOSIS OF ACUTE BACTERIAL PROSTATITIS

- Symptoms include:
  - Fever
  - Chills
  - Dysuria
  - Tense/boggy, extremely tender prostate
- Bacteremia may result from manipulation of the inflamed gland—minimal rectal examination is indicated
- Gram stain and culture of the urine can identify the causative agent

# DIAGNOSIS OF CHRONIC BACTERIAL PROSTATITIS

- Marked by varying degrees of perineal pain and obstructive or irritative voiding symptoms
- The prostate often feels normal
- Compare first-void or midstream urine with expressed prostatic secretion or urine collected post-massage:
  - Expressed sample should reveal leukocytosis and the causative agent
  - Sterile expressant with leukocytosis suggests nonbacterial prostatitis

# TREATMENT OF ACUTE BACTERIAL PROSTATITIS

- Antibiotics—may require hospitalization
  - Severe inflammation allows antibiotics to penetrate the prostate
  - Initial antibiotic selection is based on urine Gram stain results, with subsequent consideration of sensitivity profiles
  - Fluoroquinolones are highly effective in most cases
- Prompt response to empiric therapy is expected
- If recovery is delayed, consider CT or MRI to evaluate for an abscess

# TREATMENT OF CHRONIC BACTERIAL PROSTATITIS

- **Antibiotics are less effective** because of poor penetration of the prostate by most of these drugs
  - 6–16 weeks of therapy offers a cure rate of 30%–40%
  - **Continuous low-dose antibiotic suppression therapy** can be offered to patients with frequent symptomatic relapse
- **Total prostatectomy** offers cure but has a high risk-to-benefit ratio
- **Transurethral resection of the prostate** is safer but cures only one third of patients



# TREATMENT OF NONBACTERIAL PROSTATITIS

- Treated symptomatically
- A small percentage of cases involve occult infections—  
empiric antibiotic therapy is often used
- To reduce pain and discomfort:
  - Anti-inflammatory agents
  - Sitz baths
  - Fluid adjustments (avoid caffeine)
  - Anticholinergic agents
  - $\alpha$ -Adrenergic antagonists

*Recommendations for **Prostate Disease and Cancer**, based on the American Board of Internal Medicine Foundation's Choosing Wisely® Campaign:*

- Do not perform PET, CT, and radionuclide bone scan in the staging of early prostate cancer at low risk of metastasis
- A routine bone scan is unnecessary in men with low-risk prostate cancer
- Do not order creatinine or upper-tract imaging for patients with benign prostatic hyperplasia
- Do not treat an increased PSA with antibiotics for patients not experiencing other symptoms

- Treatment options for BPH include watchful waiting, drug therapies, minimally invasive procedures, and more extensive surgery
- The choice of BPH treatment is influenced by the extent of symptoms, the presence of complications from outflow obstruction, and patient preference
- The use of 5 $\alpha$ -reductase inhibitors for BPH is especially indicated when the prostate gland is large
- Patients should be informed that recommendations regarding screening for prostate cancer using PSA differ among experts. The decision to screen a patient for prostate cancer should be made using a shared-decision making approach.

# SUMMARY (2 of 2)

- Treatment options for localized prostate cancer include watchful waiting, active surveillance, resection of the gland and seminal vesicles, and radiation therapy
- How the patient balances the potential benefits and burdens of the various options will influence the choice of therapy
- For patients with chronic prostatitis, efforts should be made to identify the causative organism
- Even with a prolonged course of appropriate antibiotics, cure of chronic prostatitis can be expected in fewer than half of patients

## CASE (1 of 3)

- An 83-year-old man comes for follow-up after catheterization in the ED for acute urinary retention.
  - Catheterization yielded 450 mL urine.
- At follow-up, he describes recent increasing difficulty with urination and worsening constipation.
  - He had previously reported mild lower urinary tract symptoms that were not bothersome.
- He recently began taking an OTC “multisymptom relief” product for a cold.
- He is independent in ADLs and IADLs.

Which one of the following should be included in the immediate treatment plan?

- A. Start an  $\alpha$ -blocker.
- B. Start a  $5\alpha$ -reductase inhibitor.
- C. Stop the over-the-counter medication.
- D. Refer for urodynamic studies.

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GNRS5 Teaching Slides modified from GRS9 Teaching Slides

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