The Changing Landscape of Prostate Cancer

helping make the complicated, understandable

Marc B. Garnick, MD FACP
Clinical Professor of Medicine
Beth Israel Deaconess Medical Center
Harvard Medical School
Medical Director, Cancer Services  NHS

7 October 2008 BH
Disclosure of Financial Relationships

Marc B. Garnick MD, FACP

Has relationship(s) with the following proprietary entity(s) producing health care goods or services.

HARVARD MEDICAL SCHOOL/HARVARD HEALTH PUBLICATIONS
Editor in Chief, Perspectives on Prostate Disease
Topics for Discussion

• Prostate Gland: Basic facts and anatomy
• How is prostate cancer diagnosed?
• PSA
  • Screening – Should you have a PSA test?
• Treatments
  • Maximally Invasive to surveillance (no active treatment)
  • How do we decide who to treat and
  • How do we decide upon the specific treatment?
• Prevention
• The future
For the same patient with the diagnosis, the options range from Radical Treatment________No Treatment so how can we decide?
Prostate Cancer Factoids

• ~200,000 incidence
• 1,200,000 prevalence
• 29,000 deaths/year
• FAMILIAL Prostate CA
  • +Father+Brother ↑ 2X
  • AA+FH ↑ Detection Rates 3 fold

• AFRICAN AMERICANS
  • 1.6 x risk of getting and dying of pr ca
• OBESITY: ↑ Mortality
How is prostate cancer diagnosed?
Most common methods

• Elevated PSA leading to prostate biopsy
• Physical exam that detects a prostate abnormality, leading to biopsy (DRE)
• Urinary symptoms, leading to urological evaluation
• Back pain leading to physical exam, radionuclide scan and prostate biopsy (rarely bone biopsy or other metastatic site)
• Surgery for benign prostatic hyperplasia; “Chips” contain prostate cancer
The Gleason Score

• Two Numbers, each 1 to 5 (most and second most common)
• Based upon Biopsy
  • Gleason 1 = looks like normal prostate tissue
  • Gleason 5 = aggressive looking cancer
• Most cancers are 3+3 or 3+4; (6 or 7)
• More aggressive cancers are 4+3; 4+4; 4+5 or 5+5
Prostate Anatomy – Understanding Complications

Scientific American 279: 74 ‘98

Beverly Hospital
Beth Israel Deaconess Medical Center

TWICE THE KNOWLEDGE
twicethetrust.org
PSA in 2008

What is a “normal” PSA?

PCPT* Data

We are redefining a “normal” PSA

*Prostate Cancer Prevention Trial
Prostate Cancer with “Normal” PSA

• 9,459 to placebo; 2,950 with PSA <4 ng/mL, negative DRE and biopsied after 7 years
• 15.2% (449) had cancer; 14.9% with GS ≥ 7
• PSA 0-0.5 ng/mL: 6.6% cancer …… 12.5%
• 0.6-1.0 10.1 %
• 1.1-2.0 17.0 %
• 2.1-3.0 23.9 %
• 3.1-4.0 26.0 % …… 25%
PSA Based
Prostate Cancer Screening:
Pros and Cons
Current Status
Lead/Length Bias and Overdiagnosis

Screened    _____Tx_____________________ †
Unscreened __________________Tx+1___ †

“overdiagnosis”
Screened    _____Dx_____________________________ †
Unscreened _________________________________ † (Dx)

Years

Beverly Hospital
Beth Israel Deaconess Medical Center

TWICE THE KNOWLEDGE
twicethetrust.org
A Balanced View

• Major national societies (AUA, ACS, ACP) have changed policy guidelines; emphasize patient education and being involved in “shared” decision
## PSA Screening

<table>
<thead>
<tr>
<th>YES</th>
<th>NO</th>
<th>AMBIGUOUS</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACS</td>
<td>FRANCE</td>
<td>WSJ → NO</td>
</tr>
<tr>
<td>&gt;40 DRE</td>
<td>SWEDEN</td>
<td>NYT → YES</td>
</tr>
<tr>
<td>&gt;50 DRE, PSA</td>
<td>CANADA</td>
<td>USA Today → Maybe</td>
</tr>
<tr>
<td>SENATOR DOLE</td>
<td>IUCC</td>
<td>ESPN cold pizza → NO</td>
</tr>
<tr>
<td>Anyone, Anytime</td>
<td>USPSTF-2008</td>
<td>Patriot Ledger – tomorrow’s op ed</td>
</tr>
</tbody>
</table>
How do we decide upon treatment?

Who and When and What?
What About Treatments?

• Surgery: open, laparoscopic, robotic assisted (the robot)
• Radiation
  • External beam
  • 3-D conformal/intensity modulated radiation therapy/cyberknife/tomo
  • Interstitial (brachytherapy) seeds
    • Fiducials – not to be confused with seeds
  • Protons/neutrons
• HIFU/Cryo (Canada and EU) – FOCAL therapies
• Hormone Therapy
• Chemotherapy
• Active surveillance
3-D CRT/IMRT/IGRT

• Conventional (70.2 Gy) vs Conformal + Protons (79.2 Gy)

• Increase in rectal cancer post RT (PMID 15825064)
What’s New and Newer? BrachyRx and Robotic Sx

• Robotic Laparoscopic Radical Prostatectomy
  • “da Vinci”
  • 3D; 7 degrees of Freedom
  • No tremor
  • 12 x magnification
  • Early on, similar results
  • $$: 1.2MM; 100K/yr; 1.5K disposables/case

• Don’t know if it is any better

Scientific American 279: 74 ‘98
1. Which Clinical Cancers Should Be Treated?

- **2002**: Scandanavian Study: RP v Watchful
  - No difference in survival

- **2005**:
  - Some difference in survival
    - 5% absolute death reduction at 10 years (PMID 15888698)
    - Attribution Biases
    - NNT: 17
    - THESE WERE NOT SCREENED PATIENTS

- **2008**:
  - No difference in survival
Active Surveillance Results

• N = 299 (Canadian) PMID: 16414494, 16474710
• Free of treatment at 8 years: 65%
• Overall Survival: 85%
• PrCa specific survival: 99%
• 3 Cancer Deaths

• N = 380 (JHH)
• Free of treatment: 60%
• JHH (J. Epstein, personal communication)
Complementary Approaches to Prostate Cancer

Dietary, Lifestyle and “Herbal” Aspects
<table>
<thead>
<tr>
<th>Micronutrients/Foods and Prostate Cancer/Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Animal Fat</td>
</tr>
<tr>
<td>Vitamin A</td>
</tr>
<tr>
<td>Vitamin E</td>
</tr>
<tr>
<td>Vitamin C</td>
</tr>
<tr>
<td>Selenium</td>
</tr>
<tr>
<td>Lycopene</td>
</tr>
<tr>
<td>Soy</td>
</tr>
<tr>
<td>Calcium</td>
</tr>
<tr>
<td>α-linolenic acid</td>
</tr>
<tr>
<td>PC SPES</td>
</tr>
<tr>
<td>Lifestyle changes</td>
</tr>
<tr>
<td>Obesity</td>
</tr>
<tr>
<td>Strong + epidemiologic data</td>
</tr>
<tr>
<td>No direct evidence</td>
</tr>
<tr>
<td>Preclinical and clinical data</td>
</tr>
<tr>
<td>Mixed data</td>
</tr>
<tr>
<td>One positive study (2º EP)</td>
</tr>
<tr>
<td>Epidemiologic data</td>
</tr>
<tr>
<td>Strong epidemiologic data</td>
</tr>
<tr>
<td>&gt;7000mg bad; &lt;700mg better</td>
</tr>
<tr>
<td>From fish, ok; not plants</td>
</tr>
<tr>
<td>(DES-like) Off Market</td>
</tr>
<tr>
<td>Benefit suggested (PMID: 16094059)</td>
</tr>
<tr>
<td>BAD</td>
</tr>
</tbody>
</table>
A word about prevention

• Finasteride and dutasteride – the “shrinkers”
• Reduction in incidence of prostate cancer
• Initial controversy about the type of cancer that was detected
• Reanalysis
• Even front page analysis in NYT could not decide!!
A few parting thoughts

- Relationship with BPH and prostate cancer – no
- Testosterone administration willy nilly? No
  - Our approach
- Sexual Activity – we encourage it
- If you have had prostate cancer- “penile rehabilitation” is probably important
Thanks for your attention

Questions welcome