



## Factors Affecting PSA Levels

- Most important determinant of a man's PSA level is the presence of prostatic disease
  - BPH
  - Prostatitis/UTI
  - Prostate cancer
- Disruption of the prostatic architecture produces elevations in PSA
- PSA "leaks" into the general circulation
  - Prostatic massage
  - Instrumentation (Foley placement, cystoscopy, biopsy, surgery)
  - NO significant rise with DRE
  - Rise with ejaculation controversial: wait 48 hours

## PSA Quandary

- Not all men with prostate cancer have elevated PSA levels and not all men with elevated PSA levels have prostate cancer
  - PSA is a poor tumor marker if expressed as an absolute value
    - Question of "normal" levels
      - $\leq 0.4$  ng/mL
      - $\leq 0.2.5$  ng/mL (AA males or high-risk males)
  - Significance of a given PSA value should be taken in the context of family history, race, and DRE findings

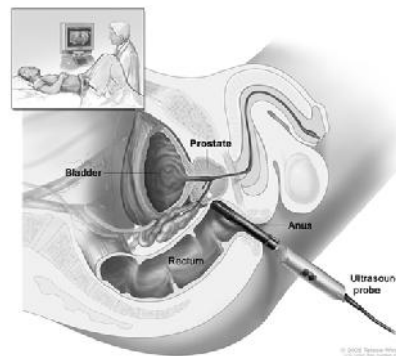
## Prostate Cancer (CaP)

- Most common noncutaneous cancer in men
- Second most common cause of cancer death in men
- Approximately 241,740 new cases in 2012\*
- Approximately 28,170 men will die in 2012\*
- Overall risk of having CaP, 16% in lifetime or 1:6\*
- Average age at diagnosis is 67\*

"More men will die WITH prostate cancer than OF prostate cancer."

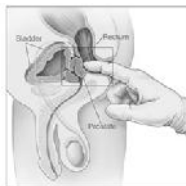
\*Statistics courtesy of the American Cancer Society

## Transrectal U/S + Biopsy



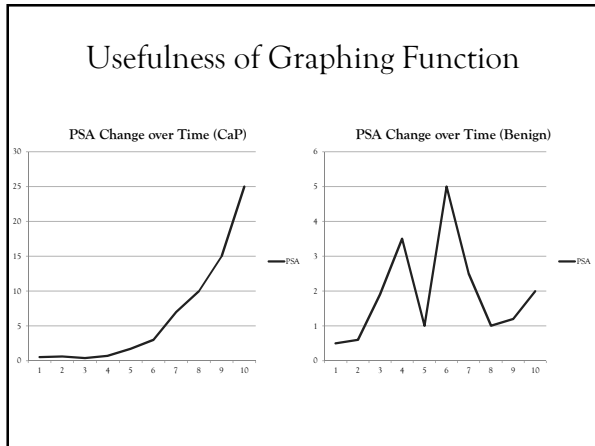
## Diagnosis of Prostate Cancer

- Early prostate cancer is rarely associated with symptoms
  - Abnormal DRE
    - Induration or nodule (asymmetry)
  - Elevated PSA
  - DRE < PSA < DRE + PSA
    - Both PSA + DRE provide greatest detection rate
  - Confirmation by transrectal U/S + biopsy



## When is Biopsy Warranted?

- A PSA level that is considered suspicious for prostate cancer should be remeasured before performing a prostate biopsy, because of fluctuations in PSA that could create false-positive elevations (Eastham et al, 2003)
- It is the trend or change in PSA over time that best signals when a biopsy should be done
  - Linear elevation is a danger sign
  - Wide fluctuations in PSA may actually signal a benign state (Garzotto, personal communication)
    - ?transient inflammation



### Staging of Prostate Cancer

<p><b>T1</b> Clinically insignificant, tumor not palpable or visible by imaging</p> <p><b>T1a</b> No clinical finding during transurethral resection of prostate; &lt; 5% of tissue resected</p> <p><b>T1b</b> No clinical finding during transurethral resection of prostate; &gt; 5% of tissue resected</p> <p><b>T1c</b> Tumor identified by needle biopsy or a technique of elevated PSA</p>	<p><b>T2</b> Tumor confined within capsule (palpable or visible on imaging)</p> <p><b>T2a</b> Involves half of a lobe or less</p> <p><b>T2b</b> Involves more than half of a lobe and less than half of the prostate</p> <p><b>T2c</b> Tumor involves both lobes</p>	<p><b>T3</b> Tumor extends through urethra; external, bladder neck or seminal vesicle</p> <p><b>T3a</b> Unilateral extracapsular extension</p> <p><b>T3b</b> Bilateral extracapsular extension</p> <p><b>T3c</b> Tumor involves seminal vesicles</p>	<p><b>T4</b> The tumor has spread or affected to tissues next to the prostate (other than the seminal vesicles)</p> <p><b>T4a</b> The tumor has spread to the rectal wall (distal); the external sphincter (muscles that help control urination), or the rectum</p> <p><b>T4b</b> The tumor has spread to the floor (up to the wall of the pelvis)</p>
<p><b>NO-3</b></p>	<p><b>MO-1</b></p>	<p><b>M0</b> Cancer has not spread to any lymph nodes</p> <p><b>M1</b> Cancer has spread to a single regional lymph node (node to the right) and is not larger than 2 centimeters</p> <p><b>M2</b> Cancer has spread to one or more regional lymph nodes and is larger than 2 centimeters (2 cm), but not larger than 5 centimeters</p> <p><b>M3</b> Cancer has spread to a lymph node and is larger than 5 centimeters</p> <p><b>M4</b> The cancer has not metastasized (spread) beyond the regional lymph nodes</p> <p><b>M5</b> The cancer has metastasized to distant lymph nodes (outside of the pelvis), bones, or other distant organs such as lungs, liver, or brain</p>	

- ### What About Free PSA?
- Unbound fraction of PSA, “% free PSA”, can help establish the significance of an elevated PSA value
    - Risk stratification and reduction of unnecessary biopsies
  - Generally used for PSA values between 4 and 10 ng/mL
    - “Diagnostic gray zone”
  - 5-35% of PSA is unbound to serum proteins
  - Men with CaP have a greater bound fraction of PSA
  - > 18% free:total PSA corresponds to low risk of CaP
    - Size matters: for larger glands, cut point declines to 14%

- ### What are “Good” Cancers?
- Gleason score 6 (3+3) or less
  - Small-volume tumors
  - Low-risk patients
  - Indolent PSA rise
    - PSA as a measure of biologic activity of the cancer

### How Bad is the Prostate Cancer?

**Gleason's Pattern Scale**

1. Small, uniform glands. Well differentiated
2. More space (stroma) between glands. Moderately differentiated
3. Distinctly infiltration of cells from glands at margins. Poorly differentiated
4. Irregular masses of neoplastic cells with few glands. Anaplastic
5. Lack of or occasional glands, sheets of cells.

- ### Treatment of Localized CaP
- Active surveillance (watchful waiting)
  - Radical prostatectomy
  - Radiation therapy
    - Brachytherapy
    - External beam radiation therapy (IMRT)
  - Cryotherapy
  - “HIFU” (High-frequency focused ultrasound)

## Morbidities of Therapy

- Active surveillance
  - Advancement of tumor
- Radical prostatectomy
  - Surgery, pain, incapacitation, incontinence, erectile dysfunction
- Radiation therapy
  - Need for adjuvant androgen deprivation, fatigue, cystitis, proctitis, hematuria, rectal bleeding, erectile dysfunction

## The Data is Muddy

- Are we finding more cancers - Yes.
- Are we finding more early-stage cancers - Yes.
- Are we over-treating some cancers and causing unnecessary morbidity - Yes.
- Are we saving lives by screening - Maybe.

## Morbidities of Therapy

- Cryotherapy
  - Inadequate therapy, fistula, incontinence, rectal pain, urethral sloughing, erectile dysfunction
- High-frequency focused ultrasound
  - Prolonged catheterization, urinary retention, fistula, urethral stricture, perineal pain, erectile dysfunction

## Guidelines for Screening

Recommendation	American Urological Association	American Cancer Society	U.S. Preventive Services Task Force
Shared decision making between patient and clinician	Yes	Yes (consider use of decision aid)	Yes (when patient requests screening)
Age to begin offering screening — yr			
Average-risk patients	40	50	Not applicable
High-risk patients (black patients and those with first-degree relative with prostate cancer)	40	40-45	Not applicable
Discontinuation of screening	Life expectancy <10 yr	Life expectancy <10 yr	Not applicable
Screening tests	PSA, digital rectal examination	PSA, optional digital rectal examination	Not applicable
Frequency of screening	Annual (possibly less often for men in their 40s)	Annual (every other year when PSA <2.5 ng/ml)	Not applicable
Criteria for biopsy referral	Age, family history, race or ethnic group, findings on digital rectal examination, total PSA, free PSA, PSA velocity, PSA density, previous biopsy findings, coexisting conditions	PSA >4.0 ng/ml, abnormal digital rectal examination, individualized risk assessment if PSA is 2.3-4.0 ng/ml	Not applicable

## The PSA Controversy

Dr. Willet Whitmore, the father of urologic oncology, is perhaps best remembered for his question: "For a patient with prostate cancer, if treatment for cure is necessary, is it possible? If possible, is it necessary?" This question crystallized the dilemma of decision making for patients and physicians and, in the third decade of prostate-specific antigen (PSA) screening, is now even more pertinent and pressing than ever.

## AUA Position

- *The decision to use PSA for the early detection of prostate cancer should be individualized. Patients should be informed of the known risks and the potential benefits.* (AUA 2009)
- Considerations:
  - Patient comorbidities
  - Life expectancy (>10 years)
  - Family history
    - Longevity
    - First-degree relatives with prostate cancer

## Case in Point

- 57 yo male presented for treatment of nephrolithiasis
- DRE revealed a nodule
- PSA 1.7 at diagnosis
- Biopsy performed: Gleason 4+5 prostate cancer
- Tx: Androgen deprivation therapy and radical prostatectomy
- Current status: Patient now has metastatic disease and is back on androgen deprivation therapy

## Questions?

