The Leukemia & Lymphoma Society®
Fighting Blood Cancers

LEUKEMIA | LYMPHOMA | MYELOMA

Blood Cancer: Early Diagnosis, Treatment & Survivorship

Cancer Case Studies for the Primary Care Physician

THIS EVENT IS NOT A PART OF THE OFFICIAL AAFP SCIENTIFIC ASSEMBLY

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

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PIM Postgraduate Institute for Medicine

This activity is supported in part by educational grants from Cephalon Oncology and Celgene Corporation

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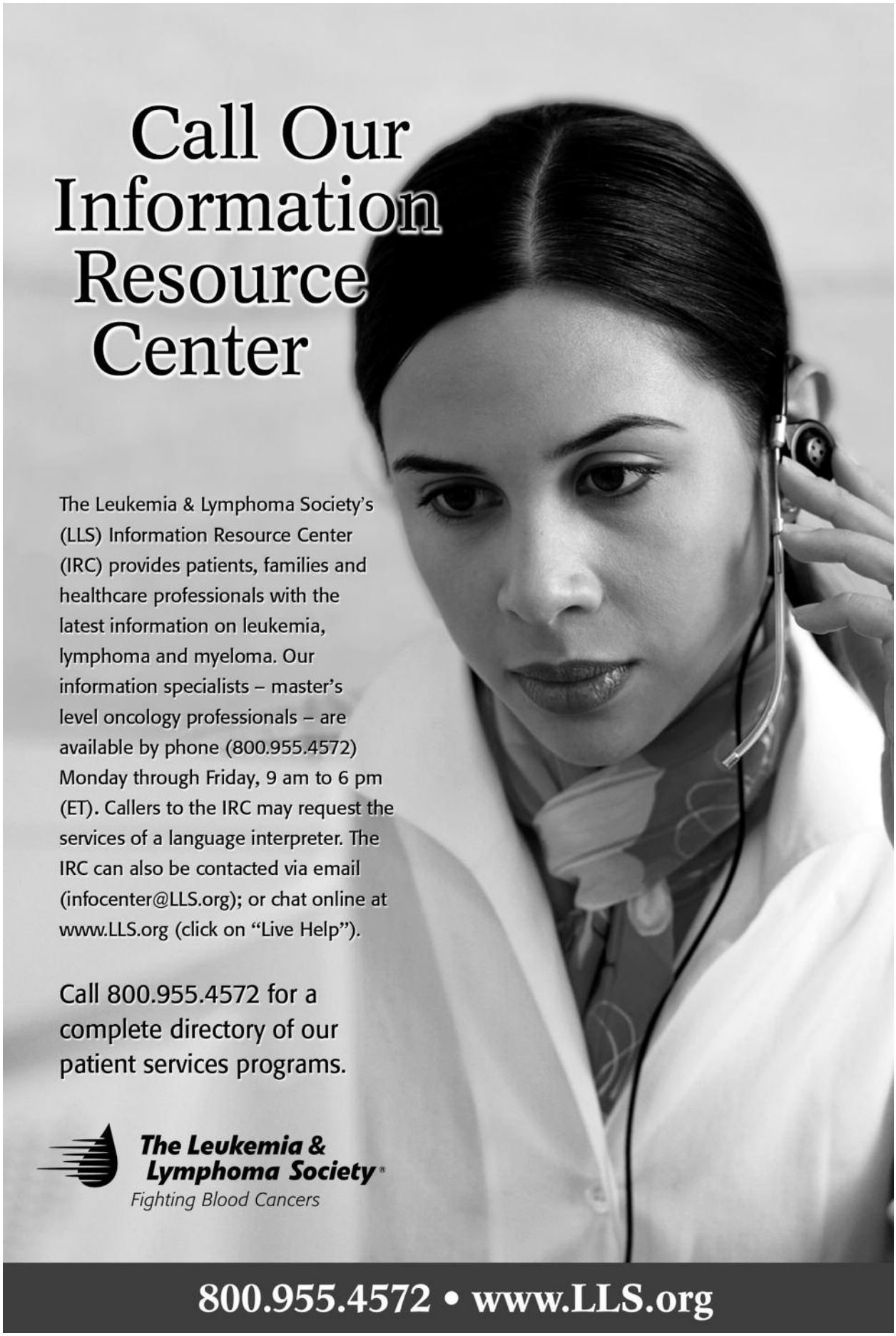
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The Leukemia & Lymphoma Society's (LLS) Information Resource Center (IRC) provides patients, families and healthcare professionals with the latest information on leukemia, lymphoma and myeloma. Our information specialists – master's level oncology professionals – are available by phone (800.955.4572) Monday through Friday, 9 am to 6 pm (ET). Callers to the IRC may request the services of a language interpreter. The IRC can also be contacted via email (infocenter@LLS.org); or chat online at www.LLS.org (click on "Live Help").
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Agenda

Program Overview

Hildy J. Dillon, MPH
Senior Vice President, Patient Services
The Leukemia & Lymphoma Society
White Plains, NY

Early Diagnosis of Blood Cancers: Symptoms Seen in the Frontline of Care

Barton A. Kamen, MD, PhD

Risk-Based Healthcare for Adult Survivors of Pediatric Cancer

Kevin C. Oeffinger, MD

Question-and-Answer Session

Overview

TARGET AUDIENCE

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

ACTIVITY PURPOSE

This activity is intended to assist healthcare professionals in recognizing the signs, symptoms, treatments and survivorship issues associated with blood cancers using representative case studies.

STATEMENT OF NEED

Blood cancers are projected to be responsible for more than 53,000 deaths in 2009.[1] Diagnosis of these conditions can be difficult, particularly in the early stages, because patients may be asymptomatic, and the signs and symptoms are nonspecific and generally related to common blood cytopenias. Treatment of these conditions is equally challenging, as malignancies and therapies alike are associated with significant short- and long-term side effects. Thus, healthcare professionals who treat patients with blood cancers must be mindful of traditional therapy targeted at achieving remission as well as supportive and follow-up care. This educational activity is designed to improve care and overall quality of life in patients with blood cancers.

[1] National Cancer Institute. Available at: http://seer.cancer.gov/csr/1975_2006/ results_single/sect_01_table.01.pdf. Accessed August 24, 2009.

EDUCATIONAL OBJECTIVES

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

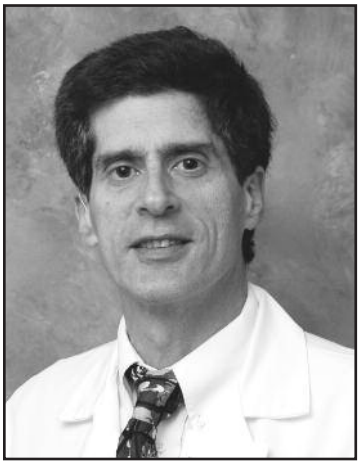
- Recognize the distinct signs and symptoms associated with hematologic malignancies to improve patient outcomes through early diagnosis
- Select appropriate methods for diagnosis in patients with signs and symptoms of hematologic malignancies
- Identify the late effects associated with treatments for hematologic malignancies
- Describe follow-up tests used to screen for malignancy recurrence to improve long-term survival

STATEMENT OF SUPPORT

This activity is supported in part by educational grants from Cephalon Oncology and Celgene Corporation.

Faculty Biographies

Barton A. Kamen, MD, PhD
Chief Medical Officer
The Leukemia & Lymphoma Society
White Plains, NY
Professor of Pediatrics and Pharmacology
The Cancer Institute of New Jersey
UMDNJ – Robert Wood Johnson Medical School
New Brunswick, NJ



Barton A. Kamen, MD, PhD, is the executive vice president and chief medical officer of The Leukemia & Lymphoma Society (LLS), as well as professor of pediatrics and pharmacology at the Cancer Institute of New Jersey at Robert Wood Johnson Medical School. Dr. Kamen has been a recipient of a scholar award from LLS, a Damon Runyon Walter Winchell Fellowship, a Burroughs Wellcome Clinical Pharmacology Award, and an American Cancer Society Clinical Research Professorship. He has authored approximately 300 peer-reviewed articles and book chapters and is the current editor-in-chief of the *Journal of Pediatric Hematology/Oncology*.

Faculty Biographies

Kevin C. Oeffinger, MD
Attending and *Member*
Director, Living Beyond Cancer
Departments of Pediatrics and Medicine
Memorial Sloan-Kettering Cancer Center
New York, NY

Kevin C. Oeffinger, MD, is an attending physician and director of Living Beyond Cancer, a program for adult survivors of pediatric cancer at Memorial Sloan-Kettering Cancer Center in New York City. After receiving his medical degree from the University of Texas Medical School at San Antonio (Texas), he completed residency training at Baylor College of Medicine in Houston, Texas, and went on to pursue advanced research training in the National Cancer Institute's Division of Cancer Epidemiology and Genetics. Dr. Oeffinger's research interests focus on better understanding the long-term health problems related to cancer and cancer therapy, particularly cardiovascular health and follow-up care optimization. His findings have been reported in over 50 peer-reviewed publications, including *Journal of Clinical Oncology*, *Journal of Pediatric Hematology/Oncology*, *Cancer*, and *Journal of the American Medical Association*.

Accreditation & Credit

PHYSICIAN CONTINUING MEDICAL EDUCATION CREDIT

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 for Medicine (PIM) and Robert Michael Educational Institute LLC (RMEI). PIM is accredited by the ACCME to provide continuing medical education for physicians.

Credit Designation

PIM designates this educational activity for a maximum of 1.5 *AMA PRA Category 1 Credits™*. Physicians should only claim credit commensurate with the extent of their participation in the activity.

AAFP Credit

This activity has been reviewed and is acceptable for up to 1.5 prescribed credits by the American Academy of Family Physicians (AAFP).

NURSES AND SOCIAL WORKERS CONTINUING EDUCATION CREDIT

Nursing Professionals

Approval for nurses has been obtained by the National Office of The Leukemia & Lymphoma Society under provider number CEP 5832 to award 1.5 continuing education contact hours through the California Board of Registered Nursing.

Social Workers

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 1.5 CE clinical clock hours.

AMERICANS WITH DISABILITIES ACT

Event staff will be glad to assist you with any special needs (ie, physical, dietary, etc). Please contact RMEI prior to the live event at (866) 770-RMEI.

FEE INFORMATION

There is no fee for this educational activity.

Disclosures & Disclaimer

DISCLOSURE OF CONFLICTS OF INTEREST

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:

- **Dr. Barton A. Kamen** has no affiliations with commercial interests to disclose.
- **Dr. Kevin Oeffinger** has no affiliations with commercial interests to disclose.

The following **planners and managers** reported the following financial relationships:

The Leukemia & Lymphoma Society
- **Hildy J. Dillon, MPH,** has no affiliations with commercial interests to disclose.

Robert Michael Educational Institute LLC
- **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.
- **Linda Graham, RN, BSN,** has no affiliations with commercial interests to disclose.
- **Trace Hutchison, PharmD,** has no affiliations with commercial interests to disclose.
- **Julia Kirkwood, RN, BSN,** has no affiliations with commercial interests to disclose.
- **Jan Schultz, RN, MSN, CCMEP,** has no affiliations with commercial interests to disclose.

DISCLOSURE OF UNLABELED USE

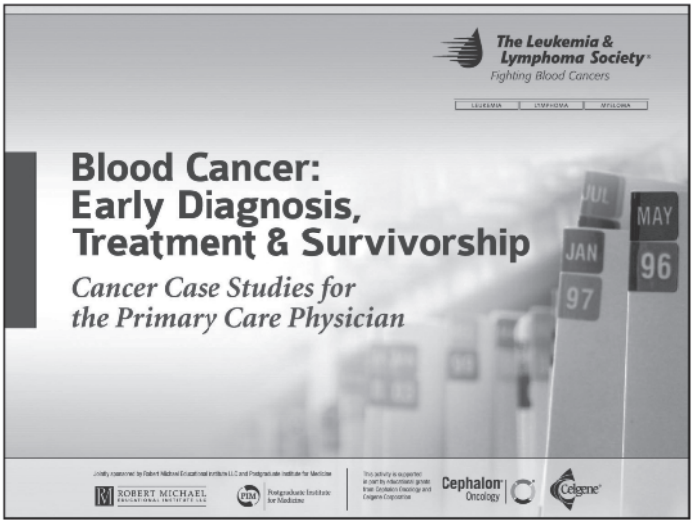
This educational activity may contain discussion of published and/or investigational uses of agents that are not indicated by the FDA. Postgraduate Institute for Medicine (PIM), Robert Michael Educational Institute LLC (RMEI), The Leukemia & Lymphoma Society (LLS), Cephalon Oncology and Celgene Corporation 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, RMEI, LLS, Cephalon Oncology and Celgene Corporation. 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.

Presentations



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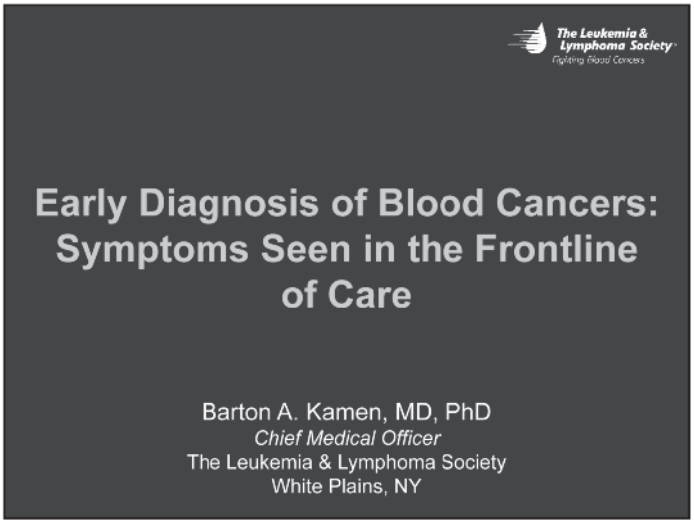

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Presentations

The Leukemia & Lymphoma Society
Fighting Blood Cancers

Disclosure of Conflicts of Interest

Barton A. Kamen, MD, PhD

Dr. Barton A. Kamen has no affiliations with commercial interests to disclose.

I thank you,
and I salute you for being on the front line of patient care.

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The Leukemia & Lymphoma Society
Fighting Blood Cancers

Goal for This Session:

- Review the scope of the problem of blood cancers
- Discuss symptoms, signs and laboratory and radiological findings as you might see them at initial presentation

Format will include some actual (or representative) cases I have seen in the ER or clinic over 30 years and will emphasize the young adult population

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Presentations

The Leukemia & Lymphoma Society
Fighting Blood Cancers

Scope of the Problem

Approximately 135,000 new cases of blood and related cancers in the US in 2007

Lymphomas	
Non-Hodgkin	63,000
Hodgkin	8,000
Leukemias	
CLL	15,000
CML	5,000
AML	13,000
ALL	5,000
Myeloma	20,000

ALL=acute lymphocytic leukemia; AML=acute myelogenous leukemia; CLL=chronic lymphocytic leukemia; CML=chronic myelogenous leukemia.
Lichtman MA. *The Oncologist*. 2008;13:126-188.

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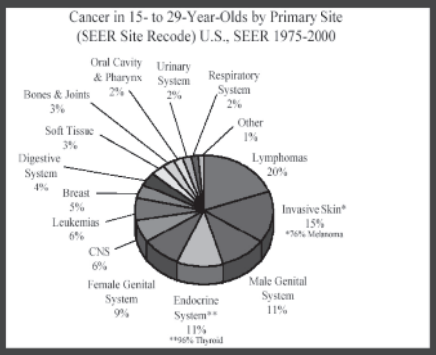
The Leukemia & Lymphoma Society
Fighting Blood Cancers

Scope of Problem in Young Adults



Bleyer A, et al. Available at: www.seer.cancer.gov/publications/aya/aya_mono_complete.pdf. Accessed September 18, 2009.

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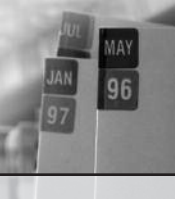
Presentations



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Leukemias & Lymphoreticular Malignancies in Pediatrics and Young Adults

Age (years)	% of all cancers
0–15	40–45
15–19	35–40
20–25	35–40
25–29	15–20
30–34	12–15
35–39	10–12

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WHY Is Early Detection Important?

Intuitively:
Earlier detection = lower stage = better outcome?

Not necessarily always true, but
patient may be healthier and Rx morbidity less

Abel GA, et al. *Leuk Lymphoma*. 2008;49:1352-1359.
Rosen PJ, et al. *Blood*. 2007;110:3312.

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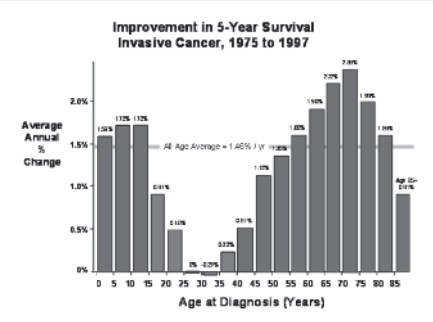
Improvements in Cancer Survival



Bleyer A, et al. Available at: www.seer.cancer.gov/publications/aya/aya_mono_complete.pdf. Accessed September 18, 2009.

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Outcomes of Patients Treated on Either Pediatric or Adult ALL Clinical Trials

Study Group	Years	Age (years)	EFS by Regimen Type (%)	
			Pediatric	Adult
USA	1988–2001	16–20	63	34
Dutch	1985–1999	15–18	69	34
Sweden	1992–2000	15–20	74	39
UK	1997–2002	15–17	65	49

EFS=event-free survival.
Barry EV, Silverman LB. *Curr Hematol Malig Rep*. 2008;3:161-166.

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Presentations

Diagnostic Strategies

Symptom	Sign	Lab/Radiology
Fatigue	Pale	Anemia
Shortness of breath	Wheezing	Chest x-ray
Pain (arthralgia, bone)	Swelling Petechiae None	Pancytopenia Leukocytosis "WNL"
Headache	Bruising Petechiae CNS findings	Pancytopenia Leukocytosis CT scans
Sweating; fever	Lymphadenopathy	CBC, CT chest

CBC=complete blood count; CNS=central nervous system; CT=computed tomography; WNL=within normal limits.

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Diagnostic Strategies (*Cont'd*)

Symptom	Sign	Lab/Radiology
Loss of appetite	Lymphadenopathy Jaundice Splenomegaly	CBC, CT scans Metabolic panel
Pruritus	Rash(es)	CBC, eosinophilia
Bloating, swelling Nausea, vomiting	Pitting edema Organomegaly	CBC Metabolic panel
NONE	NONE	CBC, chest x-ray, UA

UA=urinalysis.

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Symptom	Sign	Lab/Radiology
Fatigue	Pale	Anemia

Anemias: Normocytic
Microcytic
Macrocytic

Marrow failure syndromes:
Premalignant conditions, such as myelodysplasia

Haematological Malignancy Diagnostic Service. The Myelodysplastic Syndromes. www.hmds.org.uk/index.html.
Robbins SL. *Textbook of Pathology*, 2nd ed. Philadelphia, PA: WB Saunders; 1964.

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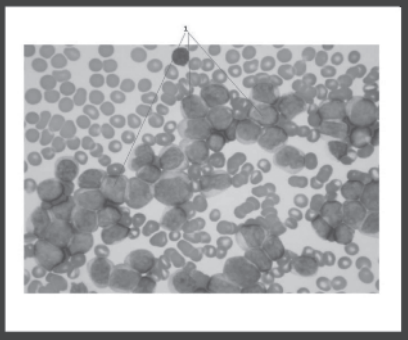

Teenage boy with 6-week history of increasing pallor
- Hemoglobin: 3 g/dL
- Mean corpuscular volume: 98 fL
- Platelets: 30,000/mm^3

Treated with weekly IM vitamin B12

Hyperleukocytosis: 900,000/mm^3

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Presentations

Hyperleukocytosis Signs and Symptoms

- Cerebral and pulmonary circulation most commonly affected
  - CNS
    - Change in mental state
    - Seizures
    - Headaches
    - Papilloedema
  - Respiratory
    - Dyspnoea
    - Hypoxemia
    - Right ventricular failure
    - Bilateral "fluffy infiltrates" on chest x-ray
  - Other
    - Renal failure
    - Priapism
    - Dactylitis

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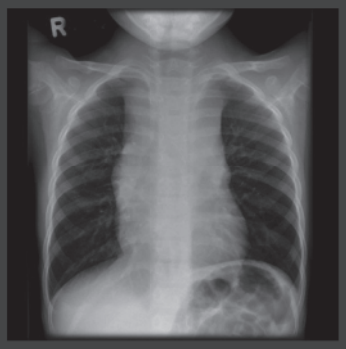
All That Wheezes Is Not Asthma!



Young boy treated for presumed reactive airway disease

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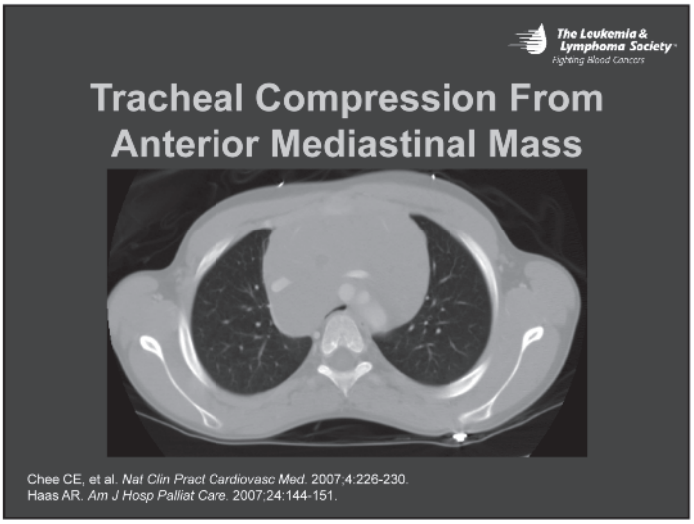
Presentations



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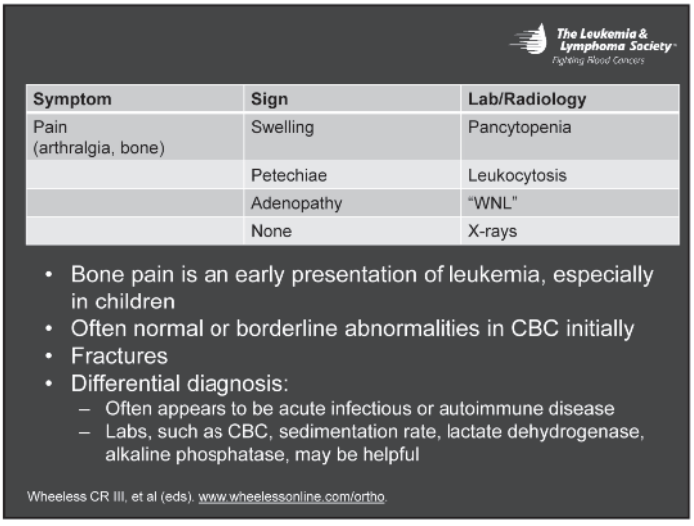

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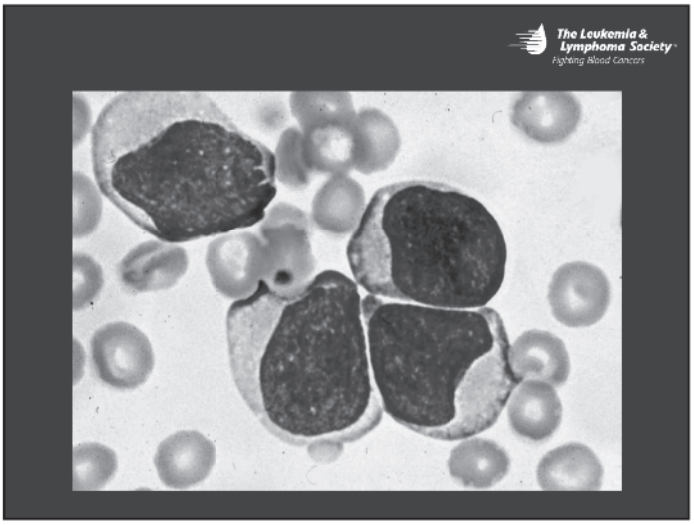

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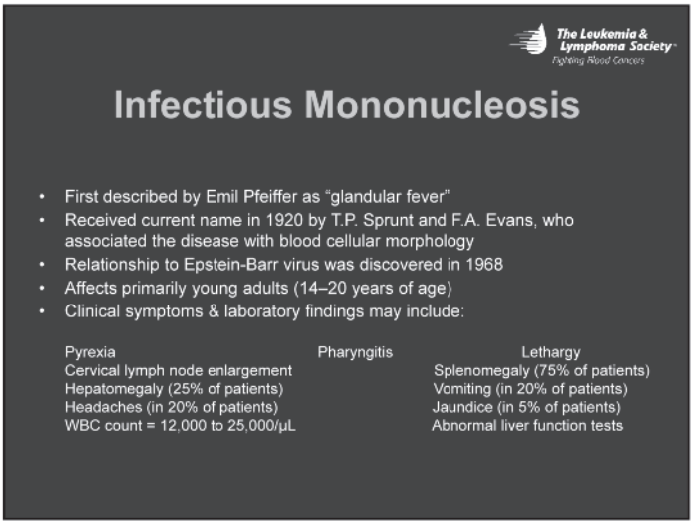

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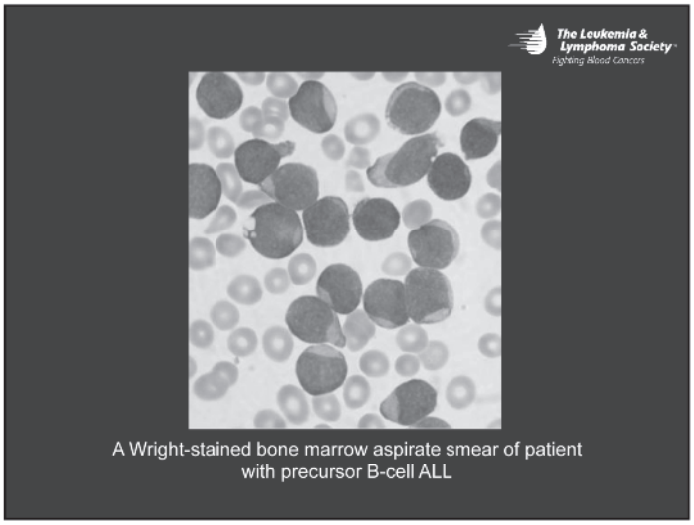

A Wright-stained bone marrow aspirate smear of patient with precursor B-cell ALL

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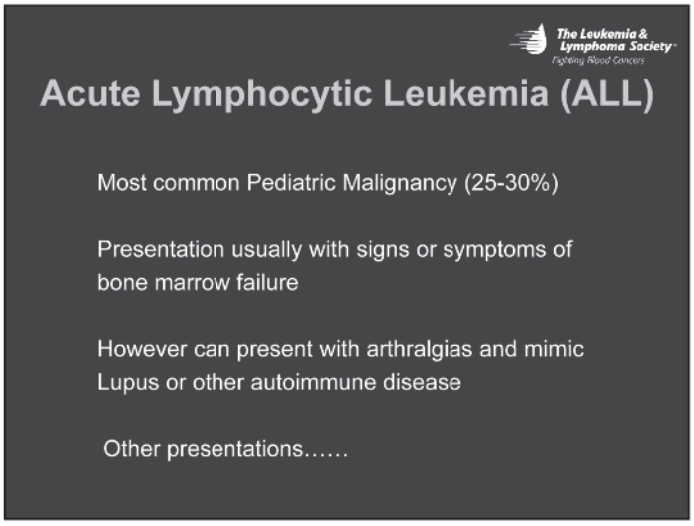

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Presentations

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Symptom	Sign	Lab/Radiology
Headache	Bruising	Pancytopenia
	Petechiae	Leukocytosis
	CNS findings	CT scans

- Leukemia and lymphoma, some types more than others, have a predilection for the CNS spread or even primary presentation (CNS lymphoma)
- Findings may be typical of any mass effect seen with a hemorrhage or tumor
- Invasion of specific cranial nerves can present with focal deficits

Jaffe ES, et al. *World Health Organisation Classification of Tumours.*

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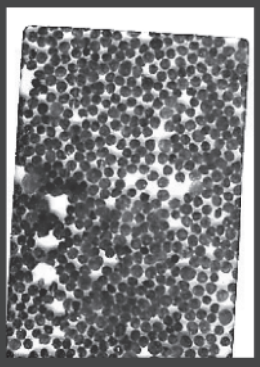
The Leukemia & Lymphoma Society
Fighting Blood Cancers

CSF Cytology



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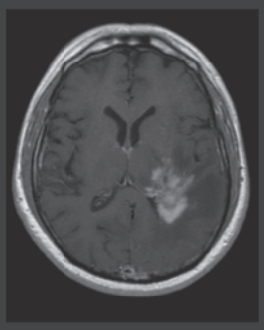
Presentations

Primary CNS Lymphoma in Immunocompromised Patients

- Usually no systemic disease at diagnosis
- Typically (95%) a B-cell non-Hodgkin lymphona (NHL)
- Almost always super-tentorial



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Symptom	Sign	Lab/Radiology
Sweating	Lymphadenopathy	CBC, CT chest
Fever		

- Unexplained fever, especially night sweats, are often seen part of the initial presentation of lymphomas; pathophysiological basis is likely cytokine release
- CBC may be normal or show anemia of chronic disease (microcytic) if the presentation is indolent (or if the patient is too tolerant of the presenting symptoms)

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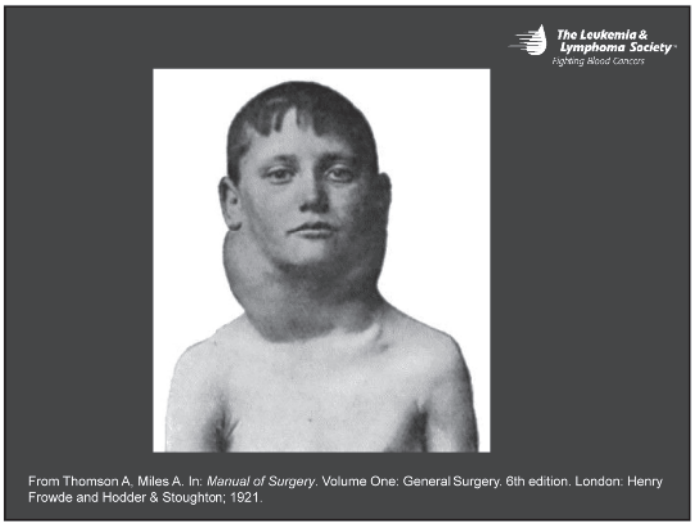
Presentations



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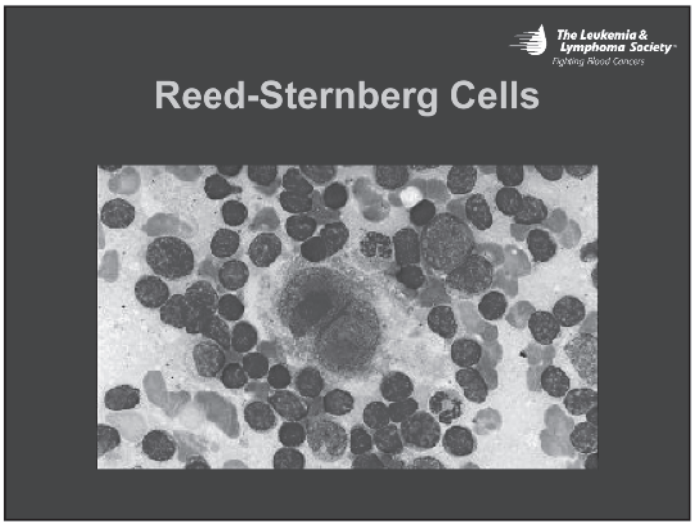

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Presentations

Symptom	Sign	Lab/Radiology
Loss of appetite	Lymphadenopathy	CBC, CT scans
	Jaundice	
	Splenomegaly	

One of the initial descriptions of a young man with what was probably CML: massive abdominal organomegaly, jaundice

Wood GB. *A Treatise on the Practice of Medicine*, 1845.

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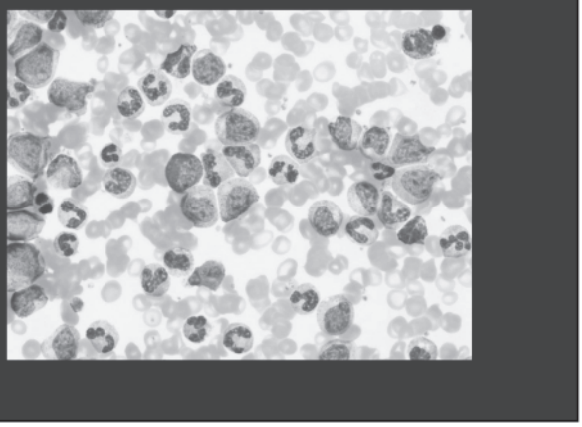

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Presentations

Burkitt's Lymphoma

Symptom	Sign	Lab/Radiology
Bloating, swelling	Pitting edema	CBC
Nausea, vomiting	Organomegaly	Metabolic panel

Organ failure: metabolic (tumor lysis syndrome) and anatomic compromise

- Acute onset of edema, clinical symptoms may be related to uremia, acute renal failure associated with aggressive B-cell lymphoma or leukemia (Burkitt's)
- May be both anatomic and metabolic causes for organ failure
- Rapid appreciation and treatment is critical
- Often dialysis is initiated before chemotherapy

Coiffier B. et al. *J Clin Oncol*. 2008;26:2767-2778.

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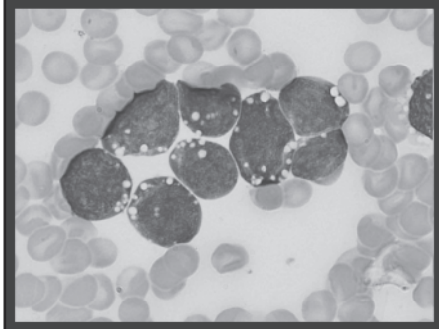
L3 (aka Burkitt's Leukemia)



Presentation: abdominal pain

Serum Chemistries

BUN	50 mg/dL
Creatinine	1.8 mg/dL
Uric acid	15 mg/dL
Phosphorus	8 mg/dL
Calcium	4 mg/dL

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Presentations

The Leukemia & Lymphoma Society
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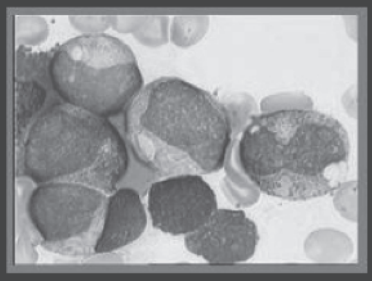
Promyelocytic Leukemia (AML-M3)

A proclivity to present with DIC



DIC=disseminated intravascular coagulopathy.
From The British Society for Haematology image library. Image submitted by Dr. Mike Scott. Available at: http://www.b-s-h.org.uk/ImageLibrary.asp; with permission.

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Leukemia Cutis Resembling a Flare-Up of Psoriasis

Symptom	Sign	Lab/Radiology
Pruritus	Rash(es)	CBC, eosinophilia
Pruritus	No rash	

From Ferreira M, et al. *Dermatology Online Journal*. 2006;12(3):13; with permission.

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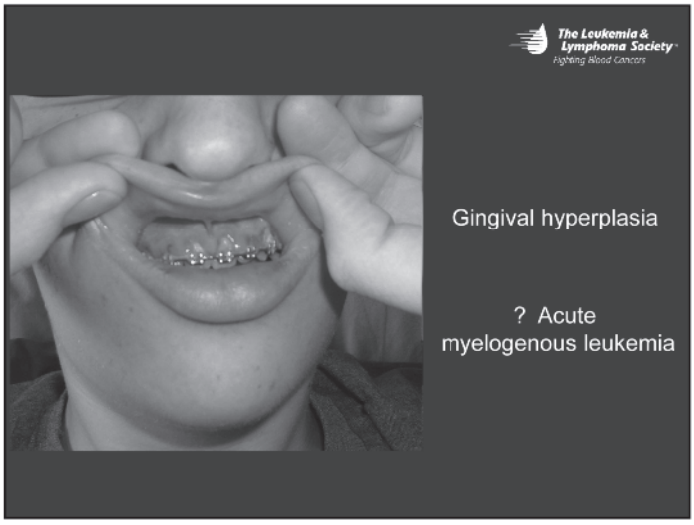
Presentations



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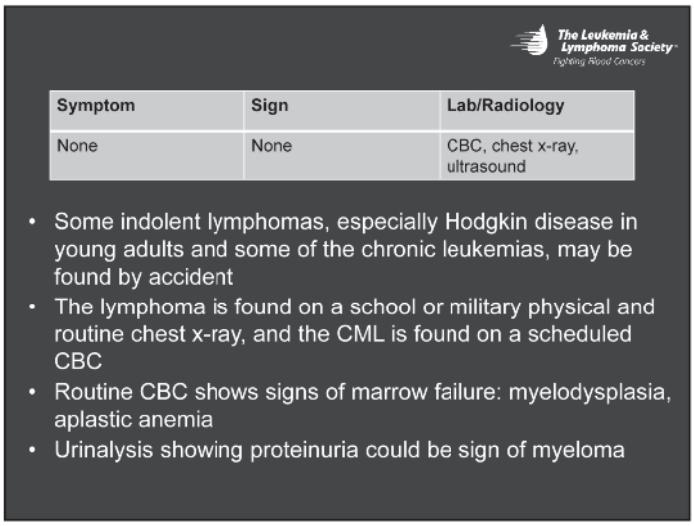

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Presentations

The Leukemia & Lymphoma Society
Fighting Blood Cancers

What we know is infinitely less than all that remains unknown.

– William Harvey (1578–1657)

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Why are we doing what we are doing?

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Risk-Based Healthcare of Adult Survivors of Pediatric Cancer

Kevin C. Oeffinger, MD
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Disclosure of Conflicts of Interest

Kevin C. Oeffinger, MD

Dr. Kevin C. Oeffinger has no affiliations with commercial interests to disclose.

Presentations

Outline

- Background
- Mortality and morbidity
- Three illustrative cancers
- Risk-based healthcare of survivors
  - Emphasize the potential to modify outcomes through risk-based care

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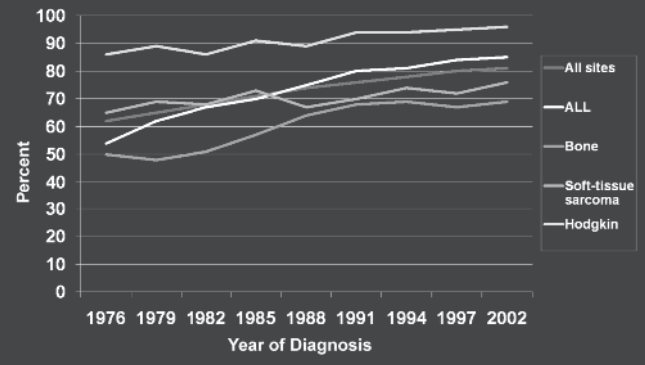
5-Year Survival Rates, Ages 0–19 Years



Horner MJ, et al. http://seer.cancer.gov/csr/1975_1976. Accessed August 28, 2009.

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Pediatric Cancer Survivors

- Over 80% 5-year survival
- 329,000 childhood cancer survivors in the United States
- About 1:570 young adults in the United States is a pediatric cancer survivor

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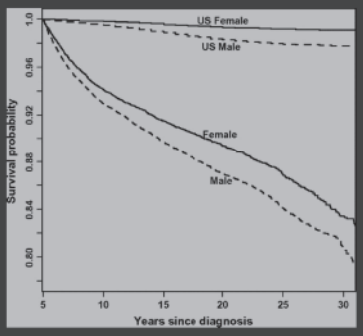
Mortality Rates of >5-Year Childhood Cancer Survivors vs US Population



- Late causes of mortality:
  - Second cancers
  - Cardiac disease
  - Pulmonary disease
- Standard mortality ratio is higher for women than men

Mertens AC, et al. *J Natl Cancer Inst.* 2008;100:1368-1379; with permission.

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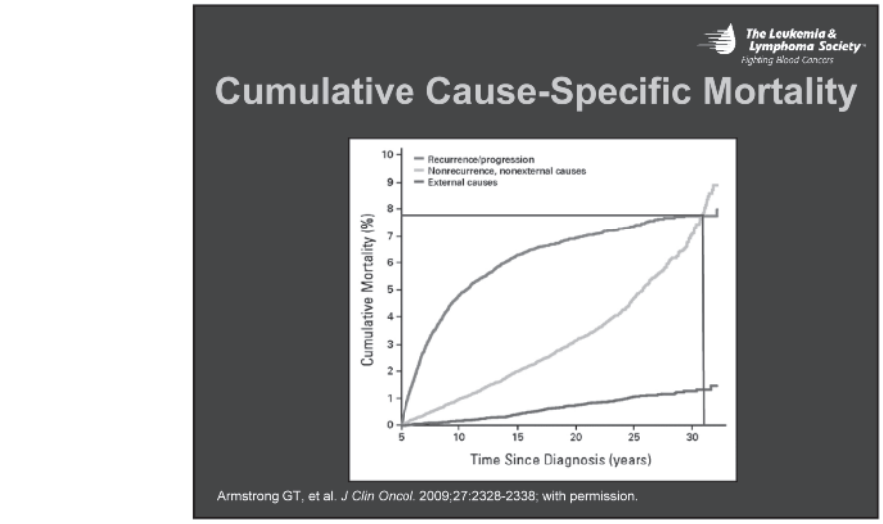

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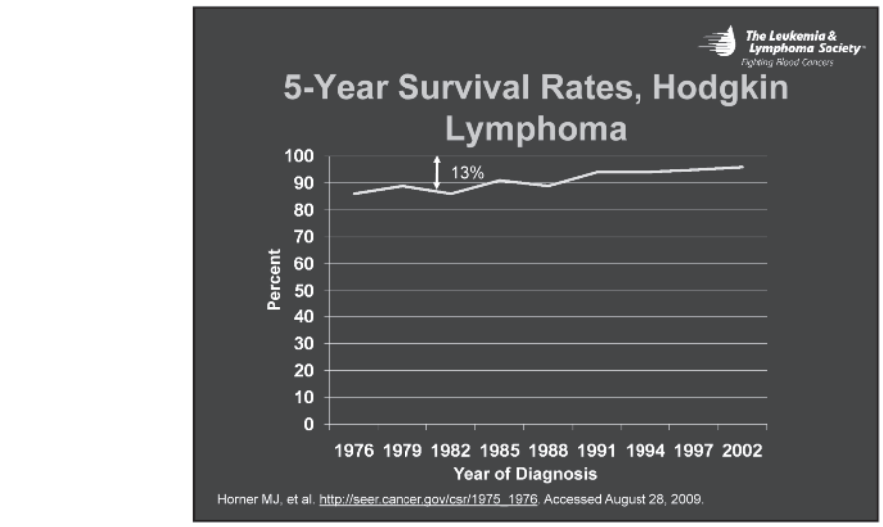

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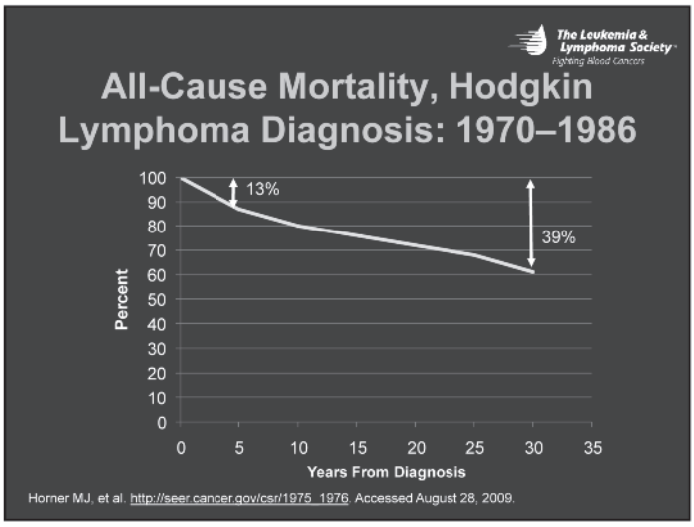

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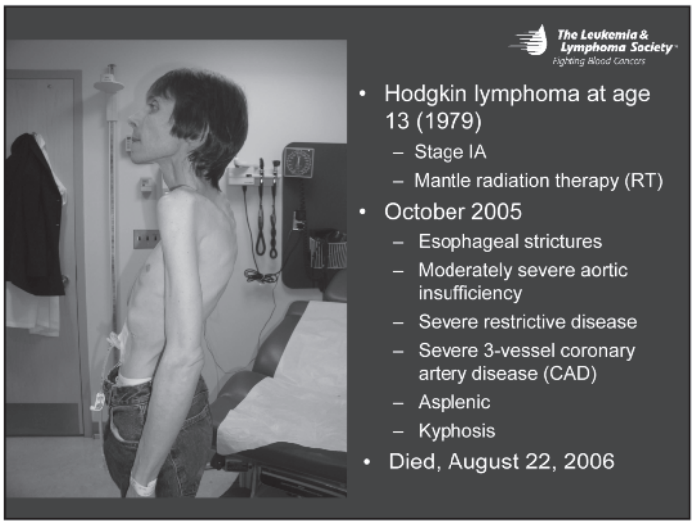

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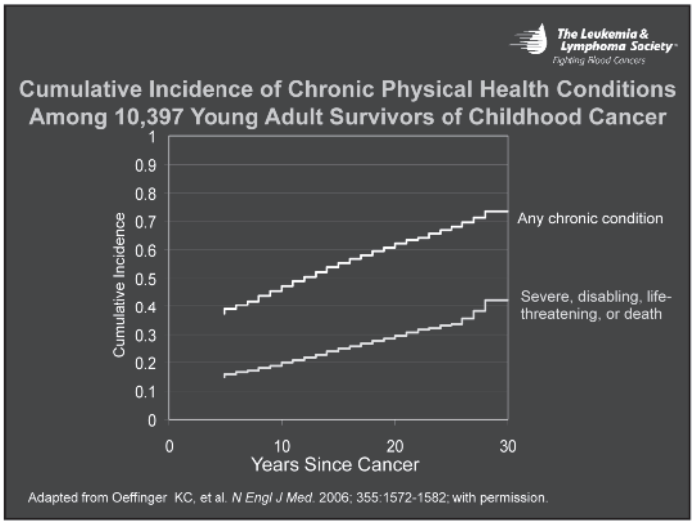

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System	Exposure	Potential Late Effects
Cardiac	RT Anthracyclines	Valvular disease Pericarditis Myocardial infarction Congestive heart failure
Pulmonary	RT Carmustine (BCNU)/lomustine (CCNU)	Restrictive lung disease Exercise intolerence
Renal/urologic	RT Platinums Ifosfamide/cyclophosphamide	Atrophy or hypertrophy Renal insufficiency or failure
Endocrine	RT Alkylating agents	Growth failure Pituitary, thyroid, adrenal disease Ovarian or testicular failure Delayed 2° sex characteristics Infertility
Central nervous system	RT Intrathecal chemotherapy	Learning disabilities Cognitive dysfunction
Psychologic	Cancer	Post-traumatic stress Employment and educational problems Insurance discrimination Adaptation/problem solving
Second malignancies	RT Alkylating agents Epipodophyllotoxins	Solid tumors Leukemia Lymphoma

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Illustrative Examples

- Breast cancer following chest RT
- Coronary artery disease post chest RT
- Cardiovascular disease post–acute lymphoblastic leukemia (ALL)
- Key points:
  - Common rather than rare
  - Window of time – clinically silent
  - Role of prevention and early intervention

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- 11-year-old girl
  - Cervical adenopathy
  - Mediastinal mass

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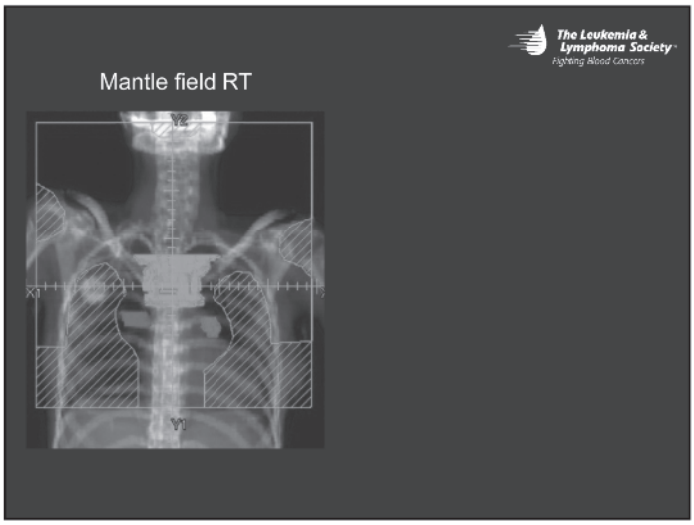

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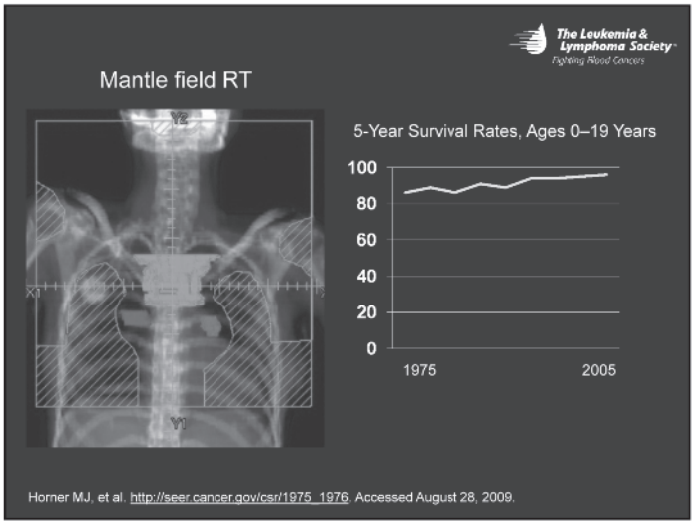

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- Hodgkin lymphoma at age 17 (1982)
  - MOPP
  - Mantle 3639 cGy/lung 1630 cGy
  - MACOP/B – doxorubicin 200 mg/m^2
- Breast cancer – age 33 years
  - Infiltrating ductal CA – 4.5 mm
  - $T_1N_0M_0$
  - Modified radical mastectomy
  - Doxorubicin 221 mg/m^2
- Congestive heart failure – age 34
  - Ejection fraction = 20%–25%
  - Ejection fraction increased to 40% on 3 drugs

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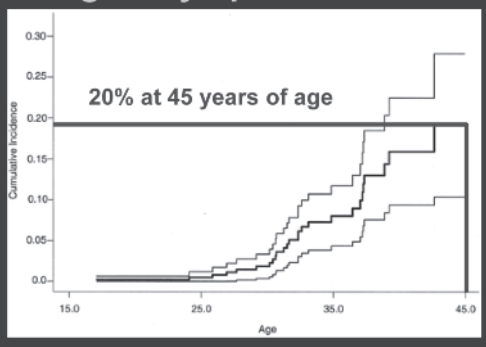
Cumulative Incidence of Breast Cancer in Hodgkin Lymphoma Survivors



Adapted from Bhatia S, et al. *J Clin Oncol*. 2003;21:4386-4394; with permission.

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Breast Cancer Post-RT

- Onset – 8 years post-RT
- Median interval – 16 years post-RT
- Median age at diagnosis – early 30s
- 5-year prognosis strongly associated with stage of disease at diagnosis
- Limitations in treatment options
  - RT
  - Anthracyclines

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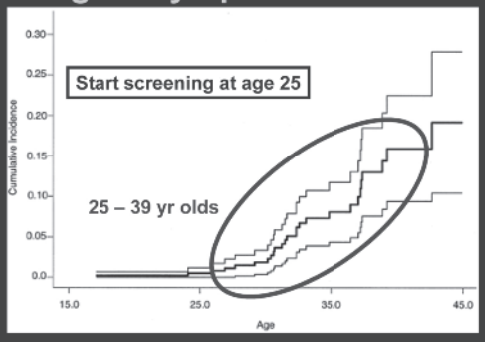
Cumulative Incidence of Breast Cancer in Hodgkin Lymphoma Survivors



Adapted from Bhatia S, et al. *J Clin Oncol*. 2003;21:4386-4394; with permission.

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Early Detection of Breast Cancer

- Starting at the age of 25 or 8 years after RT:
  - Breast self-examination every month
  - Examination by a clinician every 6 months
  - Mammogram annually with breast MRI as an adjunct where available

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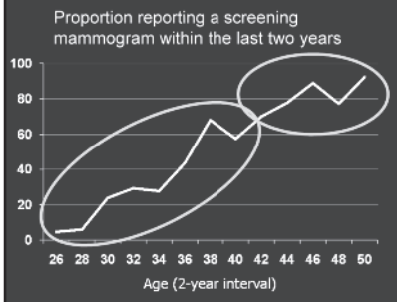
Breast Cancer Surveillance Practices Among Women Treated With Chest RT for a Childhood Cancer



- Breast cancer screening post–chest RT recommended, starting at age 25
- Of 551 survivors treated with chest RT:
  - 47% of women ages 25–39 had never had a mammogram
  - 53% of women ages 40–50 were being regularly screened

Oeffinger KC, et al. *JAMA*. 2009; 301:404-414.

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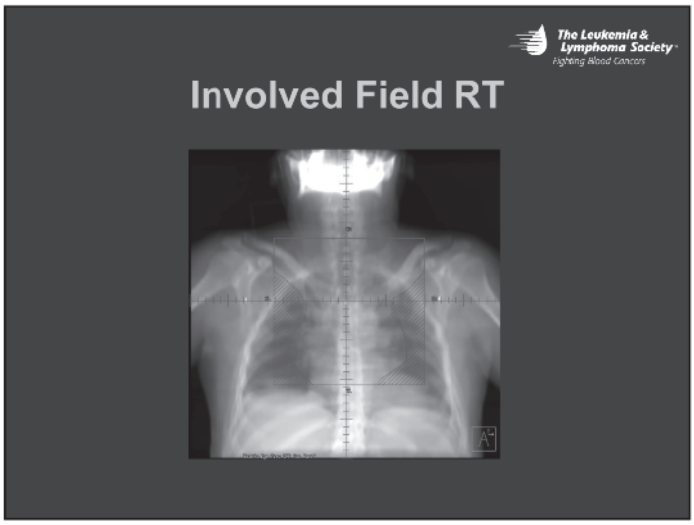

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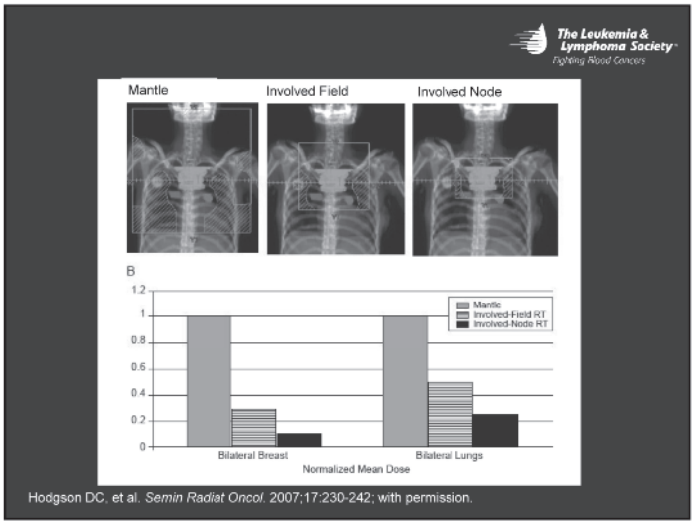

Hodgson DC, et al. *Semin Radiat Oncol.* 2007;17:230-242; with permission.

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Mantle/Mediastinal RT

- Average of 11.2 years follow-up – standardized mortality ratio of myocardial infarction (MI) = 3.2
- By 30 years, cumulative incidence of MI = 12.9%
- By 20 years post–moderate dose RT (37.2 Gy), actuarial risk of symptomatic CAD = 21.2%
- Heidenreich PA, et al. *J Clin Oncol*. 2007;25:43-49.
  - 294 asymptomatic Hodgkin lymphoma survivors
  - Stress echo and radionucleotide perfusion scan
  - 21% with abnormal testing
  - 11% with CAD proven by cardiac catheterization
  - Functional (not anatomic) method of detection

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CT Coronary Angiography

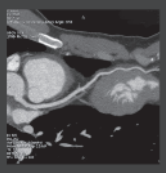

Figure 1.
CT showing a normal left anterior descending artery with curved reconstruction.

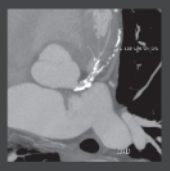

Figure 2.
CT showing a curved reconstruction of left main and proximal left anterior descending arteries with numerous calcified plaques.

Rademaker J, et al. *Am J Roentgenol*. 2008;191:32-37.

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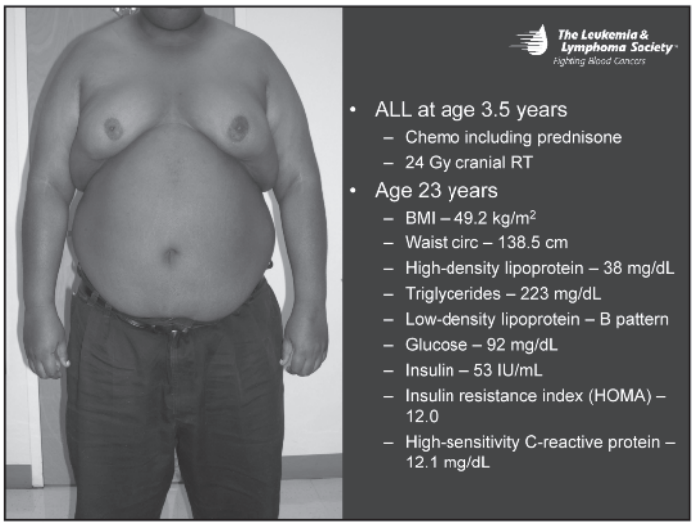

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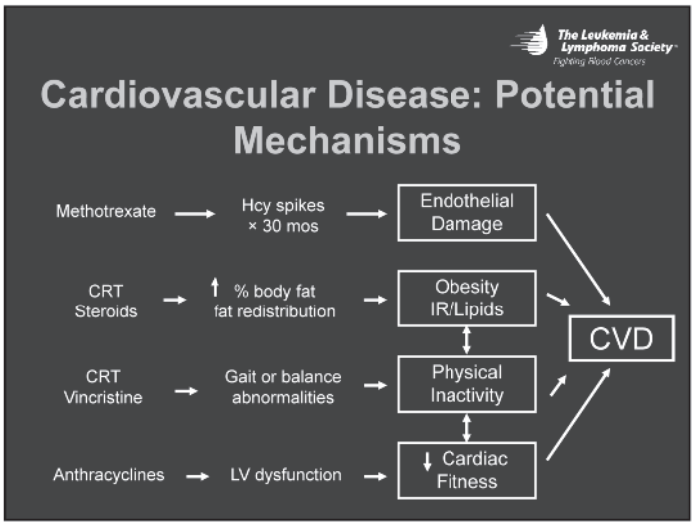

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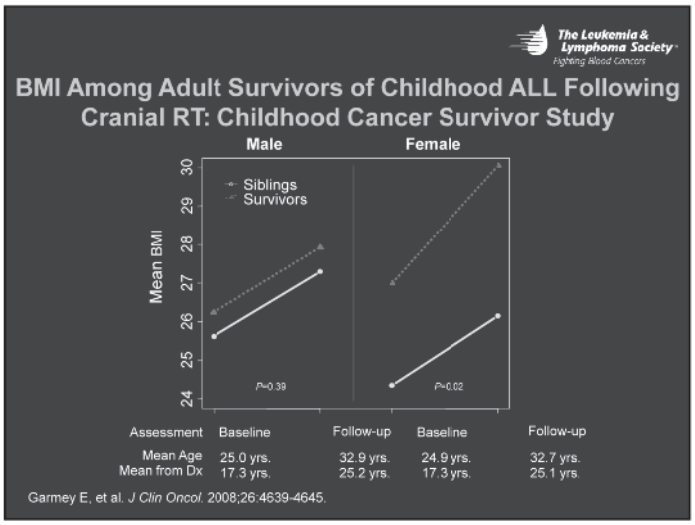
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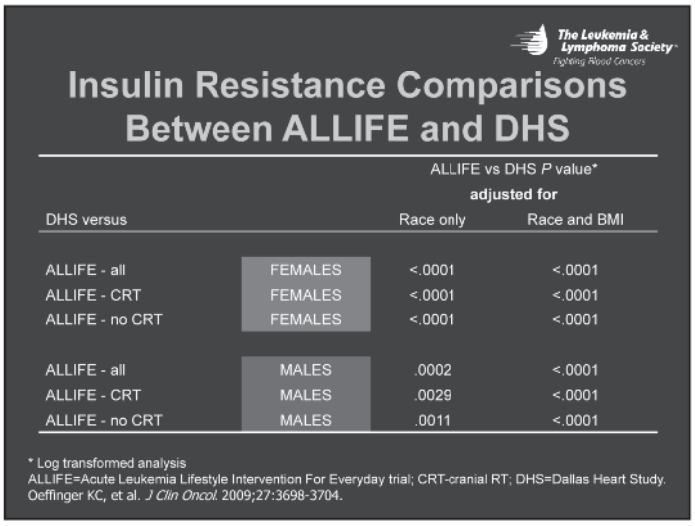
BMI Among Adult Survivors of Childhood ALL Following Cranial RT: Childhood Cancer Survivor Study
Male
Female
Siblings
Survivors
Mean BMI
30
29
28
27
26
25
24
P=0.39
P=0.02
Assessment Baseline Follow-up Baseline Follow-up
Mean Age 25.0 yrs. 32.9 yrs. 24.9 yrs. 32.7 yrs.
Mean from Dx 17.3 yrs. 25.2 yrs. 17.3 yrs. 25.1 yrs.
Garmey E, et al. J Clin Oncol. 2008;26:4639-4645.

69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Insulin Resistance Comparisons Between ALLIFE and DHS
ALLIFE vs DHS P value*
adjusted for
DHS versus
Race only
Race and BMI
ALLIFE - all FEMALES <.0001 <.0001
ALLIFE - CRT FEMALES <.0001 <.0001
ALLIFE - no CRT FEMALES <.0001 <.0001
ALLIFE - all MALES .0002 <.0001
ALLIFE - CRT MALES .0029 <.0001
ALLIFE - no CRT MALES .0011 <.0001
* Log transformed analysis
ALLIFE=Acute Leukemia Lifestyle Intervention For Everyday trial; CRT-cranial RT; DHS=Dallas Heart Study.
Oeffinger KC, et al. J Clin Oncol. 2009;27:3698-3704.

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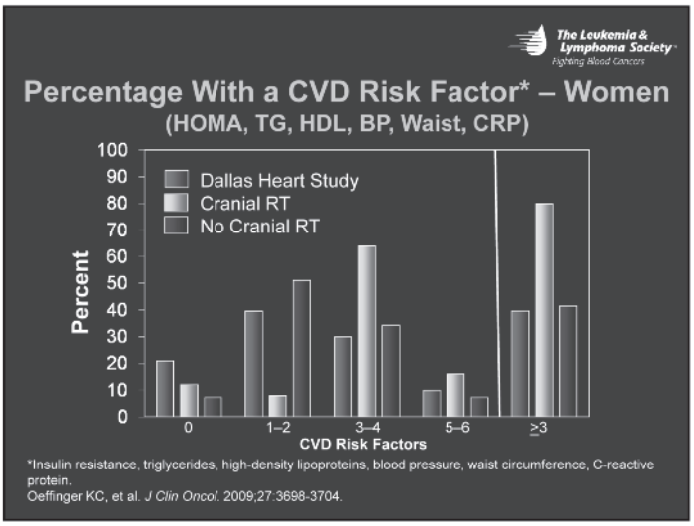

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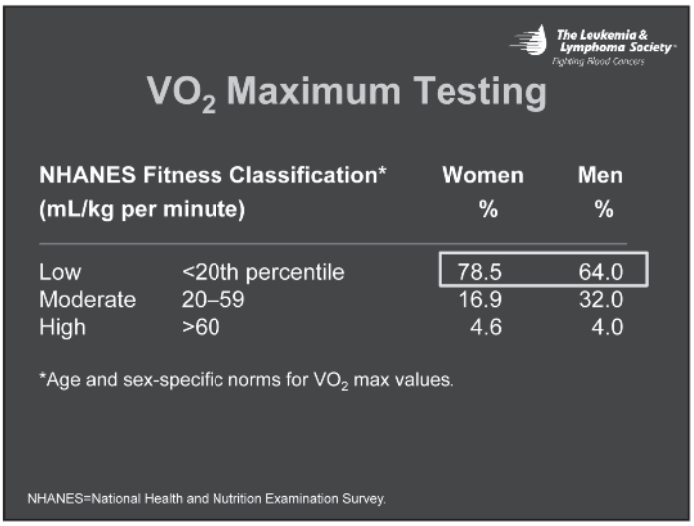

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Model for Risk-Based Care

- High-risk population
- Wide array of potential late effects
- Risk often does not plateau with aging
- Clinically silent period for many late effects – 20–30 years
- Potentially modifiable by secondary or tertiary prevention and early diagnosis and intervention

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Plan for Risk-Based Care

- Monitor for recurrence of cancer
- Surveillance for second cancers and late effects
  - Early diagnosis and intervention
- Prevention
  - Tobacco use, physical activity, calcium intake
- Counseling and education

National Cancer Policy Board and Institute of Medicine. *Childhood Cancer Survivorship: Improving Care and Quality of Life*. 2003.
Oeffinger KC, Hudson MM. *CA Cancer J Clin*. 2004;54:208-236.

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Standardized Screening

- Late Effects Screening Guidelines from the Children's Oncology Group
- www.survivorshipguidelines.org
- Melissa Hudson/Wendy Landier
- Multidisciplinary
- Strength of the association of treatment exposure to late effects
- Principles of screening/surveillance in a high-risk population

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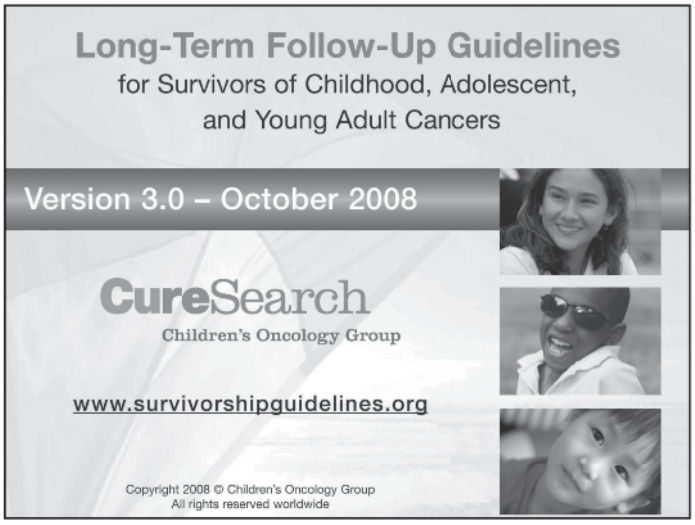

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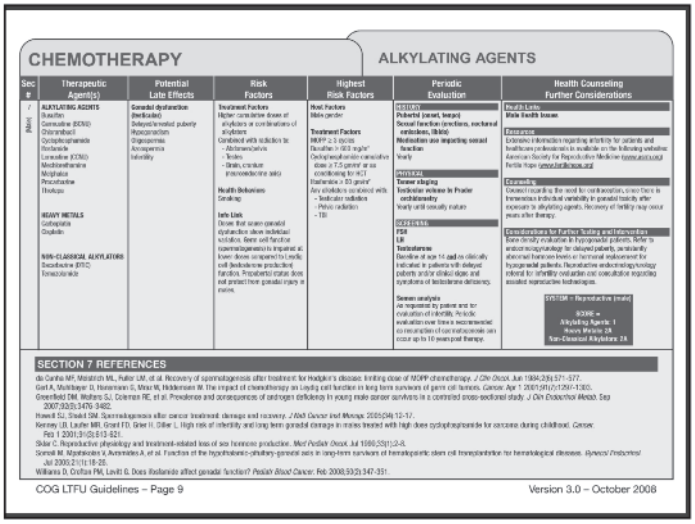

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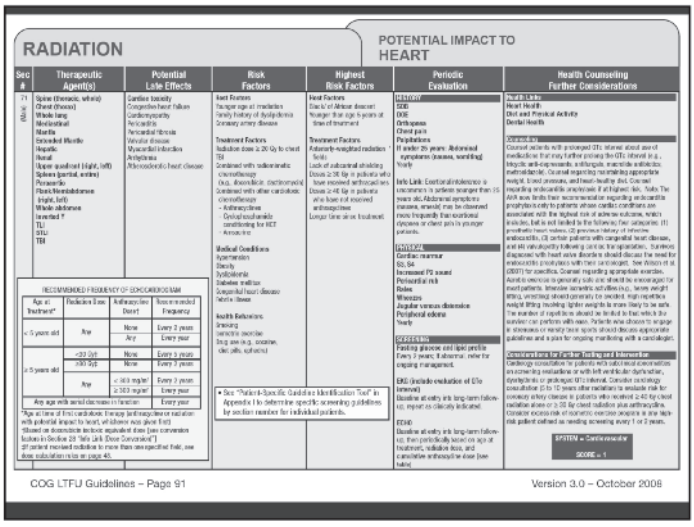

RADIATION

POTENTIAL IMPACT TO HEART

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
71 (Abd.)	Spine (thoracic, whole) Chest (thoracic) Whole lung Mediastinal Mantle Extended Mantle Hepatic Renal Upper quadrant (right, left) Spleen (partial, entire) Pancreatic Flank/hemiabdomen (right, left) Whole abdomen Inverted Y TLI STLI TBI	Cardiac toxicity Congestive heart failure Cardiomyopathy Pericarditis Pericardial fibrosis Valvular disease Myocardial infarction Arrhythmia Atherosclerotic heart disease	Heart Factors Younger age at irradiation Family history of dyslipidemia Coronary artery disease Treatment Factors Radiation dose ≥ 20 Gy to chest TBI Combined with radiomimetic chemotherapy (e.g., doxorubicin, dactinomycin) Combined with other cardiotoxic chemotherapy - Anthracyclines - Cyclophosphamide conditioning for HCT - Amsacrine Medical Conditions Hypertension Obesity Dyslipidemia Diabetes mellitus Congenital heart disease Valve disease Health Behaviors Smoking Sedentary lifestyle Drug use (e.g., cocaine, diet pills, ephedra)	Heart Factors Black/of African descent Younger than age 5 years at time of treatment Treatment Factors Anteriorly-weighted radiation fields Lack of subcarinal shielding Doses ≥ 30 Gy in patients who have received anthracyclines Doses ≥ 40 Gy in patients who have not received anthracyclines Longer time since treatment	HISTORY SOB DOE Orthopnea Chest pain Palpitations If under 25 years: Abdominal symptoms (nausea, vomiting) Yearly Info Link: Exercise intolerance is uncommon in survivors younger than 15 years old. Abdominal symptoms (nausea, emesis) may be observed more frequently than exertional dyspnea or chest pain in younger patients. EXAM Cardiac murmur S3, S4 Increased PS sound Pericardial rub Rales Wheezes Jugular venous distension Peripheral edema Yearly DIAGNOSTIC Fasting glucose and lipid profile Every 2 years; if abnormal, refer for ongoing management. EKG (include evaluation of QTc interval) Baseline at entry into long-term follow-up, repeat as clinically indicated. ECHO Baseline at entry into long-term follow-up, then periodically based on age at treatment, radiation dose, and cumulative anthracycline dose (see table)	Health Links Heart Health Diet and Physical Activity Dental Health Counseling Counsel patients with prolonged QTc interval about use of medications that may further prolong the QTc interval (e.g., tricyclic anti-depressants, antifungals, macrolide antibiotics, methadone). Counsel regarding maintaining appropriate weight, blood pressure, and heart-healthy diet. Counsel regarding cardiac prophylaxis if at highest risk. Note: The AHA now limits their recommendation regarding cardiac prophylaxis only to patients whose cardiac conditions are associated with the highest risk of adverse outcome, which includes, but is not limited to the following four categories: (1) prosthetic heart valves, (2) previous history of infective endocarditis, (3) certain patients with congenital heart disease, and (4) cardiopathy following cardiac transplantation. Survivors diagnosed with heart valve disorders should discuss the need for endocarditis prophylaxis with their cardiologist. See Wilson et al. (2007) for specifics. Counsel regarding appropriate exercise. Aerobic exercise is generally safe and should be encouraged for most patients. Intensive isometric activities (e.g., heavy weight lifting, wrestling) should generally be avoided. High-repetition weight lifting involving lighter weights is more likely to be safe. The number of repetitions should be limited to that which the survivor can perform with ease. Patients who choose to engage in strenuous or varsity-level sports should discuss appropriate guidelines and a plan for ongoing monitoring with a cardiologist. Considerations for Further Testing and Intervention Cardiology consultation for patients with subclinical abnormalities on screening evaluations or with left ventricular dysfunction, dysrhythmia or prolonged QTc interval. Consider cardiology consultation 2 to 10 years after radiation to evaluate risk for coronary artery disease in patients who received ≥ 40 Gy chest radiation alone or ≥ 30 Gy chest radiation plus anthracycline. Consider excess risk of isometric exercise program in one high-risk patient defined as needing screening every 1 or 2 years. SYSTEM = Cardiovascular SCORE = 1

RECOMMENDED FREQUENCY OF ECHOCARDIOGRAM

Age at Treatment*	Radiation Dose	Anthracycline Dose	Recommended Frequency
< 5 years old	Any	None	Every 2 years
		Any	Every year
≥ 5 years old	<30 Gy†	None	Every 3 years
	≥30 Gy†	None	Every 2 years
	Any	< 300 mg/m²	Every 2 years
		≥ 300 mg/m²	Every year
Any age with serial decrease in function			Every year

*Age at time of first candidacy. Therapy (anthracycline or radiation with potential impact to heart, all above was given first)
†Based on doxorubicin isotoxic equivalent dose (see conversion factors in Section 23 "We'll Link Dose Concurrent")
‡If patient received radiation to more than one specified field, see dose calculation rules on page 45.

• See "Patient-Specific Guideline Identification Tool" in Appendix I to determine specific screening guidelines by section number for individual patients.

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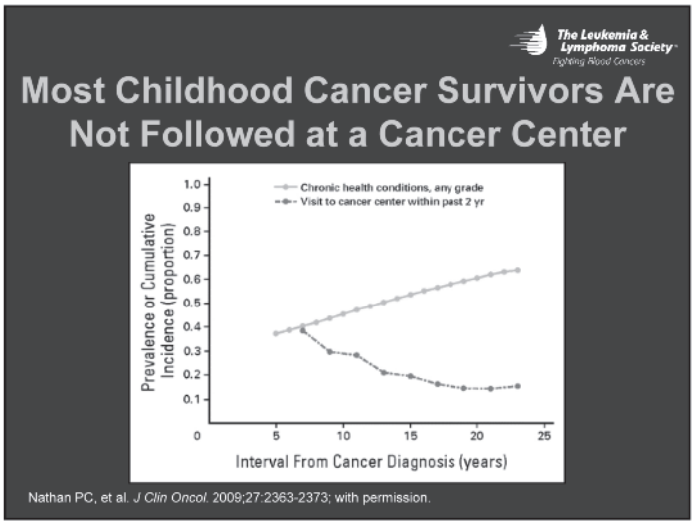

Nathan PC, et al. *J Clin Oncol.* 2009;27:2363-2373; with permission.

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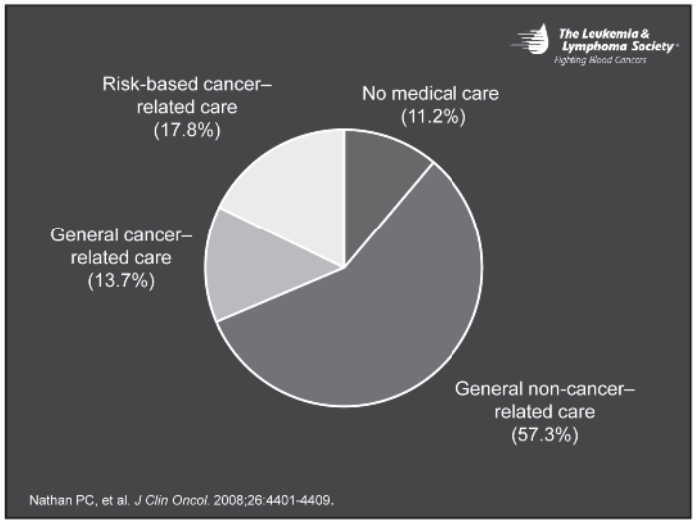
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Risk-based cancer–related care (17.8%)
No medical care (11.2%)
General cancer–related care (13.7%)
General non-cancer–related care (57.3%)
Nathan PC, et al. J Clin Oncol. 2008;26:4401-4409.

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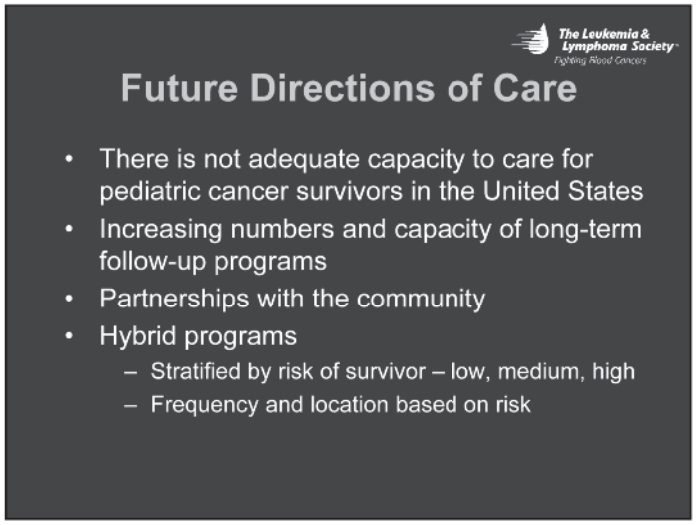
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Future Directions of Care
• There is not adequate capacity to care for pediatric cancer survivors in the United States
• Increasing numbers and capacity of long-term follow-up programs
• Partnerships with the community
• Hybrid programs
– Stratified by risk of survivor – low, medium, high
– Frequency and location based on risk

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Summary

- Cancer survivors face long-term risks
- Many late effects are modifiable
- Goal of risk-based survivor care
  - Reduce morbidity and mortality rates
  - Enhance quality of life

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Acknowledgments

- American Academy of Family Physicians
- The Leukemia & Lymphoma Society
- Leslie Robison, PhD
- Melissa Hudson, MD
- Ann Mertens, PhD
- Charles Sklar, MD
- ALLIFE Co-Investigators
- Our survivors and their families

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Question-and-Answer Session

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Thank You

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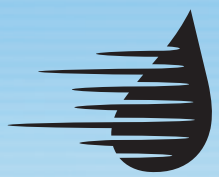

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