Physical Late and Long-Term Effects

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Late and Long-Term Effects

• Late effects
  – Develop months to years after cancer treatment

• Long-term
  – Develop during treatment and continue for months to years following
Subsequent or Second Cancers
Subsequent Primary Cancers

Using SEER data of 1.54 million cancer survivors (mean age, 60.4 years; 48.8% women), follow up 7.3 years.

- Male survivors (excluding those with prostate cancer)
  - Higher incidence (11%) and mortality (45%) from a subsequent primary cancer.
  - Most common subsequent cancers were lung, prostate, bladder/urinary, colorectal.

- Female cancer survivors
  - Higher incidence (10%) and mortality (33%) from a subsequent primary cancer.
  - Most common subsequent cancers were breast, colorectal, uterine.

Sung H et al. JAMA 2021
Increased risk of second malignant neoplasms in children and AYA survivors

AYAs = individuals diagnosed aged 15 to 39

Lee JS. Cancer 2016
Increased risk of second malignant neoplasms in children and AYA survivors

Lee JS. Cancer 2016.

$ - SMN occurring at least 5 years after original diagnosis

*p<0.05
Multiple primary cancers etiologic factors

Wood M E et al. JCO 2012;30:3734-3745
Multiple primary cancers etiologic factors

Lifestyle
- Tobacco
- Alcohol
- Diet
- Other

Environment
- Contaminants
- Occupation
- Viruses
- Other

Host factors
- Age and sex
- Genetics
- Immune function
- Hormonal, other

Interactions and other influences
- Gene-environment
- Gene-gene

Wood M E et al. JCO 2012;30:3734-3745
Treatment-Related Risks of Subsequent Cancers

• Chemotherapy
  – Early to late risk of leukemias, solid tumors
    • Type of drug
    • Higher drug doses
    • Longer treatment time
    • Higher dose intensity

• Radiation therapy
  – Most are not seen for at least 10 years after XRT
    • Dose of radiation
    • Area treated
    • Age at treatment
    • Chemotherapy
    • Smoking
    • Years since XRT

Radiation therapy and Subsequent Cancer

Figure 6.2 Subsequent cancers associated with radiation. Circles represent fields of radiation.
Screening For Subsequent Cancers

- Breast cancer screening if prior chest wall radiation as child
  - Earlier start for mammography – age 25 or 8 years post XRT whichever is later
  - Addition of breast MRI
- Colorectal cancer – start at age 30 if childhood XRT to abdomen
- Lung cancer
  - CT scan, especially for head/neck cancers and smokers
- Thyroid – clinical examination, thyroid US
- Patients and physicians need to be vigilant about symptoms!!!
Non-cancer Late and Long-term Effects
Non-cancer late and long-term effects

**Surgery**
- Lymphedema
- Pain
- Functional limitations
- Sexual dysfunction
- Body image
- Infertility
- Ostomy
Non-cancer late and long-term effects

Chemotherapy (examples)

- Cardiac dysfunction (doxorubicin, daunorubicin, trastuzumab)
- Pulmonary fibrosis (bleomycin)
- Neuropathy (vincristine, vinblastine, paclitaxel, docetaxel, oxaliplatin, cisplatin)
- Hearing loss (cisplatin)
- Premature menopause, infertility (cyclophosphamide, nitrogen mustard)
Late and Long-Term Effects

**Hormonal therapy**

- **Tamoxifen**
  - Clotting, uterine cancer, hot flashes, vaginal dryness

- **Aromatase inhibitors**
  - Osteoporosis, musculoskeletal pain

- **Androgen deprivation**
  - Hot flashes, osteoporosis, metabolic syndrome, breast tenderness, reduced libido/ED, fatigue
Radiation therapy and Non-Cancer Effects

CNS vascular disease
Neurocognitive effects
CNS hormonal imbalances
Hypothyroid/nodules
Cervical/shoulder syndrome
Carotid stenosis
Neuropathy/plexopathy
Pulmonary fibrosis
Coronary/vascular/valvular disease
Gastritis/colitis/ileitis
Proctitis
Cystitis
Vaginal stenosis
Benign skin conditions

Figure 6.1 Secondary non-cancer effects associated with radiation. Circles represent fields of radiation.
Immunotherapy

### Table 3. Relative Risk of Selected Severe (Grade 3) or Life-Threatening or Disabling (Grade 4) Health Conditions among Cancer Survivors, as Compared with Siblings.

<table>
<thead>
<tr>
<th>Condition</th>
<th>Survivors (N = 10,397)</th>
<th>Siblings (N = 3034)</th>
<th>Relative Risk (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Major joint replacement*</td>
<td>1.61 (0.03)</td>
<td>0.03</td>
<td>54.0 (7.6–386.3)</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>1.24 (0.10)</td>
<td>0.10</td>
<td>15.1 (4.8–47.9)</td>
</tr>
<tr>
<td>Second malignant neoplasm†</td>
<td>2.38 (0.33)</td>
<td>0.33</td>
<td>14.8 (7.2–30.4)</td>
</tr>
<tr>
<td>Cognitive dysfunction, severe</td>
<td>0.65 (0.10)</td>
<td>0.10</td>
<td>10.5 (2.6–43.0)</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>1.11 (0.20)</td>
<td>0.20</td>
<td>10.4 (4.1–25.9)</td>
</tr>
<tr>
<td>Cerebrovascular accident</td>
<td>1.56 (0.20)</td>
<td>0.20</td>
<td>9.3 (4.1–21.2)</td>
</tr>
<tr>
<td>Renal failure or dialysis</td>
<td>0.52 (0.07)</td>
<td>0.07</td>
<td>8.9 (2.2–36.6)</td>
</tr>
<tr>
<td>Hearing loss not corrected by aid</td>
<td>1.96 (0.36)</td>
<td>0.36</td>
<td>6.3 (3.3–11.8)</td>
</tr>
<tr>
<td>Legally blind or loss of an eye</td>
<td>2.92 (0.69)</td>
<td>0.69</td>
<td>5.8 (3.5–9.5)</td>
</tr>
<tr>
<td>Ovarian failure‡</td>
<td>2.79 (0.99)</td>
<td>0.99</td>
<td>3.5 (2.7–5.2)</td>
</tr>
</tbody>
</table>

* For survivors, major joint replacement was not included if it was part of cancer therapy.
† For both groups, this category excludes basal-cell and squamous-cell carcinoma (grade 2). For siblings, this category includes a first cancer.
‡ Values are for women only.
CENTRAL ILLUSTRATION: Overview of Clinical Practice in Childhood Cancer Survivors at Risk for Cardiotoxicity

- Childhood Cancer Treatment
  - Overall 5-Year Survival 83%

- 10.6%
  - Heart failure incidence within 40 years after cardiotoxic treatment

- Multivariable Risk Prediction
  - Cardiotoxic exposure
  - Cardiovascular risk factors
  - Genetics
  - Cardiac function

- Radiotherapy
- Mitoxantrone, anthracyclines
- Coronary artery disease
- Heart failure
- Pericardial disease
- Valvular disease
- Arrhythmia

- EARLY
- LATE
- Life-long risk

- Potential Primary Prevention
  - Dexrazoxane
  - Liposomal anthracyclines
  - Slow infusion

- Cardiac Surveillance and Management
  - Echocardiograms at least every 5 years
  - Electrocardiograms at follow-up initiation
  - Cardiovascular risk factor management

All Survivors at Age 45 (%)
- Coronary artery disease
- Heart failure
- Valvular disease
- Arrhythmia

Figure 1. ABCDEs to promote Cardiovascular Health in Cancer Survivors.
**Surveillance: Systems Based Approach**

**Evaluate symptoms/physical exam/educate!**

- **CNS**
  - Radiation
  - Chemotherapy
    - Consider imaging
- **Visual**
  - Radiation/prednisone
    - Regular eye examinations
- **Endocrine**
  - Radiation (CNS/thyroid)
    - Consider labs (TSH/FT4), cortisol, GH, thyroid US, DEXA
- **Pulmonary**
  - Radiation
  - Chemotherapy (bleomycin)
    - Consider PFTs, CXR, ?Lung CT
- **Cardiovascular**
  - Radiation
  - Chemotherapy (doxorubicin)
    - Echo, EKG, stress test, consider carotid US, lipids, manage risk factors

*Stem cell transplant – any/all of the effects based on pre-conditioning regimen*
Surveillance: Systems Based Approach

Evaluate symptoms/physical exam/educate!

- Gastrointestinal
  - Radiation
  - Chemotherapy (alkylators)
  - Consider EGD, early colonoscopy

- Hematologic
  - Chemotherapy (alkylators)
  - Yearly CBC to follow counts/MCV (?10 yrs)

- Genitourinary/renal
  - Radiation
  - Chemotherapy (alkylators)
  - Consider urinalysis, BMP, minerals

- Reproductive
  - Surgery
  - Chemotherapy (alkylators)
  - Consider labs (testosterone, LH/FSH, AMH), referral to reproductive endocrinology

*Stem cell transplant – any/all of the effects based on pre-conditioning regimen*
Surveillance: Systems Based Approach

Evaluate symptoms/physical exam/educate!

- Breasts
  - Radiation
  - Mammogram, MRI

- Neurological/CIPN
  - Chemotherapy
  - Radiation
  - Duloxetene, PT

- Muscular
  - Radiation
  - Surgery
  - Physical therapy, exercise program

- Psychological
  - Chemotherapy
  - Radiation
  - Surgery
  - Mental health evaluation, treatment, lifestyle

*Stem cell transplant – any/all of the effects based on pre-conditioning regimen*
### Surveillance: Systems Based Approach

**Evaluate symptoms/physical exam/educate!**

<table>
<thead>
<tr>
<th>Condition</th>
<th>Precaution/Specification</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sexual</td>
<td>- Surgery&lt;br&gt;- Chemotherapy&lt;br&gt;- Radiation</td>
</tr>
<tr>
<td></td>
<td>Referral to sexual therapy, mental health, specialized GYN</td>
</tr>
<tr>
<td>Dental</td>
<td>- Chemotherapy&lt;br&gt;- Radiation</td>
</tr>
<tr>
<td></td>
<td>Regular dental care</td>
</tr>
<tr>
<td>Dermatologic</td>
<td>- Radiation</td>
</tr>
<tr>
<td></td>
<td>Regular skin examination</td>
</tr>
<tr>
<td>Immunological</td>
<td>- Splenectomy&lt;br&gt;- Radiation, BMT</td>
</tr>
<tr>
<td></td>
<td>Vaccination, early treatment of infections</td>
</tr>
</tbody>
</table>

*Stem cell transplant – any/all of the effects based on pre-conditioning regimen*
Collaboration and Communication
Health Care Deja vu

So, what seems to be the trouble today?

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So, what seems to be the trouble today?

Oh for Pete's sake! Don't these people ever talk to one another?!
The expanding role of primary care in cancer control

The nature of cancer control is changing, with an increasing emphasis, fuelled by public and political demand, on prevention, early diagnosis, and patient experience during and after treatment. In the same time, primary care is increasingly promoted, by governments and health funders worldwide, as the preferred setting for most health care for reasons of increasing need, to mitigate health-care costs, and to accommodate patient preferences for care closer to home. It is timely, then, to consider how this expanding role for primary care can work for cancer control, which has long been dominated by highly technical interventions centred on treatment, and in which the contribution of primary care has been largely perceived as marginal. In this Commission, expert opinion from primary care and public health professionals with academic and clinical cancer experience—from epidemiologists, psychologists, policy-makers, and cancer specialists—has contributed to a detailed consideration of the evidence for cancer control provided in primary care and community care settings. Ranging from primary prevention to end-of-life care, the scope for new models of care is explored, and the actions needed to effect change are outlined. The strengths of primary care—its continuing, coordinated, and comprehensive care for individuals and families—are particularly evident in prevention and diagnosis, in shared follow-up and survivorship care, and in end-of-life care. A strong theme of integration of care runs throughout, and its elements (clinical, vertical, and functional) and the tools needed for integrated working are described in detail. All of this change, as it evolves, will need to be underpinned by new research and by continuing and shared professional development.
Primary and Cancer Specialists Relationship

- poor and delayed communication between PCPs and cancer specialists
- cancer specialists’ endorsement of a specialist-based model of care
- PCPs’ belief that they play an important role in the cancer care continuum
- PCPs’ willingness to participate in the cancer care continuum
- cancer specialists’ and PCPs’ uncertainty regarding the knowledge or training of the PCP to provide care, and
- discrepancies between PCPs and oncologists regarding roles and expectations
Possible Solutions

• Electronic medical records
• Use of standardized communication strategies
• Practicing in one healthcare delivery system
• Direct communication (i.e. telephone, email)
• Existing relationship

Thank you!

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