The Late Effects, Assessment & Follow-up (LEAF) Clinic
Conflicts of Interest

- None
- No disclosures to make
Objectives

• Consider
  • The definition of late effects
    • Etiology and incidence of chronic health problems in adult childhood cancer survivors (ACCS)
  • Nature
    • Physical
      • Organ function
      • Second cancers
    • Psychological
  • Factors which determine the severity of late effects
  • Current international recommendations regarding screening and prevention
  • The function of the new LEAF clinic
    • Who works in the clinic and what our roles are
    • How to contact us and refer patients
Published in 1978
Survival Rates

Childhood cancer survival

Proportion surviving after 2 years [%]

Year of Diagnosis

- M. Hodgkin
- Wilms Tumour
- Acute lymphoblastic Leukemia
- Non-Hodgkin Lymphoma
- Ewing Sarcoma
- Osteosarcoma
- Rhabdomyosarcoma
- Malignant Germ Cell Tumours
- Neuroblastoma
- Brain Tumours
- Acute myeloid Leukemia

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U.S. Mortality and Survival Rates

Figure 3. Trends in Pediatric Cancer Mortality Rates by Site, Ages 0-19, 1975-2010

Table 4. Pediatric Cancer Five-year Observed Survival Rates for Two Time Periods, Ages 0-19

<table>
<thead>
<tr>
<th>Year of Diagnosis</th>
<th>1975-79</th>
<th>2003-09*</th>
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<tbody>
<tr>
<td>All ICCC sites</td>
<td>63</td>
<td>83</td>
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<tr>
<td>Leukemia</td>
<td>48</td>
<td>84</td>
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<tr>
<td>Acute lymphocytic leukemia</td>
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<td>90</td>
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<tr>
<td>Acute myeloid leukemia</td>
<td>21</td>
<td>64</td>
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<tr>
<td>Lymphomas and reticuloendothelial neoplasms</td>
<td>72</td>
<td>91</td>
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<tr>
<td>Hodgkin lymphoma</td>
<td>87</td>
<td>97</td>
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<tr>
<td>Non-Hodgkin lymphoma</td>
<td>47</td>
<td>85</td>
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<tr>
<td>Brain and CNS</td>
<td>59</td>
<td>75</td>
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<tr>
<td>Ependymoma</td>
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<td>81</td>
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<td>Medulloblastoma</td>
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<td>Neuroblastoma and ganglioneuroblastoma</td>
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<td>Retinoblastoma</td>
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<td>99</td>
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<td>Wilms tumor</td>
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<tr>
<td>Bone tumors</td>
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<td>73</td>
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<tr>
<td>Osteosarcoma</td>
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<td>71</td>
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<tr>
<td>Ewing sarcoma</td>
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<tr>
<td>Rhabdomyosarcoma</td>
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<td>64</td>
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<tr>
<td>Testicular germ cell tumors</td>
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<tr>
<td>Ovarian germ cell tumors</td>
<td>75</td>
<td>94</td>
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<tr>
<td>Thyroid carcinoma</td>
<td>99</td>
<td>98</td>
</tr>
<tr>
<td>Melanoma</td>
<td>83</td>
<td>95</td>
</tr>
</tbody>
</table>

ONS = Other nervous system.

Note: Lines are fitted trends based on Joinpoint analyses.

Average annual percent change (APC) for cancers with significant trends during most recent period: ALL (-3.1 during 1988-2010), brain (-1.1 during 1975-2010), NHL (-4.1 during 1975-2010), soft tissue (-1.0 during 1979-2010), kidney (-1.2 during 1992-2010), HL (-4.9 during 1975-2010).

Source: National Center for Health Statistics, Centers for Disease Control and Prevention.

American Cancer Society, Surveillance Research, 2014
Incidence

- About 12,000 children in the US (between birth and 14 years of age) develop childhood cancer each year
- In Canada:
  - 1310 patients diagnosed with cancer between the ages of 0 and 19 per year
- 83% of these children will be long term survivors who have been cured of their disease
- 20 to 30 years ago many children with cancer did not survive
  - In 1950s less than 10% of childhood cancers were cured
- Improvements due to:
  - Multimodality Rx
  - Therapy intensification
- **In 2014 - estimated that 1: 530 of the adult population (ages 20 to 39) in North America was a survivor of childhood cancer**
- In 2013 - 400,000 childhood cancer survivors in US
Survivorship

• **Cancer survivor:**
  • One who remains alive and continues to function during and after overcoming a serious hardship or life-threatening disease.
  • In cancer, a person is considered to be a survivor from the time of diagnosis until the end of life.

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*Survivorship*

There are millions of people in the United States who are cancer survivors. Many say that they felt they had lots of support during their treatment, but once it ended, it was hard to make a transition to a new way of life. It was like entering a whole new world where they had to adjust to new feelings, new problems and different ways of looking at the world.

*A New Normal*

Adjusting to physical and emotional changes after cancer treatment and tips on coping with fear of recurrence.
In memoriam
Ellen Stovall
1946-2016
Survivorship
Late Effects

• Definition:
  • “Side effects that occur more than 5 years after diagnosis”

• Problems with definition:
  • Etoposide related AML (short latency)

• Generally takes many years for late effects to develop

• How are these problems detected?
  • Follow up
    • Surveillance programs
Improvement related to:

- Multimodality approach:
  - Surgery
  - Systemic therapy (chemotherapy)
  - Radiation therapy
- Therapy intensification
  - Bone marrow transplant
  - Interval compression of chemotherapy
- Better supportive care during therapy
- Development of new targeted therapeutic agents
Late Effects

• Late effects include:
  • Physical problems
    • Organ damage
      • Development affected
      • High risk of late effects in adults treated for childhood cancer
    • Secondary tumors
  • Psychological problems
    • Depression, anxiety
Late Effects

Clinical Ascertainment of Health Outcomes Among Adults Treated for Childhood Cancer

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Kirsten K. Ness, PT, PhD  
James G. Gurney, PhD  
Daniel A. Mulrooney, MD, MS  
Wassim Chemaitilly, MD  
Kevin R. Krull, PhD  
Daniel M. Green, MD  
Gregory T. Armstrong, MD, MSCE  
Kerri A. Nottage, MD  
Kendra E. Jones, MS  
Charles A. Sklar, MD  
Deo Kumar Srivastava, PhD  
Leslie L. Robison, PhD

**Importance** Adult survivors of childhood cancer are known to be at risk for treatment-related adverse health outcomes. A large population of survivors has not been evaluated using a comprehensive systematic clinical assessment to determine the prevalence of chronic health conditions.

**Objective** To determine the prevalence of adverse health outcomes and the proportion associated with treatment-related exposures in a large cohort of adult survivors of childhood cancer.

**Design, Setting, and Participants** Presence of health outcomes was ascertained using systematic exposure–based medical assessments among 1713 adult (median age, 32 [range, 18–60] years) survivors of childhood cancer (median time from diagnosis, 25 [range, 10–47] years) enrolled in the St Jude Lifetime Cohort Study since October 1, 2007, and undergoing follow-up through October 31, 2012.

**Main Outcomes and Measures** Age-specific cumulative prevalence of adverse outcomes by organ system.

**Results** Using clinical criteria, the crude prevalence of adverse health outcomes was highest for pulmonary (abnormal pulmonary function, 65.2% [95% CI, 60.4%–69.8%]), auditory (hearing loss, 62.1% [95% CI, 55.8%–68.2%]), endocrine or reproductive (any endocrine condition, such as hypothalamic-pituitary axis disorders and male germ cell dysfunction, 62.0% [95% CI, 59.5%–64.6%]), cardiac (any cardiac condition, such as heart valve disorders, 56.4% [95% CI, 53.5%–59.2%]), and neurocognitive (neurocognitive impairment, 48.0% [95% CI, 44.9%–51.0%]) function.
Late Effects

- At age 45 years:
  - 95.5% cumulative prevalence of any chronic health condition
  - 80.5% (95% CI, 73.0%-86.6%) for a serious/disabling or life-threatening chronic condition
Survivors at Risk

Researchers followed more than 1,700 adults who had been treated for cancer as children and found that those who had received certain types of treatment were very likely to develop certain health problems later in life.

Adult condition: Breast cancer
Childhood treatment: Radiation to the breast (females only)

Heart-valve disorder
Radiation to the heart

Pituitary dysfunction
Radiation to the hypothalamus-pituitary

Hearing loss
Radiation to the ear or exposure to cisplatin or carboplatin

Sources: St. Jude Children’s Research Hospital; JAMA
The Wall Street Journal
Aging and Risk of Late Effects

- ACCS who reached age 35 years without a previous grade 3 or 4 condition
  - 25.9% experienced a subsequent grade 3 to 5 health condition within next 10 years
Causes of LEs

• Tumor related
• Patient related
  • Genetic factors
• Treatment related
  • Surgery
  • Chemotherapy
  • Radiation therapy
Tumor Related Damage

- Invasion into and pressure on different structures
  - Wilms tumor
    - One kidney usually completely destroyed by disease and has to be removed
Tumor Related Damage

- **Craniopharyngioma** tumor growth and cyst expansion leads to compression of:
  - Optic apparatus
    - Blindness
  - Pituitary
    - Endocrinopathy
Surgery Related Damage

- Surgery
  - Prime modality for local control
- Lymph node dissection
  - Lymphedema
- **Splenectomy**
  - Life threatening infection
    - Pneumococcal vaccine
    - Medic Alert bracelet
Chemotherapy Related Damage

- Chemotherapy prime modality for systemic control
- Depends on agent and sensitivity of target organs
  - Adriamycin: Cardiomyopathy
  - Cisplatin: Nephrotoxicity and hearing loss
  - Alkylating agents: Infertility and second cancers
  - Vincristine: Peripheral neuropathy
  - Bleomycin: Pulmonary fibrosis
Radiation Therapy (RT)

- In children (unlike adults) affects normal growth/development
- Severity of late effects depends on:
  - Age at the time of therapy
  - Total dose given
  - Fractionation
  - Region treated:
    - Some organs more sensitive and easily damaged
    - Amount of normal tissue treated
  - Concurrent chemotherapy can sensitize normal tissues
  - Underlying genetic problems:
    - Ataxia-telangectasia
    - Radio-genomics
Organs at Risk

- Central nervous system
- Orbit
- Hearing
- Peripheral Nervous system
- Endocrine
- GU system
- Respiratory
- Gastro-intestinal
- Musculoskeletal
- Reproductive organs
- Cardiovascular
- Skin
CNS

- Brain
  - Developmental delay
    - Poor short term memory
    - Poor executive function
  - Seizures
  - Cerebrovascular events
    - Vascular malformations
    - Early aging of small blood vessels
    - Thrombotic and haemorrhagic
- Spinal cord
  - Myelitis
- Hearing loss
- Visual loss
CNS: Brain Tumors

• Long-term cognitive function in pediatric brain tumor patients
  • Expect a 10 to 20-point decline in age-adjusted intelligence quotient (IQ) scores compared to the population norms within the first 5 to 10 years
  • Depends on:
    • Age at the time of RT
    • RT volume of irradiated brain
    • RT Dose
    • VP shunt
Eye

• Ocular complications common
  • Cranial nerve palsies
  • Glucocorticoid Rx
    • Cataracts
  • High dose RT:
    • Anterior chamber damage
    • Acute glaucoma
    • Painful red eye
    • Treated by enucleation
  • Low dose RT:
    • Cataracts

Ocular Late Effects in Childhood and Adolescent Cancer Survivors: A Report from the Childhood Cancer Survivor Study

Hearing Loss

- **Radiation Therapy:**
  - Conductive: wax build up
  - Sensorineural (SNHL): direct damage to cochlea
    - SNHL (JCO study) present in 14% of pediatric brain tumor survivors
    - 12% needed hearing aids
    - Continued to deteriorate over time

- **Chemotherapy:**
  - Sensorineural
  - Cisplatin causes high frequency hearing loss
    - Sensory hair cells in the cochlea

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*Hearing Loss in Patients Who Received Cranial Radiation Therapy for Childhood Cancer*

Johnnie K. Bass, Chia-Ho Hua, Jie Huang, Arzu Onar-Thomas, Kirsten K. Ness, Skye Jones, Stephanie White, Shaurn P. Bhagat...
Bone Mineral Density

- Osteopenia common in adult survivors of childhood cancer
  - 45% in one large retrospective study
- Increased risk associated with
  - Intensive systemic chemotherapy
  - TBI as part of transplant preparative regimen
  - RT to spine (osteopenia especially severe within RT field)
  - Steroid therapy
  - Early menopause in female survivors
  - Reduced physical activity

Bone mineral density after childhood cancer in 346 long-term adult survivors of childhood cancer

Authors

Musculoskeletal

- Bone/Muscle/soft tissues
  - “Hypoplasia” – reduced growth within the RT field
Musculoskeletal
Dental Late Effects

- **Chemotherapy:**
  - Root and enamel development if given early in life

- **Radiation therapy to mouth**
  - Dental development
  - Trismus
  - Xerostomia
  - Dental decay
  - Osteoradionecrosis
    - After high dose RT
    - Then dental extraction
    - May need hyperbaric O2

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A systematic review of dental late effects in survivors of childhood cancer

Prasad L. Gawade PhD, Melissa M. Hudson MD, Sue C. Kaste DO,
Joseph P. Neglia MD, MPH, Louis S. Constine MD, Leslie L. Robison PhD,
Kirsten K. Ness PT, PhD

First published: 1 November 2013  
DOI: 10.1002/jpc.24842
Facial Hypoplasia

- **Lucy Grealy** “Autobiography of a face”
Musculoskeletal

• Bone/Muscle/soft tissues
  • Hypoplasia – reduced growth within the RT field
  • Endocrinopathy
Endocrinopathy

- Common
  - >50% of ACSS
- CCSS study:
  - 14,290 childhood cancer survivors (median 6 yrs post therapy)
  - Risk of endocrinopathy in survivors increased substantially over time
- Types of endocrinopathy
  - Pituitary dysfunction
    - GH, TSH, FSH & LH, ACTH
  - Thyroid damage
    - Primary Hypothyroidism, hyperthyroidism & thyroid nodules
  - Diabetes
  - Gonadal dysfunction
Metabolic Syndrome

• Associated with treatment for childhood cancer
• Cranial RT, TBI and abdominal RT significantly increase the risk

Etiology
• Poorly understood post chemotherapy alone
• Radiation therapy:
  • Hypothalamic effect
  • Radiation therapy to pancreas

• Characterized by:
  • Central obesity
  • Hypertension
  • Hyperlipidemia
  • Diabetes


Obesity and Metabolic Disease After Childhood Cancer.
Barnea D, Raghunathan N, Friedman DN, Tonorezos ES.
Immune Dysfunction

- Intensive chemotherapy
  - Loss of vaccine related immunity
    - Pre-existing humoral immunity against measles, mumps, rubella, and VZV after completion of chemotherapy.
  - Need post-chemotherapy revaccination in childhood cancer survivors.


**Differential loss of humoral immunity against measles, mumps, rubella and varicella-zoster virus in children treated for cancer.**

Bochennek K1, Allwinn R2, Langer R1, Becker M1, Koppier OT2, Kingebiel T1, Lehnbacher T3.
Asplenism

- No functioning spleen
  - Surgery
  - Radiation therapy to left flank or abdomen
## Asplenism

### Anatomic or Functional Asplenia

<table>
<thead>
<tr>
<th>Vaccines</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Recommended vaccines for those with anatomic or functional asplenia</strong>&lt;sup&gt;A, B&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>All routine inactivated vaccines</td>
<td>Immunize according to routine schedule.</td>
</tr>
<tr>
<td>Hib vaccine</td>
<td>All individuals 5 years of age and older require 1 dose regardless of immunization history. &lt;sup&gt;C&lt;/sup&gt;</td>
</tr>
<tr>
<td>Meningococcal quadrivalent conjugate vaccine</td>
<td>Meningococcal quadrivalent conjugate vaccine for those 2 months of age and older. (This vaccine to be given in place of meningococcal C conjugate vaccine in the routine childhood immunization schedule). Reinforcement dose(s) are recommended. &lt;sup&gt;D&lt;/sup&gt;</td>
</tr>
<tr>
<td>Pneumococcal vaccine</td>
<td>Conjugate and/or polysaccharide vaccine depending on age. Requires once only revaccination with polysaccharide vaccine.</td>
</tr>
<tr>
<td>Influenza vaccine</td>
<td>Immunize yearly (all those 6 months of age and older). Inactivated influenza vaccine should be used.</td>
</tr>
<tr>
<td>MMR vaccine&lt;sup&gt;E&lt;/sup&gt;</td>
<td>Refer to <a href="#">Immunization with Inactivated and Live Vaccines</a>. Use <a href="#">Referral Form for MMR Vaccination</a>.</td>
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<td>Varicella vaccine&lt;sup&gt;E&lt;/sup&gt;</td>
<td>Refer to <a href="#">Immunization with Inactivated and Live Vaccines</a>. Use <a href="#">Referral Form for Varicella Vaccination</a>. Separate doses by 12 weeks.</td>
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<td>Rotavirus vaccine</td>
<td>Refer to <a href="#">Immunization with Inactivated and Live Vaccines</a>. Use <a href="#">Referral Form for Rotavirus Vaccination</a>.</td>
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</table>
Cardiovascular Disease in Adult Survivors of Childhood Cancer

- **Etiology: Adriamycin and RT**
  - Adriamycin:
    - Dose related cardiomyopathy
  - Mediastinal RT for Hodgkin lymphoma (HL): 5% of patients have symptomatic heart disease 10 years later
    - Cardiomyopathy
    - Coronary artery disease
    - Pericarditis
    - Valvular disease
    - Conduction system problems
      - AV and bundle branch block
  - Neck RT: Vascular problems
    - Carotid artery disease
- Hypertension
GU/Renal disease

- Kidneys especially vulnerable
  - Chemotherapy
    - Cisplatin
      - Magnesium-wasting tubulopathy
    - Ifosfamide
      - Proximal tubular dysfunction and less frequently decreased GFR
    - Methotrexate
      - Acute renal dysfunction
  - Radiation therapy:
    - Doses greater than 20 Gy result in significant nephropathy
  - Surgery
    - Reduction in renal tissue
- Hypertension

Renal Late Effects in Patients Treated for Cancer in Childhood: A Report from the Children’s Oncology Group

Deborah P. Jones, M.D., Professor of Pediatrics, Shen L. Spunt, M.D., Associate Member, Daniel Green, M.D., Member, and James E. Springate, M.D.
Pulmonary disease

- Lungs very sensitive to both radiation therapy and chemotherapy
- Bleomycin:
  - Intra-alveolar exudates with subsequent organization
  - Hyaline membrane formation
  - Interstitial fibrosis
  - Atypical proliferation of alveolar cells
- Radiation therapy:
  - Lung inflammation (pneumonitis)
  - Chest wall deformity – restrictive defect
Chest wall deformity:
GI disease

- Intestines very sensitive to radiation therapy:
  - Malabsorption
  - Strictures
  - Adhesions and obstruction
  - Fistula
- Previous surgery increases risk
Reproductive System

- Gonads very sensitive to both RT and chemotherapy
  - Alkylating agents
  - RT to ovaries:
    - The dose of RT needed to destroy 50% of the oocytes = LD50
    - Oocytes are very sensitive with an LD50 of < 200 cGy
- Damage to developing uterus
Reproductive System

- Male infertility
- Major factors decreasing the likelihood of a cancer survivor achieving a pregnancy (Childhood Cancer Survivor Study (CCSS) 2009)
  - Radiation therapy to testes of > 7.5 Gy
  - Cumulative alkylating agent dose score of ≥2
  - Treatment with procarbazine
  - Treatment with high doses of cyclophosphamide

Reduced male fertility in childhood cancer survivors

Sun Hee Lee, MD\textsuperscript{1} and Choong Ho Shin, MD, PhD\textsuperscript{2}

Author information ➤, Article notes ➤, Copyright and License information ➤
Second Cancers

- A second cancer or second malignant neoplasm (SMN) is defined as a histologically distinct second cancer that develops after the first.

- Definition: (ICD-O)
  - Tumor in new location and not from direct spread or metastasis of the primary cancer
  - Tumor in the same location as the primary cancer but of different histological type
SMN Causes

- Factors associated with a risk of second neoplasm
  - Patient related
  - Disease related
  - Treatment related
SMN Causes

- Patient related:
  - Age
    - Increased risk if young at diagnosis
    - Time since Rx
  - Lifestyle and environment
    - Smoking
  - Underlying genetic condition
    - Clearly defined:
      - Bilateral retinoblastoma
      - NF1
      - Li-Fraumeni
        - Germ line mutation in tumor suppressor genes
    - More complex genetic factors
      - Radiogenomics
SMN Causes

- Disease related:
  - Hodgkin lymphoma
  - Ewing sarcoma
- Therapy related:
  - Chemotherapy alone
    - Alkylating agents
    - VP-16
  - Radiation therapy (RT)
  - Combined RT and chemotherapy
SMN Causes

- Proposed mechanisms for RT induced SMN:
  - DNA damage and gene mutations:
    - Rearrangements within the genome place proto-oncogenes within regions with high rates of translation
    - Double strand DNA breaks and imperfect repair
    - Tumour suppressor gene deactivation
  - Radiation-induced genomic instability
  - Telomere shortening observed in response to intensive chemotherapy and/or ionizing radiation exposure.
    - Less telomere content associated with treatment-related SMN in childhood cancer survivors.
SMN Incidence

• Significant long term risk for any child who has RT
  • 8-10% risk of second malignancies within 20 years
  • 5-20 X greater than general population (Friedman et al. Pediatrc Clin North Am 2002)

• Childhood cancer survivor study:
  • 14,364 survivors of childhood cancer diagnosed between 1970 and 1986
  • Cumulative incidence of new SNs and SMNs occurring after age 40 years was 34.6%.

Risk of Subsequent Neoplasms During the Fifth and Sixth Decades of Life in the Childhood Cancer Survivor Study Cohort

SMN Incidence

- Childhood Cancer Survivor Study
  - 30 year cumulative incidence of second malignancy = 9%
Types of Secondary Tumors

• Most common:
  • Radiation therapy induced meningioma
  • Thyroid carcinoma
  • Skin cancers
    • Basal cell
    • Melanoma
  • Breast carcinoma
  • Colorectal carcinoma
  • Sarcomas (bone)
  • Myelodysplastic syndrome (MDS) and AML
Thyroid cancer
Radiation induced Meningioma

- **RT induced meningioma**
  - Multiple
  - Atypical
  - More likely to recur after surgery
Skin Cancer

- Increased risk of cancers in previous radiation therapy field
  - Basal cell carcinoma
  - Melanoma

Skin Cancer Information

What Is Skin Cancer?
Skin cancer is the uncontrolled growth of abnormal skin cells. It occurs when unrepaired DNA damage to skin cells (most often caused by ultraviolet radiation from sunshine or tanning beds) triggers mutations, or genetic defects, that lead the skin cells to multiply rapidly and form malignant tumors.

What to Look for
- Actinic Keratosis
- Basal Cell
- Dysplastic Nevi
- Melanoma
- Squamous Cell
Breast Cancer

• Commonest solid tumor among female survivors of Hodgkin lymphoma
• Moderately high-dose mediastinal RT
  • Scatter to adjacent (breast) tissue
• Adolescent girls most at risk
Breast Cancer

- After treatment for Hodgkin lymphoma in adolescence
  - 37X risk of breast cancer
  - Bilateral disease more common
  - Increased risk:
    - Over 12 years of age at diagnosis
    - Higher dose of RT

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**Unilateral and bilateral breast cancer in women surviving pediatric Hodgkin's disease.**

Colorectal Cancer (CRC)

- 2-3% risk of CRC 30–40 years after treatment for childhood cancer and increasing.
- Associated with abdominal radiation therapy
- Risk is proportional to dose and volume of RT
  - Increased by 70% with each 10-Gy increase in RT dose.
  - Increased RT volume increased risk (group 1 OR, 1.5; P .001; group 2 OR, 1.8; P .001).
- Alkylating agent exposure associated with 8.8X increased risk of secondary CRC.
David Rakoff, 47, Comic Essayist, Dies

By MARGALIT FOX
Published: August 10, 2012

David Rakoff, a prizewinning humorist whose mordant, neurotic essays examined everything from his surreal stint portraying Sigmund Freud in a Christmastime shop window display to his all-too-real battles with cancer, died on Thursday in Manhattan. He was 47.

His death was announced by his mother, Gina Shochat-Rakoff. Mr. Rakoff’s cancer had first appeared when he was 22 and recently reappeared as a tumor in his left shoulder.

The return of his cancer, and the possibility that his arm and shoulder would have to be amputated, were the subjects of the concluding essay in Mr.
Myelodysplasia and AML

• Myelodysplastic syndrome (MDS) and AML associated with:
  • Chemotherapy
    • Alkylating agents
    • Topoisomerase II inhibitors (VP 16 also called Etoposide)
  • Radiation therapy
Myelodysplasia and AML

• Etoposide related AML:
  • Short latency period of about 30 months
  • Poor prognosis
  • Chromosomal translocations of the MLL gene at chromosome band 11q23

• Alkylating agent related AML:
  • 5-10 years post treatment
  • Risk plateaus after 10 years
  • Prognosis poor
Lung cancer

- Smoking after therapy for Hodgkin lymphoma
After Acute Leukemia Rx

• 35 year old man treated at the age of 7 for high risk acute lymphoblastic leukemia

• Chemotherapy included:
  • Adriamycin
  • IV and IT Methotrexate

• Prophylactic, low dose cranial radiation therapy (18 Gy in 10#)
Health Risks after ALL Rx

- Neuro-cognitive
  - Mild cognitive dysfunction
  - Depression and post traumatic stress syndrome
- Endocrine
  - Hypothyroidism
- Metabolic syndrome
  - Hypertension
  - Obesity
  - Hyperlipidemia
  - Diabetes
- Cardiomyopathy
- Secondary tumors
  - Skin cancers (generally basal cell cancers)
  - Thyroid cancer (and multinodular goiter)
  - Meningioma
  - Malignant brain tumor (very small risk)
- Increased risk of stroke and vascular disease
Psychosocial

- Post-traumatic stress syndrome
  - Anxiety
  - Depression

- Many brain tumor survivors:
  - Need very modified school curriculum
  - Rely on permanent disability pension:
    - Differences across the province and between different provinces regarding available programs
      - Access to vocational/recreational rehab
  - Drug costs covered by parents benefits plan
  - Other costs not covered:
    - Hearing aids
Impact on Life

- Huge range of late effects:
  - Low risk:
    - Many (but not all) previous lymphoma and leukemia patients
    - Function very well
    - Minimal risk for long-term health problems
  - High risk:
    - Any RT, high dose chemotherapy including alkylating agents and anthracylines
    - Some leukemia patients, brain tumors and solid tumors (e.g. sarcomas)
    - Lives may be “devastated”
Prevention

Information about late effects critical for prevention:

- **Initial therapy**
  - Give treatments which are less likely to cause long-term damage
    - Avoid or reduce radiation therapy
    - Targeted therapy
      - We don’t know about the late effects of these agents yet
- **Tailored therapy**
  - Genomic studies to identify people more likely to develop side effects
ASCO May 2015

• Analysis of more than 34,000 participants in the Childhood Cancer Survivor Study (CCSS)
• Mortality at 15 years after diagnosis
  • 12.4% if treated in 1970s
  • 6% if treated in 1990s

Changes in Pediatric Cancer Treatments Yield Reduced Late Mortality

JUNE 1, 2015
Cancer Survivors Who Stay Active Live Longer

By GRETCHEN REYNOLDS  MAY 16, 2012 12:01 AM  81 Comments
Prevention

• Lifestyle:
  • Diet
  • Exercise
  • Smoking
  • Sun/UV exposure
Prevention

- Information/education
  - Childhood cancer survivors
    - Know to seek advice
  - Health care professionals
    - Do the correct investigations
Screening

• Generally, follow up care depends on “risk category”
  • High risk: Hospital based and family practitioner
  • Low risk: Family practitioner

• Survivorship Care Plan:
  • Coordinated post-treatment plan
  • Built by survivor’s oncology team
  • Includes
    • Summary of the survivor’s treatment
    • Direction for future care

• Screening recommendations: COG Long Term FU Guidelines
Guidelines

Pediatric Blood & Cancer

Clinical Practice Guidelines

A worldwide collaboration to harmonize guidelines for the long-term follow-up of childhood and young adult cancer survivors: A report from the international late effects of Childhood Cancer Guideline Harmonization Group†

Leontien C.M. Kremer MD, PhD, Renée L. Mulder MSc, Kevin C. Oeffinger MD, Smita Bhatia MD, MPH, Wendy Landier RN, PhD, Gill Levitt MD, Louis S. Constine MD, W. Hamish Wallace MD, Huib N. Caron MD, PhD, Saro H. Armenian MD, MPH, Roderick Skinner MB, PhD, Melissa M. Hudson MD
Follow-up Care Plan

Getting Follow-Up Medical Care

All cancer survivors should have follow-up care. Follow-up care means seeing a doctor for regular medical checkups once you're finished with treatment. It's important to look for any changes in your health or any problems that may occur due to cancer treatment. These checkups are also a time to check for physical and emotional effects that may develop months or years after treatment ends.

Knowing what to expect after cancer treatment can help you and your family make plans, lifestyle changes, and important decisions about the future. Common questions you may
Passport for Care

Cancer. You survived. And now you've got a lot of life to live. Take care of yourself.

Passport for Care.

Long-term follow-up care recommendations for survivors of childhood cancer.
Survivorship Clinics

Survivorship Clinic

The Seattle Cancer Care Alliance Survivorship Clinic offers treatment, support, and education after treatment is complete.

To schedule a clinic appointment please call (206)286-1024 and ask for the "Survivorship Clinic".

Cancer survivorship clinics
LEAF Clinic

- Provincial survivorship program essential
  - Medical care
    - Detect and monitor for late effects
      - Screening
      - Coordinate specialist and primary care
  - Psychosocial support
    - Family counseling
    - Develop
      - Links with rehab programs
      - Support groups
      - Wellness program focusing on diet, exercise and mental wellbeing
- Education
  - Primary and specialist care
  - Families and survivors
- Research
  - Collaborative program focusing on how to reduce the risk and severity of late effects and improve survivor’s quality of life
LEAF Team

- LEAF Administrative Lead: Avril Ullett
- Medical Lead: Karen Goddard
- Nurse practitioner: Kimberley-Anne Reid
- Family counseling:
  - Bronwyn Barrett
  - Sharon Paulse
LEAF Clinic

Late Effects, Assessment & Follow-Up

The Late Effects, Assessment and Follow-Up (LEAF) Clinic is for adults who have survived childhood cancer.

Are you an adult who has survived childhood cancer?
UBC CPD E-learning

Late Effects of Childhood Cancers

0.75 Mainpro+ / MOC Section 1 credits

Target Audience: Family physicians, specialists and other health care professionals in British Columbia involved in the health care of adult patients who are survivors of childhood cancer

Guests cannot access this course, please try to log in. If you do not have an account, create a new account (it's free!).

Continue
Other Resources

• COG: [Long-Term Follow-Up Guidelines for Survivors of Childhood, Adolescent, and Young Adult Cancers](#)
Other Resources

- National Cancer Institute:
What didn’t kill me made me Stronger
Thank you!

• Karen Goddard
  • kgoddard@bccancer.bc.ca