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The Leukemia & Lymphoma Society®
Fighting Blood Cancers

FOLLOW-UP CARE FOR BLOOD CANCER SURVIVORS:

The Critical Role of Primary Care Providers

Jointly sponsored by
Robert Michael Educational Institute LLC
and Postgraduate Institute for Medicine

This activity is supported by
an educational grant from

CONTENTS

The Critical Role of Primary Care Providers

ACTIVITY OVERVIEW

The Leukemia & Lymphoma Society®
Fighting Blood Cancers

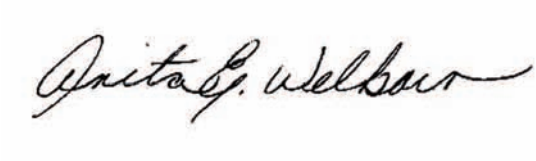
Thank you for joining us for *Follow-Up Care for Blood Cancer Survivors: The Critical Role of Primary Care Providers*, a continuing education activity originally presented during a live webcast presented on June 10, 2010.

We also thank our esteemed speakers for sharing their time and expertise. Through this activity, they will describe the role of primary care practitioners in caring for cancer survivors; describe the long-term and late effects associated with treatments for blood cancers; identify clinical trials evidence for late effects of treatments and survivorship in blood cancers; identify signs or symptoms that suggest the need for increased observation, testing and/or referral for possible recurrence or other morbidity in blood cancer survivors; and list the screening tests and optimal schedule for monitoring of blood cancer survivors for routine cancer prevention and detection of long- and late-term effects of treatment.

This workbook includes the presenters' slides to help guide you through the activity.

We hope that you will find this activity rewarding and informative.

Sincerely,



Anita Welborn, LMSW
Vice President, Patient Services Operations
The Leukemia & Lymphoma Society

AGENDA

The Critical Role of Primary Care Providers

Program Overview
Anita E. Welborn, LMSW

Follow-Up Care for Blood Cancer Survivors: The Critical Role of Primary Care Providers
Judith E. Karp, MD
Robert J. Arceci, MD, PhD

Question-and-Answer Session

Summary and Conclusion
Anita E. Welborn, LMSW

PROGRAM OVERVIEW

TARGET AUDIENCE

This activity has been designed to meet the educational needs of primary care physicians, nurses, social workers and other healthcare professionals involved in the management of patients with blood cancers.

ACTIVITY PURPOSE

This webcast is intended to inform healthcare professionals about monitoring and managing long- and late-term effects of treatment for blood cancer survivors.

STATEMENT OF NEED

Advances in improved diagnostic methods and treatment of hematologic malignancies have led to an increased number of cancer survivors. Although most therapeutic modalities for cancer are beneficial and life-saving, long-term or late adverse sequelae are increasingly prevalent, serious, and persistent in survivors of pediatric and adult cancers.[1] A thorough review of a patient's medical history, treatments, and co-morbid conditions is necessary for the primary care physician to recognize late-effects of therapy and pursue appropriate interventions.[2] Limited studies effectively associate treatment exposures with future consequences; however, through the grading of late effects, appropriate surveillance and treatment interventions may be implemented.[3] Blood cancer survivors should be evaluated for cancer recurrence during follow-up visits with primary care providers (PCPs). Effective monitoring begins with PCP awareness of disease-specific signs and symptoms and includes thorough patient history and examination, along with appropriate use of laboratory tests and diagnostic procedures.

[1] Aziz NM. *Acta Oncol*. 2007;46:417-432.

[2] Ganz PA. *Prim Care Clin Office Pract*. 2009;36:721-741.

[3] Aziz NM. "Late Effects of Cancer Treatments." In: *Cancer Survivorship*. New York: Springer New York; 2007:54-76.

EDUCATIONAL OBJECTIVES

After completing this activity, the participant should be better able to:

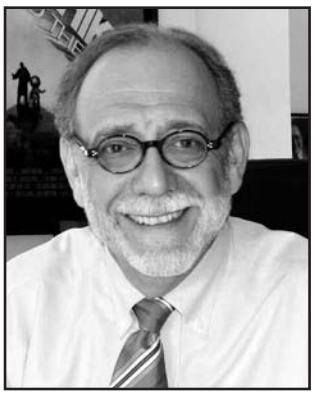
- Describe the role of primary care practitioners in caring for cancer survivors
- Describe the long-term and late effects associated with treatments for blood cancers
- Identify clinical trials evidence for late effects of treatments and survivorship in blood cancers
- Identify signs or symptoms that suggest the need for increased observation, testing and/or referral for possible recurrence or other morbidity in blood cancer survivors
- List the screening tests and optimal schedule for monitoring of blood cancer survivors for routine cancer prevention and detection of long- and late-term effects of treatment

STATEMENT OF SUPPORT

This activity is jointly sponsored by Robert Michael Educational Institute LLC and Postgraduate Institute for Medicine, and is supported by an educational grant from Genentech/Biogen Idec.

Robert J. Arceci, MD, PhD

King Fahd Professor of Pediatric Oncology
Professor of Pediatrics and Oncology,
Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins
Baltimore, MD



Robert J. Arceci, MD, PhD, is the King Fahd Professor of Pediatric Oncology and Professor of Oncology and Pediatrics at The Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins in Baltimore, Maryland. After receiving his medical degree and doctorate from the University of Rochester in New York, Dr. Arceci went on to complete his residency and fellowship training in pediatrics and pediatric hematology/oncology at The Children's Hospital and Harvard Medical School in Boston, Massachusetts. Before joining the staff at Johns Hopkins, he held faculty appointments at Harvard Medical School, Boston Children's Hospital, and the Dana Farber Cancer Institute, also in Boston.

Dr. Arceci's research focuses on translational research in pediatric malignancies and serious blood disorders, as well as on optimizing comprehensive care for children and adolescents with cancer. He has been particularly involved in the development of novel therapeutic targets and immunotherapies to improve outcomes while reducing adverse side effects in patients with cancer. He has served on several committees within the Pediatric Oncology Group, the Children's Cancer Group and the Children's Oncology Group, including Chairperson for the Myeloid Leukemia Committee and Vice-Chair of the Biology and Therapeutics Translational Committee. The author of numerous scholarly works, Dr. Arceci is considered an international authority in many challenging areas of clinical pediatric oncology, including the diagnosis and treatment of leukemia and Langerhans cell histiocytosis. He is Editor-in-Chief of *Pediatric Blood and Cancer*, a position he previously held at the *Journal of Pediatric Hematology/Oncology*; he has also served as Associate Editor of the *Journal of Pediatrics*. Dr. Arceci has also edited or co-edited several textbooks, including the 2006 text *Pediatric Hematology*. He was the originator of the internationally acclaimed movie on childhood cancer, *A Lion in the House*, filmed by documentary filmmakers Steven Bognar and Julia Reichert.

FACULTY BIOGRAPHIES

Judith E. Karp, MD

Professor of Oncology and *Medicine*
Director, Leukemia Program
Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins
Baltimore, MD

Judith E. Karp, MD, is a Professor of Oncology and Medicine and Director of the Leukemia Program at Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins Hospital in Baltimore, MD. She received her medical degree from Stanford University School of Medicine, completed an internship and residency at Stanford University Hospital and Johns Hopkins Hospital and completed her Oncology Fellowship at the Johns Hopkins University School of Medicine. Her research interests focus on the experimental therapeutics of acute leukemias, including development of timed sequential therapy, new biologic agents for older adults with acute leukemias and new approaches to the treatment of refractory acute leukemias including secondary leukemias that evolve from myelodysplasia or from prior cytotoxic chemotherapies.

Dr. Karp has been an active member of The Leukemia & Lymphoma Society's Medical and Scientific Affairs Committee since 1995 and served as Vice-Chair for Clinical Research from 1998-2002. Dr. Karp was instrumental in the development of LLS grant programs including the Translational Research Program and the Scholar Award in Clinical Research. She received the prestigious Dr. John J. Kenny Award from The Leukemia & Lymphoma Society in 2007.

PHYSICIAN CONTINUING EDUCATION

Accreditation Statement

This activity has been planned and implemented in accordance with the Essential Areas and policies of the Accreditation Council for Continuing Medical Education (ACCME) through the joint sponsorship of Postgraduate Institute of Medicine (PIM) and Robert Michael Educational Institute LLC (RMEI). PIM is accredited by the ACCME to provide continuing medical education for physicians.

Credit Designation

Postgraduate Institute for Medicine designates this educational activity for a maximum of 1.75 *AMA PRA Category 1 Credits*™. Physicians should only claim credit commensurate with the extent of their participation in the activity.

PHYSICIAN ASSISTANT & NURSE PRACTITIONER CONTINUING EDUCATION

Physician assistants and nurse practitioners should contact their respective licensure and certification bodies for information on use/conversion of *AMA PRA Category 1 Credits*™.

NURSES AND SOCIAL WORKERS

Approval for nurses has been obtained by the National Office of The Leukemia & Lymphoma Society under provider number CEP 5832 to award 1.75 continuing education contact hours through the California Board of Registered Nursing.

The Leukemia & Lymphoma Society (LLS), provider number 1105, is approved as a provider for social work continuing education by the Association of Social Work Boards (ASWB) www.aswb.org Approved Continuing Education Program (ACE). Approval Period: 12/2008–12/2011. LLS maintains responsibility for the program. Social workers should contact their regulatory board to determine course approval. Social workers will receive 1.75 CE clinical clock hours.

DISCLOSURES & DISCLAIMER

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Postgraduate Institute for Medicine (PIM) assesses conflict of interest with its instructors, planners, managers and other individuals who are in a position to control the content of CME activities. All relevant conflicts of interest that are identified are thoroughly vetted by PIM for fair balance, scientific objectivity of studies utilized in this activity, and patient care recommendations. PIM is committed to providing its learners with high quality CME activities and related materials that promote improvements or quality in healthcare and not a specific proprietary business interest of a commercial interest.

The **faculty** reported the following financial relationships or relationships to products or devices they or their spouse/life partner have with commercial interests related to the content of this CME activity:

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- **Judith E. Karp, MD,** has no affiliations with commercial interests to disclose.

The **planners and managers** reported the following financial relationships or relationships to products or devices they or their spouse/life partner have with commercial interests related to the content of this CME activity:

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- Sherri Kramer, MD, has no affiliations with commercial interests to disclose.
- Laura Altobelli, MS, has no affiliations with commercial interests to disclose.

Postgraduate Institute for Medicine

- Jan Hixon, RN, BSN, MA, has no affiliations with commercial interests to disclose.
- Trace Hutchison, PharmD, has no affiliations with commercial interests to disclose.
- Julia Kimball, RN, BSN, has no affiliations with commercial interests to disclose.
- Samantha Mattiucci, PharmD, has no affiliations with commercial interests to disclose.
- Jan Schultz, RN, MSN, CCMEP, has no affiliations with commercial interests to disclose.
- Patricia Staples, MSN, NP-C, CCRN, has no affiliations with commercial interests to disclose.

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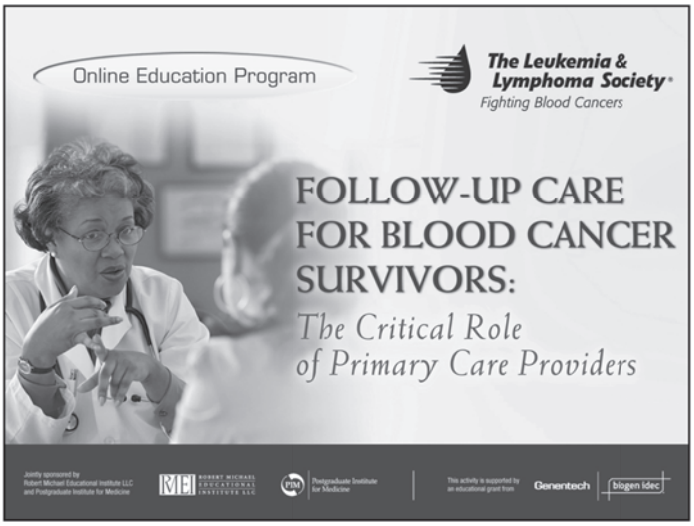
This educational activity may contain discussion of published and/or investigational uses of agents that are not indicated by the FDA. Postgraduate Institute for Medicine (PIM), Robert Michael Educational Institute LLC (RMEI), The Leukemia & Lymphoma Society (LLS), Genentech/Biogen Idec do not recommend the use of any agent outside of the labeled indications.

The opinions expressed in the educational activity are those of the faculty and do not necessarily represent the views of PIM, Robert Michael Educational Institute LLC (RMEI), The Leukemia & Lymphoma Society (LLS), Genentech/Biogen Idec. Please refer to the official prescribing information for each product for discussion of approved indications, contraindications, and warnings.

DISCLAIMER

Participants have an implied responsibility to use the newly acquired information to enhance patient outcomes and their own professional development. The information presented in this activity is not meant to serve as a guideline for patient management. Any procedures, medications, or other courses of diagnosis or treatment discussed or suggested in this activity should not be used by clinicians without evaluation of their patient's conditions and possible contraindications on dangers in use, review of any applicable manufacturer's product information, and comparison with recommendations of other authorities.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FOLLOW-UP CARE FOR BLOOD CANCER SURVIVORS:
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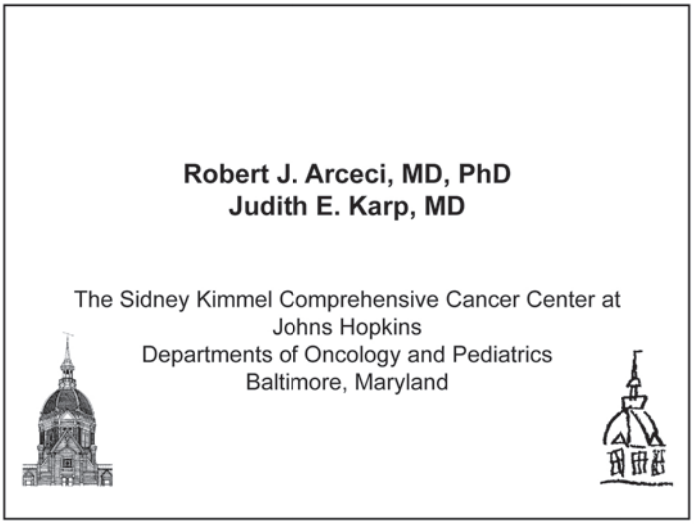
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PRESENTATION

Disclosure of Conflicts of Interest

Robert J. Arceci, MD, PhD
Judith E. Karp, MD

Drs. Robert J. Arceci and Judith E. Karp have no affiliations with commercial interests to disclose.

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The Scope of the Issue: 2010

	Estimated Incidence	Estimated Deaths
Leukemia	45,000	22,000
Lymphoma	66,000	20,000
Hodgkin	8500	too few to estimate!
Myeloma	21,000	11,000
Total	140,000	52,000

Number of blood cancer survivors in the US in 2010: *913,000* (includes 57,000 living with myelodysplastic syndrome [MDS])

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Survivors of Childhood Cancer

- 80% to 85% 5-year survival
- There are approximately 329,000 survivors of childhood cancer in the United States
- This is equivalent to about 1 of every 640 adults between the ages of 20 and 39 years of age

Hewitt M, et al (eds). *Childhood Cancer Survivorship: Improving Care and Quality of Life;* 2003.

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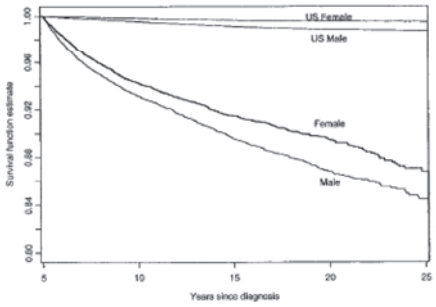
Survivorship

All-Cause Mortality – Gender-Specific Survival



Mertens AC, et al. *J Clin Oncol.* 2001;19:3163-3172, with permission.

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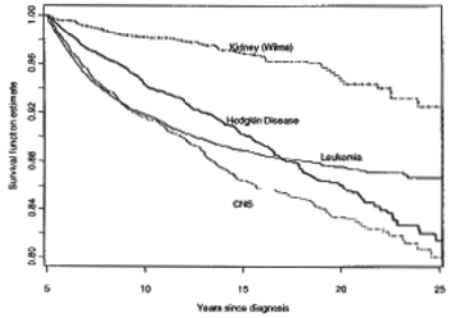
PRESENTATION

Survivorship
All-Cause Mortality – Disease-Specific Survival



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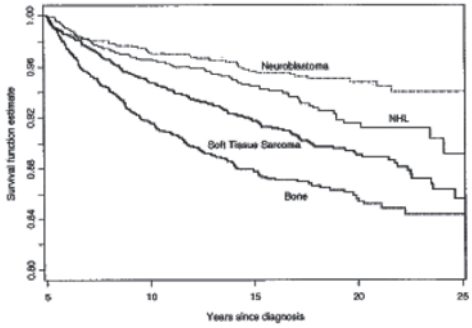
Survivorship
All-Cause Mortality – Disease-Specific Survival



Mertens AC, et al. *J Clin Oncol.* 2001;19:3163-3172, with permission.

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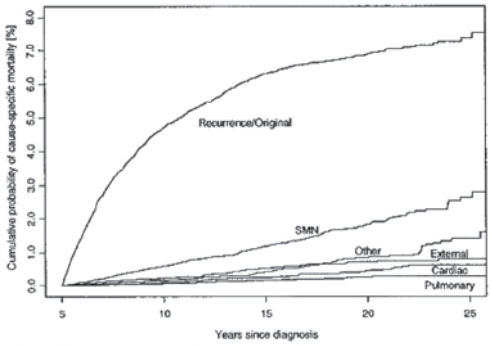
Survivorship

Cumulative Cause-Specific Mortality



Mertens AC, et al. *J Clin Oncol*. 2001;19:3163-3172, with permission.

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Patient #1

- 18-year-old woman with stage 3B Hodgkin lymphoma
  - Treated with combination chemotherapy, including steroids, cyclophosphamide, etoposide, vinblastine and bleomycin, along with low-dose involved-field (mediastinum) radiation
  - Complete response obtained
    - Developed osteonecrosis of right hip during therapy
  - Two years after stopping therapy, she developed progressive shortness of breath on exercising; work-up showed restrictive lung disease
  - Nine years after stopping therapy, she developed right-sided invasive breast cancer with axillary nodal involvement

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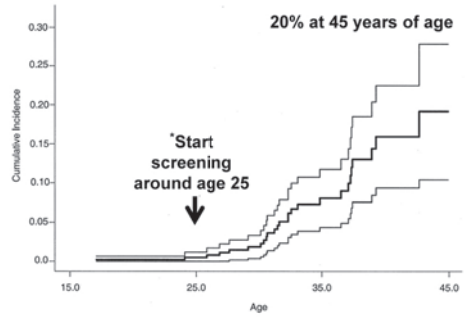
PRESENTATION

Survivorship

Cumulative Incidence of Breast Cancer in Survivors of Hodgkin Lymphoma



*Or 8 years post-radiation therapy.
Bhatia S, et al. *J Clin Oncol.* 2003;21:4386-4394, with permission.

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Patient #2

- 52-year-old woman with stage IIA left-sided breast cancer
  - Mastectomy followed by six cycles of dose-dense multi-agent chemotherapy, including anthracyclines and granulocyte colony-stimulating factor (G-CSF), followed by chest wall irradiation
  - Four years later, hematocrit 30%, platelets 110K
  - Progressive pancytopenia × 3 months → bone marrow shows MDS with trilineage dysplasia and complex cytogenetics
  - Transforms to full-blown acute myelogenous leukemia (AML) over 3 months
  - Undergoes intensive chemotherapy (including anthracyclines) – pretreatment left ventricular ejection fraction 55%–60%
  - Does not achieve complete remission
  - Post-treatment left ventricular ejection fraction 35% with symptomatic congestive heart failure

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Causes and Manifestations of Late Complications of Therapy for Hematologic Malignancies

Organ System	Causative Agents	Clinical Manifestations
Cardiac	Anthracyclines	Heart failure
	Chest radiation	Coronary artery disease
	Iron overload	
Pulmonary	Bleomycin	Pulmonary fibrosis
	Radiation	Restrictive lung disease
	Graft-versus-host disease (GVHD)	Bronchiolitis obliterans

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Causes and Manifestations of Late Complications of Therapy for Hematologic Malignancies

Organ System	Potential Causative Agents	Clinical Manifestations
Renal	Ifosfamide, platinated agents	Fanconi syndrome
Endocrine/ reproductive	Steroids	Obesity, diabetes
	Radiation	Pituitary dysfunction
	High-dose alkylators*	Infertility
Hepatic	Clofarabine, gemtuzumab ozogamicin, infections (viral, fungal), steroids, hyperalimentation, iron overload	Jaundice, ascites Liver failure

* In adolescents and young adults

PRESENTATION

Causes and Manifestations of Late Complications of Therapy for Hematologic Malignancies

Organ System	Potential Causative Agents	Clinical Manifestations
Neurologic	Central nervous system (CNS) radiation	Cognitive impairment Seizures
	Intrathecal chemotherapy	Peripheral neuropathy
	Neurotoxics (vincas, taxanes)	
Bone/joint	Steroids, radiation	Osteonecrosis
Immune	Steroids	Infection
	GVHD Anti-GVHD drugs	Chronic gastrointestinal disorders
	Clofarabine, fludarabine	Chronic skin disorders

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Secondary Malignancies as Late Complications of Therapy for Hematologic Malignancies

- Cytotoxic drugs
  - Myelodysplasia
  - Leukemia
- Radiation:
  - Breast cancer (chest wall external beam radiation [XRT])
  - Brain tumors, including meningiomas (CNS XRT)
  - Sarcomas, bone tumors
  - Skin cancers
  - Thyroid cancer

* In adolescents and young adults

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Ravages of High-Dose, Long-Term Steroids

- Obesity
- Diabetes
- Osteonecrosis
- Immunodeficiency
- Relative adrenal insufficiency
- Hypertension
- Pyschologic disturbance

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Psychologic Impact of Cancer Survivorship

- Survival anxiety
- Survival appreciation
- "Chemo brain"
- Chronic fatigue
- Body image

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PRESENTATION

Key Elements of Survivorship

- Childhood Cancer Survivorship Study
  - Retrospective study of 10,397 survivors of childhood cancer and 3034 siblings
  - Patients treated before 1986
  - Determined
    - Frequency of chronic conditions
    - Severity (mind to life-threatening or disabling)
    - Relative risks for chronic conditions

Oeffinger KC, et al. *N Engl J Med*. 2006;355:1572-1582, with permission.

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Key Elements of Survivorship

- Findings
  - Age
    - Average age of survivors: 26.6 years (range, 18–48 years)
    - Average age of siblings: 29.2 years (range, 18–56 years)
  - Time from cancer diagnosis to survey was 17.5 years
  - Of the survivors:
    - 46% were women
    - 16% were members of minority groups

Oeffinger KC, et al. *N Engl J Med*. 2006;355:1572-1582, with permission.

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Key Elements of Survivorship

- Findings
  - ~60% of survivors had at least one chronic condition
  - ~25% of survivors had a severe or life-threatening condition
  - ~40% had 2 or more and 25% of survivors had 3 or more chronic health problems

Oeffinger KC, et al. *N Engl J Med*. 2006;355:1572-1582, with permission.

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Relative Risk of Selected Severe or Life-Threatening Health Conditions, Cancer Survivors Versus Siblings

Condition	Survivors, % (n=10,397)	Siblings, % (n=3034)	Relative Risk (95% Confidence Interval)
Major joint replacement	1.61	0.03	54.0 (7.6–386.3)
Congestive heart failure	1.24	0.10	15.1 (4.8–47.9)
Second malignant neoplasms	2.38	0.33	14.8 (7.2–30.4)
Cognitive dysfunction, severe	0.65	0.10	10.5 (2.6–43.0)
Coronary artery disease	1.11	0.20	10.4 (4.1–25.9)
Cerebrovascular accident	1.56	0.20	9.3 (4.1–21.2)
Renal failure or dialysis	0.52	0.07	8.9 (2.2–36.6)
Hearing loss, uncorrectable with aid	1.96	0.36	6.3 (3.3–11.8)
Legally blind or loss of an eye	2.92	0.69	5.8 (3.5–9.5)
Ovarian failure	2.79	0.99	3.5 (2.7–5.2)

Oeffinger KC, et al. *N Engl J Med*. 2006;355:1572-1582, with permission.

PRESENTATION

Survivorship

- Findings
  - Relative risk was 3.3 times greater for survivor than for siblings to have a chronic condition
  - Relative risk was 8.2 times greater for survivors than for siblings to have a severe or life-threatening condition
  - Relative risk was 4.9 times greater for survivors to have 2 or more chronic health conditions than siblings

Oeffinger KC, et al. *N Engl J Med*. 2006;355:1572-1582, with permission.

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Survivorship

- Findings
  - Cumulative incidence of chronic health conditions is about 73%
  - Cumulative incidence of having a severe, disabling or life-threatening condition or death from a chronic condition is about 42%

Oeffinger KC, et al. *N Engl J Med*. 2006;355:1572-1582, with permission.

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Groups at Highest Risk for Having a Severe Condition

Cancer Diagnosis or Treatment Exposure	Relative Risk (95% Confidence Interval)		
	Grade 1–4	Grade 3 or 4	≥2 Conditions
Siblings	1.0	1.0	1.0
All cancer groups	3.3 (3.0–3.5)	8.2 (6.9–9.7)	4.9 (4.4–5.5)
Bone tumor	10.3 (8.9–12.0)	38.9 (31.2–48.5)	10.7 (8.9–12.8)
CNS tumor	7.1 (6.3–8.2)	12.6 (10.3–15.5)	12.4 (10.5–14.6)
*Hodgkin lymphoma	4.6 (4.2–5.1)	10.2 (8.3–12.5)	8.7 (7.4–10.2)
Sarcoma	3.5 (3.1–4.0)	8.9 (7.2–11.0)	5.2 (4.4–6.2)
*Non-Hodgkin lymphoma	3.2 (2.8–3.6)	6.8 (5.3–8.6)	4.3 (3.6–5.2)
Neuroblastoma	2.0 (1.7–2.4)	4.7 (3.5–6.4)	2.5 (2.0–3.2)
*Leukemia	2.2 (2.0–2.4)	4.1 (3.4–5.1)	2.5 (2.5–3.3)
Wilms' tumor	1.9 (1.7–2.2)	4.1 (3.2–5.4)	2.5 (2.0–3.1)

Oeffinger KC, et al. *N Engl J Med*. 2006;355:1572-1582, with permission.

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Groups at Highest Risk for Having a Severe Condition

Cancer Diagnosis or Treatment Exposure	Relative Risk (95% Confidence Interval)		
	Grade 1–4	Grade 3 or 4	≥2 Conditions
No chemotherapy or radiation	1.5 (1.3–1.7)	1.2 (1.0–1.5)	1.3 (1.1–1.5)
Chemotherapy			
Any chemotherapy	3.2 (2.9–3.4)	8.1 (6.8–9.6)	4.5 (4.0–5.0)
Alkylating agent	3.8 (3.5–4.2)	9.9 (8.3–11.8)	5.6 (5.0–6.4)
Anthracycline	4.3 (3.9–4.7)	11.0 (9.2–13.1)	5.8 (5.0–6.6)
Radiation therapy			
Any irradiation	3.4 (3.1–3.6)	7.9 (6.6–9.4)	5.2 (4.6–5.9)
Brain irradiation	3.1 (2.8–3.3)	7.0 (5.8–8.5)	4.8 (4.2–5.5)
Chest irradiation	4.7 (4.3–5.2)	10.6 (8.8–12.7)	8.2 (7.1–9.4)
Abdominal irradiation	3.7 (3.3–4.0)	8.8 (7.3–10.6)	5.8 (5.1–6.7)
Pelvic irradiation	4.2 (3.8–4.7)	10.5 (8.6–12.7)	6.8 (5.9–7.9)
Surgery			
Splenectomy	4.7 (4.2–5.2)	10.2 (8.3–12.5)	8.5 (7.2–10.0)
Nephrectomy	2.1 (1.8–2.4)	4.7 (3.5–6.2)	2.7 (2.2–3.4)

Oeffinger KC, et al. *N Engl J Med*. 2006;355:1572-1582, with permission.

PRESENTATION

Groups at Highest Risk for Having a Severe Condition

Cancer Diagnosis or Treatment Exposure	Relative Risk (95% Confidence Interval)		
	Grade 1–4	Grade 3 or 4	≥2 Conditions
Specific combinations			
Chest irradiation + bleomycin	7.8 (6.2–9.8)	13.6 (9.8–18.7)	13.3 (10.1–17.6)
Chest irradiation + anthracycline	6.0 (5.2–6.9)	13.0 (10.4–16.3)	9.7 (8.1–11.8)
Chest irradiation + abdominal or pelvic irradiation	4.7 (4.2–5.2)	10.9 (8.9–13.2)	8.5 (7.3–9.9)
Anthracycline + alkylating agent	4.3 (3.9–4.8)	10.9 (9.0–13.1)	6.0 (5.2–6.9)
Abdominal or pelvic irradiation + alkylating agent	4.0 (3.6–4.4)	10.0 (8.2–12.1)	6.2 (5.4–7.2)

Oeffinger KC, et al. *N Engl J Med.* 2006;355:1572-1582, with permission.

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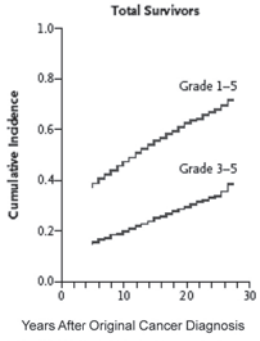
Survivorship

Cumulative Incidence of Chronic Health Conditions



Oeffinger KC, et al. *N Engl J Med.* 2006;355:1572-1582, with permission.

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Survivorship

- Major problem areas
  - Second malignancies
  - Coronary heart disease/heart failure
  - Pulmonary fibrosis
  - Endocrine problems (gonadal failure, osteoporosis, thyroid disease, pituitary dysfunction)

Oeffinger KC, et al. *N Engl J Med.* 2006;355:1572-1582.

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Survivorship

- Major problems by diagnosis
  - Bone tumors
    - Musculoskeletal problems, congestive heart failure
  - Brain tumors
    - Cognitive dysfunction; seizures; visual, hearing, endocrine problems
  - Hodgkin lymphoma
    - Cardiovascular diseases, second cancers, thyroid dysfunction

Oeffinger KC, et al. *N Engl J Med.* 2006;355:1572-1582.

Survivorship

- Major problems by race
  - Not related to having a severe chronic condition
  - Black non-Hispanic survivors are more likely than white non-Hispanic survivors to have any chronic condition
- Major problems by age
  - Older age more frequently associated with having any condition, severe conditions or multiple conditions

Oeffinger KC, et al. *N Engl J Med*. 2006;355:1572-1582.

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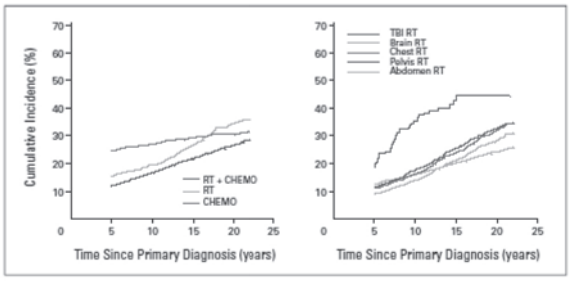
Timing of Chronic Conditions



Diller L, et al. *J Clin Oncol*. 2009;27:2339-2355, with permission.

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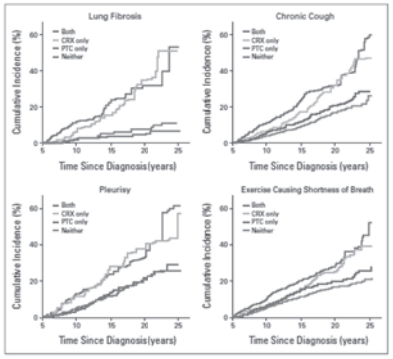
Timing of Chronic Conditions



Diller L, et al. *J Clin Oncol*. 2009;27:2339-2355, with permission.

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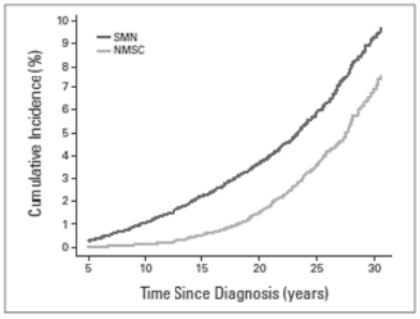
Timing of Secondary Cancers



Meadows AT, et al. *J Clin Oncol*. 2009;27:2356-2362, with permission.

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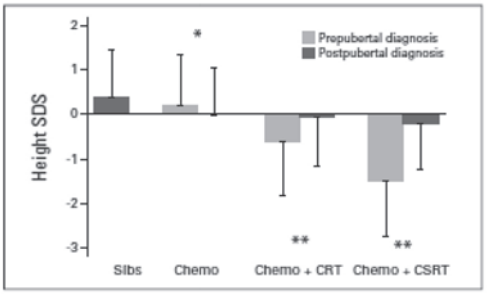
Height Issues



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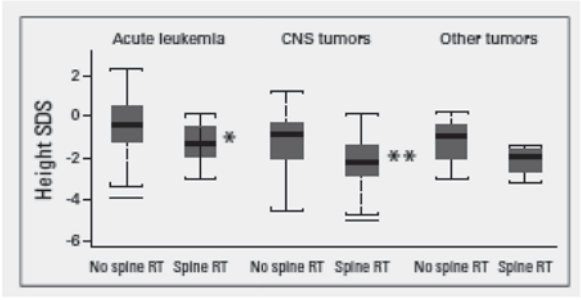
Height Issues



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Height Issues

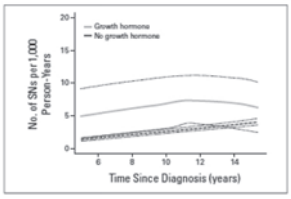

Table 3. Multivariate Analysis of Risk of Second Neoplasm in Patients Treated With Growth Hormone by Initial Diagnosis[40]

Diagnosis	RR	95% CI	*P*
Acute leukemia	4.98	1.95 to 12.74	< .001
CNS tumors	2.34	0.96 to 5.70	.06
CNS tumors (meningiomas excluded)	1.46	0.31 to 6.79	.69
Rhabdomyosarcoma	1.82	0.41 to 8.01	.43

Abbreviation: RR, relative risk.

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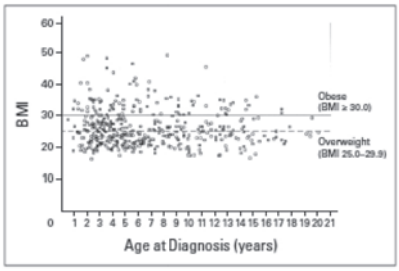
Obesity



Diller L, et al. *J Clin Oncol.* 2009;27:2339-2355, with permission.

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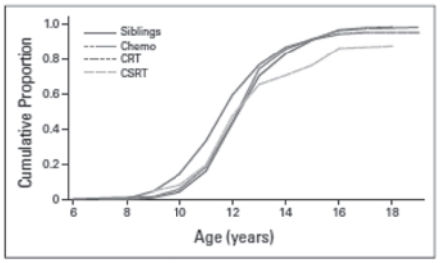
PRESENTATION

Menarche



Risk factors for early menarche: radiation therapy (odds ratio, 6.2); craniospinal radiation therapy (odds ratio, 8.6)

Diller L, et al. *J Clin Oncol.* 2009;27:2339-2355, with permission.

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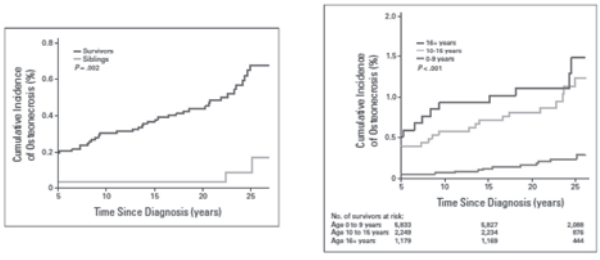
Osteonecrosis



Diller L, et al. *J Clin Oncol.* 2009;27:2339-2355, with permission.

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An Alternative Assessment of Survivorship

75% Cure
− 25% Having one serious condition
= 50%

75% Cure
− 40% Having >2 serious conditions
= 35%

75% Cure
− 66% Having at least one condition
= 8%

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Barriers to Optimal Care of Cancer Survivors

- Mechanisms of support needed
- Standard methodologies for neurocognitive, psychosocial and physical well-being are needed
- Insurability
- Job discrimination
- National database
- Need for linking long-term care and survivorship issues to disease experts
- Need for linking long-term care and survivorship issues to primary care providers (note: fewer than 20% of survivors followed by cancer centers)

Arceci R. *CA Cancer J Clin.* 2002;52:377-379.
AACR Pediatric Task Force.

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PRESENTATION

Barriers to Optimal Care of Cancer Survivors

- Survivor-related barriers
  - Knowledge
    - Most survivors not aware of their treatment details or potential late effects
    - 30% to 50% remember receiving anthracyclines
    - Only 70% recalled site of radiation
    - 33% of splenectomized patients knew
    - Only 15% reported having received a summary of their cancer treatment
    - Family history

Oeffinger KC, Wallace WH. *Pediatr Blood Cancer*. 2006;46:135-142.

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Barriers to Optimal Care of Cancer Survivors

- Physician-related barriers
  - Awareness and access to information
    - Not enough formal long-term follow-up programs (LTFUP)
    - Many programs do not follow survivors through adulthood
    - 96% of pediatric oncologists follow patients for at least 5 years after end of treatment, but 52% follow patients for life
    - Lack of dedicated nursing staff
    - Lack of communication between cancer center and primary care physicians

Oeffinger KC, Wallace WH. *Pediatr Blood Cancer*. 2006;46:135-142.

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Barriers to Optimal Care of Cancer Survivors

- Healthcare system–related barriers
  - Coverage beyond minor years
  - Loss of work, loss of coverage

Oeffinger KC, Wallace WH. *Pediatr Blood Cancer*. 2006;46:135-142.

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Survivorship Barriers to Care

Oeffinger KC, Wallace WH. *Pediatr Blood Cancer*. 2006;46:135-142, with permission.

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PRESENTATION

Survivorship: Problems & Solutions

- Mechanisms of support needed
- Standard methodologies for neurocognitive, psychosocial and physical well-being are needed
- Insurability
- Job discrimination
- National database
- Need for linking long-term care and survivorship issues to disease experts
- Need for linking long-term care and survivorship issues to primary care providers (note: fewer than 20% of survivors followed by cancer centers)

Arceci R. *CA Cancer J Clin.* 2002;52:377-379.
AACR Pediatric Task Force.

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Essential Elements of Survivorship Care

- Surveillance
- Prevention
- Intervention
- Coordination

Institute of Medicine. *From Cancer Patient to Cancer Survivor: Lost in Transition;* 2005.

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Risk-Directed Screening and Care

- Useful Guidelines from Children's Oncology Group
  - www.survivorshipguidelines.org
- Passport for Care (Texas Children's Cancer Center)
  - www.passportforcare.org
- Prevention, counseling, education
- Intervention

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Biology, Predispositions and Survivorship Involvement for All Ages

www.hopkinskimmelcancercenter.org

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PRESENTATION

Biology, Predispositions and Survivorship Involvement for All Ages

THE SIDNEY KIMMEL COMPREHENSIVE CANCER CENTER

CENTER INFORMATION

Specialty Centers and Clinics

Survivorship Program - The Michael J. Garil Leukemia Survivors Program at Johns Hopkins
www.hopkinskimmelcancercenter.org/survivorsprogram
Phone: (410) 614-5062

The Michael J. Garil Leukemia Survivors Program supports Kimmel Cancer Center research designed to better understand the reasons certain patients are predisposed to the long-term effects of cancer therapy as well as how adverse late effects impact on the lives of survivors. The program also offers follow-up services such as screening and prevention of late effects of leukemia treatment in children and adults.

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www.survivorshipguidelines.org

CureSearch
Children's Oncology Group

OUR MISSION
To cure and prevent childhood and adolescent cancer through scientific discovery and compassionate care.

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

Long-Term Follow-Up Program Resource Guide

This comprehensive guide to establishing and enhancing long-term follow-up programs for childhood cancer survivors was developed collaboratively by the Children's Oncology Group Nursing Discipline and Late Effects Committee. Over 50 individuals from multiple disciplines contributed to this Long-Term Follow-Up Program Resource Guide, providing a broad perspective from a variety of long-term follow-up programs within the Children's Oncology Group.

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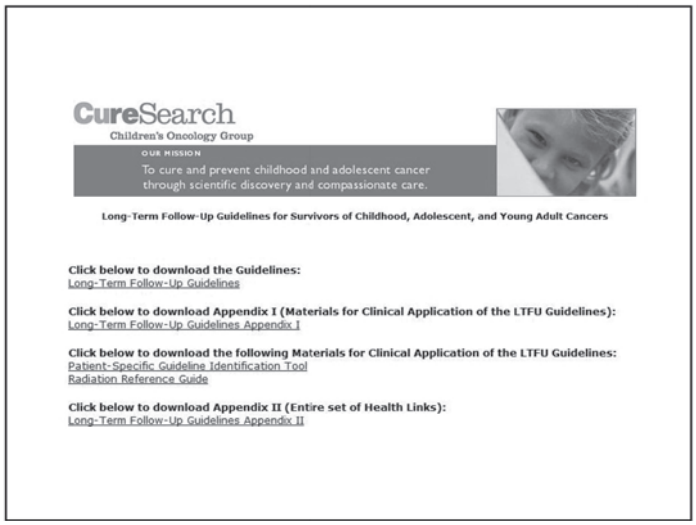
CureSearch
Children's Oncology Group
OUR MISSION
To cure and prevent childhood and adolescent cancer through scientific discovery and compassionate care.
Long-Term Follow-Up Guidelines for Survivors of Childhood, Adolescent, and Young Adult Cancers
Click below to download the Guidelines:
Long-Term Follow-Up Guidelines
Click below to download Appendix I (Materials for Clinical Application of the LTFU Guidelines):
Long-Term Follow-Up Guidelines Appendix I
Click below to download the following Materials for Clinical Application of the LTFU Guidelines:
Patient-Specific Guideline Identification Tool
Radiation Reference Guide
Click below to download Appendix II (Entire set of Health Links):
Long-Term Follow-Up Guidelines Appendix II

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CureSearch
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OUR MISSION
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Long-Term Follow-Up Guidelines for Survivors of Childhood, Adolescent, and Young Adult Cancers
Click below to download individual Health Links:
Introduction to Long-Term Follow-Up
Introduction to Long-Term Follow-Up (Spanish)
Emotional Issues
Emotional Issues (Spanish)
Educational Issues
Finding and Paying for Healthcare
Finding and Paying for Healthcare (Spanish)
Diet and Physical Activity
Diet and Physical Activity (Spanish)
Eye Health
Cataracts
Hearing Loss
Growth Hormone Deficiency
Central Adrenal Insufficiency
Hyperprolactinemia
Hypopituitarism
Dental Health
Osteoradionecrosis
Thyroid Problems
Heart Health
Pulmonary Health
Bleomycin Alert
Gastrointestinal Health
Liver Health
Hepatitis
Splenic Precautions
Kidney Health
Single Kidney Health
Bladder Health
Cystectomy
Neurogenic Bladder
Female Health Issues
Male Health Issues
Precocious Puberty
Bone Health
Osteonecrosis
Amputation
Limb Sparing Procedures
Scoliosis and Kyphosis
Peripheral Neuropathy
Raynaud's Phenomenon
Chronic Pain
Skin Health
Breast Cancer
Colorectal Cancer
Reducing the Risk of Second Cancers
Reducing the Risk of Second Cancers (Spanish)

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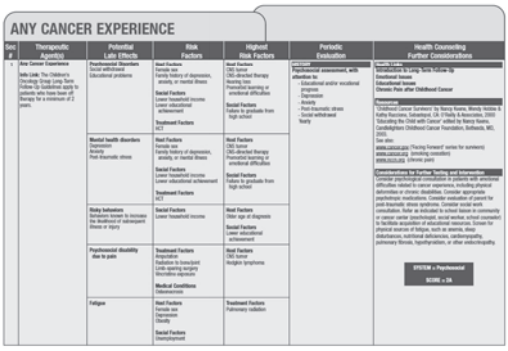
Examples of Exposure and Follow-Up Recommendations



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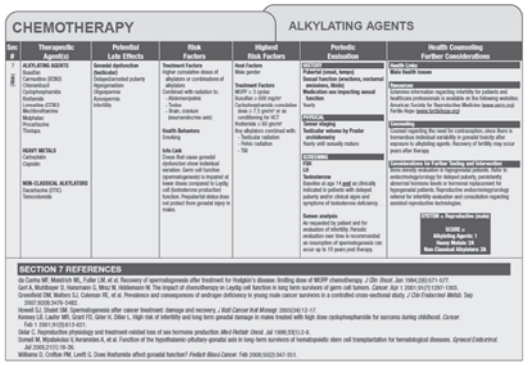
Examples of Exposure and Follow-Up Recommendations



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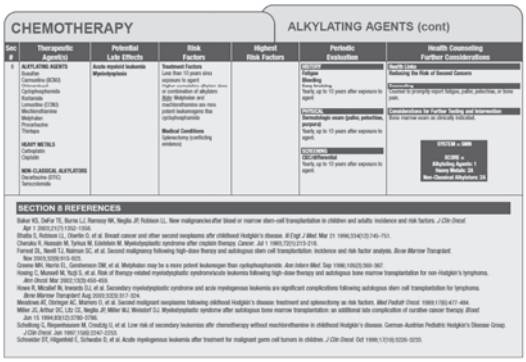
Examples of Exposure and Follow-Up Recommendations



CHEMOTHERAPY — ALKYLATING AGENTS (cont)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
8	ALKYLATING AGENTS Busulfan Carmustine (BCNU) Chlorambucil Cyclophosphamide Ifosfamide Lomustine (CCNU) Mechlorethamine Melphalan Procarbazine Thiotepa HEAVY METALS Carboplatin Cisplatin NON-CLASSICAL ALKYLATORS Dacarbazine (DTIC) Temozolomide	Acute myeloid leukemia Myelodysplasia	Treatment Factors Less than 10 years since exposure to agent Higher cumulative alkylator dose or combination of alkylators Also: Melphalan and mechlorethamine are more potent leukemogens than cyclophosphamide Medical Conditions Splenectomy (conflicting evidence)		HISTORY Fatigue Bleeding Easy bruising Yearly, up to 10 years after exposure to agent CLINICAL Dermatologic exam (pallor, petechiae, purpura) Yearly, up to 10 years after exposure to agent SCREENING CBC with Differential Yearly, up to 10 years after exposure to agent	Health Links Reducing the Risk of Second Cancers Counseling Counsel to promptly report fatigue, pallor, petechiae, or bone pain. Considerations for Further Testing and Intervention Bone marrow exam as clinically indicated. SYSTEM = SMN SCORE = Alkylating Agents: 1 Heavy Metals: 2A Non-Classical Alkylators: 2A

SECTION 8 REFERENCES

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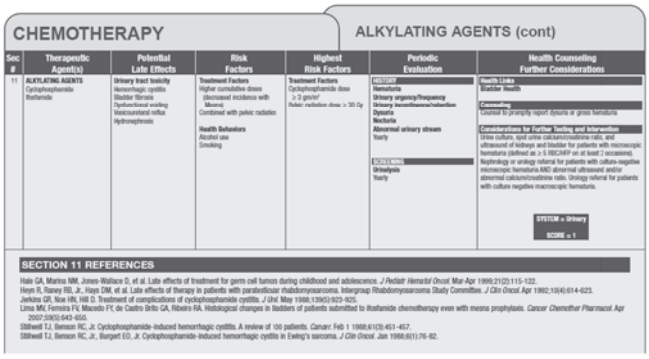
Examples of Exposure and Follow-Up Recommendations



CHEMOTHERAPY — ALKYLATING AGENTS (cont)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
11	ALKYLATING AGENTS Cyclophosphamide Ifosfamide	Urinary tract toxicity Hemorrhagic cystitis Bladder fibrosis Dysfunctional voiding Vesicoureteral reflux Hydronephrosis	Treatment Factors Higher cumulative doses (decreased incidence with Mesna) Combined with pelvic radiation Health Behaviors Alcohol use Smoking	Treatment Factors Cyclophosphamide dose > 3 gm/m² Pelvic radiation dose > 30 Gy	HISTORY Hematuria Urinary urgency/frequency Urinary incontinence/retention Dysuria Nocturia Abnormal urinary stream Yearly SCREENING Urinalysis Yearly	Health Links Bladder Health Counseling Counsel to promptly report dysuria or gross hematuria Considerations for Further Testing and Intervention Urine culture, spot urine calcium/creatinine ratio, and ultrasound of kidneys and bladder for patients with microscopic hematuria (defined as > 5 RBC/HPF on at least 2 occasions). Nephrology or urology referral for patients with culture-negative microscopic hematuria AND abnormal ultrasound and/or abnormal calcium/creatinine ratio. Urology referral for patients with culture negative macroscopic hematuria. SYSTEM = Urinary SCORE = 1

SECTION 11 REFERENCES

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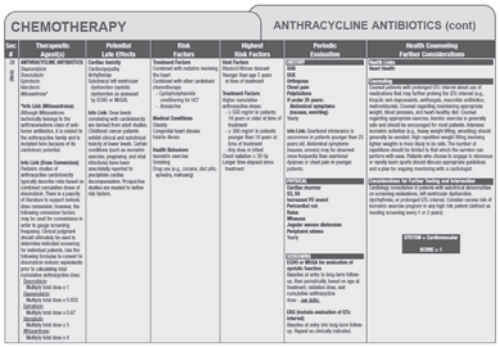
PRESENTATION

Examples of Exposure and Follow-Up Recommendations



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Examples of Exposure and Follow-Up Recommendations

RECOMMENDED FREQUENCY OF ECHOCARDIOGRAM OR MUGA SCAN

Age at Treatment*	Radiation with Potential Impact to the Heart§	Anthracycline Dose†	Recommended Frequency
<1 year old	Yes	Any	Every year
	No	<200 mg/m²	Every 2 years
		≥200 mg/m²	Every year
1-4 years old	Yes	Any	Every year
	No	<100 mg/m²	Every 5 years
		≥100 to <300 mg/m²	Every 2 years
		≥300 mg/m²	Every year
≥5 years old	Yes	<300 mg/m²	Every 2 years
		≥300 mg/m²	Every year
	No	<200 mg/m²	Every 5 years
		≥200 to <300 mg/m²	Every 2 years
		≥300 mg/m²	Every year
Any age with decrease in serial function			Every year

*Age at time of first cardiotoxic therapy (anthracycline or radiation [see fields below], whichever was given first)
§See Section 7†
†Based on doxorubicin isotoxic equivalent dose [see conversion factors in Section 28 "Info Link (Dose Conversion)"]

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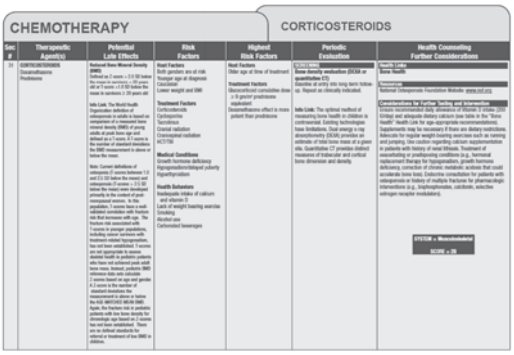
Examples of Exposure and Follow-Up Recommendations



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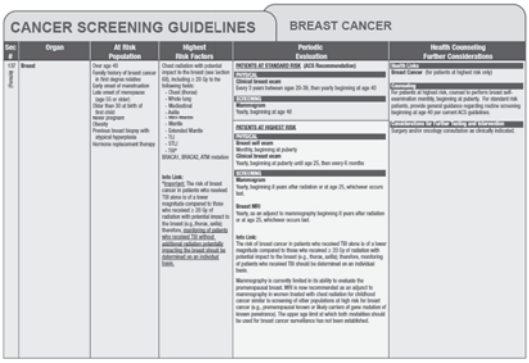
Examples of Exposure and Follow-Up Recommendations



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PRESENTATION

What About Survivors of Adult Cancers?

- Adults who survive cancers that occur during their adulthood incur patterns of drug- and modality-related complications that are similar to those seen in children but with some age-related differences
- Survivors of adult cancers and their therapies may have increased risks for secondary leukemias, osteonecrosis, iron overload, chronic infections, chronic fatigue, depression and GVHD
- On the other hand, survivors of adult cancers and their therapies may have fewer problems with neurocognitive disorders and fertility issues

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Role of the Primary Physician: The Patient's First Line of Defense

- Management of the cancer survivor
  - Careful serial history and physical examination, including a detailed composite of all previous anti-cancer therapies (names, total doses, dates of administration)
  - Awareness of potential complications of anti-cancer drugs and modalities – target organs, onset relative to therapy administration, clinical manifestations
  - Pre-emptive screening and follow-up
  - Prompt referral to appropriate specialist
  - Notify the patient's original oncologist: we may not know unless you tell us!

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Question-and-Answer Session

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TrialCheck®
A Clinical Trial Search Service

- Healthcare professionals, patients and caregivers can immediately access listings of clinical trials for leukemia, lymphoma, myeloma and other blood cancers
- Search results show clinical trials targeted to a patient's diagnosis, disease type and stage, and zip code preference
- To have an IRC Specialist conduct a personalized clinical trial search with you, call the **Information Resource Center (IRC) at (800) 955-4572,** or you may access the search tool at **www.LLS.org/clinicaltrials**.

Co-Pay Assistance Program

- The Leukemia & Lymphoma offers financial assistance to qualified patients to help with treatment-related expenses and insurance premiums. Funding is available for chronic myelogenous leukemia (CML), chronic lymphocytic leukemia (CLL), Hodgkin lymphoma, non-Hodgkin lymphoma (NHL), myelodysplastic syndromes (MDS), myeloma and Waldenström macroglobulinemia. Patients may apply online or over the phone with a Co-Pay Specialist.

- Toll-free Phone: 1-877-LLS-COPAY **or** 1-877-557-2672
- Website: www.LLS.org/copay

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The Leukemia & Lymphoma Society®

Fighting Blood Cancers

Mission Statement

The Leukemia & Lymphoma Society's mission: Cure leukemia, lymphoma, Hodgkin's disease and myeloma, and improve the quality of life of patients and their families

For information on leukemia, lymphoma and myeloma, call The Leukemia & Lymphoma Society's Information Resource Center at (800) 955-4572 or visit www.LLS.org.

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