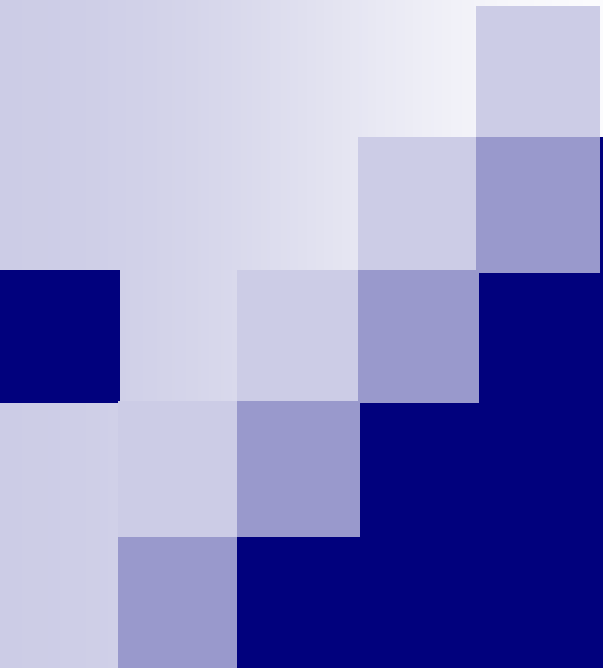


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Prostate Cancer: Overview, Screening, Treatment, Prevention

Presented at “Cancer Updates for the
Primary Care Provider” on July 20, 2002
by John T. Gwozdz, M.D.

Prostate Cancer Outline Slide #1

■ Overview

- Location of Prostate Gland
- Who is at risk for prostate cancer
- Seriousness of disease
- Myths vs. Reality and publications – showing why to screen

■ Screening

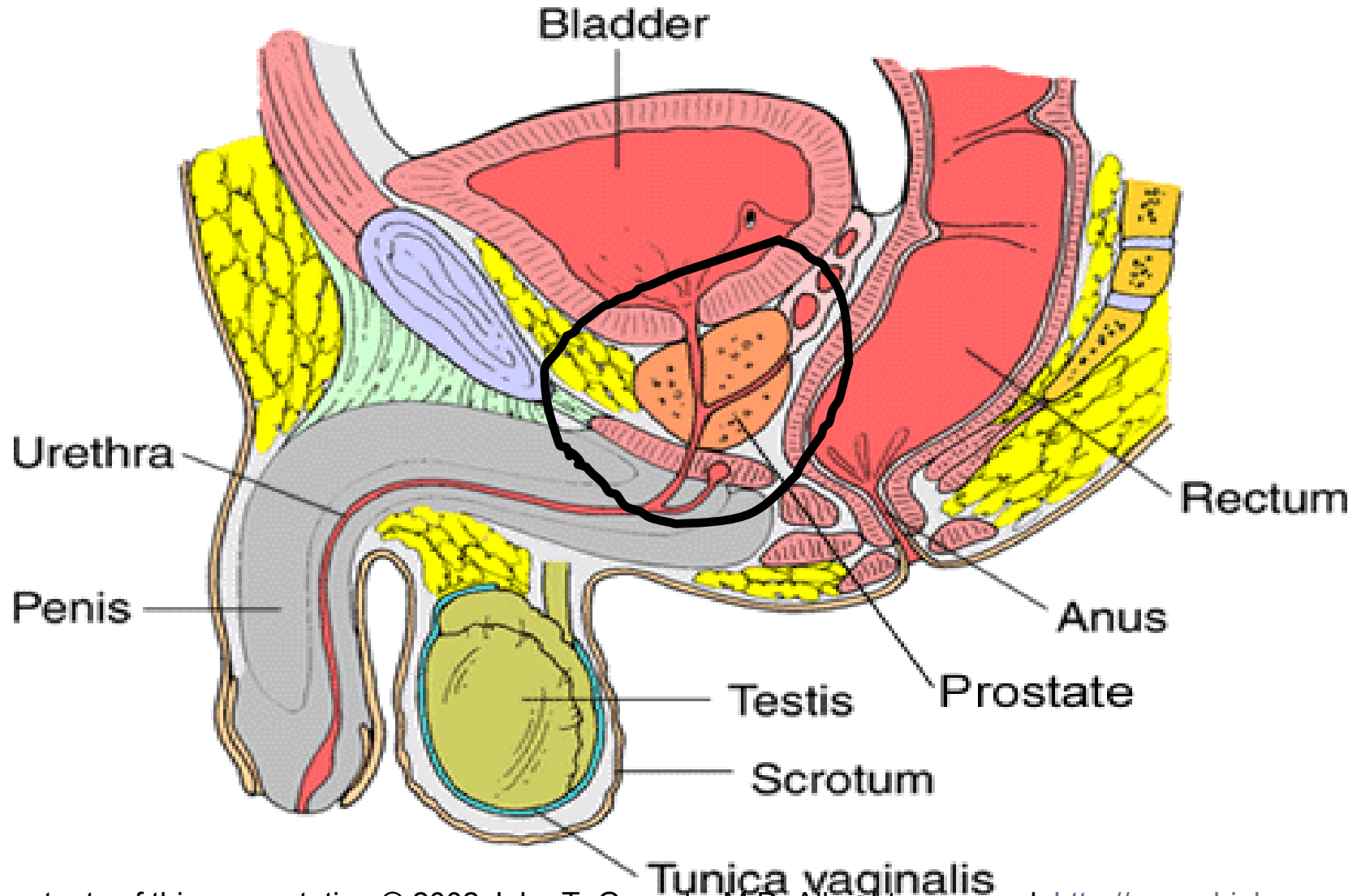
- How to screen
- Screening Guidelines
- When to refer to a urologist
- What does the urologist do

Prostate Cancer Outline Slide #2

■ Treatment

- Prognostic Factors dictate treatment success rate
- Who NOT to treat
- Treatment options
 - Surgery/Radical Prostatectomy
 - Prostate Seed Implants
 - External beam RT/IMRT
 - Hormonal Therapy Alone
 - Observation/No Treatment

Location of Prostate Gland



Who is at Risk for Prostate Cancer

- All males are at risk for prostate cancer.
- As age increases risk increases.
- There is no known causative agent.
- African Americans and positive family history have increased risk.

Seriousness of Disease

- 189,000 men are expected to be diagnosed with prostate cancer in 2002
- It is the second leading cause of cancer death in men. 30,200 men are expected to die of prostate cancer in 2002.
- > 10X's WTC deaths/yr., a huge socioeconomic impact

Myths vs. Reality

Myth: No proof of increase cure with treatment.

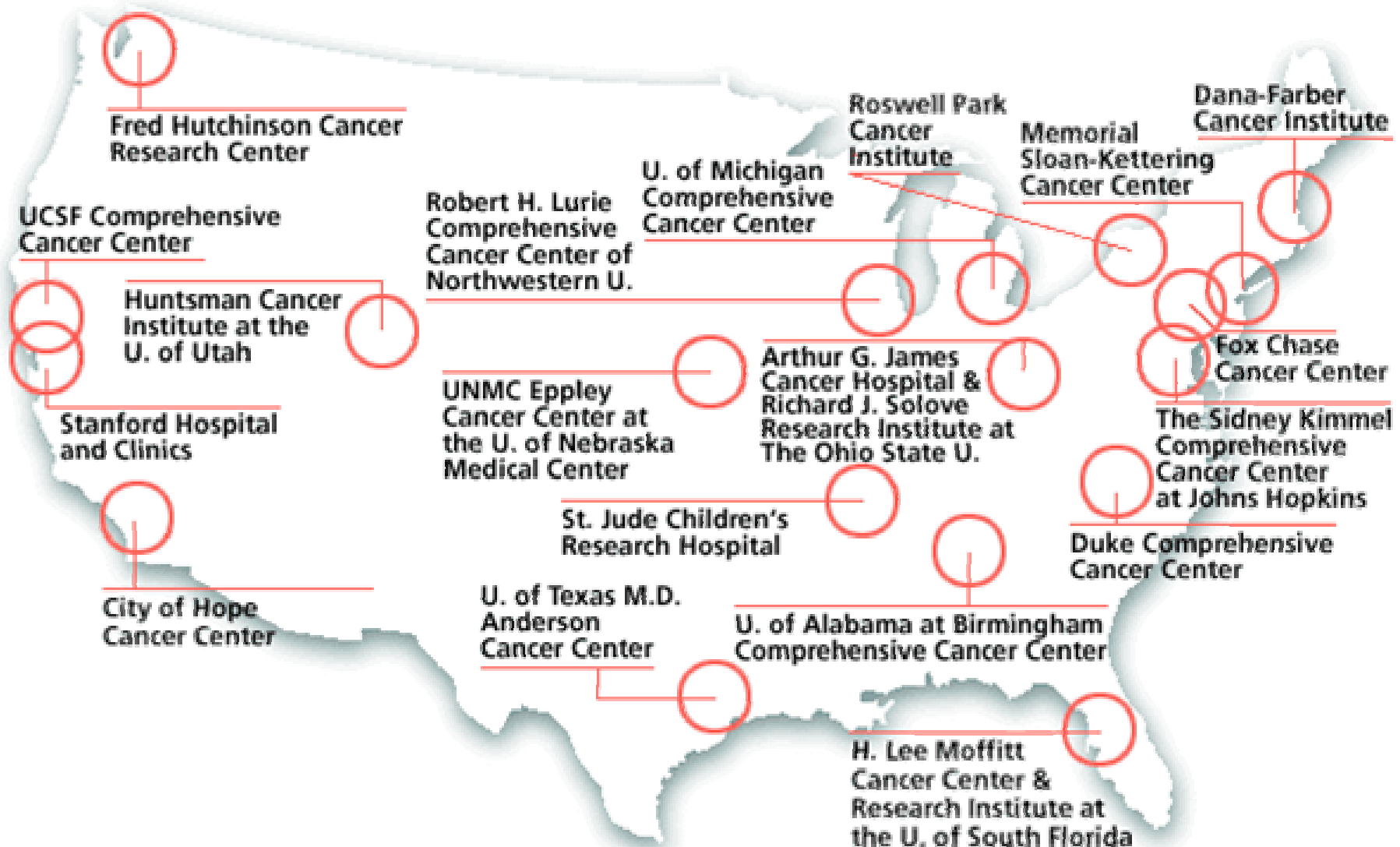
Reality: Population based data shows that with early detection and treatment there are now fewer deaths from prostate cancer.

Myths vs. Reality - Note

According to the ACS and NCCN, when screening is performed, 83% of all prostate cancers are discovered in these early stages and if treated with conventional treatment have a 5 year survival rate of 100%.

(More than 70% of prostate cancer patients who have not died from something other than prostate cancer live 20 or more years after conventional treatment)

Member hospitals of NCCN



Myths vs. Reality

Myth: The toxicity of treatment outweighs the benefit of treatment.

Reality: Current era treatment has very modest long term side effects compared to uncontrolled tumor growth (more in treatment section).

Screening led to decline in mortality

J Urol 1999 Feb; 161(2): 529-33

Conclusion: These data demonstrate that despite the increase in prostate cancer mortality rates in the mid to late 1980s, mortality rates in 1993 to 1997 are lower than in the years before serum PSA testing. While chance cannot be ruled out, the data suggest that increased screening for prostate cancer, particularly through PSA testing, may have led to declines in mortality from prostate cancer.

Decline in mortality relates to treatment success

- J Natl Cancer Inst 1999 Jun 16;91

Conclusions: When screening is assumed to be at least as efficacious as hypothesized in the PLCO trial, it is unlikely that the entire decline in prostate cancer mortality can be explained by PSA testing based on current beliefs concerning lead time. Only very short lead times would produce a decline in mortality of the magnitude that has been observed.

PLCO Trial

- Prostate, Lung, Colorectal, Ovarian cancer screening trial
- Screening guidelines were developed based on cost savings and are slightly different from those of ACS and NCCN
- Note: Their results were not stratified by age, and a significant proportion of the participants were older men.

Screening leads to decline in distant stage disease

- J Natl Cancer Inst 1999 Jun 16;91

Implications: The decline in the incidence of distant stage disease holds the promise that testing for prostate-specific antigen may lead to a sustained decline in prostate cancer mortality.

Myths vs. Reality

Myth: Physicians are too busy to discuss screening or they don't want to burden the patient with screening information.

Reality: Most patients want the information and would much prefer to avoid metastatic prostate cancer morbidity. Additionally, there is medicolegal risk in not screening if a patient later is diagnosed with a terminal stage when screening was not offered previously.

Cost of Screening is acceptable

Cancer Control 2001 Mar-Apr;8(2):133-40

Conclusions: The cost of prostate cancer screening appears to be acceptable. Randomized studies of PSA-based screening are currently ongoing, although the results may not be available for a decade. Currently, the best evidence is derived from population-based studies that appear to show a benefit to prostate cancer screening.

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How to screen

- Prostate-Specific Antigen (PSA)
Blood Test
- PSA II blood test (Percent free-PSA
for PSA 2.5 to 10)
- Digital Rectal Exam (DRE)
- Takes 2 minutes

PSA

- Prostate specific antigen (PSA) is a substance made by the normal prostate gland detectable with this blood test.
- Most men have levels under 4 nanograms per milliliter (ng/mL) of blood.
- When prostate cancer develops, the PSA level usually goes above 4.
- If the PSA is above 4 but less than 10, the patient has about a 25% chance of having prostate cancer.
- If the PSA is above 10, the patients chance of having prostate cancer is over 67% and increases further as their PSA level increases.

PSA II

- Percent free PSA (or PSA II) blood test indicates how much PSA circulates free compared to how much is bound.
- If the patient's PSA results are in the borderline range (4-10 ng/mL), a low *percent free PSA* (less than 10%) means that the likelihood of having prostate cancer is about 50% and that you should recommend that they have a biopsy.
- According to the ACS, a recent study found that if men with borderline PSA results had prostate biopsies only when their percent free PSA was 25% or less, about 20% of unnecessary prostate biopsies could be avoided.

DRE

- Digital Rectal Exam (DRE) is when the doctor inserts a gloved, lubricated finger into the patient's rectum to feel for any irregular or abnormally firm area that might be a cancer.
- Most cancers begin in the back part of the gland that can be reached by a rectal exam. While it is uncomfortable, it only takes a short time.
- Although DRE is less effective than the PSA blood test in finding prostate cancer, it can sometimes find cancers in men with normal PSA levels.

ACS & NCCN Screening Guidelines

- Annual DRE beginning at age 50
- Annual PSA blood test beginning at age 50
- Begin screening at age 45 for men at increased risk (African-American men, men with a family history of prostate cancer)
- Screening is not recommended for men with a life expectancy of less than 10 years

PLCO Screening Guidelines

- Annual DRE

- PSA blood test
 - PSA > 2 ng/mL test every year
 - PSA < 2 ng/mL, but > 1 ng/mL test every 2 years
 - PSA < 1 ng/mL test every 5 years

When to Refer to a Urologist

- Standard PSA level => 4.0 ng/ml
- Standard PSA level between 2.5 and 10.0 ng/ml AND a low free/total PSA ratio as indicated by the PSA II test (lab provides tables to interpret results)
- Suspicious-feeling prostate on a DRE (anything other than a smooth homogeneous, non-rock hard texture)

What does urologist do?

- Review data
- Transrectal biopsies when indicated (a simple out patient procedure with minimal risk)
- Discuss results/treatment options

Prostate Cancer Outline Slide #2

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Prognostic Factors Dictate Treatment Options

- Stage
- Gleason Score
- PSA
- Age
- Co-morbidities
- Patient preferences

Who NOT to treat

- Patient who does not want treatment
- Patients whose survival is expected to be < 10 years and early disease as below:
 - PSA < 10
 - G1 ≤ 6
 - Stage T1C

Who NOT to treat – Why 10 years?

Even early prostate cancer can progress and kill in 10 years, if patient lives that long. Physician must attempt to accurately predict who will die of co-morbidities before cancer causes symptoms. It is often difficult to predict survival for chronic illnesses COPD, CAD, DM.

Treatment Options

- Radical Prostatectomy (surgery)
- Radiation therapy (seeds or external)
- Hormone therapy
- Chemotherapy
- Observation/No treatment
- Alternative or Complementary Therapies

Surgery/Radical Prostatectomy

Ideal for patients with small enough tumors to cut it all out and whom will be able to recover from the procedure.

- Pts with T1 – T2 disease N0, M0
- Low Gleason score, low PSA
- < 70 years old
- Good operative risks
- Prefers surgery

Control Rates and Typical Side Effects of Surgery

■ Control rates:

- Early stage pts: 80 – 95% long term control (10 years)
- Advance local stage: 10 – 40% long term control

■ Typical side effects:

- Incontinence: up to 35% of men
- Impotence: 65 to 90% of men

Prostate Seed Implants

Ideal for an older patient who is unwilling to come in for 8 weeks of treatment and has a smaller, low grade tumor. The patient must be capable of tolerating anesthesia.

- ≥ 70 years old, debated.
- OK anesthesia risks
- T1C, T2a, G1 \leq 6, PSA $<$ 10
- Patient preference

Control Rates & Typical Side Effects of Seed Implants

■ Control rates:

- Early stage pts: 80 – 95% long term control (10 years)

■ Typical side effects:

- Impotence < 50%
- Urinary frequency/obstructive symptoms (temporary for most patients)
- Significant rectal problems (burning, pain & diarrhea) – less than 5% of men (usually temporary)

External RT/IMRT

External beam RT/IMRT can treat bigger tumor best. No anesthesia is required, but it does require 2 months of daily treatment in Amarillo (15 minutes/day).

- ≥ 70 years old
- Small or Large tumors T2, T3
- Any Gleason, especially 7 or higher
- Any PSA $< 20 - 30$, especially > 10 .
- Patient preference

Control Rates and Typical Side Effects of External Beam Radiation

■ Control rates:

- Early stage pts: 80 – 95% long term control (10 years)
- Advance local stage: 10 – 40% long term control

■ Typical side effects:

- Fatigue
- Diarrhea/proctitis – temporary
- Urine frequency – temporary
- Impotence up to 70%

Myths vs. Reality

Myth: Patient feels lousy after radiation and wonders if radiation caused it.

Reality: Patient probably didn't feel good before:

- 50+ lbs overweight
- Smokers, drinkers
- Don't regularly exercise
- Poor diet
- HTN, CAD, DM, Depression, Hypothyroid, Arthritis

If the above are taken care of > 95% have excellent quality of life post radiation.

Hormonal Therapy Alone

Hormonal treatment never cures on its own, but may control growth for 3-7 years.

- N+, M+
- PSA > 30
- GI > 8

All above have excessively high failure (>50%) rates with surgery or RT

Possible Side Effects of Hormonal Therapy

- Reduced or absent libido – 100%
- Impotence – 100%
- Hot flashes – menopausal type
- Breast tenderness < 50%
- Growth of breast tissue < 20%
- Liver disease < 10%
- Bone loss – everyone eventually

Observation/No Treatment

Ideal when patient prefers not to be treated and fully accepts no further screening and potential eventual death from cancer.

- < 10 year survival from co-morbidities
- GI<6, PSA < 10, T1-2
- Low rise in PSA over time

In other words other diseases progressing faster than cancer or patient just refuses care permanently.



Note Regarding Observation/No Treatment

Patients too often change their minds after PSA rises more. Thus the patient self selects to have a lower chance of cure and all the same risks of complications by waiting until cancer is more advanced to pursue treatment.

Possible Side Effects of No Treatment

- Inability to pass urine, pelvic pain, bleeding into urine, tumor growth into rectum with rectal symptoms
- lymphatic obstruction with massive leg swelling
- Bone mets causing pain, fracture and immobility resulting in extremely low quality of life, possibly for years

Chemotherapy

Currently, chemotherapy is mostly used experimentally in young patients with metastatic disease who failed hormonal therapy.

Alternative Medicines

- Not much good research done yet.
- Most agents have antiandrogen effects that will at least temporarily drop PSA. This is NOT a cure even though patients are told otherwise.

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