AYA & XYZ: Care of the Childhood Cancer Survivor & Adolescent/Young Adult Oncology

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DISCLOSURES

I have no relevant disclosures
OBJECTIVES

• Describe the health issues that affect adult survivors of childhood cancer
• Discuss appropriate follow up strategies for the general internist
• Discuss the unique considerations for Adolescent/Young Adult (AYA) patients with oncology diagnoses for the general internist and hospitalist
The Good News

Children with cancer are surviving into adulthood

- Acute lymphoblastic leukemia (cancer of the blood): 4% survival in 1962 vs. 94% in present.
- Hodgkin lymphoma (cancer of lymph system): 50% survival in 1962 vs. 95% in present.
- Non-Hodgkin lymphoma (cancer of infection fighting cells): 7% survival in 1962 vs. 80% in present.
- Retinoblastoma (cancer affecting eyes): 75% survival in 1962 vs. 95% in present.
- Neuroblastoma (tumor of peripheral nervous tissue): 10% survival in 1962 vs. 75% in present.
- Wilms tumor (kidney tumor): 50% survival in 1962 vs. 90% in present.
- Osteosarcoma (bone cancer): 20% survival in 1962 vs. 70% in present.
- Rhabdomyosarcoma (solid tumor of muscle cells): 30% survival in 1962 vs. 65% in present.
- Ewing sarcoma (a type of bone cancer): 5% survival in 1962 vs. 65% in present.
- Medulloblastoma (a type of brain tumor): 10% survival in 1962 vs. 85% in present.

* Cancer survival of five years or greater based on national averages from 2001-2007.
Childhood Cancer Diagnostic Groups, Ten-Year Actuarial Survival, Children (Aged 0-14), Great Britain, 1971-2005


More than 25% of adult survivors report at least one severe, life-threatening or disabling condition 25 years after treatment (compared to 5% in siblings of similar age).

As time from diagnosis increases, risk of recurrence plateaus but risk of late effects continues to increase.

Mechanism Causing Late Effects

Late Effects – What are they?

<table>
<thead>
<tr>
<th>Avascular Necrosis (AVN)</th>
<th>Male Reproductive Issues</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bone Health</td>
<td>Hepatitis</td>
</tr>
<tr>
<td>Osteoradionecrosis</td>
<td>Hyperprolactinemia</td>
</tr>
<tr>
<td>Breast Cancer</td>
<td>Hypopituitarism</td>
</tr>
<tr>
<td>Chronic Pain</td>
<td>Limb Salvage</td>
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<tr>
<td>Educational Issues</td>
<td>Managing Amputation</td>
</tr>
<tr>
<td>Emotional Health</td>
<td>Organs</td>
</tr>
<tr>
<td>Gastrointestinal System</td>
<td>Heart Problems</td>
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<tr>
<td>Hormones and Reproduction</td>
<td>Kidney Health</td>
</tr>
<tr>
<td>Central Adrenal Insufficiency</td>
<td>Lung (Pulmonary) Health</td>
</tr>
<tr>
<td>Early Puberty</td>
<td>Liver Health</td>
</tr>
<tr>
<td>Female Reproductive Issues</td>
<td>Spleen</td>
</tr>
<tr>
<td>Growth Hormone (GH) Deficiency;</td>
<td>Bladder Health</td>
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<tr>
<td></td>
<td>Neurogenic Bladder</td>
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<tr>
<td></td>
<td>Peripheral Neuropathy</td>
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<td></td>
<td>Raynaud’s Phenomenon</td>
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<td></td>
<td>Scoliosis and Kyphosis</td>
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<tr>
<td></td>
<td>Secondary Cancers</td>
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<tr>
<td></td>
<td>Colorectal Cancer</td>
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<tr>
<td></td>
<td>Sensory</td>
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<tr>
<td></td>
<td>Dental Health</td>
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<td></td>
<td>Eye Problems</td>
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<td></td>
<td>Hearing Problems</td>
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<tr>
<td></td>
<td>Skin Health</td>
</tr>
<tr>
<td></td>
<td>Thyroid Problems</td>
</tr>
</tbody>
</table>
Childhood Cancer Survivor Study (CCSS)

- Cohort study with 14370 survivors and 3737 sibling controls from 26 institutions diagnosed between 1970-1986
- Included those treated for leukemia, CNS tumors, Hodgkin’s lymphoma, Non-Hodgkin’s lymphoma, Wilm’s tumor, Neuroblastoma, soft tissue sarcomas, and bone tumors
- 25 years after treatment:
  - 27.5% of adult survivors report at least one severe, life-threatening, or disabling condition
  
  VS.

  5.2% of age matched siblings
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</td>
<td>0.03</td>
<td>54.0 (7.6–386.3)</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>1.24</td>
<td>0.10</td>
<td>15.1 (4.8–47.9)</td>
</tr>
<tr>
<td>Second malignant neoplasm†</td>
<td>2.38</td>
<td>0.33</td>
<td>14.8 (7.2–30.4)</td>
</tr>
<tr>
<td>Cognitive dysfunction, severe</td>
<td>0.65</td>
<td>0.10</td>
<td>10.5 (2.6–43.0)</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>1.11</td>
<td>0.20</td>
<td>10.4 (4.1–25.9)</td>
</tr>
<tr>
<td>Cerebrovascular accident</td>
<td>1.56</td>
<td>0.20</td>
<td>9.3 (4.1–21.2)</td>
</tr>
<tr>
<td>Renal failure or dialysis</td>
<td>0.52</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</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</td>
<td>0.69</td>
<td>5.8 (3.5–9.5)</td>
</tr>
<tr>
<td>Ovarian failure‡</td>
<td>2.79</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.
# Treatment Related Late Effects

<table>
<thead>
<tr>
<th>Chronic Condition</th>
<th>Treatment Exposures</th>
<th>AF</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coronary artery disease</td>
<td>Radiation to heart</td>
<td>57.1</td>
<td>36.3 to 71.0</td>
</tr>
<tr>
<td>Heart failure</td>
<td>Anthracyclines, radiation to heart</td>
<td>100.0</td>
<td>—</td>
</tr>
<tr>
<td>Hypertension</td>
<td>Ifosfamide, platinum, methotrexate, radiation to kidney, nephrectomy, radiation to HPA</td>
<td>9.3</td>
<td>-16.3 to 29.2</td>
</tr>
<tr>
<td>Cataracts</td>
<td>Busulfan, corticosteroids, radiation to eye</td>
<td>43.7</td>
<td>25.3 to 57.5</td>
</tr>
<tr>
<td>Osteoporosis</td>
<td>Methotrexate, corticosteroids, radiation to HPA</td>
<td>50.6</td>
<td>22.1 to 68.7</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>Radiation to HPA</td>
<td>41.7</td>
<td>12.2 to 61.3</td>
</tr>
<tr>
<td>Hypogonadism</td>
<td>Alkylating agents, radiation to reproductive system</td>
<td>98.3</td>
<td>91.2 to 98.6</td>
</tr>
<tr>
<td>Cognitive decline</td>
<td>Antimetabolites, cranial radiation, surgery</td>
<td>63.1</td>
<td>55.1 to 69.7</td>
</tr>
</tbody>
</table>

**NOTE.** AF represents the percentage of the cases in the St. Jude Lifetime Cohort Study related to a specific treatment exposure and is calculated as follows: (Absolute risk of the outcome in those with the listed treatment exposures – Absolute risk of the outcome in those without the treatment exposure)/(Absolute risk of the outcome in those with the treatment exposure) multiplied by 100.

Abbreviations: AF, attributable fraction; HPA, hypothalamic-pituitary axis.
Survivorship Brings Increased Risk of Chronic Health Conditions
Second Malignancies

- Leading cause of non-relapse death
- Cumulative incidence of up to 20% at 30 years following diagnosis
- Majority are solid tumors/sarcomas
  - Related to radiation exposure, especially younger age, increased dose
  - Risk increases over time after radiation exposure
- Treatment-related MDS/AML
  - Related to chemotherapy exposures
Solid Subsequent Malignant Neoplasms

Reprinted from International Journal of Radiation Oncology, Biology, Physics, 94, Inskip, et al, Radiation-Related New Primary Solid Cancers in the Childhood Cancer Survivor Study: Comparative Radiation Dose Response and Modification of Treatment Effects, 800-807, © 2016, with permission from Elsevier
Cardiovascular Late Effects

• Leading cause of non-oncologic death in survivors

• Congestive Heart Failure due to Cardiomyopathy
  • Dose-dependent risk after exposure to anthracycline chemotherapy
  • Slightly increased risk after chest XRT

• Coronary Artery Disease
  • Radiation therapy predisposes to ischemic heart disease
  • Higher risk with co-morbidities- hypertension, dyslipidemia, obesity

• Pericarditis, valvular heart disease, conduction abnormalities
I need HELP!!!

http://www.survivorshipguidelines.org/

Ask for a treatment summary from treating oncologist- includes cumulative doses, areas of radiation
Dexamethasone ➔ Avascular Necrosis

### CHEMOTHERAPY

<table>
<thead>
<tr>
<th>Section</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>32</td>
<td>Dexamethasone Doseplanse</td>
<td>Osteonecrosis (Avascular Necrosis)</td>
<td>Host Factors</td>
<td>Both genders are at risk; Host polymorphonuclear cells can cause increased risk.</td>
<td>Treatment Factors</td>
<td>Osteonecrosis radiation syndrome used before 1975 due to delivery of greater dose to skin and bones.</td>
</tr>
</tbody>
</table>

### CORTICOSTEROIDS (cont)

- MRI after symptom onset
- Yearly musculoskeletal exam
**Daunorubicin ➔ Cardiomyopathy**

<table>
<thead>
<tr>
<th>Age at Treatment*</th>
<th>Radiation with Potential Impact to the Heart§</th>
<th>Anthracycline Dose†</th>
<th>Recommended Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1 year old</td>
<td>Yes</td>
<td>Any</td>
<td>Every year</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>&lt;200 mg/m²</td>
<td>Every 2 years</td>
</tr>
<tr>
<td></td>
<td></td>
<td>≥200 mg/m²</td>
<td>Every year</td>
</tr>
<tr>
<td>1-4 years old</td>
<td>Yes</td>
<td>Any</td>
<td>Every year</td>
</tr>
<tr>
<td></td>
<td>&lt;100 mg/m²</td>
<td>Every 5 years</td>
<td></td>
</tr>
<tr>
<td></td>
<td>≥100 to &lt;300 mg/m²</td>
<td>Every 2 years</td>
<td></td>
</tr>
<tr>
<td></td>
<td>≥300 mg/m²</td>
<td>Every year</td>
<td></td>
</tr>
<tr>
<td>≥5 years old</td>
<td>Yes</td>
<td>&lt;300 mg/m²</td>
<td>Every 2 years</td>
</tr>
<tr>
<td></td>
<td>≥300 mg/m²</td>
<td>Every year</td>
<td></td>
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<td>≥200 to &lt;300 mg/m²</td>
<td>Every 2 years</td>
<td></td>
</tr>
<tr>
<td></td>
<td>≥300 mg/m²</td>
<td>Every year</td>
<td></td>
</tr>
<tr>
<td>Any age with decrease in serial function</td>
<td></td>
<td>Every year</td>
<td></td>
</tr>
</tbody>
</table>
Cyclophosphamide $\rightarrow$ hemorrhagic cystitis

Yearly urinalysis
How can we reduce late effects?

Change the therapy we give, or how we give it:
- Reduce therapies or replace toxic therapies (e.g. decrease amount of brain radiation)
- Use better technologies (e.g. new radiation approaches)

Detect late effects earlier to prevent progression (risk-based care, screening/surveillance)

Change lifestyle factors that contribute to late effects (e.g. diet, exercise, smoking, sunscreen, regular medical care)
When do you get a Mammogram?

If you have received radiation therapy to the chest at a dose of 20 Gy or higher, you should have a yearly mammogram and breast MRI starting at age:

A) 40
B) 25 or 8 years after you received radiation (whichever is last)
C) 10 years after the earliest relative to get diagnosed
When do you get a Mammogram?

If you have received radiation therapy to the chest at a dose of 20 Gy or higher, you should have a yearly mammogram and breast MRI starting at age:

A) 40

B) 25 or 8 years after you received radiation (whichever is last)

C) 10 years after the earliest relative to get diagnosed
Colon Cancer Screening

Radiation therapy to the abdomen, pelvis, or spine at doses of 30 Gy or higher during childhood, adolescences or young adulthood should have a colonoscopy:

A) Every 5 years starting at age of 35 or 10 years after radiation
B) Age 50
C) 10 years before age at which first degree relative
Colon Cancer Screening

Radiation therapy to the abdomen, pelvis, or spine at doses of 30 Gy or higher during childhood, adolesences or young adulthood should have a colonoscopy:

A) Every 5 years starting at age of 35 or 10 years after radiation
B) Age 50
C) 10 years before age at which first degree relative
Adolescent/Young Adult Oncology

National Cancer Institute: Adolescent/Young Adults (AYA) age 15-39 = vulnerable population
  ◦ Different biology/genetics of cancers
  ◦ Psychosocial needs
  ◦ Survivorship
  ◦ Survival differences

How do we approach and treat AYAs?
-> Different answer for different diseases

Bleyer et al. NCI SEER AYA Monograph 2006;
Adolescent/Young Adult Oncology

Clinical trial enrollment in the National Comprehensive Cancer Network

- 10% of 15 to 19-year-old patients
- 1-2% of 20 to 39-year-old patients

Single Pediatric Institution

- 92% of 0-4 year old patients
- 72% of 15-21 year old patients

Common Cancer Types in AYAs

Source: SEER 18, 2007-2011, ages 15-39

*includes testicular cancer
**excludes breast, cervical, colon and other less prevalent cancers
***includes malignant bone tumors and other less prevalent cancers
Relative survival rates are lower in AYAs for some diseases

Compared to younger patients

Compared to younger & older patients

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AYA Trends in CNS Tumors

Site of treatment associated with better outcomes in AYA population
AYA Trends in ALL (Acute Lymphoblastic Leukemia)

Pediatric regimen vs. adult regimen
25/25 pts- pediatric protocol achieved CR
19/22 pts- adult protocol achieved CR

OS at 3 years 80% peds group and 59% in adult group

EFS at 3 years 80% peds group and 45% in adult group

Increased intensity chemo well tolerated, no statistically significant increase in adverse events
Survival is not different but treatment related mortality much higher in AYA patients
AYA outcomes - Ewings Sarcoma

AYA M:F 1.8 (p <0.01)

Psychosocial stressors

- Educational/Employment Concerns
- Health Insurance
- Emotional Challenges
- Self-Esteem/Body Image
- Family Interactions
- Lack of Medical Home
- Desire for Autonomy
- Sexual Health
- Peer Relations
- Financial Concerns
- Risky Behaviors
- Fertility

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Questions?

Cancer Sucks

in every color
References


