PROSTATE CANCER UPDATE
DISCLOSURES

I, “BRUCE WAYNE” PORTERFIELD
HAVE NOTHING TO DISCLOSE.
OBJECTIVES

- Epidemiology
- Early detection and screening
- Review of clinical disease states
- Treatment options by disease states
- Manifestations of metastatic disease
- Conclusion
### Estimated New Cancer Cases* in the US in 2014

<table>
<thead>
<tr>
<th></th>
<th>Men</th>
<th>Women</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>855,220</td>
<td>810,320</td>
</tr>
<tr>
<td>Prostate</td>
<td>27%</td>
<td>Breast</td>
</tr>
<tr>
<td>Lung &amp; bronchus</td>
<td>14%</td>
<td>13% Lung &amp; bronchus</td>
</tr>
<tr>
<td>Colon &amp; rectum</td>
<td>8%</td>
<td>8% Colon &amp; rectum</td>
</tr>
<tr>
<td>Urinary bladder</td>
<td>7%</td>
<td>6% Uterine corpus</td>
</tr>
<tr>
<td>Melanoma of skin</td>
<td>5%</td>
<td>6% Thyroid</td>
</tr>
<tr>
<td>Kidney &amp; renal pelvis</td>
<td>5%</td>
<td>4% Non-Hodgkin lymphoma</td>
</tr>
<tr>
<td>Non-Hodgkin lymphoma</td>
<td>4%</td>
<td>4% Melanoma of skin</td>
</tr>
<tr>
<td>Oral cavity &amp; pharynx</td>
<td>4%</td>
<td>3% Kidney &amp; renal pelvis</td>
</tr>
<tr>
<td>Leukemia</td>
<td>4%</td>
<td>3% Pancreas</td>
</tr>
<tr>
<td>Liver &amp; intrahepatic bile duct</td>
<td>3%</td>
<td>3% Leukemia</td>
</tr>
<tr>
<td>All other sites</td>
<td>20%</td>
<td>21% All other sites</td>
</tr>
</tbody>
</table>

*Excludes basal cell and squamous cell skin cancers and in situ carcinoma except urinary bladder.*
Estimated Cancer Deaths in the US in 2014

<table>
<thead>
<tr>
<th>Cancer Site</th>
<th>Men 310,010</th>
<th>Women 275,710</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lung &amp; bronchus</td>
<td>28%</td>
<td>26% Lung &amp; bronchus</td>
</tr>
<tr>
<td>Prostate</td>
<td>10%</td>
<td>15% Breast</td>
</tr>
<tr>
<td>Colon &amp; rectum</td>
<td>8%</td>
<td>9% Colon &amp; rectum</td>
</tr>
<tr>
<td>Pancreas</td>
<td>7%</td>
<td>7% Pancreas</td>
</tr>
<tr>
<td>Liver &amp; intrahepatic bile duct</td>
<td>5%</td>
<td>5% Ovary</td>
</tr>
<tr>
<td>Leukemia</td>
<td>5%</td>
<td>4% Leukemia</td>
</tr>
<tr>
<td>Esophagus</td>
<td>4%</td>
<td>3% Uterine corpus</td>
</tr>
<tr>
<td>Urinary bladder</td>
<td>4%</td>
<td>3% Non-Hodgkin lymphoma</td>
</tr>
<tr>
<td>Non-Hodgkin lymphoma</td>
<td>3%</td>
<td>3% Liver &amp; intrahepatic bile duct</td>
</tr>
<tr>
<td>Kidney &amp; renal pelvis</td>
<td>3%</td>
<td>2% Brain &amp; other nervous system</td>
</tr>
<tr>
<td>All other sites</td>
<td>24%</td>
<td>23% All other sites</td>
</tr>
</tbody>
</table>

Presenter: Bruce W. Porterfield, MD, PhD
Trends in Cancer Incidence Rates* Among Men, US, 1975-2010

*Age-adjusted to the 2000 US standard population and adjusted for delays in reporting.
†Includes the intrahepatic bile duct.
Source: Surveillance, Epidemiology, and End Results (SEER) Program, National Cancer Institute, 2013.

Presenter: Bruce W. Porterfield, MD, PhD
The Lifetime Probability of Developing Cancer for Men, 2008-2010*

<table>
<thead>
<tr>
<th>Site</th>
<th>Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>All sites†</td>
<td>1 in 2</td>
</tr>
<tr>
<td>Prostate</td>
<td>1 in 7</td>
</tr>
<tr>
<td>Lung &amp; bronchus</td>
<td>1 in 13</td>
</tr>
<tr>
<td>Colon &amp; rectum</td>
<td>1 in 20</td>
</tr>
<tr>
<td>Urinary bladder‡</td>
<td>1 in 26</td>
</tr>
<tr>
<td>Melanoma of the skin¶</td>
<td>1 in 34</td>
</tr>
<tr>
<td>Non-Hodgkin lymphoma</td>
<td>1 in 42</td>
</tr>
<tr>
<td>Kidney &amp; renal pelvis</td>
<td>1 in 49</td>
</tr>
<tr>
<td>Leukemia</td>
<td>1 in 60</td>
</tr>
<tr>
<td>Oral cavity &amp; pharynx</td>
<td>1 in 66</td>
</tr>
<tr>
<td>Liver &amp; intrahepatic bile duct</td>
<td>1 in 82</td>
</tr>
</tbody>
</table>

* For those free of cancer at beginning of age interval.
† All sites exclude basal cell and squamous cell skin cancers and in situ cancers except urinary bladder.
‡ Includes invasive and in situ cancer cases
¶ Statistic for white men.

Source: DevCan: Probability of Developing or Dying of Cancer Software, Version 0.7.0 Statistical Research and Applications Branch, National Cancer Institute, 2013.
## Five-year Relative Cancer Survival Rates (%) by Race, 2003-2009

<table>
<thead>
<tr>
<th>Site</th>
<th>White</th>
<th>Black</th>
<th>Absolute Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Sites</td>
<td>67</td>
<td>59</td>
<td>8</td>
</tr>
<tr>
<td>Breast (female)</td>
<td>90</td>
<td>79</td>
<td>11</td>
</tr>
<tr>
<td>Colon</td>
<td>65</td>
<td>56</td>
<td>9</td>
</tr>
<tr>
<td>Esophagus</td>
<td>18</td>
<td>11</td>
<td>7</td>
</tr>
<tr>
<td>Leukemia</td>
<td>56</td>
<td>50</td>
<td>6</td>
</tr>
<tr>
<td>Non-Hodgkin lymphoma</td>
<td>70</td>
<td>62</td>
<td>8</td>
</tr>
<tr>
<td>Oral cavity &amp; pharynx</td>
<td>64</td>
<td>43</td>
<td>21</td>
</tr>
<tr>
<td>Prostate</td>
<td>100*</td>
<td>97</td>
<td>3</td>
</tr>
<tr>
<td>Rectum</td>
<td>67</td>
<td>61</td>
<td>6</td>
</tr>
<tr>
<td>Urinary bladder</td>
<td>78</td>
<td>65</td>
<td>13</td>
</tr>
<tr>
<td>Uterine cervix</td>
<td>69</td>
<td>59</td>
<td>10</td>
</tr>
<tr>
<td>Uterine corpus</td>
<td>84</td>
<td>61</td>
<td>23</td>
</tr>
</tbody>
</table>

5-year relative survival rates based on patients diagnosed in the SEER 18 areas from 2003 to 2009, all followed through 2010.

*99.5%

Source: Surveillance, Epidemiology, and End Results (SEER) Program, National Cancer Institute, 2013.
PROSTATE STATISTICS

Estimated New Cases in 2015: 220,800
% of All New Cancer Cases: 13.3%

Estimated Deaths in 2015: 27,540
% of All Cancer Deaths: 4.7%

Percent Surviving 5 Years: 98.9%

Percent of Cases & 5-Year Relative Survival by Stage at Diagnosis: Prostate Cancer


Presenter: Bruce W. Porterfield, MD, PhD
WHO GETS AND DIES FROM PROSTATE CANCER?

Presenter: Bruce W. Porterfield, MD, PhD
ARE THERE RISK FACTORS FOR PROSTATE CANCER?

FAMILY HISTORY
GENE MUTATIONS
DIET
WEIGHT
SMOKING
ENVIRONMENTAL
PROSTATITIS AND BPH
STDs

Table 1. Relative Risk (RR) Related to Family History of Prostate Cancer

<table>
<thead>
<tr>
<th>Risk Group</th>
<th>RR for Prostate Cancer (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brother(s) with prostate cancer diagnosed at any age</td>
<td>3.14 (2.37–4.15)</td>
</tr>
<tr>
<td>Father with prostate cancer diagnosed at any age</td>
<td>2.35 (2.02–2.72)</td>
</tr>
<tr>
<td>One affected FDR diagnosed at any age</td>
<td>2.48 (2.25–2.74)</td>
</tr>
<tr>
<td>Affected FDRs diagnosed &lt;65 y</td>
<td>2.87 (2.21–3.74)</td>
</tr>
<tr>
<td>Affected FDRs diagnosed ≥65 y</td>
<td>1.92 (1.49–2.47)</td>
</tr>
<tr>
<td>Second-degree relatives diagnosed at any age</td>
<td>2.52 (0.99–6.46)</td>
</tr>
<tr>
<td>Two or more affected FDRs diagnosed at any age</td>
<td>4.39 (2.61–7.30)</td>
</tr>
</tbody>
</table>

CI = confidence interval; FDR = first-degree relative.

*Adapted from Kicinski et al. [22]

Borrowed from National Cancer Institute

Presenter: Bruce W. Porterfield, MD, PhD
EARLY DETECTION RECOMMENDATIONS

VARYING OPINIONS

- ACS
- AUA
- UNITED STATES PREVENTATIVE SERVICES TASK FORCE (USPSTF)
- NCCN

HARM FROM SCREENING

- OVER-DIAGNOSIS
PROSTATE SPECIFIC ANTIGEN

- ACCURACY, SPECIFICITY, SENSITIVITY
- RANGE
  - CAN VARY BY AGE AND RACE
  - MOST ACCEPTED CUTOFF IS 4.0
- AGE OF TESTING
- FREQUENCY OF TESTING
- WHEN TO NOT TEST
- WHAT CAN AFFECT PSA
- WHEN TO HAVE A BIOPSY
- PSA VELOCITY
- AGE SPECIFIC RANGES
PROSTATE SCREENING
TO DO OR NOT DO...THE DRE
ADVANCES …

BIOMARKERS

- %PSA
- PROSTATE HEALTH INDEX (FREE, TOTAL AND PRO)
  - FOR SERUM PSA BETWEEN 4 AND 10NG/ML
- 4KSCORE (NOT FDA APPROVED)
NCCN PROSTATE CANCER EARLY DETECTION

NCCN Guidelines Version 2.2015
Prostate Cancer Early Detection

Baseline Evaluation

History and physical (H&P) including:
- Family history
- Medications
- History of prostate disease and screening, including prior PSA and/or isoforms, exams, and biopsies
- Race

Risk Assessment

Start risk and benefit discussion about offering prostate screening:
- Baseline PSA
- Consider baseline digital rectal examination (DRE)

Early Detection Evaluation

Age 45-75 y

- DRE normal (if done), PSA ≥1 ng/mL
  - Repeat testing at 1-2 year intervals

Age >75 y, in select patients (category 2B)

- DRE normal (if done), PSA <3 ng/mL and no other indications for biopsy
  - Repeat testing at 1-2 year intervals

- PSA <1 ng/mL
  - Repeat testing at 2-4 year intervals

See Indications for Biopsy (PROSD-3)
WHEN TO WATCH?  
WHEN TO BIOPSY? WHEN TO REFER?

NCCN Guidelines Version 2.2015  
Prostate Cancer Early Detection

INDICATIONS FOR BIOPSY

- PSA >3.0 ng/mL

  • Repeat PSA
  • DRE
  • Workup for benign disease

  - Follow up in 5–12 mo with PSA/DRE
  - or
  - Percent free PSA, 4Kscore, or phi

TRUS-GUIDED BIOPSY

Initial and Repeat

Extended-pattern biopsy (12 cores)

- Number of cores:
  - Sextant (6),
  - Lateral peripheral zone (6), and
  - Lesion-directed at palpable nodule or suspicious image

- Anteriorly directed biopsy is not supported in routine biopsy. However, the addition of a transition zone biopsy to an extended biopsy protocol may be considered in a repeat biopsy if PSA is persistently elevated.

- Multiparametric MRI may help identify regions of cancer missed on prior biopsies and should be considered in selected cases after at least 1 negative biopsy.

- For high-risk men with negative biopsies, consideration can be given to a saturation biopsy strategy (including transperineal techniques) and/or the use of multiparametric MRI followed by an appropriate biopsy technique based on the results.

- Local anesthesia can decrease pain/discomfort associated with prostate biopsy and should be offered to all patients.

Presenter: Bruce W. Porterfield, MD, PhD
DIAGNOSIS & STAGING:

GLEASON STAGE
GLEASON HISTOLOGY
GLEASON SCORE

HORMONE SENSITIVE DISEASE
- Newly diagnosed, localized disease.
- Non-metastatic, biochemical relapse.
- Metastatic hormone naïve.

CASTRATION RESISTANT DISEASE
- Non-metastatic.
- Metastatic, asymptomatic (chemotherapy naïve).
- Metastatic, symptomatic (chemotherapy naïve).
- Metastatic, post chemotherapy.

Presenter: Bruce W. Porterfield, MD, PhD
<table>
<thead>
<tr>
<th>Pathologic (pT)</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>pT2</td>
<td>Organ confined</td>
</tr>
<tr>
<td>pT2a</td>
<td>Unilateral, involving one-half of 1 lobe or less</td>
</tr>
<tr>
<td>pT2b</td>
<td>Unilateral, involving more than one-half of 1 lobe but not both lobes</td>
</tr>
<tr>
<td>pT2c</td>
<td>Bilateral disease</td>
</tr>
<tr>
<td>pT3</td>
<td>Extraprostatic extension</td>
</tr>
<tr>
<td>pT3a</td>
<td>Extraprostatic extension or microscopic invasion of the bladder neck</td>
</tr>
<tr>
<td>pT3b</td>
<td>Seminal vesicle invasion</td>
</tr>
<tr>
<td>pT4</td>
<td>Invasion of the bladder and rectum</td>
</tr>
</tbody>
</table>
PROGNOSIS AS A FUNCTION OF AGE AND GLEASON SCORE FOR LOCALIZED DISEASE

Lu-Yao et al, JAMA 2009
PROSTATE CANCER TREATMENT
DISEASE STATES

HORMONE SENSITIVE DISEASE

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Presenter: Bruce W. Porterfield, MD, PhD
TREATMENT BY DISEASE STATE: HORMONE SENSITIVE DISEASE

Newly diagnosed, localized disease
- Surgery
- XRT
- XRT + ADT
- Active surveillance

Non-metastatic, biochemical relapse.
- Observation
- Intermittent ADT

Metastatic, hormone naïve.
- ADT
- ADT + chemotherapy

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ANDROGEN DEPRAVATION THERAPY (ADT)

- Prostate cancer Driven by androgen receptor signaling

- ADT
  - Lowers testosterone levels to castration levels.
  - PSA levels decline
  - ADT considered “Gold Standard” for newly diagnosed, hormone sensitive disease
ANDROGEN SIGNALING PATHWAY

SCHER ET AL END RELATED CANCER 11 (459)

Presenter: Bruce W. Porterfield, MD, PhD
ADT: GnRH agonist and antagonist
Leuprolide
Goserelrix
Degarelix

Presenter: Bruce W. Porterfield, MD, PhD
ADT: GnRH agonist and antagonist
Leuprolide
Goserelox
Degarelix

Presenter: Bruce W. Porterfield, MD, PhD
Nonsteroidal antiandrogens
Flutamide
Nilutamide
Bicalutamide

1) Block intratumoral testosterone
2) Monotherapy can result in increased serum testosterone.

ADT: GnRH agonist and antagonist
Leuprolide
Goserelx
Degarelix

ORCHIECTOMY

Presenter: Bruce W. Porterfield, MD, PhD
NEWLY DIAGNOSED, HORMONE SENSITIVE PROSTATE CANCER

- Localized Disease
- Based on T stage, Gleason score, PSA level
- Low risk: All required
  - T2a or lower, Gleason score 6 or less, PSA < 10
- Intermediate risk:
  - T2b or higher, Gleason 7 or PSA 10-20
- High risk: Any of the following
  - T3 or higher, Gleason 8-10, PSA > 20
PROGNOSIS AS A FUNCTION OF AGE AND GLEASON SCORE FOR LOCALIZED DISEASE

Lu-Yao et al, JAMA 2009

Presenter: Bruce W. Porterfield, MD, PhD
LOW RISK LOCALIZED DISEASE

- Pivot trial: Wilt et al, NEJM 2012
- No benefit of radical prostatectomy over observation.
- Life expectancy can influence decision for definitive therapy vs palliative therapy.
- Active surveillance protocols available
INTERMEDIATE RISK TREATMENT OPTIONS

• Radiation therapy plus short term > Radiation therapy alone (RTOG 94-08).

• Radical prostatectomy or radiation + ADT for 4-6 months equivalent options
HIGH RISK TREATMENT OPTIONS

XRT + long term ADT > XRT alone
  ▪ RTOG 8531 and EORTC trials – improved overall survival
  ▪ ADT for 2-3 years

Radical prostatectomy or XRT and long term ADT are reasonable options.
  ▪ No phase 3 data.

• Pilopich et al Inter J. Radiat Oncol Biol Phys 2005
• Bolla et al Lancet Oncol 2013
• Bill-Anderson et al J Natl Cancer Inst 2008
HORMONE SENSITIVE NON-METASTATIC

No studies to guide treatment options.

- Observation vs ADT
- PSA doubling time <9 months implies more aggressive disease.

If ADT chosen, intermittent not inferior to continuous.

- Has QOL implications.

- Freedland et al JAMA 2005
- Klotz et al GU ASCO 2011
- Crook et al NEJM 2012

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METASTATIC HORMONE NAIVE

- SWOG 9346 Phase III > 1000 patients
- Continuous ADT vs intermittent ADT
- Median survival 5.8 years vs 5.1 years, respectively
- Continuous ADT slightly better than intermittent and considered Gold Standard


Presenter: Bruce W. Porterfield, MD, PhD
METASTATIC HORMONE NAIVE

- Chemotherapy vs ADT
- CHAARTED E3809, Phase III trial
- Randomization
  - ADT + Docetaxel vs ADT alone
- Endpoints
  - TTP
  - OS

- Median Survival
  - ADT + docetaxel – 57.6 months
  - ADT – 44 months
  - $p= 0.0003$
  - Highest level of effectiveness seen in patients with high volume disease.

Presenter: Bruce W. Porterfield, MD, PhD
DISEASE STATES

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Presenter: Bruce W. Porterfield, MD, PhD
Castration Resistant Disease

- Serial rising PSA or disease progression on imaging
- Castrate level serum testosterone
  - < 50 ng/ml
- Former terminology
  - Hormone refractory
  - Androgen independence

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Castration Resistant Non-Metastatic Disease

Secondary hormone manipulation

- Estrogens
  - Estradiol
  - DES
- Glucocorticoids: Prednisone
- CYP17: Ketoconazole

- Anti-androgens: Change or withdraw the drug.
  - Flutamide
  - Niludamide
  - Bicaludamide
PROSTATE CANCER SURVIVORS

- HEALTHY BEHAVIOR RECOMMENDATIONS
- CANCER SCREENING
- SIDE EFFECTS
SUMMARY

NOT ALL MEN DIAGNOSED WITH PROSTATE CANCER WILL BENEFIT FROM TREATMENT