Breakout Session: Adolescent and Young Adult Lymphoma

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THE UNIVERSITY OF CHICAGO MEDICINE Comer Children’s Hospital
Adolescent and Young Adult (AYA) Cancer

- NIH definition AYA: Cancer diagnosis between ages of 15 and 39 years
- Nearly 70,000 AYAs are diagnosed with cancer annually
  - Six times that of children 0-14 years of age

http://www.cancer.gov/research/progress/snapshots/adolescent-young-adult
Common AYA Cancers

(Dark blue = lymphomas)
Advances are slower in AYAs with Cancer

SEER Cancer Statistics, 1975-1997
The overall trends are seen for lymphoma

NCI and LiveStrong: 2006 Progress Review Group (PRG) Call to Action
What explains these outcome differences so we can address them?
WHY?
Multiple Areas to Consider

• Personal/Patient
• Family/community
• Societal
• Health professional
Why?

• Personal/Patient
  – Independence/Autonomy
    • Mobile/Period of transition
  – Lack of Awareness
  – Delays in Diagnosis
  – Compliance/Adherence
  – Health Insurance
  – Financial
  – Biology

CRITICAL MASS
THE YOUNG ADULT CANCER ALLIANCE

stupidcancer.org

WHO CARES
TEEN CANCER AMERICA

GIVE THE BIRD
TheCancerBird.com

i[2]y

ImTooYoungForThis.org
empowering young adults affected by cancer
Why?

• Family/Community
  – Lack of Awareness
  – Inadequate Resources

• Societal
  – Lack of Awareness
  – Health Insurance
  – Delays in Diagnosis
Why?

• Health Professional
  – Lack of Awareness
  – Delay in Diagnosis
  – Approach
    • Pediatric vs Adult
    • Communication
  – Clinical Trial Participation
  – Tumor Specimen Banking
    • Cellular/Molecular Mechanisms
  – Tolerance to therapy
  – Ability to relate to other patients in care facilities
Clinical trial participation by age at diagnosis

- **<15 years**: 90% are treated at center with NCI sponsored trials and 2/3 are enrolled on trial
  - Overall survival >80%
- **15 to 19 years**: 20-35% are treated at center with NCI trials and only 10% are enrolled on trials
- **20 to 39 years**: 1-2% are entered on NCI trials.

![Patients enrolled on CTEP-sponsored trials, 1997-2003](chart.png)
Does location of care matter?

- Patients 17-21 years have better outcomes on pediatric trials.

- Patients treated at NCI designated cancer centers have better outcomes.
What do AYA patients need?

- **Fertility preservation**
  - Discussion of risk
  - Referral to reproductive endocrinologist

- **Genetic testing**
  - Referral to genetic specialists

- **Clinical Trials**
  - Explore if possible with provider. [https://clinicaltrials.gov](https://clinicaltrials.gov)

- **Psychosocial issues**
  - Financial counselors
  - Counseling or group support

- **Survivorship**
  - Next part of discussion

Copies of Resource List are available
Our understanding of AYA cancer survivorship is informed by childhood and AYA survivors diagnosed with their cancer before the age of 21 years.
The Childhood and Adolescent Cancer Success Story

- 1960's: ~10%
- 2015: >80%

5-Year Survival (%)

1975-77
1978-80
1981-83
1984-86
1987-89
1990-92
1993-95
1996-98
1999-01
2002-05
2006-12

• Laboratory discovery
• More intense therapy
• Clinical trials
• Supportive care
• New therapies
  - Stem cell transplant
  - Targeted agents
  - Immunotherapy

SEER Cancer Statistics, 1975-2011
Chronic Health Issues in Cancer Survivors

Based on survivors treated between 1970-1986 in the North American Childhood Cancer Survivor Study:

• By 30 years after their cancer:
  • 3/4 have at least one chronic health condition
  • 2/5 have a severe or life threatening condition

• 8 times more likely to have a severe or life threatening health condition than their siblings

Oeffinger, NEJM, 2006
Armstrong, J Clin Oncol, 2009
## Late Effects: Physical

<table>
<thead>
<tr>
<th>Growth and Development</th>
<th>Organ Function</th>
<th>Cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Linear growth</td>
<td>Cardiac</td>
<td>Recurrent (primary)</td>
</tr>
<tr>
<td>Skeletal maturation</td>
<td>Pulmonary</td>
<td>Second cancers</td>
</tr>
<tr>
<td>Intellectual function</td>
<td>Endocrine</td>
<td></td>
</tr>
<tr>
<td>Emotional/social maturation</td>
<td>GI/Hepatic</td>
<td></td>
</tr>
<tr>
<td>Sexual development</td>
<td>Genitourinary</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Musculoskeletal</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Neurocognitive</td>
<td></td>
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<tr>
<td></td>
<td>Neurologic</td>
<td></td>
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<tr>
<td></td>
<td>Neurosensory</td>
<td></td>
</tr>
<tr>
<td>Fertility and Reproduction</td>
<td></td>
<td></td>
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<tr>
<td>Sexual functioning</td>
<td></td>
<td></td>
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<tr>
<td>Fertility</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Health of offspring</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### Late Effects: Psychosocial

<table>
<thead>
<tr>
<th>Mental Health</th>
<th>Education/Vocation</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Depression/mood disorders</td>
<td>- Academic underachievement</td>
</tr>
<tr>
<td>- Cancer-related anxiety</td>
<td>- Vocational limitations</td>
</tr>
<tr>
<td>- Post-traumatic stress</td>
<td>- Under/unemployment</td>
</tr>
<tr>
<td><strong>Physical/Body image</strong></td>
<td>- Loss of job/benefits</td>
</tr>
<tr>
<td>- Weight loss/gain</td>
<td><strong>Insurance discrimination</strong></td>
</tr>
<tr>
<td>- Loss of organs/tissues</td>
<td>- Access to health care</td>
</tr>
<tr>
<td><strong>Chronic Symptoms</strong></td>
<td><strong>Financial/economic</strong></td>
</tr>
<tr>
<td>- Fatigue/ Low energy</td>
<td>- Debt (medical/other)</td>
</tr>
<tr>
<td>- Disrupted sleep</td>
<td></td>
</tr>
<tr>
<td>- Poor memory/concentration</td>
<td><strong>Social Interaction</strong></td>
</tr>
<tr>
<td>- Chronic pain</td>
<td>- Family/peer relationships</td>
</tr>
<tr>
<td><strong>Self-care</strong></td>
<td>- Social withdrawal/isolation</td>
</tr>
<tr>
<td>- Independent living</td>
<td>- Intimacy/marriage/family</td>
</tr>
<tr>
<td></td>
<td>- Cancer-related stigma</td>
</tr>
</tbody>
</table>

**In summary:**

- Chronic Symptoms
- Education/Vocation
- Mental Health
- Physical/Body image
- Social Interaction
- Self-care
- Social Interaction
What contributes to late effects after cancer?

Late Effect Risk

Host Factors
- Age
- Gender
- Race

Premorbid conditions

Treatment Factors
- Surgery
- Chemotherapy
- Radiation therapy

Genetic
- BRCA, ATM, p53 polymorphisms

Tumor Factors
- Histology
- Site
- Biology
- Response

Health Behaviors
- Tobacco
- Diet
- Alcohol
- Exercise
- Sun

Aging

Treatment Events

Hudson, Cancer 2005
Cancer Survivorship: A New Chronic Disease Paradigm

- Distinct from classic chronic disease
- Once cured, often no signs of sequelae for often years or decades
- Traditional chronic disease model inadequate to describe evolution of health issues in survivors
How do we ensure that the health care of AYA cancer survivors is maximized..... so health risks are minimized and quality of life is optimal?
Institute of Medicine Call To Action

2003 Recommendations:

• Risk-based health care
• Monitor for cancer recurrence
• Surveillance and intervention for late effects and second cancers
• Prevention/education
  • Lifestyles, health behaviors
  • Education
  • Assistance with financial challenges
Children’s Oncology Group

Long-Term Follow-Up Guidelines
for Survivors of Childhood, Adolescent, and Young Adult Cancer

- 166 sections detailing exposure-based potential late effects and screening recommendations
- Grading of evidence linking exposure to potential late effect
- Second (adult) cancer screening recommendations for standard and high risk groups
- Health Links for patient education
An illustrative example of an AYA cancer related late effect that requires life-long risk based health care to minimize morbidity and mortality.
Case:

- J.N. is a 33 yo female who was diagnosed with Stage IIA nodular Hodgkin lymphoma in March 1990 at age 16.
- She was treated with 3900 Gy mantle radiation at the University of Chicago (UC).
- She received no chemotherapy.
- In October 2008, she developed shoulder pain. She went to her PMD who did an x-ray of the shoulder. X-ray showed a mass in breast.
- She was referred to UC, where she had a mammogram and biopsy which revealed stage I breast cancer.
- She was treated with bilateral mastectomy and tamoxifen for 5 years.
Breast Cancer Risk:
Childhood Cancer Survivor Study (CCSS)

Cumulative Risk

Age (years)

Breast Cancer Risk
Radiation Dose and Volume

Will early screening help?

- Median age is young
- Interval from radiation to breast cancer is often short (10-20 yrs)
- 5-yr survival strongly associated with stage at diagnosis (women with early stage disease have good outcomes)

Children’s Oncology Group

www.survivorshipguidelines.org

Annual mammogram and breast MRI
Starting at the age of 25 or 8 yrs after exposure to chest radiotherapy (> 20 Gy).

Are survivors receiving risk-based health care, such as early breast cancer screening for women exposed to chest radiation for an AYA lymphoma?
Where are adult survivors of childhood and AYA cancer getting their care?


- Cancer center: 14.6%
- Primary care facility: 85.4%
Cancer Center Visits and Development of Chronic Health Conditions

The rate of follow up for health care at cancer centers decreases with time from cancer diagnosis.

Development of late effects increases with time from cancer diagnosis.

Are survivors receiving exposure-specific surveillance based on available guidelines?
### Screening in survivors at average risk for SMN (USPSTF)

<table>
<thead>
<tr>
<th>Breast</th>
<th>Cervix</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mammography every 1 to 2 years for</td>
<td>Papanicolaou smear every 3 y starting at age</td>
</tr>
<tr>
<td>women aged ≥40 y</td>
<td>21 y</td>
</tr>
</tbody>
</table>

### Surveillance in survivors at high risk for SMN (COG)

<table>
<thead>
<tr>
<th>Breast</th>
<th>Colorectal</th>
<th>Skin</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥20 Gy radiation therapy to the chest</td>
<td>≥30 Gy radiation therapy to the abdomen, pelvis, or spine</td>
<td>Any radiation therapy</td>
</tr>
<tr>
<td>Annual mammography starting 8 y after radiation or age 25 y, whichever is last</td>
<td>Colonoscopy every 5 y starting at age 35 y</td>
<td>Annual dermatologic examination of irradiated areas</td>
</tr>
</tbody>
</table>
Compliance with recommended surveillance tests: average risk

Compliance with recommended surveillance tests: high-risk

Observation

• Survivors adherent to population-based screening, not with treatment exposure based, high-risk surveillance

• Lack of knowledge not lack of motivation
  – Predictor of breast cancer screening in women exposed to chest radiotherapy: physician recommendation (JAMA 2010)
Are physicians aware of IOM recommendations and available long-term follow up guidelines for childhood cancer survivors?
C.L. is a 29 year old female patient treated for Hodgkin lymphoma when she was 16 years old.

She received combination chemotherapy (including Adriamycin 150 mg/m² and Cyclophosphamide 15 g/m²) and mantle radiation (25 Gy).

Questions regarding:
- Cardiac screening
- Thyroid function
- Breast cancer screening

Henderson et al, J Clin Oncol 2010
Nathan et al, Journal of Cancer Survivorship 2013
Suh et al, Ann Intern Med 2014
Physician Knowledge of Guidelines

% concordance

Breast
Cardiac
Thyroid
All

Ped-Oncologists
Family Physicians
Gen. Internists

N=1159
N=1124
N=1110
How do we overcome barriers to survivors receiving risk-based health care?

Problems

Solutions
Address physician barriers

• Primary care physician identified needs
  (Suh et al. *Ann Intern Med* 2014)
  – Treatment summary/letter from treating oncologist
  – Access to surveillance guidelines
  – Contact with cancer center

Earlier integration of oncology and primary care in the cancer care continuum?
Institute of Medicine Call To Action

2005 Recommendations:
• Survivorship Care Plan for all cancer survivors
  • Roadmap for post-treatment care
  • Created by oncology provider
  • For survivor, primary care providers
How does the understanding of long-term outcomes of cancer survivors impact cancer treatments?
We are doing better with modern therapies.

- Risk stratification of therapy
  - Identify low risk patients and reduce therapies
    - Hodgkin lymphoma
    - ALL
- Improvements in:
  - Screening and early detection of late effects
  - Treatment of late effects
  - Supportive care

1970s
10.7% (10.1 - 11.4)
1980s
7.9% (7.4 - 8.3)
1990s
5.8% (5.4 - 6.3)

Armstrong NEJM 2016.
How oncology programs help AYA cancer patients and their families to ensure optimal outcomes and continue to address the PRG and recent ASCO recommendations?
The University of Chicago
AYA Model

• Idea born from debate in the hospital hallways over the "best" way to treat leukemia in young adults.

• Seamless care from diagnosis through survivorship.

• Joint initiative between pediatric and medical oncology.

James Nachman, MD
1949-2011

Wendy Stock, MD
The University of Chicago
AYA Model

• Clinic initiated in August 2012
  – Cancer survivors throughout the lifespan diagnosed with cancer <39 yr.
  – Clinic located in pediatric hospital.

• Support staff
  – Psychology
  – Social work (adult and pediatric)
  – Genetic counselor
  – Physical therapy
  – Research nurse
  – Clinical research associate
AYA Program Expansion

- New patients diagnosed prior to age 40 yr.
- Phase I and Solid Tumor focus
  - Ami Desai, MD
- Teen Cancer America Grant in May 2016.
  - Dedicated AYA space adjacent to pediatric clinics.
  - Dedicated AYA Program Manager.
  - Dedicated Psychology Post-Doc to provide counseling.
Summary

• AYAs with cancer are a population with unique needs that need to be addressed to ensure the best outcomes.
  – Diagnosis through long-term survivorship
  – Consider ASCO Resource List

• Research across the cancer care continuum imperative to improve these outcomes.
  – Continue to understand long term outcomes of AYA cancer survivors
    • New therapies – what are the risks associated with them.
  – Identify factors associated with disparate outcomes in the AYA population: biology, treatments, treatment location and supports?

• Building interdisciplinary AYA cancer clinical and research programs are an essential step to providing optimal AYA care.
Thank you!