Caring for the Patient with Prostate Cancer

Mary W. Dunn, MSN, RN, NP-C, OCN®

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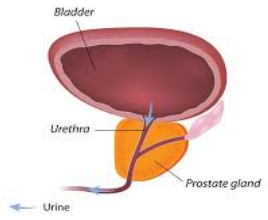
UNC LINEBERGER UNC CANCER CARE

Objectives

- Describe the types, stages, & diagnostic tests available for treating prostate cancer patients
- Discuss the treatment options, management of side effects & emotional needs of patients with prostate cancer
- Discuss the importance of collaboration & teamwork to enhance quality of care & patient outcomes

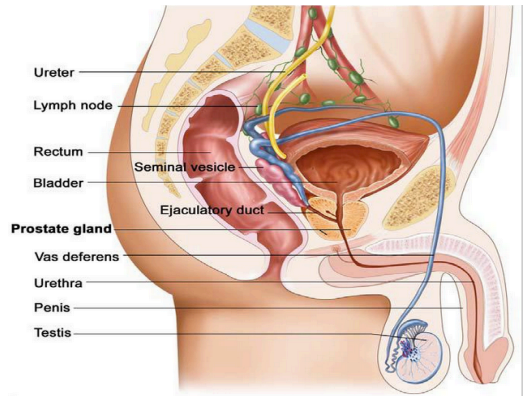
Definition

Prostate cancer is a disease in which malignant (cancer) cells form in the prostate gland



Physiology

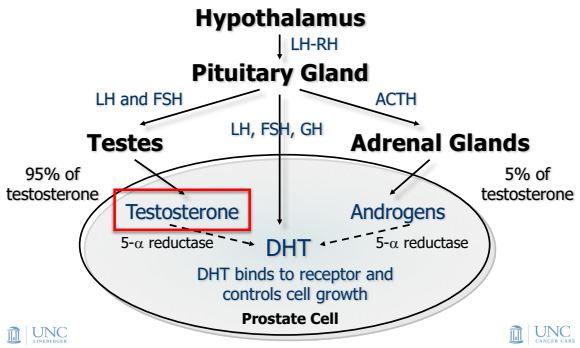
- Partly glandular and muscular organ within lower pelvis
- Accessory reproductive gland
- Secretes alkaline fluid that forms a part of the ejaculate which aids in motility and nourishment of sperm
- 4 zones: peripheral (75%), central, transition, fibromuscular
- Average size 28-47 cc



Pathophysiology

- ~90% are adenocarcinomas
  - Remaining ~10% are primarily neuroendocrine
- Disseminated disease
  - Locally via lymphatic system
  - Hematologic
- Metastasis
  - Bone: Axial skeleton
  - Lymph nodes
  - Organs less common

Hormonal Regulation of the Prostate Gland



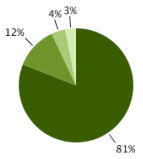
Epidemiology

- Most commonly diagnosed malignancy in men
- >2.9 million men living with prostate cancer
- Lifetime risk: 1 in 7 men
- 2nd leading cause of cancer death
- 1 in 38 die of prostate cancer
- 2017: __new dx; ___ deaths

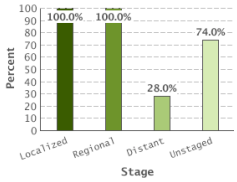
Estimated Cancer Cases and Deaths (U.S)

Estimated New Prostate Cancer Cases (2016): 180,890		Estimated Prostate Cancer Deaths (2016): 26,120	
Prostate	**21%**	Lung & bronchus	28%
Lung & bronchus	14%	**Prostate**	**8%**
Colon & rectum	8%	Colon & rectum	8%
Bladder	7%	Pancreas	7%
Melanoma	6%	Liver	6%
NHL	5%	Leukemia	4%
Kidney/renal pelvis	5%	Esophagus	4%
Oral cavity/pharynx	4%	Bladder	4%
Leukemia	3%	NHL	3%
Liver	3%	Kidney/renal pelvis	3%
Pancreas	3%	Brain/CNS	3%

American Cancer Society 2016



Localized (81%)-Confined to primary site
Regional (12%)-Spread to Regional LN
Distant (4%)-Distant mets
Unknown (3%)-Unknown



5-year relative survival by stage

Risk Factors

- Age
  - 75% diagnosed at ≥ 65 years old
- Race
  - AA men have the highest incidence and mortality
  - Complex socioeconomic disparities
- Family history
  - Men with a 1st degree relative who has prostate cancer have a twofold risk

Risk Factors

- Diet/supplements
  - Extensively studied; conflicting data
  - No conclusive data exist
- Others
  - BMO, inactivity, chemical exposure, STIs, vasectomy
  - Little or no evidence

Prevention

- 2 large RCTs studying BPH medications
  - PCPT = ~25% reduction in PRCA but more likely to have more aggressive cancer
  - REDUCE = ~27% reduction in PRCA; no reduction in more aggressive cancer
  - No study on prostate cancer mortality
  - Neither approved for prevention
  - Black box warning

Prevention

- Nutrition
  - Multiple large studies looking at fruit/veggie intake, selenium, vitamin E, vitamin C
  - No decreased incidence of prostate cancer
  - No nutritional supplements recommended for prevention
  - Counsel patients to avoid costly supplements not backed by evidence

Encourage healthy lifestyle (balanced diet, exercise, avoiding tobacco, minimal alcohol)

Screening

Over screening

Over diagnosis

Over treatment

Screening

- The only consensus is that men should be presented with benefits v risks
- AUA: 2009 PSA Best Practice Statement: Yes
- AUA: 2013 Revision
- ACS: 2014 Update: Yes
- **USPSTF: 2012 Update: No**
- ACPM: 2009 Update: No

Screening

- Prostate exam called digital rectal exam (DRE)
- Blood test called prostate specific antigen (PSA)
  - Protease found in prostate luminal cells
  - Hormone dependent
  - Adoption for screening in later 1980's

Prostate Specific Antigen

- PSA elevation
  - Infection
  - Lab error
  - Inflammation
  - Retention
  - BPH
  - Instrumentation
  - Age
  - Abnormal cells
  - Prostate cancer
- PSA decrease
  - 5 ARI
  - ADT
  - Prostatectomy
  - XRT
  - Lab error
- Not proven
  - Ejaculating
  - Bike riding
  - Rectal exam

The great debate

- Can we justify mass public screenings to detect prostate cancer?
- 6 RCTs serve as basis for screening recommendations, but not much clarity re: screening and impact on mortality
- Financial: Does cost spent on screening prolong life or prevent unnecessary death?
- Clinically significant and insignificant

Other tools

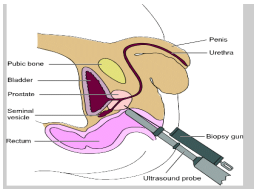
- Prostate MRI (not for screening)
- Biomarkers
  - Who to biopsy
    - PHI, 4K, Select MDx
  - Who to rebiopsy
    - PCA3, Confirm MDx
  - Surveillance v intervention
    - Oncotype, Prolaris, Decipher, Promark

Clinical Presentation

- **Usually asymptomatic**
- Lower urinary tract symptoms (LUTS)
- Bony pain
- Renal failure
- Spinal cord compression

Diagnosis

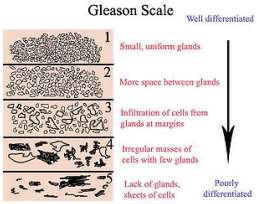
- Shared decision making to screen
- PSA, DRE
- Prostate biopsy
  - Office procedure
  - transrectal ultrasound guided
  - 12 cores
  - Minor prep



Diagnosis

- The Gleason Scoring System
  - Assigns a grade to the 2 largest areas in each biopsy
  - Ex: Gleason 4+3=7: Pattern 4 most abundant, Pattern 3 2nd most
  - Adenocarcinomas
  - New grading system

Replaces Gleason



Staging

- Variables: PSA, DRE, biopsy results, Gleason, imaging
- Clinical (PSA, DRE, imaging) v. Pathologic
- Risk categories: Very low risk-Very high risk
- AJCC Prostate Cancer Staging

Staging

Staging

Group	T	N	M	PSA	Gleason
I	T1a-c	N0	M0	PSA <10	Gleason ≤6
	T2a	N0	M0	PSA <10	Gleason ≤ 6
	T1-2a	N0	M0	PSA X	Gleason X
IIA	T1a-c	N0	M0	PSA <20	Gleason 7
	T1a-c	N0	M0	PSA ≥10<20	Gleason ≤ 6
	T2a	N0	M0	PSA≥10<20	Gleason ≤ 6
	T2a	N0	M0	PSA <20	Gleason 7
	T2b	N0	M0	PSA <20	Gleason ≤ 7
	T2b	N0	M0	PSA X	Gleason X
IIB	T2c	N0	M0	Any PSA	Any Gleason
	T1-2	N0	M0	PSA ≥ 20	Any Gleason
	T1-2	N0	M0	Any PSA	Gleason ≥ 8
III	T3a-b	N0	M0	Any PSA	Any Gleason
IV	T4	N0	M0	Any PSA	Any Gleason
	Any T	N1	M0	Any PSA	Any Gleason
	Any T	Any N	M1	Any PSA	Any Gleason

Treatment

Localized Prostate Cancer/no distant disease

Treatment

Active Surveillance

- Typical criteria: PSA <10, Gleason 6, Stage T1c-T2a, >10 yr life expectancy, low volume
- Follow up: PSA & DRE every 3-6 months, biopsy annually
- Intervention: Change on biopsy, concerning PSA trend
- Not appropriate for all men meeting criteria
- Other: Age, comorbidities, anxiety, commitment to follow up schedule

Treatment

Radical prostatectomy

- Surgical removal of the prostate gland and seminal vesicles
- Open, laparoscopic, robotic techniques
- Considerations: Age, comorbidities, prior abdominal surgeries
- 1 night in the hospital, leave with catheter
- Side effects: Erectile dysfunction, urine leakage, infertility
- Follow up: every 3 months x 1 year; every 6 months until year 5, annually until year 10

Treatment

Radiation Therapy

- Intensity Modulated Radiation Therapy: gives higher dose to prostate and less to surrounding tissue
- Uses a machine outside the body to deliver radiation
- Usually 5 days/week, 4-6 week
- If >intermediate risk disease will get hormone shots
- Side effects: urinary symptoms, diarrhea, rectal irritation, fatigue, erectile dysfunction

Treatment

Brachytherapy

- Radioactive seeds implanted into the prostate
- Low risk disease; prostate size matters
- Side effects: Urinary retention, painful urination, erectile dysfunction

Treatment

Cryotherapy

- Surgical freezing of the prostate
- Causes cell death
- Candidates: Unfit for surgery or radiation
- Side effects: Erectile dysfunction (near 100%), rectal pain, urinary symptoms

High-intensity focused ultrasound (HIFU)

- Ablates tissue using heat
- Side effects: urinary symptoms, erectile dysfunction

Localized Prostate Cancer

Risks of Recurrence

- High grade tumors (≥ GL 7)
- High stage tumors (≥ T3)
- High pre-treatment PSA (≥ 10)
- Positive surgical margin
- Seminal vesicle invasion
- Capsular penetration
- Positive Lymph Nodes

After recurrence, a PSADT > 15 months is associated with a low risk of death from prostate cancer over 10 years.

Advanced Prostate Cancer

Recurrent prostate cancer following definitive therapy, locally recurrent disease, systemic recurrence, or clinical (symptomatic) recurrence.

Advanced Prostate Cancer

Types of Recurrence

1. Biochemical: PSA recurrence. Most common.
    1. Post-XRT: A rise of 2ng/ml or above the nadir PSA
    2. Post-RP: PSA >0.2ng/ml x 2 (AUA) or detectable PSA x 2 (NCCN)
    3. Post-cryo: No set value
2. Local: Cancer identified within the prostate
3. Distant: Cancer identified in distant organs
4. Clinical: Local or distant, symptomatic

Treatment

Salvage

- After radiation
  - Prostatectomy
  - Hormone shots
  - Surveillance
- After surgery
  - Radiation
  - Hormone shots
  - Surveillance

Treatment

Timing of hormone treatment

- No distant tumors
  - Can delay
- Distant tumors
  - Typically start soon after distant tumors are found

Prostate tumors require testosterone

Treatment

Hormone shots/androgen deprivation therapy (ADT)

1. Surgical Castration
   1. Removal of both of the testicles
2. Medical Castration
   1. LHRH agonists, LHRH antagonists
   2. Injections, implants

Side effects: Hot flashes, fatigue, moodiness, weight gain, enlarged breast tissue, osteoporosis, sexual dysfunction

Treatment

Metastatic Castrate Sensitive Disease

- Men who have distant disease when they are first diagnosed
- New data support use of chemotherapy plus ADT for these men
- Criteria: Newly diagnosed, high volume disease
- Clinical trial data showed significant median overall survival in chemo/hormone arm vs. hormone arm alone (13.6 months longer)
- Docetaxel chemotherapy + hormone shots

Treatment

Advanced Prostate Cancer responds to castration for an average of 2-3 years before the PSA begins to rise.

Then what?

Treatment

Castrate Resistant Disease

- PSA rises, testosterone remains castrate
- Always keep hormone shots
- Obtain imaging studies prior to starting additional treatment & prior to each treatment change

Treatment

Non metastatic castration resistant disease

PSA rising, testosterone low, no evidence of distant tumors

1. Antiandrogen pill; block cells ability to bind hormone
    1. E.g. Casodex
2. Ketoconazole plus steroids; reduces gonadal and adrenal androgen synthesis

Treatment

Metastatic Castration Resistant Disease

- PSA rises, testosterone remains low, evidence of distant tumors
- Sites of metastatic spread
  - Lymph nodes (pelvis, retroperitoneal)
  - Bones
  - Visceral (liver, lung)

Treatment

Metastatic Castration Resistant Disease

Chemotherapy

1. Docetaxel: Given through an IV once every 3 weeks x 10
2. Cabazitaxel: Given through an IV once every 3 weeks x 10

Side effects: Hypersensitivity, hair loss, numbness, rash, fatigue, fluid retention, GI disturbance

Treatment

Metastatic Castration Resistant Disease

Pills

1. Abiraterone
   1. Inhibits an enzyme needed for androgen synthesis in the testicles, adrenal glands, and tumors
2. Enzalutamide
   1. Inhibits androgen binding to androgen receptors

Side effects: Fatigue, body aches, hot flashes

Treatment

Metastatic Castration Resistant Disease

Immunotherapy (stimulates an immune response)

- Sipuleucel-T
  - Cells taken from patient, prepared by company, then infused back to patient
  - Side effects: Chills, fever, fatigue, body aches

Radiotherapy

- Radium-223
  - Alpha particle emitting radioactive agent
  - Mimics calcium and forms complexes with bone

Treatment

- When do you change treatment?
  - Take into account PSA, testosterone, clinical picture, radiographic scans
  - After chemo, wait to see what PSA does
  - On PO meds, when you see a consistent rise in PSA and/or worsening clinical picture
  - Get CT AP and bone scan prior to each change in treatment to establish a new baseline
  - Example: Provenge→Abi→Docetaxel→Enza→Cabazitaxel→Radium

Advanced Prostate Cancer Treatment Summary

- Recurrent
  - Biochemical
    - Detectable PSA
  - Localized
    - Biopsy confirmed to prostate
  - Distant
    - Mets on imaging
  - Clinical
    - Symptomatic
- Treatment
  - Varies depending on extent, age, previous tx, co morbidities, etc
  - Adjuvant, salvage, systemic options
- Non-metastatic, castrate resistant
  - ADT + antiandrogen or ketoconazole/hydro
- Metastatic, castrate sensitive
  - ADT + 6 cycles Docetaxel
- Metastatic, castrate resistant
  - ADT +
  - Immunotherapy, PO antiandrogen inhibitor, chemotherapy, radiotherapy

Supportive Care

- Bone health
  - Zolendronic Acid
  - Denosumab
  - Calcium and Vitamin D
  - Weight Bearing exercise
- Urinary Symptoms
  - Radiation
  - Prostate “roto rooter”
  - Tubes

Supportive Care

- Bone pain
  - Medications (pills, patches, etc)
  - Palliative radiation
  - Surgery for fracture

Supportive Care

There is no cure for metastatic prostate cancer

ALWAYS incorporate best supportive care

ALWAYS let patients know that just because there are multiple treatment options does not mean they have to exhaust them

Side Effect Management

Erectile Dysfunction

1. Vacuum Erectile Device (VED)
2. Pills (PDE5 inhibitors)
3. Urethral suppository
4. Penile injections
5. Penile prosthesis

The Lineup

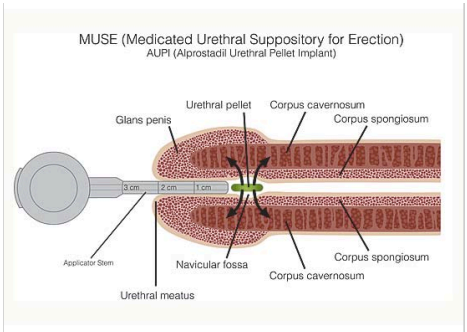
Sildenafil (Viagra): April 1998

Vardenafil (Levitra): August 2003

Tadalafil (Cialis): Nov 2003

Vardenafil (Staxyn): June 2010

Avanafil (Stendra): April 2012




NO, NO... NOT THAT ONE... THE BIG ONE ON THE TOP SHELF!!!
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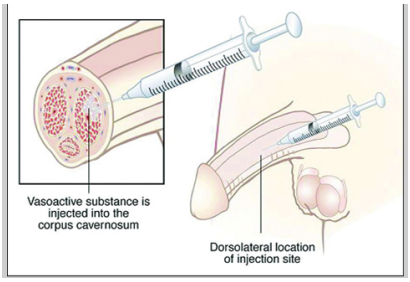
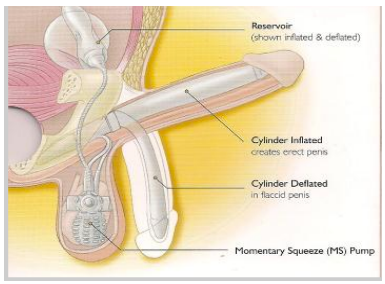

Vasoactive substance is injected into the corpus cavernosum
Dorsolateral location of injection site


Reservoir
(shown inflated & deflated)
Cylinder Inflated
creates erect penis
Cylinder Deflated
in flaccid penis
Momentary Squeeze (MS) Pump

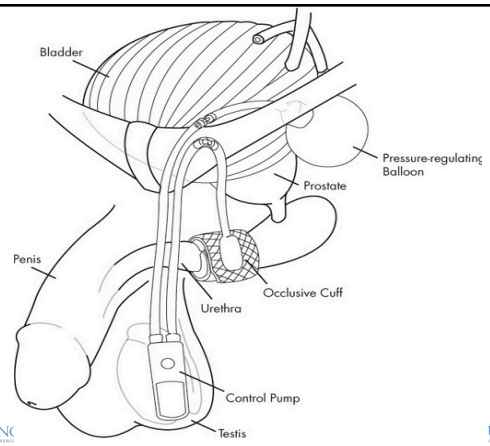
Pros & Cons

Treatment	Pros	Cons
PO PDE-5I	• Easy to take • Discreet • Travel	• Poor efficacy after surgery • Side effects • Costly
VED	• Noninvasive • Highly efficacy rates • Fairly easy to use • Travel • Incorporate into foreplay • One-time cost	• Cumbersome • Messy • Penis may appear purple • Penis wobbly at base • Discomfort
MUSE	• Easy to use • Less invasive than injections	• Low efficacy • Side effects • Pain • Costly
ICI	• High efficacy • Reliable • No tension ring • Erection lasts longer than other tx	• Invasive • Side effects • Refrigeration • Anxiety
Implant	• High efficacy • High satisfaction	• Permanent • Side effects • Surgical procedure • Surgical costs

Side Effect Management

Urinary Incontinence

- Muscle/nerve damage to urinary sphincter
- Pads, diapers
- Kegel exercise
- Pelvic floor physical therapy
- Severe/refractory
  - Artificial urinary sphincter



Side Effect Management

Hot flashes

- 80% on ADT
- Behavior change: Loose cotton clothing, fans, ice, avoid alcohol, caffeine, spicy foods, cool temperature
- Medications: SSRI, Gabapentin
- Most men do not require treatment

Side Effect Management

Sexual Dysfunction

- ED: See previous slides
- Decreased sex drive
  - 30-90% of men on ADT
  - No effective tx in the setting of prostate cancer
  - Libido is dependent on sufficient levels of T
- Penile shrinkage
  - On ADT = due to hypogonadal state
  - After surgery = unchallenged muscle tone, esp if loss of nocturnal erections
  - VED: Stretches and fills penis with blood

Side Effect Management

Fatigue

–Exercise
–Sleep hygiene
–Accept assistance from others
–Energy conservation
–Check for other causes

Side Effect Management

Emotional

- Encourage open discussion
- Validate feelings
- Involve partner and/or family
- Refer to mental health professional

Collaboration

- Nurses (oncology, urology, inpatient, clinic, infusion, navigators, research, CNAs)
- Advanced Practice Providers (NPs, APRNs, PAs)
- Physicians (urologists, medical oncologists, radiation oncologists, pathologists, radiologists)
- Mental health providers (psychologists, counselors, SW, sex therapists)
- Pharmacists, pharmacy techs
- Recovery team (PT, OT, home health, nutrition)
- Ancillary staff (radiology techs, phlebotomy, clinical trial personnel, administrative, financial counselors, volunteers)

Health Care Provider Considerations

- Counsel patients about screening
- Manage uncertainty
- Educate about treatment options
- Side effect management
- Refer to support groups
- Post-treatment survivorship
- Refer to other providers
- Quality of Life
- Incorporate best supportive care
- End of life care

Resources

- American Cancer Society
- National Cancer Institute
- Man-to-Man
- American Society of Clinical Oncology
- National Comprehensive Cancer Network
- American Prostate Society
- His Prostate Cancer
- Male Care
- Prostate Cancer Foundation
- US Too