

LUTS, BPH, Carcinoma Prostate

Dept. of Surgery

LUTS: definition

- Storage (irritative) symptoms:
 - Urgency
 - Urinary frequency
 - Nocturia
 - Urinary incontinence
- Voiding (obstructive) symptoms
 - Hesitancy, poor stream, terminal dribbling

Causes of LUTS

- Obstructive
 - BPH
 - Prostate/bladder/rectal cancer
 - Bladder neck/urethral strictures
 - Antimuscarinic drugs
 - Autonomic neuropathy/neurogenic bladder

Causes of LUTS

- Irritative
 - BPH
 - Bladder/prostate cancer
 - Infection
 - Bladder stones
 - Neurological
 - Dementia
 - Diabetes
 - Stroke

Assessment

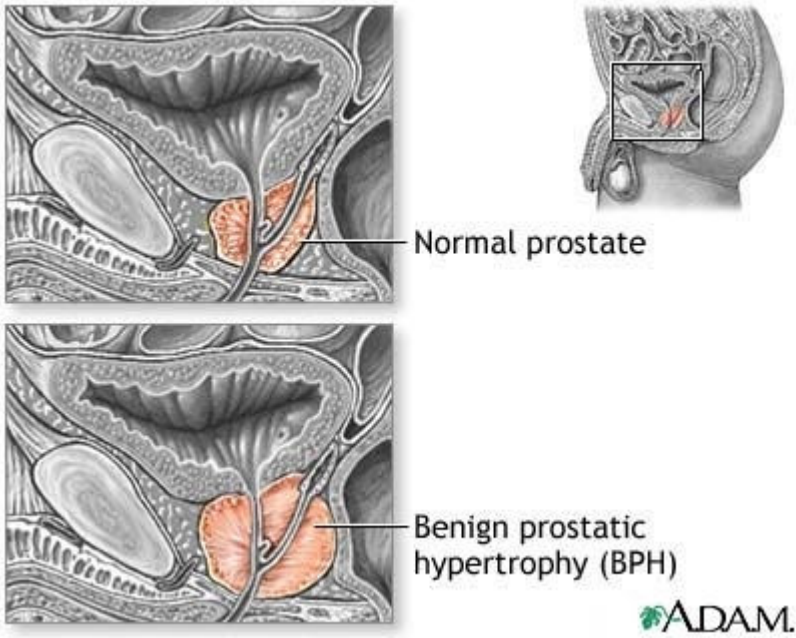
- History – type of LUTS, duration of Sx, how bothersome are they?
- Examination – abdomen (distended bladder), external genitalia, DRE
- International Prostate Symptom Score:
 - Used to assess severity of symptoms
 - Score of 0-5 for seven symptoms (total 35):
 - 0-7 – mildly symptomatic
 - 8-19 – moderately symptomatic
 - 20-35 – severely symptomatic

Management

- Urine dip +/- culture
- U&E
 - Chronic retention
 - Recurrent UTI
 - Hx of renal stones
- PSA
- Urinary frequency-volume chart
 - Ask patient to note down when they drink fluid/pass water and to comment on type of fluid
 - Allows to differentiate between frequency of urine, polyuria and nocturia

- Obstructive symptoms
 - Lifestyle changes.
 - Alpha blocker: e.g tamsulosin
 - 5 α – reductase inhibitors
- Irritative symptoms
 - Exclude/manage treatable causes
 - Urine containment devices
 - Supervised bladder retraining
 - Anticholinergics e.g oxybutinin

Benign Prostatic Hyperplasia



- Generalised disease of the prostate due to hormonal derangement which leads to enlargement of the gland (increase in the number of epithelial cells and stromal tissue) to cause compression of the urethra leading to symptoms

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Etiology

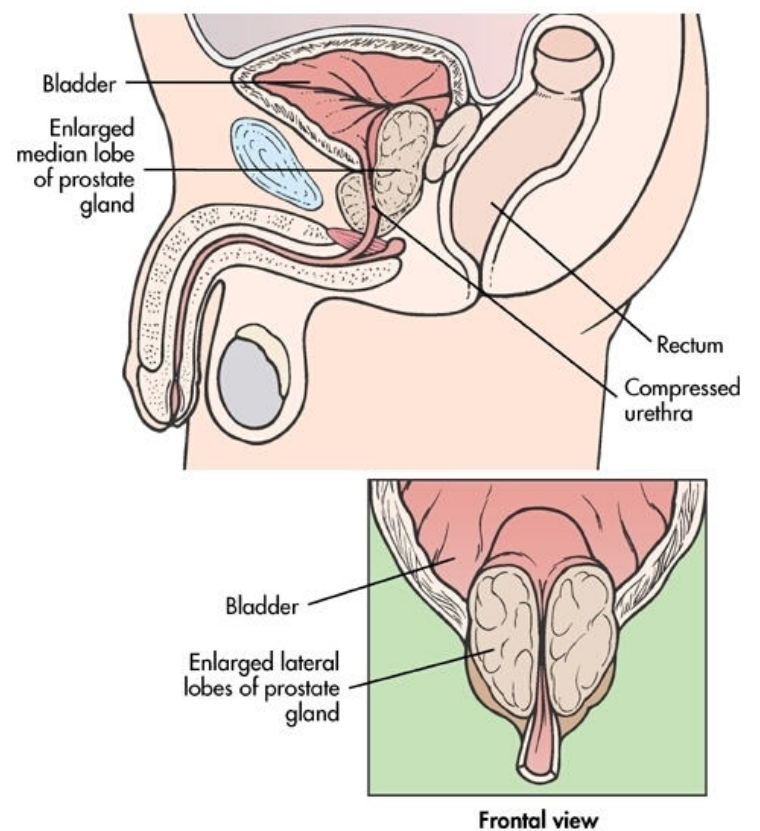
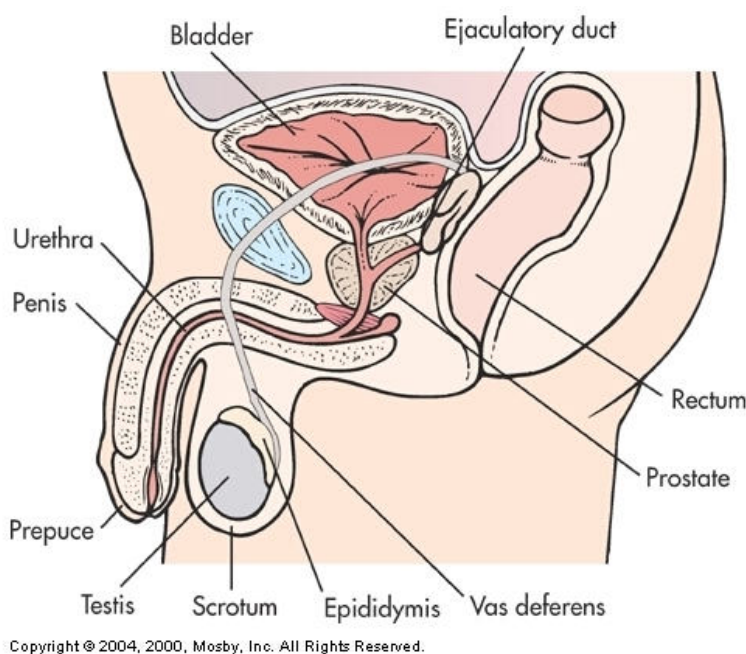
- Cause not completely understood
- Reawakening of the urogenital sinus to proliferate
- Change in hormonal milieu with alterations in the testosterone/estrogen balance
- Induction of prostatic growth factors
- Increased stem cells/decreased stromal cell death
- Accumulation of dihydroxytestosterone, stimulation by estrogen and prostatic growth hormone actions

BPH facts

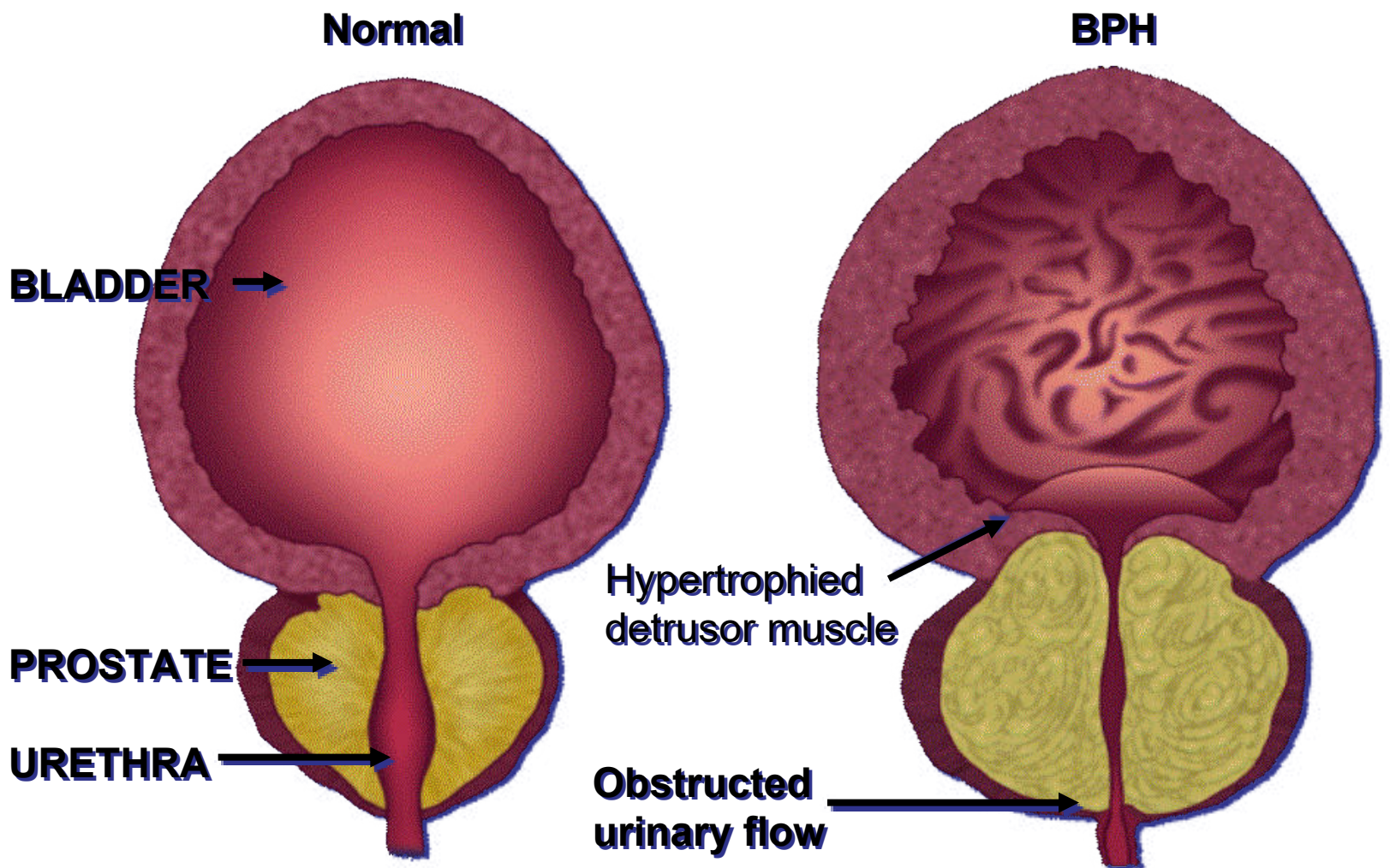
- Occurs in 50% of men over 50 and in 80% of men over 80 have BPH
- BPH progresses differently in every individual
- Many men with BPH may have mild symptoms and may never need treatment
- BPH **does not** predispose to the development of prostate cancer

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Benign Prostatic Hyperplasia



BPH Pathophysiology



Pathophysiology

- Slow and insidious changes over time
- Complex interactions between prostatic urethral resistance, intravesical pressure, detrusor functionality, neurologic integrity, and general physical health.
- Initial hypertrophy → detrusor decompensation → poor tone → diverticula formation → increasing urine volume → hydronephrosis → upper tract dysfunction

Complications

- Urinary retention
- UTI
- Sepsis secondary to UTI
- Residual urine
- Calculi
- Renal failure
- Hematuria
- Hernias, hemorrhoids, bowel habit change

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Clinical manifestations

- Voiding symptoms
 - decrease in the urinary stream
 - Straining
 - Dribbling at the end of urination
 - Intermittency
 - Hesitancy
 - Pain or burning during urination
 - Feeling of incomplete bladder emptying

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Clinical manifestations

- Irritative symptoms
 - urinary frequency
 - urgency
 - dysuria
 - bladder pain
 - nocturia
 - incontinence
 - symptoms associated with infection

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Benign Prostatic Hyperplasia

- Leading to “**symptom bother**” and **worsened QOL**

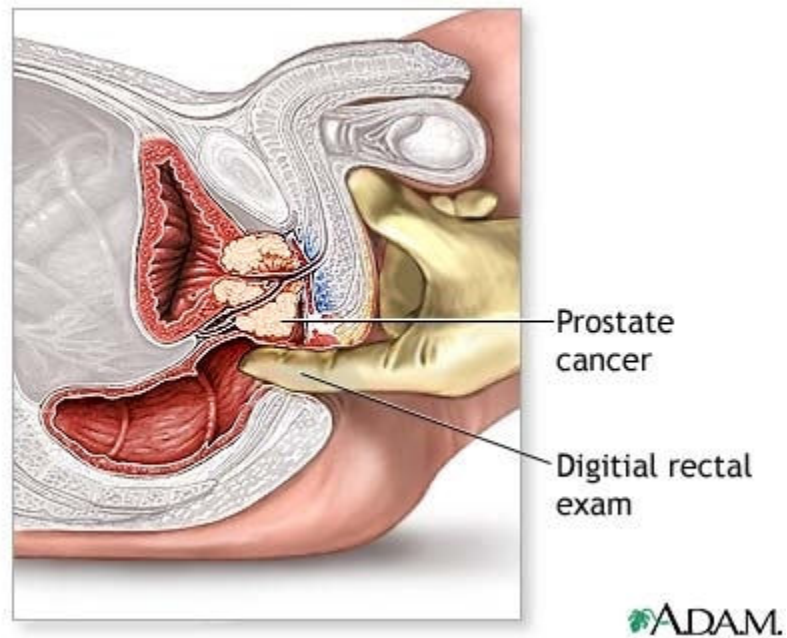
Other Relevant History

- GU History (STD, trauma, surgery)
- Other disorders (eg. neurologic, diabetes)
- Medications (anti-cholinergics)
- Functional Status

Diagnostic Tests

- History & Examination
 - Abdominal/GU exam
 - Focused neuro exam
- Digital rectal exam (DRE)
- Validated symptom questionnaire.
- Urinalysis
- Urine culture
- BUN, Cr
- Prostate specific antigen (PSA)
- Transrectal ultrasound – biopsy
- Uroflometry
- Postvoid residual

DRE



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- Urine cytology in patients with:
 - Predominance of irritative voiding symptoms.
 - Smoking history
- Flow rate and post-void residual
 - Not necessary before medical therapy but should be considered in those undergoing invasive therapy or those with neurologic conditions
- Upper tract evaluation if hematuria, increased creatinine
- Cystoscopy

Differential Diagnosis

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

Treatment Indications Absolute vs Relative

- | | |
|---|-----------------------------------|
| • Severe obstruction | • Moderate symptoms of prostatism |
| • Urinary retention | • Recurrent UTI's |
| • Signs of upper tract dilatation and renal insufficiency | • Hematuria |
| | • Quality of life issues |

Therapy

- Watchful waiting and behavioral modification
- Medical Management
 - Alpha blockers
 - 5-alpha reductase inhibitors
 - Combination therapy
- Surgical Management
 - Office based therapy
 - OR based therapy
- Urethral stents

Carcinoma Prostate

Epidemiology

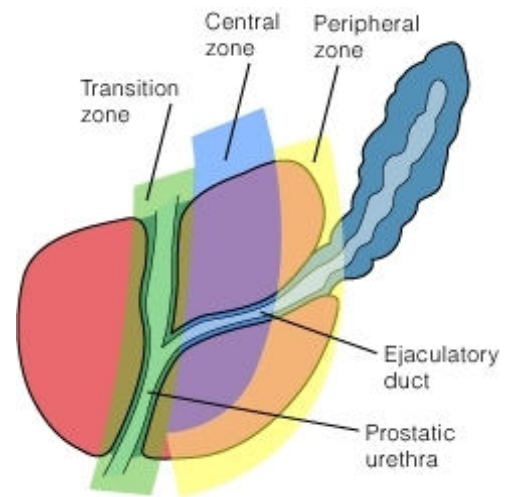
- Risk factors
 - Increasing age
 - Family history
 - African-American
 - Dietary factors.
- Nutritional factors have protective effect against prostate cancer
 - Reduced fat intake
 - Soy protein
 - Lycopene
 - Vitamin E
 - Selenium
- Race
 - Incidence doubled in African Americans compared to white Americans.
- Genetics
 - Common among relatives with early-onset prostate cancer
 - Susceptibility locus (early onset prostate cancer)
 - Chromosome 1, band Q24
 - An abnormality at this locus occurs in less than 10% of prostate cancer patients.

Pathophysiology

- Adenocarcinoma
 - 95% of prostate cancers
 - Developing in the acini of prostatic ducts
- Rare histopathologic types of prostate carcinoma
 - Occur in approximately 5% of patients
 - Include
 - Small cell carcinoma
 - Mucinous carcinoma
 - Endometrioid cancer (prostatic ductal carcinoma)
 - Transitional cell cancer
 - Squamous cell carcinoma
 - Basal cell carcinoma
 - Adenoid cystic carcinoma (basaloid)
 - Signet-ring cell carcinoma
 - Neuroendocrine cancer

Pathophysiology

- Peripheral zone (PZ)
 - 70% of cancers
- Transitional zone (TZ)
 - 20%
 - Some claim
 - TZ prostate cancers are relatively nonaggressive
 - PZ cancers are more aggressive
 - Tend to invade the periprostatic tissues.



Clinical Manifestations

- Early state (organ confined)
 - Asymptomatic
- Locally advanced
 - Obstructive voiding symptoms
 - Hesitancy
 - Intermittent urinary stream
 - Decreased force of stream
 - May have growth into the urethra or bladder neck
 - Hematuria
 - Hematospermia
- Advanced (spread to the regional pelvic lymph nodes)
 - Edema of the lower extremities
 - Pelvic and perineal discomfort

Clinical Manifestations

- **Metastasis**
 - Most commonly to bone (frequently asymptomatic)
 - Can cause severe and unremitting pain
 - Bone metastasis
 - Can result in pathologic fractures or
 - Spinal cord compression
 - Visceral metastases (rare)
 - Can develop pulmonary, hepatic, pleural, peritoneal, and central nervous system metastases late in the natural history or after hormonal therapies fail.

Detection and Diagnosis

- PSA level
 - Helpful in asymptomatic patients
 - > 60% of patients with prostate cancer are asymptomatic
 - Diagnosis is made solely because of an elevated screening PSA level
 - A palpable nodule on digital rectal examination
 - Next most common clinical presentation
 - Prompts biopsy
 - Much less commonly, patients are symptomatic
 - Advanced disease
 - Obstructive voiding symptoms
 - Pelvic or perineal discomfort
 - Lower extremity edema
-
- Symptomatic bone lesions.

Detection and Diagnosis

- Digital rectal examination
 - Low sensitivity and specificity for diagnosis
 - Biopsy of a nodule or area of induration
 - Reveals cancer 50% of the time
 - Suggests
 - Prostate biopsy
 - » Should be undertaken in all men with palpable nodules.

Detection and Diagnosis

- Transrectal ultrasound with biopsies
 - Indicated when
 - The PSA level is elevated
 - The percent-free PSA is less than 25%, or
 - An abnormality is noted on digital rectal examination
 - Type of biopsy
 - Sextant biopsies (base, midgland, and apex on each side)
 - Generally obtained
 - Seminal vesicles are biopsied in high-risk patients

Detection and Diagnosis

- A bone scan
 - Warranted only
 - PSA level greater than 10ng/mL
- Computed Tomography or magnetic resonance imaging
 - Abdominal and pelvic CT or MRI is usually unrevealing in patients with a PSA level less than 20ng/mL. .

Small, E., Cecil Textbook of Medicine, Prostate Cancer, 2004, WB Saunders, an Elsevier imprint

Prostate Cancer

Prognosis

- Prognosis correlates with histologic grade and extent (stage) of disease
- Adenocarcinoma
 - > 95% of prostate cancers
 - Multifocality is common
- Grading
 - Ranges from 1 to 5
- Gleason score
 - Definition
 - Sum of the two most common histologic patterns seen on each tissue specimen
 - Ranges
 - From 2 (1 + 1)
 - To 10 (5 + 5)
 - Category
 - Well-differentiated (Gleason scores 2, 3, or 4)
 - Intermediate differentiation (Gleason scores 5, 6, or 7)
 - Poorly differentiated (Gleason scores 8, 9, or 10).

Prostate Cancer

Staging

- Stage T1
 - Nonpalpable prostate cancer
 - Detected only on pathologic examination
 - Incidentally noted after
 - Transurethral resection for benign hypertrophy (T1a and T1b) or
 - On biopsy obtained because of an elevated PSA (T1c-the most common clinical stage at diagnosis)
- Stage T2
 - Palpable tumor
 - Appears to be confined to the prostatic gland (T2a if one lobe, T2b if two lobes)
- Stage T3
 - Tumor with extension through the prostatic capsule (T2a if focal, T2b if seminal vesicles are involved)
- Stage T4
 - Invasion of adjacent structures
 - Bladder neck
 - External urinary sphincter
 - The rectum
 - The levator muscles
 - The pelvic sidewall
- Nodal metastases
 - Can be microscopic and can be detected only by biopsy or lymphadenectomy, or they can be visible on imaging studies
- Distant metastases
 - Predominantly to bone
 - Occasional visceral metastases occur.

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Treatment

- **PRINCIPLES OF THERAPY**
 - May include
 - Watchful waiting
 - Androgen deprivation
 - External beam radiotherapy
 - Retropubic or perineal radical prostatectomy
 - with or without postoperative radiotherapy to the prostate margins and pelvis
 - Brachytherapy (either permanent or temporary radioactive seed implants)
 - with or without external beam radiotherapy to the prostate margins and pelvis.

- Surgery
 - Traditional
 - Robotic
- Radiation
 - Brachytherapy
 - External beam
- Cryotherapy
- Androgen Deprivation
- Watchful waiting

Treatment – Hormone resistant

- **HORMONE-RESISTANT PROSTATE CANCER**
- Climbing PSA
 - First manifestation of resistance to androgen deprivation
 - In the setting of anorchid levels of testosterone
- Therapy
 - Discontinuation of antiandrogen therapy (flutamide, bicalutamide, nilutamide) while continuing with LHRH agonists
 - Results in a PSA decline
 - Can be associated with symptomatic improvement
 - Can persist for 4 to 24 months or more
 - Secondary hormonal manipulations
 - Ketoconazole or
 - Estrogens
 - Chemotherapeutic regimens
 - Mitoxantrone plus corticosteroids or
 - Estramustine plus a taxane
- Monitoring
 - Serial PSA levels (best)
 - A decline of 50% or more is probably clinically significant

- **PALLIATIVE CARE**

- Bone pain
 - Advanced prostate cancer
 - Analgesics
 - Glucocorticoids
 - Anti-inflammatory agents
 - Can alleviate bone pain
- Widespread bony metastases not easily controlled with analgesics or local radiation
 - Strontium-89 and samarium-153
 - Selectively concentrated in bone metastases
 - Alleviate pain in 70% or more of treated patients.