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

Introductory Materials

Version 6.0
October 2023
Abstract

Release date: October 2023

Status: Updated from Version 5.0 incorporating modifications based on recommendations from the Children’s Oncology Group’s Long-Term Follow-Up Guideline Core Committee and its associated multidisciplinary Task Forces.

Overview: These risk-based, exposure-related clinical practice guidelines provide recommendations for screening and management of late effects in survivors of pediatric malignancies. (“Pediatric malignancies” are defined as those malignancies commonly associated with the pediatric population that may arise during childhood, adolescence or young adulthood.) A complementary set of patient education materials, known as “Health Links” accompany the guidelines in order to enhance patient follow-up visits and broaden the application of these guidelines. Additional accompanying materials include detailed instructions, templates for cancer treatment summary forms, a radiation reference guide, and a tool to assist in identifying guideline applicability for individual survivors based on therapeutic exposures. The information provided in these guidelines is important for primary healthcare providers in the fields of pediatrics, oncology, internal medicine, family practice, and gynecology, as well as subspecialists in many fields. Implementation of these guidelines is intended to increase awareness of potential late effects and to standardize and enhance follow-up care provided to survivors of pediatric malignancies throughout their lifespan.

Source: Version 6.0 of the Children’s Oncology Group Long-Term Follow-Up Guidelines for Survivors of Childhood, Adolescent, and Young Adult Cancers, and related Health Links, can be downloaded in their entirety from www.survivorshipguidelines.org.

Suggested Citations for COG Long-Term Follow-Up Guidelines

Guidelines

Guidelines Methodology

Health Links Background and Application
Disclaimer and Notice of Proprietary Rights

Introduction to Late Effects Guidelines and Health Links: The Long-Term Follow-Up Guidelines for Survivors of Childhood, Adolescent, and Young Adult Cancers and accompanying Health Links were developed by the Children's Oncology Group as a collaborative effort of the Late Effects Committee and Nursing Discipline and are maintained and updated by the Children's Oncology Group's Long-Term Follow-Up Guidelines Core Committee and its associated Task Forces.

For Informational Purposes Only: The information and contents of each document or series of documents made available by the Children's Oncology Group relating to late effects of cancer treatment and care or containing the title Long-Term Follow-Up Guidelines for Survivors of Childhood, Adolescent, and Young Adult Cancers or the title Health Link, whether available in print or electronic format (including any digital format, e-mail transmission, or download from the website), shall be known hereinafter as “Informational Content”. All Informational Content is for informational purposes only. The Informational Content is not intended to substitute for medical advice, medical care, diagnosis or treatment obtained from a physician or healthcare provider.

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Contributors Panel of Experts

The following members of the Children’s Oncology Group Long-Term Follow-Up (LTFU) Guidelines Core Committee participated in comprehensive review and scoring of Version 6.0 of the Children’s Oncology Group Long-Term Follow-Up Guidelines for Survivors of Childhood, Adolescent, and Young Adult Cancers:

### CORE COMMITTEE

**Smita Bhatia, MD, MPH**
Co-Chair, COG LTFU Guidelines Core Committee  
Professor and Vice Chair, Pediatrics  
Director, Institute for Cancer Outcomes and Survivorship  
Children’s Hospital of Alabama  
University of Alabama at Birmingham  
Birmingham, AL

**Matthew J. Ehrhardt, MD, MS**
Co-Chair, COG LTFU Guidelines Core Committee  
Associate Member, Department of Oncology  
St. Jude Children’s Research Hospital  
Memphis, TN

**Melissa M. Hudson, MD**
Co-Chair, COG LTFU Guidelines Core Committee  
Member, Department of Oncology  
Co-Leader, Cancer Control & Survivorship Program  
Director, Cancer Survivorship Division and After Completion of Therapy Program  
St. Jude Children’s Research Hospital  
Memphis, TN

**Louis S. Constine, MD, FASTRO, FACR**
The Philip Rubin Professor of Radiation Oncology and Pediatrics  
Vice Chair, Department of Radiation Oncology  
Director, The Judy DiMarzo Cancer Survivorship Program  
James P. Wilmot Cancer Institute  
University of Rochester Medical Center  
Rochester, NY

**Wendy Landier, PhD, CRNP**
M.D., CRNP, OCN, ONS, FAAN  
Co-Chair, COG LTFU Guidelines Core Committee  
Member, Department of Oncology  
Member, Cancer Control and Survivorship Program  
Director, Cancer Survivorship Division and After Completion of Therapy Program  
St. Jude Children’s Research Hospital  
Memphis, TN

**Saro Armenian, DO, MPH**
Professor, Departments of Pediatrics and Population Sciences  
Director, Institute for Cancer Outcomes and Survivorship  
Children’s Hospital of Alabama  
University of Alabama at Birmingham  
Birmingham, AL

**Alicia Kunin-Batson, PhD**
Co-Chair, COG LTFU Guidelines Core Committee  
Associate Member, Department of Pediatrics  
Director, Pediatric Survivorship Fellowship  
Memorial Sloan Kettering Cancer Center  
New York, NY

**Danielle N. Friedman, MD, MS**
Co-Chair, COG LTFU Guidelines Core Committee  
Associate Member, Department of Pediatrics  
Director, Pediatric Survivorship Fellowship  
Memorial Sloan Kettering Cancer Center  
New York, NY

**Kay W. Chang, MD**
Professor, Department of Otolaryngology  
Stanford University School of Medicine  
Palo Alto, CA

**Ming Hui Chen, MD, MMSc, FACC, FASE**
Associate Professor of Pediatrics  
Director, Cardiovascular Health for Cancer Survivors Program  
Boston Children’s Hospital  
Dana Farber Cancer Institute  
Harvard Medical School  
Boston, MA

**Smita Bhatia, MD, MPH**
Co-Chair, COG LTFU Guidelines Core Committee  
Professor and Vice Chair, Pediatrics  
Director, Institute for Cancer Outcomes and Survivorship  
Children’s Hospital of Alabama  
University of Alabama at Birmingham  
Birmingham, AL

**Melissa A. Acquazzino, MD, MS**
Associate Professor, Pediatrics  
Medical Director Pediatric Cancer Survivorship Clinic  
University of Nebraska Medical Center and  
Children’s Hospital & Medical Center  
Omaha, NE

**Daniel C. Bowers, MD**
Professor, Pediatrics and Neurological Surgery  
Director, After the Cancer Experience Program  
UT Southwestern Medical School  
Dallas, TX

**Sharon Castellino, MD, MSc**
Professor of Pediatrics  
Emory University  
Director, Leukemia/Lymphoma Program  
Aftac Cancer and Blood Disorders Center  
Children’s Healthcare of Atlanta  
Atlanta, GA

**Wassim Chemaitilly, MD**
Clinical Director, Division of Endocrinology and Diabetes  
UPMC Children’s Hospital of Pittsburgh  
Professor of Pediatrics  
University of Pittsburgh School of Medicine  
Pittsburgh, PA

**Johnnie K. Bass, AuD, PhD**
Research Audiologist, Rehabilitation Services  
St. Jude Children’s Research Hospital  
Memphis, TN
Contributors
Panel of Experts continued

The following members of the Children's Oncology Group Long-Term Follow-Up (LTFU) Guidelines Core Committee participated in comprehensive review and scoring of Version 6.0 of the Children's Oncology Group Long-Term Follow-Up Guidelines for Survivors of Childhood, Adolescent, and Young Adult Cancers:

Eric J. Chow, MD, MPH
Associate Professor, Pediatrics
Director, Cancer Survivor Program
University of Washington School of Medicine
Seattle Children’s Hospital
Seattle, WA

Douglas Cipkala, MD
Children’s Center for Cancer and Blood Disorders
Peyton Manning Children’s Hospital at Ascension St. Vincent
Assistant Clinical Professor Marian University College of Osteopathic Medicine
Indianapolis, IN

Laurie E. Cohen, MD
Professor of Pediatrics
Chief, Division of Pediatric Endocrinology and Diabetes
Associate Director, Reassessment and Evaluation After Cancer Treatment (REACT) Clinic
The Children’s Hospital at Montefiore
Albert Einstein College of Medicine
Bronx, NY

Karen E. Effinger, MS, MD
Associate Professor Pediatrics
Medical Director, Cancer Survivor Program
Emory University
Children’s Healthcare of Atlanta
Atlanta, GA

Natia Esiashvili, MD
Professor, Chief Quality Officer, Department of Radiation Oncology
Emory University
Atlanta, GA

Paul G. Fisher, MD, MHS
Interim Chair, Department of Neurology and Neurological Sciences
Professor, Neurology and Pediatrics
Stanford University
Palo Alto, CA

Kayla L. Foster, MD, MPH
Assistant Professor, Pediatrics
Texas Children’s Cancer and Hematology Centers
Baylor College of Medicine
Houston, TX

M. Monica Gramatges, MD, PhD
Associate Professor, Pediatrics
Associate Chief, Oncology
Texas Children’s Cancer and Hematology Center
Baylor College of Medicine
Houston, TX

Daniel M. Green, MD
Member, Departments of Oncology and Epidemiology and Cancer Control
St. Jude Children’s Research Hospital
Memphis, TN

Gregory M.T. Guilcher, MD, FRCP, FAAP
Associate Professor of Oncology and Pediatrics
Pediatric Medical Director, Alberta Blood and Marrow Transplant Program
Cumming School of Medicine, University of Calgary
Calgary, AB, Canada

Tara O. Henderson, MD, MPH
Arthur and Marian Edelstein Professor of Pediatrics
Chief, Cancer and Blood Diseases Service Line CCHA
Section Chief, Pediatric Hematology, Oncology and Stem Cell Transplantation
The University of Chicago
Chicago, IL

David Hodgson, MD, MPH, FRCP(C)
Professor, Department of Radiation Oncology
Princess Margaret Cancer Centre, University of Toronto
Medical Director, Pediatric Oncology Group of Ontario
POGO Chair, Childhood Cancer Control, University of Toronto
Toronto, Canada

Lisa B. Kenney, MD, MPH
Senior Physician, David B. Perini Jr., Quality of Life Clinic
Dana-Farber Boston Children’s Cancer and Blood Disorders Center
Assistant Professor of Pediatrics, Harvard Medical School
Boston, MA

James Klosky, PhD, ABPP
Professor, Department of Pediatrics
Emory University School of Medicine &
Director of Psychology and Neuropsychology
Aflac Cancer and Blood Disorders Center
Children’s Healthcare of Atlanta
Atlanta, GA

Kevin R. Krull, PhD, ABPP
Chair, Department of Psychology and Biobehavioral Sciences
St. Jude Children’s Research Hospital
Memphis, TN
Contributors
Panel of Experts continued

The following members of the Children's Oncology Group Long-Term Follow-Up (LTFU) Guidelines Core Committee participated in comprehensive review and scoring of Version 6.0 of the *Children’s Oncology Group Long-Term Follow-Up Guidelines for Survivors of Childhood, Adolescent, and Young Adult Cancers*:

**Lillian R. Meacham, MD**
Professor of Pediatrics
Emory University
Chair for Cancer Survivorship
Director of the Fertility Preservation and Reproductive Health Program
Children’s Healthcare of Atlanta
Atlanta, GA

**Cesar A. Migliorati, DDS, MS, PhD**
Professor, Oral Medicine
Department of Oral and Maxillofacial Diagnostic Sciences
University of Florida College of Dentistry
Gainesville, Florida

**Daniel A. Mulrooney, MD, MS**
Associate Member, Department of Oncology
Deputy Director, After Completion of Therapy Clinic
St. Jude Children's Research Hospital
Memphis, TN

**Paul C. Nathan, MD, MSc, FRCP**
Professor, Paediatrics and Health Policy, Management & Evaluation
Director, Aftercare Program
The Hospital for Sick Children
University of Toronto
Toronto, Ontario, Canada

**Kirsten K. Ness, PT, PhD**
Member, Department of Epidemiology and Cancer Control
St. Jude Children’s Research Hospital
Memphis, TN

**Kevin C. Oeffinger, MD**
Professor, Medicine and Community and Family Medicine
Director, Center for Onco-Primary Care and Supportive Care and Survivorship Center
Duke University Medical Center
Durham, NC

**Linda Rivard, RN, BSN, CPON**
Survivorship Coordinator/P.O.S.T. Clinic
Patient Advocate
Pediatric Hematology/Oncology
Advocate Children’s Hospital
Oak Lawn, IL

**Fiona Schulte, PhD**
Associate Professor, Department of Oncology, Division of Psychosocial Oncology
Cumming School of Medicine, University of Calgary
Hematology, Oncology and Transplant Program
Alberta Children’s Hospital
Calgary, Canada

**Ami J. Shah, MD**
Clinical Professor of Pediatrics
Division of Hematology/Oncology/Stem Cell Transplantation and Regenerative Medicine
Stanford School of Medicine
Lucile Packard Children’s Hospital
Palo Alto, CA

**Sheri L. Spunt, MD, MBA**
Endowed Professor of Pediatric Cancer
Department of Pediatrics
Stanford University School of Medicine
Stanford, CA

**Stephanie Smith, MD, MPH**
Instructor, Pediatric Oncology
Lucile Packard Children’s Hospital Stanford
Stanford University School of Medicine
Palo Alto, CA

**Nicole Ullrich, MD, PhD, MMSci**
Professor, Neurology
Director of Neurologic NeuroOncology
Dana-Farber/Boston Children’s Cancer and Blood Disorders Center
Harvard Medical School
Boston, MA
# Contributors

## Task Force Membership 2019-2023

<table>
<thead>
<tr>
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<td>Douglas A. Cipkala, MD, Chair</td>
<td>Saint Vincent Hospital and Health Care Center</td>
<td>Pediatric Hematology Oncology</td>
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<td>Pinki Prasad, MD, MPH, Silo Leader</td>
<td>Children's Hospital New Orleans</td>
<td>Pediatric Hematology Oncology</td>
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<td>Tambra R. Dahlheimer, RN, CPNP, CNP</td>
<td>University of Minnesota, Masonic Cancer Center</td>
<td>Pediatric Hematology Oncology</td>
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<td>Kristin Knight, MS, CCC-A, FAA</td>
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<td>Etan Orgel, MD</td>
<td>Keck School of Medicine, University of Southern California</td>
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<td>Catherine Woodman, MD</td>
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<td>Children's Hospital of Philadelphia UMPC</td>
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<td>Nathalie Alois, MD</td>
<td>Université de Montréal</td>
<td>Pediatric Endocrinology</td>
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<td>St. Jude Children's Research Hospital</td>
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<td>Sogol Mostoufi-Moab, MD, MSCE</td>
<td>Children's Hospital of Philadelphia UMPC</td>
<td>Pediatric Oncology &amp; Endocrinology</td>
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<td>Susan V. Shannon, RN, MSN, CPNP, CPON</td>
<td>Miller Children’s and Women’s Hospital Long Beach</td>
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<td>St. Jude Children's Research Hospital</td>
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<td><strong>Clinical Care Translation</strong></td>
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<td>Children's Hospital and Medical Center of Omaha</td>
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<td>Sanford USD Medical Center - Sioux Falls</td>
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<td>Advocate Children's Hospital-Oak Lawn</td>
<td>Pediatric Hematology Oncology</td>
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<td>Daniel Smith, RN, DNP, FNP</td>
<td>St. Jude Children's Research Hospital</td>
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<td>S. Ashley Speckhart, MD</td>
<td>Maine Medical Center, Maine Children’s Cancer Program</td>
<td>Pediatric Hematology Oncology</td>
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<td>Katheryn Tomlinson, RN, BSN</td>
<td>Children's Hospital of Wisconsin</td>
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<td>Christine S Yun, MSN, PNP, CPON</td>
<td>Children's Hospital of Orange County</td>
<td>Pediatric Hematology Oncology</td>
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<td>Emily S. Tonorezos, MD, MPH, Silo Leader</td>
<td>National Cancer Institute</td>
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<td>City of Hope</td>
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<td>UT Southwestern/Simmons Cancer Center-Dallas</td>
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<td>Vincent Horne, MD</td>
<td>Baylor College of Medicine, Texas Children's Hospital</td>
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<td>Children's Healthcare of Atlanta - Egleston</td>
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<td>Megan Pruett, MSN, CPNP</td>
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<td>Roswell Park Comprehensive Care Center</td>
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<td>Seth Rotz, MD</td>
<td>Cleveland Clinic</td>
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<td>Jenna Sopfe, MD</td>
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<td>Karen E. Effinger, MD, MS, <em>Chair</em></td>
<td>Children's Healthcare of Atlanta - Egleston</td>
<td>Pediatric Hematology Oncology</td>
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<td>Kathy J. Ruble, RN, CRNP, PhD, AOCN, <em>Silvo Leader</em></td>
<td>Johns Hopkins University</td>
<td>Pediatric Hematology Oncology</td>
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<td>John K. Petty, MD</td>
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<td>Julia O'Malley Stepeske, RN, BSN, CPON</td>
<td>Advocate Children's Hospital-Park Ridge</td>
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<td>Greg Guilcher, MD, FRCP, FAAP, <em>Chair</em></td>
<td>University of Calgary, Alberta Children's Hospital</td>
<td>Hematopoietic Cell Transplantation and Pediatric Oncology</td>
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<td>Ascension Hospital System Indianapolis</td>
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<td>Yale School of Medicine</td>
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<td>LaVette S. Bowles, MN, Npc</td>
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<td>UC Davis</td>
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<td>Carmen Wilson, PhD</td>
<td>St. Jude Children's Research Hospital</td>
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<td>Lauren Zeitlinger, DO</td>
<td>Orthopedic Specialties of Central PA - UPMC</td>
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<td>Alicia Kunin-Batson, PhD, Chair&lt;br&gt;Ellen van der Plas, PhD, Silo Leader&lt;br&gt;Yin Ting Cheung, PhD&lt;br&gt;Lisa Jacola, PhD, ABPP-CN&lt;br&gt;Katharine Rae Lange, MD&lt;br&gt;Kim Raghurab, PhD</td>
<td>University of Minnesota/Masonic Cancer Center&lt;br&gt;University of Arkansas, Arkansas Children's Hospital&lt;br&gt;Chinese University of Hong Kong&lt;br&gt;St. Jude Children's Research Hospital&lt;br&gt;Hackensack Meridian Children's Health&lt;br&gt;Texas Children's Hospital/Baylor College of Medicine</td>
<td>Neuropsychology&lt;br&gt;Cognitive Neuroscience&lt;br&gt;Pharmacoeconomics&lt;br&gt;Pediatric Neuropsychology&lt;br&gt;Pediatric Hematology Oncology&lt;br&gt;Neuropsychology</td>
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<td>Douglas A. Cipkala, MD, Chair&lt;br&gt;Zsila S. Sadighi, MD, Silo Leader&lt;br&gt;Emma Chang, MD&lt;br&gt;Jessica Goodman, MD&lt;br&gt;Fatema Malbari, MD&lt;br&gt;Susan McGovern, MD, PhD&lt;br&gt;Neha Patel, MD&lt;br&gt;Suzanne M. Russo, MD</td>
<td>Ascension Hospital System Indianapolis&lt;br&gt;University of Texas, MD Anderson St. Luke's Children's Cancer Institute&lt;br&gt;Peyton Manning Children's Hospital&lt;br&gt;Texas Children's Hospital/Baylor College of Medicine&lt;br&gt;University of Texas, MD Anderson&lt;br&gt;Cleveland Clinic&lt;br&gt;UH Seidman Cancer Center</td>
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<td><strong>New Agents</strong></td>
<td>Stephanie Smith, MD, MPH, Chair&lt;br&gt;Maya Lodish, MD, MHSc, Silo Leader&lt;br&gt;Neel S. Bhatt, MD, MBBS, MPH&lt;br&gt;Sharon M. Castellino, MD, MSc&lt;br&gt;Matthew J. Ehrhardt, MD, MS&lt;br&gt;Michael Gleason, MD, MSPH&lt;br&gt;Brinda Mehta, MBBS&lt;br&gt;Esther Adekeye-Oladojo, PhD, MS, RPh&lt;br&gt;Serina Patel, MD&lt;br&gt;Robert Raphael, MD&lt;br&gt;Jessica Sun, MD</td>
<td>Lucile Packard Children's Hospital Stanford University&lt;br&gt;UCSF&lt;br&gt;Seattle Children's Hospital&lt;br&gt;Children's Healthcare of Atlanta - Egleston&lt;br&gt;St. Jude Children's Research Hospital&lt;br&gt;Texas Children's Hospital/Baylor College of Medicine&lt;br&gt;Children's Hospital of Illinois&lt;br&gt;New York (NYU/LIU)&lt;br&gt;Children's Hospital/London Health Sciences Center&lt;br&gt;UCSF&lt;br&gt;Duke University</td>
<td>Medicine and Pediatrics&lt;br&gt;Pediatric Endocrinology&lt;br&gt;Pediatric Hematology Oncology&lt;br&gt;Pediatric Gastroenterology/Hepatology&lt;br&gt;Pediatric Hematology Oncology&lt;br&gt;Pediatric Hematology Oncology&lt;br&gt;Pediatric Hematology Oncology&lt;br&gt;Pediatric Hematology Oncology&lt;br&gt;Pediatric Hematology Oncology&lt;br&gt;Pediatric Hematology Oncology</td>
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<td>Douglas A. Cipkala, MD, Chair&lt;br&gt;Pinki K. Prasad, MD, MPH, Silo Leader&lt;br&gt;Charline Boente, MD</td>
<td>Saint Vincent Hospital and Health Care Center&lt;br&gt;Children's Hospital New Orleans&lt;br&gt;Indiana University, Riley Hospital for Children</td>
<td>Pediatric Oncology&lt;br&gt;Pediatric Oncology&lt;br&gt;Pediatric Ophthalmology</td>
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<td><strong>Oral/Dental</strong></td>
<td>Karen E. Effinger, MD, MS, Chair&lt;br&gt;Kathy J. Ruble, RN, CPNP, PhD, Silo Leader&lt;br&gt;Zachary Abramson, MD, DMD&lt;br&gt;Sahaja Acharya, MD&lt;br&gt;Cathleen M. Cook, MD&lt;br&gt;Julia O'Malley Stempeske, RN, BSN, CPON&lt;br&gt;Nathaniel Treister, DMD, DMSc&lt;br&gt;Rebecca Williams, DMD</td>
<td>Children's Healthcare of Atlanta - Egleston&lt;br&gt;Johns Hopkins University/Sidney Kimmel Cancer Center&lt;br&gt;St. Jude Children's Research Hospital&lt;br&gt;Johns Hopkins University&lt;br&gt;East Carolina University&lt;br&gt;Advocate Children's Hospital-Park Ridge&lt;br&gt;Dana-Farber/Harvard Cancer Center&lt;br&gt;Perth Children's Hospital</td>
<td>Pediatric Hematology Oncology&lt;br&gt;Pediatric Hematology Oncology&lt;br&gt;Pediatric Hematology Oncology&lt;br&gt;Pediatric Hematology Oncology&lt;br&gt;Pediatric Hematology Oncology&lt;br&gt;Pediatric Hematology Oncology&lt;br&gt;Pediatric Hematology Oncology&lt;br&gt;Pediatric Hematology Oncology&lt;br&gt;Pediatric Hematology Oncology</td>
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*Contributors Task Force Membership 2019-2023 (cont)*
# Contributors

## Task Force Membership 2019-2023 (cont)

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<th>Task Force</th>
<th>Task Force Members</th>
<th>COG Institution</th>
<th>Expertise</th>
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<tbody>
<tr>
<td><strong>Psychosocial</strong></td>
<td>Fiona Schulte, PhD, Chair</td>
<td>University of Calgary, Alberta Children's Hospital</td>
<td>Psychology</td>
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<td></td>
<td>Rebecca Foster, PhD, Silo Leader</td>
<td>Washington University, St. Louis Children's Hospital</td>
<td>Pediatric Psychology</td>
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<td>Tara M. Brinkman, PhD</td>
<td>St. Jude Children's Hospital Research</td>
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<td>Katie Devine, PhD, MPH</td>
<td>Rutgers Cancer Institute of New Jersey</td>
<td>Pediatric Hematology Oncology</td>
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<td></td>
<td>Kristin Foster, DNP, C-PNP, C-PMHNPC</td>
<td>University of Iowa Hospitals and Clinics</td>
<td>Pediatric Psychology</td>
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<td>Cynthia Karlson, PhD</td>
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<td>Jordan Gilleland Marshak, PhD, ABPP</td>
<td>Children's Healthcare of Atlanta</td>
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<td>Sunnys Mayes, PhD, ABPP</td>
<td>University of Louisville, Norton Children's Cancer Institute</td>
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<td>Sapna Oberoi, MBBS, MD, DM</td>
<td>Max Rady School of Medicine, University of Manitoba</td>
<td>Pediatric Hematology Oncology</td>
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<td>Wendy G. Pelletier, MSW, RSW</td>
<td>Alberta Children's Hospital</td>
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<td>Karen Long-Traynor, PhD</td>
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<td>St. Jude Children's Research Hospital</td>
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<td>St. Jude Children's Research Hospital</td>
<td>Pediatric Hematology Oncology</td>
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<td>Neel S. Bhatt, MD, MBBS, MPH, Silo Leader</td>
<td>Seattle Children's Hospital</td>
<td>Pediatric Hematology Oncology</td>
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<td>Jennifer E. Agrusa, MD</td>
<td>University of Michigan, C. S. Mott Children's Hospital</td>
<td>Pediatric Hematology Oncology</td>
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<td>Aarati Didwania, MD</td>
<td>Northwestern University Feinberg School of Medicine</td>
<td>Internal Medicine</td>
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<td>Mary Frances McAleer, MD, PhD</td>
<td>MD Anderson</td>
<td>Radiation Oncology</td>
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<td>Daniel Weiner, MD</td>
<td>Children's Hospital of Pittsburgh, UPMC</td>
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<td><strong>Subsequent Malignant Neoplasms</strong></td>
<td>Danielle N. Friedman, MD, MS, Co-Chair</td>
<td>Memorial Sloan Kettering Cancer Center</td>
<td>Pediatric Hematology Oncology</td>
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<td>Monica M. Gramatges, MD, PhD, Co-Chair</td>
<td>Texas Children's Hospital/Baylor College of Medicine</td>
<td>Pediatric Hematology Oncology</td>
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<td>Dana Barnea, MD</td>
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<td>Taumoha Ghosh, MD</td>
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<td>Pediatric Hematology Oncology</td>
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<td>Tara O. Henderson, MD, MPH</td>
<td>University of Chicago Comprehensive Cancer Center</td>
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<td>David Hodgson, MD, MPH, FRCP</td>
<td>University of Toronto</td>
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<td>Lenat Joffe, MD</td>
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<td>Katharine Rae Lange, MD</td>
<td>Hackensack Meridian Children's Health</td>
<td>Biostatistics, Survivorship</td>
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<td>Chaya Moskowitz, PhD</td>
<td>Memorial Sloan Kettering Cancer Center</td>
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<td>Paul C. Nathan, MD, MSc, FRCP</td>
<td>Hospital for Sick Children</td>
<td>Family Medicine</td>
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<td>Kevin C. Deffinger, MD</td>
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<td>Radiation Oncology</td>
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<td>Kenneth Roberts, MD</td>
<td>Yale University School of Medicine/Smillow Cancer Hospital</td>
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<td>Loyola University Medical Center</td>
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<td>University of Minnesota/Masonic Cancer Center</td>
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<td>Tung Wynn, MD</td>
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<td>Alia Zaidi, MD</td>
<td>St. Jude Children's Research Hospital</td>
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Task Force Membership 2019-2023 (cont)

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<tr>
<td>Urinary Tract</td>
<td>Karen E. Effinger, MD, MS, Chair</td>
<td>Children's Healthcare of Atlanta - Egleston</td>
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<td>Kathleen Kieran, MD, MS, Silo Leader</td>
<td>Seattle Children's Hospital</td>
<td>Pediatric Urology</td>
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<td>Kala Kamdar, MD</td>
<td>Texas Children's Hospital/Baylor College of Medicine</td>
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<td>Anne Crowley Mauck, RN, MSN, CPNP</td>
<td>Virginia Commonwealth University/Massey Cancer Center</td>
<td>Pediatric Hematology Oncology</td>
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<td>Kerry M. Moss, MD</td>
<td>Connecticut Children's Medical Center</td>
<td>Pediatric Hematology Oncology</td>
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<td>Daniel A. Mulrooney, MD, MS</td>
<td>St. Jude Children's Research Hospital</td>
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<td>Jonathon C. Routh, MD, MPH</td>
<td>Duke University Medical Center</td>
<td>Pediatric Urology</td>
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<td>Sheri L. Spunt, MD</td>
<td>Lucile Packard Children's Hospital Stanford University</td>
<td>Pediatric Hematology Oncology</td>
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Contributors

Guideline Development Task Force - Initial Versions

The Children's Oncology Group Nursing Discipline and Late Effects Committee collaboratively developed the initial versions (1.0, 1.1, and 1.2) of the Children's Oncology Group Long-Term Follow-Up Guidelines for Survivors of Childhood, Adolescent, and Young Adult Cancers. The following individuals comprised the original Guideline Development Task Force:

**Development Task Force**

- Melissa M. Hudson, MD, Task Force Co-Chair, St. Jude Children's Research Hospital, Memphis, TN
- Wendy Landier, PhD, CPNP, Task Force Co-Chair, Children's Hospital of Alabama, Birmingham, AL
- Joan Darling, PhD, COG Patient Advocate Committee, Lincoln, NE
- Kathy Forte, RN, MS, CPNP, Children's Healthcare of Atlanta - Egleston, Atlanta, GA
- Allison Hester, RN, MSN, CPNP, Arkansas Children's Hospital, Little Rock, AR
- Debra A. Kent, RN, MSN, CPNP, Cincinnati Children's Hospital Medical Center, Cincinnati, OH
- Teresa Sweeney, RN, MSN, CPNP, St. Jude Children's Research Hospital, Memphis, TN

**Special Acknowledgment:**

- Smita Bhatia, MD, MPH, Children's Hospital of Alabama, Birmingham, AL for her leadership in overseeing the initial development of the COG LTFU Guidelines as Chair of the COG Late Effects Committee, and for her continued oversight of all content in all versions of the COG LTFU Guidelines
- Louis S. “Sandy” Constine, MD, University of Rochester, Rochester, NY for his in-depth expert review and extensive contributions to all radiation-related sections in all versions of the COG LTFU Guidelines
Preface

Overview

The Children’s Oncology Group Long-Term Follow-Up Guidelines for Survivors of Childhood, Adolescent, and Young Adult Cancers (COG LTFU Guidelines) are risk-based, exposure-related clinical practice guidelines for screening and management of late effects resulting from therapeutic exposures used during treatment for pediatric malignancies. “Late effects” are defined as therapy-related complications or adverse effects that persist or arise after completion of treatment for a pediatric malignancy. “Pediatric malignancies” are defined as those malignancies commonly associated with the pediatric population that may arise during childhood, adolescence, or young adulthood.

These guidelines represent a statement of consensus from a panel of experts in the late effects of pediatric cancer treatment. The guidelines are both evidence-based (utilizing established associations between therapeutic exposures and late effects to identify high-risk categories) and grounded in the collective clinical experience of experts (matching the magnitude of the risk with the intensity of the screening recommendations).

Since therapeutic interventions for a specific pediatric malignancy may vary considerably based on the patient's age, presenting features, and treatment era, a therapy-based design was chosen to permit modular formatting of the guidelines by therapeutic exposure. Importantly, the recommended periodic screening underscores the use of a thorough history and physical examination (H&P) as the primary assessment for cancer-related treatment effects. In regard to the screening recommendations outlined for the 165 therapeutic exposures in the COG LTFU Guidelines:

- 113 (68%) are derived primarily from the H&P, of which 91 (55%) rely solely on the H&P and 22 (13%) rely on the H&P plus a baseline diagnostic study (e.g., lab, imaging)
- 44 (27%) include periodic laboratory, diagnostic imaging, or other testing
- 8 (5%) recommend no screening (agents with no known late effects)

Interventions exceeding minimal screening are provided for consideration in individuals with positive screening tests. Medical citations supporting the association of each late effect with a specific therapeutic exposure are included. Patient education materials complementing the guidelines have been organized into Health Links that feature health protective counseling on 45 topics, enhancing patient follow-up visits and broadening application of the guidelines. Additional accompanying materials include detailed instructions, templates for cancer treatment summary forms, a radiation reference guide, a tool to assist in identifying guideline applicability for individual survivors based on therapeutic exposures, and templates for letters appealing denied insurance claims.

Goal

Implementation of these guidelines is intended to increase quality of life and decrease complication-related healthcare costs for pediatric cancer survivors by providing standardized and enhanced follow-up care throughout the lifespan that:

- Promotes healthy lifestyles
- Provides for ongoing monitoring of health status
- Facilitates early identification of late effects
- Provides timely intervention for late effects

Focus

These guidelines are intended for use beginning two or more years following the completion of cancer therapy, and provide a framework for ongoing late effects monitoring in childhood cancer survivors; however, these guidelines are not intended to provide guidance for follow-up of the pediatric cancer survivor's primary disease.

Target Population

The recommendations for periodic screening evaluations provided in the COG LTFU Guidelines are appropriate for asymptomatic survivors of childhood, adolescent, or young adult cancers who present for routine exposure-related medical follow-up. More extensive evaluations are presumed, as clinically indicated, for survivors presenting with signs and symptoms suggesting illness or organ dysfunction.

Intended Users

The COG LTFU Guidelines were developed as a resource for clinicians who provide ongoing healthcare to survivors of pediatric malignancies. The information within these guidelines is important for clinicians (e.g., physicians, nurse practitioners, physician assistants, nurses) in the fields of pediatrics, oncology, internal medicine, family practice, and gynecology, as well as subspecialists in many fields (e.g., endocrinology, cardiology, pulmonology). A basic knowledge of ongoing issues related to the long-term follow-up needs of this patient population is assumed. Healthcare professionals who do not regularly care for survivors of pediatric malignancies are encouraged to consult with a pediatric oncology long-term follow-up center if any questions or concerns arise when reviewing or using these guidelines.

Although the information within the guidelines will certainly prove valuable to the survivors themselves, at this time the only version available is targeted to healthcare professionals. Therefore, survivors who choose to review these guidelines are strongly encouraged to do so.
Preface (cont)

with the assistance of a healthcare professional knowledgeable about long-term follow-up care for survivors of childhood, adolescent, and young adult cancers. This is important in order to put the recommendations in perspective, avoid over-testing, address potential anxieties, and provide a comprehensive evaluation of the survivor’s health status. The Children’s Oncology Group itself does not provide individualized treatment advice to survivors or their families, and strongly recommends discussing this information with a qualified medical professional.

Developer

The COG LTFU Guidelines were developed as a collaborative effort of the Children’s Oncology Group Late Effects Committee and the Nursing Discipline Committee and Patient Advocacy Committee. All Children’s Oncology Group members have complied with the COG conflict of interest policy, which requires disclosure of any potential financial or other conflicting interests.

Evidence Collection

Pertinent information from the published medical literature over the past 20 years (updated as of October 2023) was retrieved and reviewed during the development and updating of these guidelines. For each therapeutic exposure, a complete search was performed via MEDLINE (National Library of Medicine, Bethesda, MD). Keywords included “childhood cancer therapy,” “complications,” and “late effects,” combined with keywords for each therapeutic exposure. References from the bibliographies of selected articles were used to broaden the search.

Methods

In 2002, the leadership of the Children’s Oncology Group Late Effects Committee and Nursing Discipline appointed a 7-member task force, with representation from the Late Effects Committee, Nursing Discipline, and Patient Advocacy Committee. The task force was convened to review and summarize the medical literature and develop a draft of clinical practice guidelines to direct long-term follow-up care for pediatric cancer survivors. The task force followed a modified version of the guideline development process established by the National Comprehensive Cancer Network (NCCN), integrating available literature with expert opinion using reiterative feedback loops.

The original draft went through several iterations within the task force prior to initial review. Multidisciplinary experts in the field, including nurses, physicians (pediatric oncologists and other subspecialists), patient advocates, behavioral specialists, and other healthcare professionals, were then recruited by the task force to provide an extensive, targeted review of the draft, including focused review of selected guideline sections. Revisions were made based on these recommendations. The revised draft was then sent out to additional multidisciplinary experts for further review. A total of 62 individuals participated in the review process. The guidelines subsequently underwent comprehensive review and scoring by a panel of experts in the late effects of pediatric malignancies, comprised of multidisciplinary representatives from the COG Late Effects Committee.

In a parallel effort led by the Nursing Clinical Practice Subcommittee, complementary patient education materials (Health Links) were developed. Each Health Link underwent two levels of review; first by the Nursing Clinical Practice Subcommittee to verify accuracy of content and recommendations, and then by members of the Late Effects Committee (to provide expert medical review) and Patient Advocacy Committee (to provide feedback regarding presentation of content to the lay public).

Pre-Release Review

The initial version of the guidelines (Version 1.0 – Children’s Oncology Group Late Effects Screening Guidelines) was released to the Children’s Oncology Group membership in March 2003 for a six-month trial period. This allowed for initial feedback from the COG membership, resulting in additional review and revision of the guidelines by the Late Effects Committee prior to public release.

Revisions

The guidelines were initially released to the public (Version 1.1 – Childhood Cancer Survivor Long-Term Follow-Up Guidelines) on the Children’s Oncology Group website in September 2003. Following this release, clarification regarding the applicability of the guidelines to the adolescent and young adult populations of cancer survivors was requested. In response, additional minor modifications were made and the title of the guidelines was changed. A revised version (Version 1.2 – Long-Term Follow-Up Guidelines for Survivors of Childhood, Adolescent, and Young Adult Cancers) was released to the public on the Children’s Oncology Group website in March 2004.

In order to keep the guidelines current and clinically meaningful, the COG Late Effects Committee organized multidisciplinary task forces in March 2004. These task forces are charged with the responsibility for monitoring the medical literature in regard to specific system-related clinical topics relevant to the guidelines (e.g., cardiovascular, neurocognitive, fertility/reproductive), providing periodic reports to the COG Outcomes and Survivorship Committee, and recommending revisions to the guidelines and their associated health education materials and references (including the addition of therapeutic exposures) as new
information becomes available. Task force members are assigned according to their respective areas of expertise and clinical interest and membership is updated every 5 years. A list of these task forces and their membership is included in the “Contributors” section of this document, reflecting contributions and recommendations relevant to the current release of these guidelines (Version 6.0 – October 2023).

All revisions proposed by the task forces were evaluated by a panel of experts, and if accepted, assigned a score (see “Scoring Explanation” section of Preface). Proposed revisions that were rejected by the expert panel were returned with explanation to the relevant task force chair. If desired, task force chairs were given an opportunity to respond by providing additional justification and resubmitting the rejected task force recommendation(s) for further consideration by the expert panel.

Plan for Updates

The multidisciplinary task forces described above will continue to monitor the literature and report to the COG Long-Term Follow-Up Guideline Core Committee during each guideline review/update cycle. Periodic revisions to these guidelines are planned as new information becomes available, and at least every 5 years. Clinicians are advised to check the Children’s Oncology Group website periodically for the latest updates and revisions to the guidelines, which will be posted at www.survivorshipguidelines.org.

Scoring Explanation

These guidelines represent a statement of consensus from a multidisciplinary panel of experts in the late effects of pediatric cancer treatment. The guidelines outline minimum recommendations for specific health screening evaluations in order to detect potential late effects arising as a result of therapeutic exposures received during treatment of childhood, adolescent, and young adult cancers.

Each score relates to the strength of the association of the identified late effect with the specific therapeutic exposure based on current literature, and is coupled with a recommendation for periodic health screening based on the collective clinical experience of the panel of experts. This is due to the fact that there are no randomized clinical trials (and none forthcoming in the foreseeable future) on which to base recommendations for periodic screening evaluations in this population; therefore, the guidelines should not be misconstrued as representing conventional “evidence-based clinical practice guidelines” or “standards of care”.

Each item was scored based on the level of evidence currently available to support it. Scores were assigned according to a modified version of the National Comprehensive Cancer Network “Categories of Consensus,” as follows:

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<td>1. There is high-level evidence linking the late effect with the therapeutic exposure</td>
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<td>2. The screening recommendation is appropriate based on the collective clinical experience of panel members</td>
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<td>2A</td>
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<td>There is non-uniform consensus of the panel that:</td>
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<tr>
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<td>2. The screening recommendation is appropriate based on the collective clinical experience of panel members</td>
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<tr>
<td>3</td>
<td>There is major disagreement that the recommendation is appropriate.</td>
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Uniform consensus: Near-unanimous agreement of the panel with some possible neutral positions.
Non-uniform consensus: The majority of panel members agree with the recommendation; however, there is recognition among panel members that, given the quality of evidence, clinicians may choose to adopt different approaches.
High-level evidence: Evidence derived from high quality case control or cohort studies.
Lower-level evidence: Evidence derived from non-analytic studies, case reports, case series, and clinical experience.

All “Category 1” recommendations reflect uniform consensus among the reviewers. “Category 2” recommendations are designated as “2A” (there is uniformity of consensus among the reviewers regarding strength of evidence and appropriateness of the screening recommendation) or “2B” (there is non-uniform consensus among the reviewers regarding strength of evidence and appropriateness of the screening recommendation).

Rather than submitting recommendations representing major disagreements, items scored as “Category 3” were either deleted or revised by the panel of experts to provide at least a “Category 2B” score for all recommendations included in the guidelines.
Preface (cont)

Recommendations and Rationale

Screening and follow-up recommendations are organized by therapeutic exposure and included throughout the guidelines. Pediatric cancer survivors represent a relatively small but growing population at high risk for various therapy-related complications. Although several well-conducted studies on large populations of childhood cancer survivors have demonstrated associations between specific exposures and late effects, the size of the survivor population and the rate of occurrence of late effects does not allow for clinical studies that would assess the impact of screening recommendations on the morbidity and mortality associated with the late effect. Therefore, scoring of each exposure reflects the expert panel’s assessment of the level of literature support linking the therapeutic exposure with the late effect coupled with an assessment of the appropriateness of the recommended screening modality in identifying the potential late effect based on the panel’s collective clinical experience.

Potential Benefits and Harms

Potential benefits of implementing these guidelines into clinical practice include earlier identification of and intervention for late onset therapy-related complications in this at-risk population, potentially reducing or ameliorating the impact of late complications on the health status of survivors. In addition, ongoing healthcare that promotes healthy lifestyle choices and provides ongoing monitoring of health status is important for all cancer survivors.

Potential harms of guideline implementation include increased patient anxiety related to enhanced awareness of possible complications, as well as the potential for false-positive screening evaluations, leading to unnecessary further workup. In addition, costs of long-term follow-up care may be prohibitive for some survivors, particularly those lacking health insurance, or those with insurance that does not cover the recommended screening evaluations.

Patient Preferences

Ultimately, as with all clinical guidelines, decisions regarding screening and clinical management for any specific patient should be individually tailored, taking into consideration the patient’s treatment history, risk factors, co-morbidities, and lifestyle. These guidelines are therefore not intended to replace clinical judgment or to exclude other reasonable alternative follow-up procedures. The Children’s Oncology Group recognizes that specific patient care decisions are the prerogative of the patient, family, and healthcare provider.

Implementation Considerations

Implementation of these guidelines is intended to standardize and enhance follow-up care provided to survivors of pediatric malignancies throughout the lifespan. Considerations in this regard include the practicality and efficiency of applying these broad guidelines in individual clinical situations. Studies to address guideline implementation and refinement are a top priority of the COG Long-Term Follow-Up Guideline Core Committee; studies of feasibility of guideline use have been reported in limited institutions and others are currently underway. Issues being addressed include description of anticipated barriers to application of the recommendations in the guidelines and development of review criteria for measuring changes in care when the guidelines are implemented. Additional concerns surround the lack of current evidence establishing the efficacy of screening for late complications in pediatric cancer survivors. While most clinicians believe that ongoing surveillance for these late complications is important in order to allow for early detection and intervention for complications that may arise, development of studies addressing the efficacy of this approach is imperative in order to determine which screening modalities are optimal for asymptomatic survivors.

In addition, the clinical utility of this lengthy document has also been a top concern of the COG Long-Term Follow-Up Guideline Core Committee. While recognizing that the length and depth of these guidelines is important in order to provide clinically-relevant, evidence-based recommendations and supporting health education materials, clinician time limitations and the effort required to identify the specific recommendations relevant to individual survivors have been identified as barriers to their clinical application. Therefore, the COG Long-Term Follow-Up Guideline Core Committee has partnered with the Baylor School of Medicine to develop a web-based interface, known as “Passport for Care,” that generates individualized exposure-based recommendations from these guidelines in a clinician-focused format for ease of patient-specific application of the guidelines in the clinical setting. The Passport for Care® application is available to Children’s Oncology member institutions at no cost. For additional information, please contact Monica Gramatges, MD, PhD (gramatge@bcm.edu) or Susan Krause (skrause@texaschildrens.org).

Funding Source

This work was supported by the Children’s Oncology Group Chair’s Grant (U10 CA098543) and the National Clinical Trials Network Group Operations Center Grant (U10 CA180886) from the National Cancer Institute. The Version 6.0 update, including typesetting, was supported by the St. Baldrick’s Foundation.
## Instructions for Use

### Guideline Organization

The Children’s Oncology Group *Long-Term Follow-Up Guidelines for Survivors of Childhood, Adolescent, and Young Adult Cancers* are organized according to therapeutic exposures, arranged by column as follows:

<table>
<thead>
<tr>
<th>Section Number</th>
<th>Unique identifier for each guideline section.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Therapeutic Agent</td>
<td>Therapeutic intervention for malignancy, including chemotherapy, radiation, surgery, blood/serum products, hematopoietic cell transplant, and other therapeutic modalities.</td>
</tr>
<tr>
<td>Potential Late Effects</td>
<td>Most common late treatment complications associated with specified therapeutic intervention.</td>
</tr>
<tr>
<td>Periodic Evaluations</td>
<td>Recommended screening evaluations, including health history, physical examination, laboratory evaluation, imaging, and psychosocial assessment. Recommendation for minimum frequency of periodic evaluations is based on risk factors and magnitude of risk, as supported by the medical literature and/or the combined clinical experience of the reviewers and panel of experts.</td>
</tr>
</tbody>
</table>
| Health Counseling/ Further Considerations | **Health Links:** Health education materials developed specifically to accompany these guidelines. Title(s) of Health Link(s) relevant to each guideline section are referenced in this column. Health Link documents are included in Appendix II, and are also available on the COG website at www.survivorshipguidelines.org.  
**Resources:** Books and websites that may provide the clinician with additional relevant information.  
**Counseling:** Suggested patient counseling regarding measures to prevent/reduce risk or promote early detection of the potential treatment complication.  
**Potential Considerations for Further Testing and Intervention:** Recommendations for further diagnostic evaluations beyond minimum screening for individuals with positive history and/or physical examination findings or positive screening tests, recommendations for consultation and/or referral, and recommendations for management of exacerbating or predisposing conditions. |

### System/Score

| System/Score | Body system (e.g., auditory, musculoskeletal) most relevant to each guideline section.  
Score assigned by expert panel representing the strength of data from the literature linking a specific late effect with a therapeutic exposure coupled with an assessment of the appropriateness of the screening recommendation based on collective clinical experience. See “Scoring Explanation” in the Preface for more information. |

### Additional Information

| Additional Information | Patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk for developing the complication and additional information pertinent to the late effects or its evaluation (previously known as “Info Links”) |

### References

| References | References are listed immediately following each guideline section. Included are medical citations that provide evidence for the association of the therapeutic intervention with the specific treatment complication and/or evaluation of predisposing risk factors. In addition, some general review articles have been included in the Reference section for clinician convenience. |
Instructions for Use (cont)

Using the COG LTFU Guidelines to Develop Individualized Screening Recommendations

In order to accurately derive individualized screening recommendations for a specific childhood cancer survivor using the Children's Oncology Group Long-Term Follow-Up Guidelines for Survivors of Childhood, Adolescent, and Young Adult Cancers, the following procedure should be followed. (Note: For ease of use, a Patient-Specific Guideline Identification Tool has been developed to streamline the following process and is included in Appendix I).

1. Obtain the survivor’s Cancer Treatment Summary (see templates for comprehensive and abbreviated summaries in Appendix 1). Note: In order to generate accurate exposure-based follow-up recommendations from these guidelines, the following information regarding the survivor’s diagnosis and treatment is required, at minimum:

   Demographics
   - Name
   - Sex
   - Date of birth

   Cancer Diagnosis
   - Diagnosis
   - Date of diagnosis
   - Date cancer therapy was completed

   Cancer Treatment: Chemotherapy
   - Names of all chemotherapy agents received
     - For a list of chemotherapy agents addressed by these guidelines (Sections 11-43), see the “Chemotherapy” portion of the Patient-Specific Guideline Identification Tool in Appendix I.
     - For generic and brand names of chemotherapy agents, see Chemotherapy Agents in Appendix I.
   - Cumulative dose of all anthracycline chemotherapy received (i.e., doxorubicin, daunorubicin, idarubicin, mitoxantrone and epirubicin)
     - See Section 34 of Guidelines for anthracycline isotoxic dose-equivalent conversion.
     - For doses in mg/kg, multiply by 30 to obtain equivalent dosing in mg/m² (example: 2 mg/kg = 60 mg/m²).
   - For carboplatin, whether any dose was myeloablative (i.e., given as conditioning for HCT)
   - For cytarabine and methotrexate:
     - Route of administration (i.e., IV, IM, SQ, PO, IT, IO)
     - If IV, designation of “high dose” (any single dose ≥ 1000 mg/m²) versus “standard dose” (all single doses < 1000 mg/m²)

2. Compile a list of guideline sections relevant to the survivor based off the list generated in step 1.
   - Sections 1 - 7: Applicable to all survivors
   - Section 8: Survivors diagnosed before 1972
   - Section 9: Survivors diagnosed between 1977 and 1985
   - Section 10: Survivors diagnosed between 1977 and 1985
   - Section 11: All survivors who received chemotherapy
   - Sections 12-43: For survivors who received chemotherapy, include relevant sections
   - Sections 44, 45, 96: All survivors who received radiation
Instructions for Use (cont)

- Sections 46 - 95, 97- 98: For survivors who received radiation, include relevant sections
- Sections 100 - 105: All survivors who underwent HCT
  - Section 100 is for males only
  - Section 101 is for females only
- Section 99: For survivors who underwent autologous HCT
- Sections 106 - 114: For survivors who underwent allogeneic HCT, include relevant sections
- Sections 115 - 151: For survivors who underwent surgery, include relevant sections
- Sections 152 - 163: For survivors who received other therapeutic modalities, include relevant sections
- Section 164-165: Applicable to all survivors

1. Review all guideline sections generated in the list above, and develop a plan for screening the individual survivor, taking into consideration the survivor’s relevant risk factors, current health, co-morbidities, health-related behaviors and preferences.

Note: The above procedure is applicable to generation of follow-up guidelines from the current version of this document; however, the COG Long-Term Follow-Up Guidelines Core Committee recognizes that as new evidence becomes available and these guidelines are updated, additional details regarding the childhood cancer survivor’s therapeutic exposures may be required in order to generate comprehensive recommendations. Therefore, we strongly advise that a comprehensive treatment summary be prepared for each childhood cancer survivor, including a record of all therapeutic exposures with applicable dates, details of administration, and cumulative doses of all agents, including those not currently addressed by these guidelines.

The COG Long-Term Follow-Up Guidelines Core Committee recognizes that the time required to identify patient-specific recommendations from these guidelines is significant, and has been identified as a barrier to clinical use. Therefore, COG has partnered with the Baylor School of Medicine to develop a web-based interface, known as “Passport for Care,” that generates individualized exposure-based recommendations from these guidelines in a clinician-focused format for ease of patient-specific application in the clinical setting. The Passport for Care® application is available to Children’s Oncology member institutions at no cost. For additional information, please contact Monica Gramatges, MD, PhD (gramatge@bcm.edu) or Susan Krause (skrause@texaschildrens.org).

We are hopeful that this revised version of the Children’s Oncology Group Long-Term Follow-Up Guidelines for Survivors of Childhood, Adolescent, and Young Adult Cancers will enhance the follow-up care provided to this unique group of cancer survivors. If you have questions, suggestions, or concerns regarding use of these guidelines, please contact:

Co-Chairs, COG Long-Term Follow-Up Guidelines Core Committee:

Matthew J. Ehrhardt, MD, MS  Danielle N. Friedman, MD, MS
St. Jude Children’s Research Hospital  Memorial Sloan Kettering Cancer Center
Memphis, TN  New York, NY
(901) 595-5913  (212) 639-7376
matt.ehrhardt@stjude.org  friedmad@mskcc.org

Melissa M. Hudson, MD  Louis S. “Sandy” Constine, MD
St. Jude Children’s Research Hospital  University of Rochester Medical Center
Memphis, Tennessee  Rochester, NY
(901) 595-4781  (585) 275-5622
melissa.hudson@stjude.org  louis_constine@urmc.rochester.edu

Wendy Landier, PhD, CPNP  Smita Bhatia, MD, MPH
Children’s Hospital of Alabama  Children’s Hospital of Alabama
University of Alabama at Birmingham  University of Alabama at Birmingham
Birmingham, Alabama  Birmingham, Alabama
(205) 638-2120  (205) 638-2120
wlandier@peds.uab.edu  sbhatia@peds.uab.edu
New to Version 6.0

All guideline sections have been reviewed by the Long-Term Follow-Up Guidelines Task Forces and modifications have been made per their recommendations and with the approval of the Expert Panel. The most significant modifications are detailed below.

**Simplification**

A continued overall goal of Version 6.0 of the COG Long-Term Follow-Up Guidelines is to simplify the format and content of the guidelines in order to focus on clinically relevant content, reduce the burden of medical record data abstraction necessary to determine tailored recommendations for survivors, reduce the complexity of guideline application to individual survivors, and better align COG’s screening recommendations with those of the International Guideline Harmonization Group. Version 6.0 therefore features the following modifications:

- Guideline navigation has been simplified through the use of hyperlinks. Hyperlinks are denoted with blue text and assist in moving more easily through the guideline contents. Additionally, there is often a hyperlink at the bottom of most pages to direct the user back to a section or the guideline table of contents.
- Simplification of design/format with a focus on clinical information that drives screening
- Continuation of defined and simplified radiation fields
  - All radiation fields from Version 5.0 are still mapped to body parts
  - In most cases, knowing the general area of the body that received radiation is now all that is necessary in order to generate tailored radiation-related recommendations for survivors
  - It is not necessary to know or record specific radiation doses (with a few exceptions)
- Radiation dose cut-offs largely eliminated
  - Emerging evidence indicates that some late effects (e.g., breast and colorectal cancers) are occurring below the previously determined minimum dose thresholds
  - The dose cut-offs that remain are for late effects that require screening beyond the history and physical examination and for which evidence indicates that there is a low risk of developing the late effect below the radiation threshold
- All Risk Factors and Highest Risk Factors have been moved to Additional Information

**General Updates**

- Some History and Physical Exam elements have been reworded for consistency between sections
- Revisions have been made to Counseling and Potential Considerations in most sections
- References have been updated in all applicable sections
- Secondary malignancy has been renamed Subsequent throughout the guidelines
- References to veno-occlusive disease (VOD) has been removed throughout the guidelines and replaced with the current sinusoidal obstruction syndrome (SOS) term
- Templates remain in Appendix I to assist with drafting appeal letters for denied insurance claims

**New Sections/Late Effects**

The following new sections/late effects have been added:

- Subsequent malignancy and/or Risk of malignancy in offspring related to any cancer experience (section 7)
- Hypothyroidism related to (partial) Thyroidectomy (section 151)
- Xerostomia and/or Salivary gland dysfunction and/or Chronic sialadenitis related to radioiodine therapy (I-131 thyroid ablation) (section 154)
- Growth attenuation related to BCR-ABL tyrosine kinase inhibitors (section 159)
- Hypothyroidism related to BCR-ABL tyrosine kinase inhibitors (section 160)
- Insufficient information regarding late effects from Other targeted biologic therapies (section 161)
- Immunologic complications related to B-cell directed antibody-based therapies (section 162)
- Insufficient information regarding late effects from Other antibody-based immune therapies (section 163)
- General health screening regarding vaccinations (section 165)

**Sections/Late Effects Removed**

The following sections or late effects have been removed from Version 6.0 of the COG LTFU Guidelines:

- Clinical leukoencephalopathy related to high dose cytarabine (section 24 of Version 4.0)
- Lymphoma related to HCT (section 106 of Version 4.0)
New to Version 6.0 (cont)

- Renal toxicity related to methotrexate (section 28 changed to “No Known Renal Late Effects” in Version 5.0)
- Reduced bone mineral density related to methotrexate (section 27 changed to “No Known BMD Late Effects” in Version 6.0)
- The Cancer Screening Guidelines Sections (156-164 in Version 5.0) for average risk individuals have been removed due to inconsistencies across cooperative groups and practice standards, as well as timing alignment with suggested changes and publication. Your health care providers will offer guidance based on current recommendations and guidelines.

Late Effects Renamed

- Reduced ovarian follicular pool renamed as Diminished ovarian reserve (DOR) (15, 93, 137)
- Secondary benign or malignant neoplasm occurring in or near radiation field renamed as Subsequent benign or malignant neoplasm occurring in or near radiation field (44)

Newly Combined Sections

These sections from Version 5.0 have been combined into one section (164) in Version 6.0:

- Breast cancer screening guidelines standard risk (previous section 156)
- Cervical cancer screening guidelines standard risk (previous section 157)
- Colorectal cancer screening guidelines standard risk (previous section 158)
- Endometrial cancer screening guidelines standard risk (previous section 159)
- Lung cancer screening guidelines standard risk (previous section 160)
- Oral cancer screening guidelines standard risk (previous section 161)
- Prostate cancer screening guidelines standard risk (previous section 162)
- Skin cancer screening guidelines standard risk (previous section 163)
- Testicular cancer screening guidelines standard risk (previous section 164)

New Potential Late Effects Subcategories Added

- Subsequent malignancy (section 7)
- Risk of malignancy in offspring (section 7)
- Altered skin pigmentation (section 106)

Major Screening Changes

Guidelines for Genetic Risk Assessment for Cancer Predisposition (7)
Screening for Decreased Bone Mineral Density after Methotrexate (28)
Cardiomyopathy Screening (34, 77)
Cancer Screening for Average Risk Individuals (previously 156-164)

Guidelines for Genetic Risk Assessment for Cancer Predisposition (Section 7)
There is risk for subsequent malignancy and/or malignancy in offspring based on genetic predisposition which warrants further assessment based on the determined risk factors.

Screening for Decreased Bone Mineral Density after Methotrexate (Section 28)
No association has been found concerning decreased BMD and methotrexate; screening is no longer recommended, but the section remains for reference

Cardiomyopathy Screening (Sections 34, 77)

- Echocardiogram screening is not recommended for individuals with both <15Gy radiation dose (with potential impact to heart) and a cumulative doxorubicin equivalent anthracycline dose <100 mg/m²
- Anthracycline dose conversion of mitoxantrone changed to “multiply total dose x 10” versus the previous recommendation to multiply the total dose x 4

Cancer Screening for Average Risk Individuals

The Average Risk Cancer screening guidelines (Version 5.0 sections 156-164) have been removed and replaced with a combined screening guideline section (164) for average risk individuals. Patients with high risk needs related to their cancer treatment are meticulously addressed in their specific sections. Standard risk patients should consult with their healthcare provider for general health maintenance based on age and gender. High risk patients are those with a history of the following exposure(s):

- Breast cancer: radiation (TBI, chest, axilla) review section 73
- Cervical cancer: HCT review section 100
- Colorectal cancer: radiation (TBI, abdominal, pelvic, spinal [lumbar, sacral, whole]) review section 85
- Lung cancer: radiation (TBI, chest, axilla) review section 75
- Oral cancer: radiation (TBI, head/brain, neck) review section 43 and/or GVHD should review section 107
- Skin cancer: radiation review section 44, with a history of HCT review section 100/101, and/or with a history of cGVHD review section 106
New to Version 6.0 (cont)

Additional Screening Change Highlights

- Testicular hormonal dysfunction related to alkylating agents and/or testicular radiation: Screening with AM testosterone in high-risk patients starting at age 18 years is recommended (12, 90)
- Cyclophosphamide equivalent dose calculator (CED) has been added to assist in determining high risk status (12, 13, 14, 15, 92, 93)
- Cataracts related to corticosteroids, alkylating agents, and/or radiation recommends a yearly evaluation by an ophthalmologist or optometrist (18, 39, 61)
- Reduced bone mineral density related to steroids and HCT: Adjustments for gender and menopause status regarding z-score, as well as the age metric changing from 20 to 50 years old. Guidelines for follow up are indicated with a specific algorithm for ease of implementation. Vitamin D recommendations updated to reflect AAP guidelines with age specific parameters (37, 104)
- Monthly breast “self-exam” is no longer recommended (73)

Health Links

- The Health Links have been modified to reflect all Version 6.0 Guideline changes.
- Five Health Links have been renamed:
  - Diet and Physical Activity is now Staying Healthy through Nutrition and Physical Activity
  - Educational Issues is now School After Cancer Treatment
  - Emotional Issues is now Mental Health After Cancer Treatment
  - Female Health Issues after Cancer Treatment is now Ovarian and Reproductive Health after Cancer Treatment
  - Male Health Issues after Cancer Treatment is now Testicular and Reproductive Health after Cancer Treatment
- Two new Health Links for Version 6.0:
  - Vaccines after Treatment for Cancer Survivors Treated with Hematopoietic Cell Transplant (HCT)
  - Vaccines after Treatment for Cancer Survivors Treated with Chemotherapy and/or Radiation (Non-HCT)

General Recommendations Regarding Use of the Simplified COG LTFU Guidelines, V 6.0

- The COG Long-Term Follow-Up Guidelines are designed to offer general guidance and are not meant to provide or replace the medical advice or judgment of clinicians caring for individual survivors.
- The recommendations in Version 6.0 of these Guidelines rely more extensively on history and physical examination and less on screening evaluations, when compared to prior Guideline versions.
- We recognize that recommendations for over-screening may occur (primarily due to elimination of radiation dose-cutoffs and simplification of radiation fields); however, additional screening will generally result in recommendations for components of the history and physical examination only.
- It is important for clinicians to recognize that not all survivors may be at-risk for all late effects that are associated with the broader exposure categories in Version 6.0; for example, survivors with radiation fields that are known to be limited to a specific targeted area within a broader field. Thus, if clinicians have more detailed information that supports refraining from a specific screening for a particular patient, clinical judgment should be used to guide the individual evaluation.
- Since a number of previously recommended screening evaluations are now to be considered based on findings from the history and physical examination, clinicians need to carefully discern which history and physical examination findings should trigger further evaluations. Additional, more intensive screening and/or diagnostic workup are recommended for any survivors for whom the clinician believes there is reason to suspect the presence of a late effect.
- If clinicians have more detailed information that supports additional screening (or refraining from screening), clinicians are encouraged to modify their recommendations for individual survivors based on their knowledge of that survivor’s specific therapeutic exposures during treatment and their current clinical status.
## Abbreviations & Parameters

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Definition</th>
</tr>
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<tbody>
<tr>
<td>AAP</td>
<td>American Academy of Pediatrics</td>
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<tr>
<td>ABR</td>
<td>Auditory brainstem response</td>
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<tr>
<td>ACIP</td>
<td>Advisory Committee on Immunization Practices</td>
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<tr>
<td>ACS</td>
<td>American Cancer Society</td>
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<tr>
<td>AHA</td>
<td>American Heart Association</td>
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<tr>
<td>ALL</td>
<td>Acute lymphoblastic leukemia</td>
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<tr>
<td>ALT</td>
<td>Alanine aminotransferase</td>
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<tr>
<td>AMH</td>
<td>Anti-Mullerian hormone</td>
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<tr>
<td>AML</td>
<td>Acute myeloid leukemia</td>
</tr>
<tr>
<td>AST</td>
<td>Aspartate aminotransferase</td>
</tr>
<tr>
<td>ATG</td>
<td>Anti-thymocyte globulin</td>
</tr>
<tr>
<td>ATM</td>
<td>Ataxia telangiectasia cancer susceptibility gene (located on chromosome 11)</td>
</tr>
<tr>
<td>AVN</td>
<td>Avascular necrosis</td>
</tr>
<tr>
<td>BMD</td>
<td>Bone mineral density</td>
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<tr>
<td>BMI</td>
<td>Body mass index</td>
</tr>
<tr>
<td>BRCA1</td>
<td>Breast cancer susceptibility gene 1 (located on chromosome 17)</td>
</tr>
<tr>
<td>BRCA2</td>
<td>Breast cancer susceptibility gene 2 (located on chromosome 13)</td>
</tr>
<tr>
<td>BUN</td>
<td>Blood urea nitrogen</td>
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<tr>
<td>Ca</td>
<td>Calcium</td>
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<tr>
<td>CAD</td>
<td>Coronary artery disease</td>
</tr>
<tr>
<td>CBC</td>
<td>Complete blood count</td>
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<tr>
<td>CGG</td>
<td>Children’s Cancer Group</td>
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<tr>
<td>CDC</td>
<td>Centers for Disease Control</td>
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<tr>
<td>cGVHD</td>
<td>Chronic graft versus host disease</td>
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<tr>
<td>CI</td>
<td>Chloride</td>
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<tr>
<td>CNS</td>
<td>Central nervous system</td>
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<tr>
<td>CO₂</td>
<td>Carbon dioxide</td>
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<tr>
<td>COG</td>
<td>Children’s Oncology Group</td>
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<tr>
<td>CRT</td>
<td>Cranial radiation therapy</td>
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<tr>
<td>CT</td>
<td>Computed tomography</td>
</tr>
<tr>
<td>CVRF</td>
<td>Cardiovascular risk factors</td>
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<tr>
<td>dB</td>
<td>Decibel</td>
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<tr>
<td>DES</td>
<td>Diethylstilbestrol</td>
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<tr>
<td>DI</td>
<td>Diabetes Insipidus</td>
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<tr>
<td>DLCO</td>
<td>Diffusion capacity of carbon monoxide</td>
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<tr>
<td>DOR</td>
<td>Diminished ovarian reserve</td>
</tr>
<tr>
<td>DTI</td>
<td>Diffusion-tensor imaging</td>
</tr>
<tr>
<td>DWI</td>
<td>Diffusion-weighted imaging</td>
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<tr>
<td>DXA</td>
<td>Dual energy x-ray absorptiometry</td>
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<tr>
<td>ECHO</td>
<td>Echocardiogram</td>
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<tr>
<td>EKG</td>
<td>Electrocardiogram</td>
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<tr>
<td>EIA</td>
<td>Enzyme immunoassay</td>
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<tr>
<td>FAP</td>
<td>Familial adenomatous polyposis</td>
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<tr>
<td>FM</td>
<td>Frequency modulated</td>
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<tr>
<td>FNA</td>
<td>Fine needle aspiration</td>
</tr>
<tr>
<td>FNM</td>
<td>Focal nodular hyperplasia</td>
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<td>FSH</td>
<td>Follicle stimulating hormone</td>
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<tr>
<td>G-CSF</td>
<td>Granulocyte colony stimulating factor</td>
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<tr>
<td>GH</td>
<td>Growth hormone</td>
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<td>Gastrointestinal</td>
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<td>Hemoglobin A1c</td>
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<td>Hepatitis B core antibody</td>
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<td>HBsAg</td>
<td>Hepatitis B surface antigen</td>
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<tr>
<td>HCT</td>
<td>Hematopoietic cell transplant</td>
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<td>HCV</td>
<td>Hepatitis C virus</td>
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<td>HDL</td>
<td>High-density lipoproteins</td>
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<td>HIB</td>
<td>Haemophilus influenzae type B</td>
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<tr>
<td>HIV</td>
<td>Human immunodeficiency virus</td>
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<td>HLA</td>
<td>Human leukocyte antigen</td>
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<tr>
<td>HNPPC</td>
<td>Hereditary nonpolyposis colorectal cancer</td>
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<td>HPF</td>
<td>High power field</td>
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<td>HPV</td>
<td>Human papillomavirus</td>
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<td>Height</td>
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<td>Hz</td>
<td>Hertz</td>
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<tr>
<td>IBD</td>
<td>Inflammatory bowel disease</td>
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<td>K</td>
<td>Potassium</td>
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<tr>
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<td>Intra-Ommaya</td>
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<td>IQ</td>
<td>Intelligence quotient</td>
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<td>IVIG</td>
<td>Intravenous immunoglobulin</td>
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<td>kg</td>
<td>Kilogram</td>
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<tr>
<td>KUB</td>
<td>Kidneys, ureters, bladder radiograph</td>
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<td>LH</td>
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<td>LV</td>
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<td>m²</td>
<td>Square meter</td>
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### Abbreviations & Parameters (cont.)

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<td>mg</td>
<td>Milligram</td>
<td>SCUBA</td>
<td>Self-contained underwater breathing apparatus</td>
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<td>Mg</td>
<td>Magnesium</td>
<td>SD</td>
<td>Standard deviation</td>
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<td>MMF</td>
<td>Mycophenolate mofetil</td>
<td>SOS</td>
<td>Sinusoidal obstruction syndrome</td>
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<td>MOPP</td>
<td>Mechlorethamine, Oncovin, Procarbazine, Prednisone</td>
<td>SQ</td>
<td>Subcutaneous</td>
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<tr>
<td>MR</td>
<td>Magnetic resonance</td>
<td>STLII</td>
<td>Subtotal lymphoid irradiation</td>
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<tr>
<td>MRA</td>
<td>Magnetic resonance angiography</td>
<td>T4</td>
<td>Thyroxine</td>
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<tr>
<td>MRI</td>
<td>Magnetic resonance imaging</td>
<td>TBI</td>
<td>Total body irradiation</td>
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<td>Na</td>
<td>Sodium</td>
<td>TLI</td>
<td>Total lymphoid irradiation</td>
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<tr>
<td>NF1</td>
<td>Neurofibromin 1 (neurofibromatosis) cancer susceptibility gene (located on chromosome 17)</td>
<td>TPN</td>
<td>Total parenteral nutrition</td>
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<td>NHL</td>
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<td>Non-steroidal anti-inflammatory drugs</td>
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<tr>
<td>p53</td>
<td>Cancer susceptibility gene associated with familial cancers (located on chromosome 17)</td>
<td>USPSTF</td>
<td>United States Preventive Services Task Force</td>
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<tr>
<td>PAP</td>
<td>Papanicolaou</td>
<td>V-A</td>
<td>Ventriculoatrial</td>
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<td>PCR</td>
<td>Polymerase chain reaction</td>
<td>VOD</td>
<td>Veno-occlusive disease</td>
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<td>PFTs</td>
<td>Pulmonary function tests</td>
<td>V-P</td>
<td>Ventriculoperitoneal</td>
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<td>PNET</td>
<td>Primitive neuroectodermal tumor</td>
<td>V-V</td>
<td>Ventriculovenous</td>
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<td>PNS</td>
<td>Peripheral nervous system</td>
<td>VZIG</td>
<td>Varicella zoster immunoglobulin</td>
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<td>PO</td>
<td>By mouth</td>
<td>WAGR</td>
<td>Wilms tumor, aniridia, genitourinary anomalies, range of developmental delays</td>
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<td>PO4</td>
<td>Phosphate</td>
<td>wt</td>
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<td>PSA</td>
<td>Prostate specific antigen</td>
<td>Parameters commonly referenced in the guidelines</td>
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<td>PUVA</td>
<td>Psoralen plus ultraviolet-A radiation</td>
<td>≥1000 mg/m²</td>
<td>High dose methotrexate</td>
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<td>QTc</td>
<td>Corrected QT interval</td>
<td>&lt;1000mg/m²</td>
<td>Standard dose methotrexate</td>
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<td>RB1</td>
<td>Retinoblastoma cancer susceptibility gene (located on chromosome 13)</td>
<td>≥1000 mg/m²</td>
<td>High dose cytarabine</td>
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<tr>
<td>RBC</td>
<td>Red blood cell</td>
<td>&lt;1000mg/m²</td>
<td>Standard dose cytarabine</td>
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<td>RUQ</td>
<td>Right upper quadrant</td>
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# ANY CANCER EXPERIENCE

<table>
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<tr>
<th>Sec #</th>
<th>Therapeutic Exposure</th>
<th>Potential Late Effects</th>
<th>Periodic Evaluation</th>
<th>Health Counseling/ Further Considerations</th>
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</thead>
</table>
| 1     | Any Cancer Experience        | Adverse psychosocial/quality of life effects  
                    Social withdrawal  
                    Educational problems  
                    Relationship problems  
                    Under-employment/ Unemployment  
                    Dependent living | HISTORY  
Psychosocial assessment with attention to:  
• Educational and/or vocational progress  
• Social withdrawal  
Yearly | HEALTH LINKS  
Introduction to Long-Term Follow-Up  
Mental Health  
School After Treatment |

## HEALTH LINKS
- Introduction to Long-Term Follow-Up
- Mental Health
- School After Treatment

## RESOURCES

## POTENTIAL CONSIDERATIONS FOR FURTHER TESTING AND INTERVENTION
Preference should be given to self vs. proxy report.  
Psychological consultation in patients with emotional difficulties related to cancer experience, including physical deformities or chronic disabilities.  
Social work consultation.  
Refer as indicated to school liaison in community or cancer center (psychologist, social worker, school counselor) to facilitate acquisition of educational or vocational resources.  
Refer as indicated for neuropsychological evaluation.  

## SYSTEM = Psychosocial  
SCORE = 1

### Additional Information
Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.

- Patient factors: Younger age at diagnosis, family history of depression, anxiety, or mental illness, lower household income, lower educational attainment, school withdrawal, race/ethnicity  
- Cancer/Treatment factors: Bone tumor, CNS tumor, CNS-directed therapy, history of HCT  
- Pre-morbid/Co-morbid medical conditions: Premorbid learning or emotional difficulties, chronic conditions after cancer treatment (e.g., obesity, endocrine, pulmonary, cardiac conditions) are associated with increased risk for neurocognitive difficulties, and/or increased symptom burden (e.g., pain, fatigue) including neurocognitive problems

### References
**Section 1 References (cont)**


## Any Cancer Experience (Cont)

<table>
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<tr>
<th>Sec #</th>
<th>Therapeutic Exposure</th>
<th>Potential Late Effects</th>
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<td>Any Cancer Experience</td>
<td>Mental health disorders</td>
<td>HISTORY</td>
<td>HEALTH LINKS</td>
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<td>Depression</td>
<td>Psychosocial assessment with attention to:</td>
<td>Mental Health</td>
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<td>Anxiety</td>
<td>• Depression</td>
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<td>Post-traumatic stress</td>
<td>• Anxiety</td>
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<td>Suicidal behavior</td>
<td>• Post-traumatic stress</td>
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<td></td>
<td>• Suicidal ideation</td>
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<td>Yearly</td>
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</table>

### Additional Information

Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.

- **Patient factors:** Female sex, family history of depression, anxiety, or mental illness, lower household income, lower educational attainment, especially school withdrawal, unemployment, not in a relationship, poor social support, perceived poor physical health, no health insurance or public health insurance.
- **Cancer/Treatment factors:** CNS tumor, CNS-directed therapy, history of HCT.
- **Pre-morbid/Co-morbid medical conditions:** Chronic pain, scarring or physical disfigurement, permanent hair loss, premorbid learning or emotional difficulties, sleep/fatigue issues, substance misuse.

### References


### ANY CANCER EXPERIENCE (CONT)

<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Exposure</th>
<th>Potential Late Effects</th>
<th>Periodic Evaluation</th>
<th>Health Counseling/ Further Considerations</th>
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<td>3</td>
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<td>Risky behaviors</td>
<td>HISTORY</td>
<td>HEALTH LINKS</td>
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<td>Behaviors known to increase the likelihood of subsequent illness or injury</td>
<td>Psychosocial assessment Yearly</td>
<td>Mental Health</td>
</tr>
</tbody>
</table>

**HEALTH LINKS**
- Mental Health

**RESOURCES**
- www.smokefree.gov
- www.cancer.org/healthy/stay-away-from-tobacco

**POTENTIAL CONSIDERATIONS FOR FURTHER TESTING AND INTERVENTION**
Psychological consultation in patients with emotional difficulties related to cancer experience.

**SYSTEM = Psychosocial**  
**SCORE = 2A**

---

**Additional Information**
Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.

- Patient factors: Adolescent/Young adult at diagnosis or follow-up, male sex, lower household income, lower educational attainment, rural neighborhood, psychological distress

**References**
### ANY CANCER EXPERIENCE (CONT)

<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Exposure</th>
<th>Potential Late Effects</th>
<th>Periodic Evaluation</th>
<th>Health Counseling/ Further Considerations</th>
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<tbody>
<tr>
<td>4</td>
<td>Any Cancer Experience</td>
<td>Psychosocial disability due to pain</td>
<td>HISTORY&lt;br&gt;Psychosocial assessment&lt;br&gt;Yearly</td>
<td>HEALTH LINKS&lt;br&gt;Chronic Pain after Childhood Cancer&lt;br&gt;RESOURCES&lt;br&gt;‘Childhood Cancer Survivors: A Practical Guide to Your Future,’ by Nancy Keene, Wendy Hobbie &amp; Kathy Ruccione, Childhood Cancer Guides, 2012&lt;br&gt;POTENTIAL CONSIDERATIONS FOR FURTHER TESTING AND INTERVENTION&lt;br&gt;Psychological consultation in patients with chronic pain. Appropriate psychotropic medications, as clinically indicated. Referral to pain rehabilitation clinic.</td>
</tr>
</tbody>
</table>

### Additional Information

Consider patient and cancer/treatment factors, pre-morbidity/co-morbid health conditions, and health behaviors that may increase risk.
- Patient factors: Female sex
- Cancer/Treatment factors: CNS tumor, Hodgkin lymphoma, sarcoma/bone diagnosis, radiation to bone/joint, vincristine exposure
- Pre-morbid/Co-morbid medical conditions: History of osteonecrosis, depression, anxiety, sleep/fatigue issues, severe/life threatening chronic medical conditions

### References

Any Cancer Experience

<table>
<thead>
<tr>
<th>Section</th>
<th>Therapeutic Exposure</th>
<th>Potential Late Effects</th>
<th>Periodic Evaluation</th>
<th>Health Counseling/Further Considerations</th>
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<tbody>
<tr>
<td>5</td>
<td>Any Cancer Experience</td>
<td>Fatigue, Sleep problems</td>
<td>HISTORY</td>
<td>RESOURCES</td>
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</tbody>
</table>

**HISTORY**
- Psychosocial assessment
  - Yearly

**RESOURCES**

**POTENTIAL CONSIDERATIONS FOR FURTHER TESTING AND INTERVENTION**
- Screen for physical sources of fatigue, such as anemia, sleep disturbances, nutritional deficiencies, cardiomyopathy, pulmonary fibrosis, hypothyroidism, or other endocrinopathies.
- Referral to specialties such as endocrinology, sleep lab/study, or nutrition as indicated.
- Referral to psychology for behavioral intervention for emotional difficulties contributing to sleep/fatigue issues.
- Refer as indicated for cognitive-behavior therapy for insomnia.

**SYSTEM = Psychosocial**
**SCORE = 2A**

### Additional Information
Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.
- Patient factors: Female sex
- Cancer/Treatment factors: CNS tumor (e.g., craniopharyngioma), pulmonary radiation
- Pre-morbid/Co-morbid medical conditions: Depression, anxiety, obesity, sleep/fatigue issues, pain

### References
## ANY CANCER EXPERIENCE (CONT)

<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Exposure</th>
<th>Potential Late Effects</th>
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<tr>
<td>6</td>
<td>Any Cancer Experience</td>
<td>Limitations in healthcare and insurance access</td>
<td>HISTORY Psychosocial assessment with attention to healthcare and insurance access Yearly</td>
<td>HEALTH LINKS Finding and Paying for Healthcare</td>
</tr>
</tbody>
</table>

**SYSTEM = Psychosocial**  
**SCORE = 2A**

### Additional Information

Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.  
- Patient factors: Lower household income, lower educational attainment, unemployment

### References

### ANY CANCER EXPERIENCE (CONT)

<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Exposure</th>
<th>Potential Late Effects</th>
<th>Periodic Evaluation</th>
<th>Health Counseling/ Further Considerations</th>
</tr>
</thead>
</table>
| 7     | Any Cancer Experience| Subsequent malignancy Risk of malignancy in offspring | HISTORY: **Strongly consider assessment for cancer predisposition in the following settings:**  
- Any tumor listed in Table 1  
- Any bilateral cancer  
- >1 primary cancer  
- ≥1 first degree relative(s) with cancer  
- Other concerning family history including consanguinity  
- Diagnosis of adult-type cancer in a child (basal cell carcinoma, breast, colon, gastrointestinal, ovarian, etc.)  
- Diagnosis of cancer predisposition syndrome in a relative | RESOURCES:  
McGill Interactive Pediatric OncoGenetic Guidelines: [www.mipogg.com](http://www.mipogg.com)  
National Society of Genetic Counselors: [www.nsgc.org](http://www.nsgc.org)  
POTENTIAL CONSIDERATIONS FOR FURTHER TESTING AND INTERVENTION:  
For patients who may be at risk for cancer predisposition by history, or with a history of one of the cancer types listed in Table 1, consider:  
- Referral to genetic counseling or clinical genetics  
- Referral for preconception/prenatal counseling |}

**SYSTEM = SMN**  
**SCORE = 1**

#### Table 1

<table>
<thead>
<tr>
<th>Solid Tumor</th>
<th>Solid Tumor (cont)</th>
<th>CNS Tumor (cont)</th>
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<td>Adrenocortical carcinoma</td>
<td>Pleuropulmonary blastoma</td>
<td>Pineoblastoma</td>
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<td>Desmoid tumor</td>
<td>Renal cell carcinoma</td>
<td>Pituitary blastoma</td>
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<td>Endolymphatic sac tumor</td>
<td>Rhabdoid tumor</td>
<td>Retinoblastoma</td>
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<tr>
<td>Gastrointestinal stromal tumor</td>
<td>Schwannoma</td>
<td>Sub-ependymomal giant cell astrocytoma</td>
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<td>Malignant peripheral nerve sheath tumor</td>
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<td>Medullary thyroid cancer</td>
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<tr>
<td>Osteosarcoma</td>
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<tr>
<td>Ovarian Sertoli cell or Sertoli-Leydig cell tumor</td>
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<td>Paraganglioma</td>
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<td>Pheochromocytoma</td>
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## Blood/Serum Products

<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Exposure</th>
<th>Potential Late Effects</th>
<th>Periodic Evaluation</th>
<th>Health Counseling/ Further Considerations</th>
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</thead>
<tbody>
<tr>
<td>8</td>
<td>Diagnosed prior to 1972</td>
<td>Chronic hepatitis B</td>
<td>SCREENING</td>
<td>HEALTH LINKS</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Hepatitis B surface antigen (HBsAg)</td>
<td>Hepatitis</td>
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<td>Hepatitis B core antibody (anti-HBc or HBcAb)</td>
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<td>Once in patients who received treatment for cancer prior to 1972</td>
<td>Screening for viral hepatitis in patients with persistently abnormal liver function regardless of transfusion history.</td>
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<td>Note: Date may vary for international patients</td>
<td>Gastroenterology or hepatology consultation for patients with chronic hepatitis.</td>
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<td></td>
<td>Hepatitis A and B immunization in at-risk patients lacking immunity.</td>
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</tbody>
</table>

### Additional Information

Exposure to blood/serum products prior to initiation of hepatitis B screening of blood supply (1972 in the United States - dates may differ in other countries) is associated with risk of chronic hepatitis B. Since the vast majority of patients received some type of blood product during childhood cancer treatment, screening based on date of diagnosis/treatment is recommended unless there is absolute certainty that the patient did not receive any blood or blood products.

Relevant exposures include packed red cells, whole blood, granulocytes, platelets, fresh frozen plasma, cryoprecipitate, IVIG, VZIG, factor concentrate, and allogeneic marrow, cord blood, or stem cells.

Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk:

- Patient factors: Living in hyperendemic areas
- Cancer/Treatment factors: Chronic immunosuppression
- Health behaviors: History of IV drug use, unprotected sex, multiple partners, high-risk sexual behavior, sexually transmitted infections, tattoos, body piercing

### References

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#### BLOOD/SERUM PRODUCTS (CONT)

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<th>Potential Late Effects</th>
<th>Periodic Evaluation</th>
<th>Health Counseling/ Further Considerations</th>
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<tbody>
<tr>
<td>9</td>
<td>Diagnosed prior to 1993</td>
<td>Chronic hepatitis C</td>
<td>SCREENING</td>
<td>HEALTH LINKS</td>
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<td>Hepatitis C antibody</td>
<td>Hepatitis</td>
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<td>Once in patients who received treatment for cancer prior to 1993</td>
<td><strong>POSSIBLE CONSIDERATIONS FOR FURTHER TESTING AND INTERVENTION</strong></td>
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<td>Note: Date may vary for international patients</td>
<td>Screen for viral hepatitis in patients with persistently abnormal liver function regardless of transfusion history.</td>
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<td>Hepatitis C PCR (to establish chronic infection)</td>
<td>PCR testing for HCV in immunosuppressed patients who are negative for antibody.</td>
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<td>Once in patients with positive Hepatitis C antibody</td>
<td>Gastroenterology or hepatology consultation for management of patients with chronic hepatitis.</td>
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<td>Hepatitis A and B immunization in at-risk patients lacking immunity.</td>
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</tbody>
</table>

#### Additional Information

Exposure to blood/serum products prior to initiation of hepatitis C screening of blood supply (1993 in the United States [considering the more reliable EIA-2 screening was released in the U.S. in 1992] - dates may differ in other countries) is associated with risk of chronic hepatitis C.

Since the vast majority of patients received some type of blood product during childhood cancer treatment, screening based on date of diagnosis/treatment is recommended unless there is absolute certainty that the patient did not receive any blood or blood products.

Relevant exposures include packed red cells, whole blood, granulocytes, platelets, fresh frozen plasma, cryoprecipitate, IVIG, VZIG, factor concentrates, and allogeneic marrow, cord blood, or stem cells.

Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.

- **Patient factors:** Living in hyperendemic areas
- **Cancer/Treatment factors:** Chronic immunosuppression, exposure to blood/serum products prior to 1986 (when surrogate screening of blood donors with ALT was initiated and donors with self-reported high-risk behaviors were deferred)
- **Health behaviors:** History of IV drug use, unprotected sex, multiple partners, high-risk sexual behavior, sexually transmitted infections, tattoos, body piercing

#### References

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<th>Health Counseling/ Further Considerations</th>
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<tr>
<td>10</td>
<td>Diagnosed between 1977 and 1985</td>
<td>HIV infection</td>
<td>SCREENING</td>
<td>COUNSELING</td>
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<td>HIV testing</td>
<td>Standard counseling regarding safer sex, universal precautions and high-risk behaviors that exacerbate risk.</td>
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<td>Once in patients who received treatment for cancer between 1977 and 1985</td>
<td>POTENTIAL CONSIDERATIONS FOR FURTHER TESTING AND INTERVENTION</td>
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<td>Note: Date may vary for international patients</td>
<td>HIV/Infectious diseases specialist consultation for patients with chronic infection.</td>
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</tbody>
</table>

**Additional Information**

Exposure to blood/serum products prior to initiation of HIV screening of blood supply (between 1977 and 1985 in the United States - dates may differ in other countries) is associated with risk of HIV infection. Since the vast majority of patients received some type of blood product during childhood cancer treatment, screening based on date of diagnosis/treatment is recommended unless there is absolute certainty that the patient did not receive any blood or blood products.

Relevant exposures include packed red cells, whole blood, granulocytes, platelets, fresh frozen plasma, cryoprecipitate, IVIG, VZIG, factor concentrates, and allogeneic marrow, cord blood, or stem cells.

Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.

- Health behaviors: History of IV drug use, unprotected sex, multiple partners, high-risk sexual behavior, sexually transmitted infections, tattoos, body piercing

**References**

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<th>Sec #</th>
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<th>Periodic Evaluation</th>
<th>Health Counseling/ Further Considerations</th>
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<tbody>
<tr>
<td>11</td>
<td>Any Chemotherapy</td>
<td>Dental abnormalities</td>
<td>PHYSICAL</td>
<td>HEALTH LINKS</td>
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<td></td>
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<td>Tooth/Root agenesis</td>
<td>Oral exam</td>
<td>Dental Health</td>
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<td>Root thinning/shortening</td>
<td>Yearly</td>
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<td>Enamel dysplasia</td>
<td>SCREENING</td>
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<td>Microdontia</td>
<td>Dental exam and cleaning</td>
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<td>Ectopic molar eruption</td>
<td>Every 6 months</td>
<td>SYSTEM = Dental</td>
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<td>Dental caries</td>
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<td>SCORE</td>
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**Potential Considerations for Further Testing and Intervention**

- Regular dental care including fluoride applications.
- Baseline panorex prior to dental procedures to evaluate root development.

**Additional Information**

Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.

- Patient factors: Any patient who had not developed permanent dentition at time of cancer therapy, younger age at treatment, especially age <5 years
- Cancer/Treatment factors: Any radiation treatment involving the oral cavity or salivary glands

**References**


## Therapeutic Exposure

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<th>Sec #</th>
<th>Potential Late Effects</th>
<th>Periodic Evaluation</th>
<th>Health Counseling/Further Considerations</th>
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</thead>
<tbody>
<tr>
<td>12</td>
<td>Classical Alkylation Agents</td>
<td>Testicular hormonal dysfunction</td>
<td><strong>History</strong></td>
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<td>(male)</td>
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<td>Testosterone deficiency/insufficiency</td>
<td>Onset and tempo of puberty</td>
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<td>Delayed/Arested puberty</td>
<td>Sexual function (erections, nocturnal emissions, libido)</td>
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</table>

- **Commonly used alkylators can be converted to a cyclophosphamide equivalent dose by using: CED (mg/m²) =** 1.0 (cumulative cyclophosphamide dose (mg/m²)) + 0.244 (cumulative ifosfamide dose (mg/m²)) + 0.857 (cumulative procarbazine dose (mg/m²)) + 14.286 (cumulative chlorambucil dose (mg/m²)) + 15 (cumulative BCNU dose (mg/m²)) + 16 (cumulative CCNU dose (mg/m²)) + 40 (cumulative melphalan dose (mg/m²)) + 50 (cumulative thiotepa dose (mg/m²)) + 100 (cumulative nitrogen mustard dose (mg/m²)) + 0.857 (cumulative procarbazine dose (mg/m²)) + 14.286 (cumulative chlorambucil dose (mg/m²)) + 15 (cumulative BCNU dose (mg/m²)) + 16 (cumulative CCNU dose (mg/m²)) + 40 (cumulative melphalan dose (mg/m²)) + 50 (cumulative thiotepa dose (mg/m²)) + 100 (cumulative nitrogen mustard dose (mg/m²)) + 8.823 (cumulative busulfan dose (mg/m²))

### Additional Information

- Testicular volume is not a reliable indicator of pubertal onset/stage in boys treated with alkylating agents and/or direct testicular radiotherapy. Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.
  - Cancer/Treatment factors: Testicular cancer, higher cumulative doses of alkylators (especially cyclophosphamide dose ≥20 g/m² or ifosfamide ≥60 g/m²), combinations of alkylators, combination with MOPP, cyclophosphamide as conditioning for HCT, in combination with radiation (to abdomen/pelvis, testes [especially dose ≥20 Gy], brain/cranium [neuroendocrine axis], or TBI), and unilateral orchiectomy
  - Health behaviors: Tobacco/Marijuana use

### References

### CHEMOTHERAPY

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<tbody>
<tr>
<td>13</td>
<td>Classical Alkylating Agents</td>
<td>Impaired spermatogenesis</td>
<td>HISTORY</td>
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<tr>
<td></td>
<td>Busulfan</td>
<td>Reduced fertility</td>
<td>Onset and tempo of puberty</td>
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<td></td>
<td>Carmustine (BCNU)</td>
<td>Oligospermia</td>
<td>Sexual function (erections, nocturnal emissions, libido)</td>
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<td>Chlorambucil</td>
<td>Azoospermia</td>
<td>Medication use</td>
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<td>Cyclophosphamide</td>
<td>Infertility</td>
<td>Yearly</td>
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<td>Procarbazine</td>
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<td>Carboplatin</td>
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<td>Cisplatin</td>
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<td>Non-Classical Alkylators</td>
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<td>Dacarbazine (DTIC)</td>
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<td>Temozolomide</td>
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<td>PHYSICAL</td>
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<td>Tanner staging until sexually mature</td>
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<td>Testicular volume by Prader orchidometer</td>
<td>Yearly</td>
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**Commonly used alkylators can be converted to a cyclophosphamide equivalent dose by using:**

\[
\text{CED (mg/m}^2\text{)} = 1.0 \times (\text{cumulative cyclophosphamide dose (mg/m}^2\text{)}) + 0.244 \times (\text{cumulative ifosfamide dose (mg/m}^2\text{)}) + 0.857 \times (\text{cumulative procarbazine dose (mg/m}^2\text{)}) + 14.286 \times (\text{cumulative chlorambucil dose (mg/m}^2\text{)}) + 15 \times (\text{cumulative BCNU dose (mg/m}^2\text{)}) + 16 \times (\text{cumulative CCNU dose (mg/m}^2\text{)}) + 40 \times (\text{cumulative melphalan dose (mg/m}^2\text{)}) + 50 \times (\text{cumulative thiotepa dose (mg/m}^2\text{)}) + 100 \times (\text{cumulative nitrogen mustard dose (mg/m}^2\text{)}) + 8.823 \times (\text{cumulative busulfan dose (mg/m}^2\text{)})
\]

**SYSTEM = Reproductive (Male)**

**SCORE**

- Classical Alkylating Agents = 1
- Heavy Metals = 2A
- Non-Classical Alkylators = 2A

### Additional Information

Testicular volume is not a reliable indicator of pubertal onset/stage in boys treated with alkylating agents and/or direct testicular radiotherapy. Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.

- **Patient factors:** Medications (anabolic steroids, testosterone), occupational exposures (pesticides, heavy metals, solvents)
- **Cancer/Treatment factors:** Testicular cancer, higher cumulative doses of alkylators (especially busulfan >600 mg/m<sup>2</sup>, cyclophosphamide >4 gm/m<sup>2</sup>, CED >4 gm/m<sup>2</sup>, ifosfamide >50 gm/m<sup>2</sup>), and cisplatin >488 mg/m<sup>2</sup>, combinations of alkylators, MOPP >3 cycles, cyclophosphamide as conditioning for HCT, in combination with radiation to abdomen/pelvis, testes, brain/cranium (neuroendocrine axis), or TBI, genitourinary surgery
- **Pre-morbid/Co-morbid medical conditions:** Obesity, ejaculatory dysfunction, history of sexually transmitted infections, cGVHD
- **Health behaviors:** Tobacco/Marijuana use

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<tbody>
<tr>
<td>14 (female)</td>
<td><strong>Classical Alkylating Agents</strong>&lt;br&gt;Busulfan&lt;br&gt;Carmustine (BCNU)&lt;br&gt;Chlorambucil&lt;br&gt;Cyclophosphamide&lt;br&gt;Ifosfamide&lt;br&gt;Lonustine (CCNU)&lt;br&gt;Meclorethamine&lt;br&gt;Melphalan&lt;br&gt;Procarbazine&lt;br&gt;Thiotepa&lt;br&gt;<strong>Heavy Metals</strong>&lt;br&gt;Carboplatin&lt;br&gt;Cisplatin&lt;br&gt;Non-Classical Alkylators&lt;br&gt;Dacarbazine (DTIC)&lt;br&gt;Temozolomide&lt;br&gt;</td>
<td>Ovarian hormone deficiencies&lt;br&gt;Delayed puberty&lt;br&gt;Arrested puberty&lt;br&gt;Premature ovarian insufficiency/Premature menopause&lt;br&gt;</td>
<td><strong>HISTORY</strong>&lt;br&gt;Onset and tempo of puberty&lt;br&gt;Menstrual history&lt;br&gt;Sexual function (vaginal dryness, libido)&lt;br&gt;Menopausal symptoms&lt;br&gt;Medsication use&lt;br&gt;Yearly&lt;br&gt;<strong>PHYSICAL</strong>&lt;br&gt;Tanner staging until sexually mature&lt;br&gt;Yearly&lt;br&gt;Monitor growth until mature&lt;br&gt;Yearly&lt;br&gt;</td>
<td><strong>HEALTH LINKS</strong>&lt;br&gt;Ovarian and Reproductive Health&lt;br&gt;</td>
</tr>
</tbody>
</table>

**COUNSELING**

Higher cumulative doses of alkylating agents with or without radiation may increase risk. Dose can be estimated using CED dose calculation. Adverse impact of ovarian hormone deficiencies on growth, bone mineralization, cardiovascular disease and sexual dysfunction.

**POTENTIAL CONSIDERATIONS FOR FURTHER TESTING AND INTERVENTION**

FSH and estradiol and/or endocrine/gynecology referral for patients with:
- No signs of puberty by age 13 years
- Failure of pubertal progression
- Abnormal menstrual patterns or menopausal symptoms
- Ovarian hormone deficiency/insufficiency to weigh risks and benefits of hormonal replacement therapy

Bone density evaluation in patients with ovarian hormone deficiencies.

**SYSTEM = Reproductive (Female)**

**SCORE**

Classical Alkylating Agents = 1
Heavy Metals = 2B
Non-Classical Alkylators = 2A

Commonly used alkylators can be converted to a cyclophosphamide equivalent dose by using: 

\[
\text{CED (mg/m^2)} = 1.0 \times (\text{cumulative cyclophosphamide dose (mg/m^2)}) + 0.244 \times (\text{cumulative ifosfamide dose (mg/m^2)}) + 0.857 \times (\text{cumulative procarbazine dose (mg/m^2)}) + 14.286 \times (\text{cumulative chlorambucil dose (mg/m^2)}) + 15 \times (\text{cumulative BCNU dose (mg/m^2)}) + 16 \times (\text{cumulative CCNU dose (mg/m^2)}) + 40 \times (\text{cumulative melphalan dose (mg/m^2)}) + 50 \times (\text{cumulative thiotepa dose (mg/m^2)}) + 100 \times (\text{cumulative nitrogen mustard dose (mg/m^2)}) + 8.823 \times (\text{cumulative busulfan dose (mg/m^2)})
\]

**Additional Information**

Alkylating agent doses that cause gonadal dysfunction show individual variation. Females can typically maintain gonadal function at higher cumulative doses than males.
Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.
- Patient factors: Older age at treatment
- Cancer/Treatment factors: Higher cumulative doses of alkylators or combinations of alkylators, combination with radiation to abdomen/pelvis, lumbar or sacral spine (from ovarian scatter), or brain/cranium (neuroendocrine axis), any alkylators combined with pelvic radiation or TBI
- Health behaviors: Smoking

**References**

Section 14 References (cont)

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<tr>
<td>15 (female)</td>
<td><strong>Classical Alkylating Agents</strong>&lt;br&gt;Busulfan&lt;br&gt;Carmustine (BCNU)&lt;br&gt;Chlorambucil&lt;br&gt;Cyclophosphamide&lt;br&gt;Ifosfamide&lt;br&gt;Loxustine (CCNU)&lt;br&gt;Mechlorethamine&lt;br&gt;Melphalan&lt;br&gt;Procarbazine&lt;br&gt;Thiotepa</td>
<td><strong>Diminished Ovarian Reserve (DOR)</strong>&lt;br&gt;Infertility</td>
<td><strong>HISTORY</strong>&lt;br&gt;Menstrual and pregnancy history&lt;br&gt;Hormonal therapy&lt;br&gt;Yearly <strong>PHYSICAL</strong>&lt;br&gt;Tanner staging until sexually mature&lt;br&gt;Yearly</td>
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<table>
<thead>
<tr>
<th><strong>COMMONLY USED ALKYLATORS</strong></th>
<th><strong>CED (mg/m²)=</strong></th>
</tr>
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<tbody>
<tr>
<td>1.0 (cumulative cyclophosphamide dose (mg/m²)) + 0.244 (cumulative ifosfamide dose (mg/m²)) + 0.857 (cumulative procarbazine dose (mg/m²)) + 14.286 (cumulative chlorambucil dose (mg/m²)) + 15 (cumulative BCNU dose (mg/m²)) + 16 (cumulative CCNU dose (mg/m²)) + 40 (cumulative melphalan dose (mg/m²)) + 50 (cumulative thiotepa dose (mg/m²)) + 100 (cumulative nitrogen mustard dose (mg/m²)) + 8.823 (cumulative busulfan dose (mg/m²))</td>
<td></td>
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</tbody>
</table>

**AMH** may be low in the presence of normal FSH. AMH should be interpreted relative to age-specific reference ranges. FSH is lowered and AMH may be lowered by concurrent hormonal contraceptive use. Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.

- Patient factors: Older age at treatment
- Cancer/Treatment factors: Higher cumulative doses of alkylators or combinations of alkylators, combination with radiation to abdomen/pelvis, lumbar or sacral spine (from ovarian scatter), or brain, cranium (neuroendocrine axis), any alkylators combined with pelvic radiation or TBI
- Health behaviors: Smoking

### ALKYLATING AGENTS (CONT)

**HEALTH LINKS**

**RESOURCES**
- American Society for Reproductive Medicine: [www.asrm.org](http://www.asrm.org)
- Alliance for Fertility Preservation: [www.allianceforfertilitypreservation.org](http://www.allianceforfertilitypreservation.org)
- Livestrong Foundation: [www.livestrong.org/what-we-do/program/fertility](http://www.livestrong.org/what-we-do/program/fertility)
- Oncofertility Consortium: [https://oncofertility.msu.edu](https://oncofertility.msu.edu)

**COUNSELING**

- Need for contraception.
- Review previous fertility preservation counseling/interventions.
- Fertility recovery can be seen in the early years after the completion of therapy and occasionally thereafter.
- Potential for shorter period of fertility in family planning. Those with DOR should consider discussing reproductive health options with a reproductive endocrinologist or fertility specialist.
- Higher cumulative doses of alkylating agents with or without radiation may increase risk. Dose can be estimated using CED dose calculation.

**POTENTIAL CONSIDERATIONS FOR FURTHER TESTING AND INTERVENTION**

- **FSH and estradiol** for patients with menstrual cycle dysfunction suggestive of premature ovarian insufficiency or those who desire information about potential for future fertility.
- AMH to assess for diminished ovarian reserve.
- Reproductive endocrinology referral for antral follicle count, ovarian reserve evaluation and consultation regarding assisted reproductive technologies in at-risk patients who desire information about potential fertility and interventions to preserve future fertility.
- Alkylating agent doses that cause gonadal dysfunction show individual variation. Females can typically maintain gonadal function at higher cumulative doses than males.

<table>
<thead>
<tr>
<th>SYSTEM = Reproductive (Female)</th>
<th><strong>SCORE</strong></th>
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</thead>
<tbody>
<tr>
<td>Classical Alkylating Agents = 1</td>
<td>Heavy Metals = 2B</td>
</tr>
<tr>
<td>Non-Classical Alkylators = 2A</td>
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</table>
### Section 15 References (cont)

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<tr>
<td>16</td>
<td><strong>Classical Alkylating Agents</strong>&lt;br&gt;Busulfan&lt;br&gt;Carmustine (BCNU)&lt;br&gt;Chlorambucil&lt;br&gt;Cyclophosphamide&lt;br&gt;Ifosfamide&lt;br&gt;Loxustine (CCNU)&lt;br&gt;Mechlorethamine&lt;br&gt;Procarbazine&lt;br&gt;Thiotepa&lt;br&gt;<strong>Heavy Metals</strong>&lt;br&gt;Carboplatin&lt;br&gt;Cisplatin&lt;br&gt;<strong>Non-Classical Alkylators</strong>&lt;br&gt;Dacarbazine (DTIC)&lt;br&gt;Temozolomide</td>
<td>Acute myeloid leukemia (AML)&lt;br&gt;Myelodysplasia (MDS)</td>
<td><strong>HISTORY</strong>&lt;br&gt;Fatigue&lt;br&gt;Bleeding&lt;br&gt;Easy bruising&lt;br&gt;Yearly, up to 10 years after exposure to agent</td>
<td><strong>HEALTH LINKS</strong>&lt;br&gt;Reducing the Risk of Subsequent Cancers&lt;br&gt;<strong>COUNSELING</strong>&lt;br&gt;Promptly seek medical attention for fatigue, pallor, petechiae or bone pain.</td>
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### Additional Information

There is negligible benefit to obtaining a screening CBC in the absence of clinical signs and symptoms for AML/MDS.

Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.

- Cancer/Treatment factors: Less than 10 years since exposure to agent, higher cumulative alkylator dose or combination of alkylators, autologous HCT. Note melphalan and mechlorethamine are more potent leukemogens than cyclophosphamide.
- Pre-morbid/Co-morbid medical conditions: Evidence is conflicting that splenectomy modifies risk for AML/MDS

### References


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<td>17</td>
<td>Classical Alkylating Agents</td>
<td>Pulmonary fibrosis</td>
<td>HISTORY</td>
<td>HEALTH LINKS</td>
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<td>Busulfan</td>
<td>Cough</td>
<td>Pulmonary Health</td>
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<td></td>
<td>Carmustine (BCNU)</td>
<td>Wheezing</td>
<td>RESOURCES</td>
<td><a href="http://www.smokefree.gov">www.smokefree.gov</a></td>
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<tr>
<td></td>
<td>Lomustine (CCNU)</td>
<td>Shortness of breath</td>
<td>COUNSELING</td>
<td>Tobacco avoidance/Smoking cessation/Environmental tobacco smoke.</td>
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<td>Dyspnea on exertion</td>
<td>Influenza and Pneumococcal vaccinations.</td>
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<td>Yearly</td>
<td>POTENTIAL CONSIDERATIONS FOR FURTHER TESTING AND INTERVENTION</td>
<td>Repeat PFTs prior to general anesthesia.</td>
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<td></td>
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<td>PHYSICAL</td>
<td>Pulmonary consultation for patients with symptomatic pulmonary dysfunction.</td>
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<td></td>
<td>Pulmonary exam</td>
<td>PFTs (including DLCO and spirometry)</td>
<td>Pulmonary consultation for survivors who desire to SCUBA dive (due to potential undiagnosed pulmonary toxicities, and limited data to guide safe diving recommendations for individuals treated with pulmonary toxic therapy).</td>
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<td>Yearly</td>
<td>Baseline at entry into long-term follow-up, repeat as clinically indicated in patients with abnormal results or progressive pulmonary dysfunction</td>
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<td>SCREENING</td>
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<td>SYSTEM = Pulmonary</td>
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**Additional Information**

Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.

- Cancer/Treatment factors: Higher cumulative doses, especially BCNU ≥600 mg/m² and busulfan ≥500 mg (transplant doses), combination with bleomycin, combination with chest radiation or TBI
- Pre-morbid/Co-morbid medical conditions: Atopic history
- Health behaviors: Smoking, inhaled illicit drug use

**References**


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<td>Classical Alkylating Agents</td>
<td>Cataracts</td>
<td>HISTORY</td>
<td>HEALTH LINKS</td>
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<tr>
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<td>Busulfan</td>
<td></td>
<td>Visual changes (decreased acuity, halos, diplopia)</td>
<td>Cataracts</td>
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<td>Yearly</td>
<td>POTENTIAL CONSIDERATIONS FOR FURTHER TESTING AND INTERVENTION</td>
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<td>PHYSICAL</td>
<td>Ophthalmology consultation as clinically indicated.</td>
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<td>Visual acuity</td>
<td>Refer patients with visual deficits to school liaison in community or cancer center (psychologist, social worker, school counselor) to facilitate acquisition of educational resources.</td>
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<td>Funduscopic exam</td>
<td>SYSTEM = Ocular</td>
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<td>SCORE = 2B</td>
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<td>SCREENING</td>
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<td>Evaluation by ophthalmologist or optometrist</td>
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**Additional Information**

Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.

- Cancer/Treatment factors: Combination with corticosteroids, combination with TBI, cranial, orbital, or eye radiation, longer interval since treatment

**References**


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| 19    | Classical Alkylating Agents
Cyclophosphamide
Ifosfamide | Urinary tract toxicity
Hemorrhagic cystitis
Bladder fibrosis
Dysfunctional voiding
Vesicoureteral reflux
Hydronephrosis | HISTORY
Hematuria
Urinary urgency/frequency
Urinary incontinence/retention
Dysuria
Nocturia
Abnormal urinary stream
Yearly | HEALTH LINKS
Bladder Health
COUNSELING
Promptly report dysuria or gross hematuria.

**POTENTIAL CONSIDERATIONS FOR FURTHER TESTING AND INTERVENTION**

Urinalysis, urine culture, spot urine calcium/creatinine ratio for patients with positive history.

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, incontinence, or dysfunctional voiding.

SYSTEM = Urinary
SCORE = 1

### Additional Information

Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.

- Cancer/Treatment factors: Higher cumulative doses (decreased incidence with Mesna), especially cyclophosphamide dose ≥3 gm/m², combination with pelvic radiation, especially pelvic radiation dose ≥30 Gy
- Health behaviors: Alcohol use, smoking

### References


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</table>
| 20    | Classical Alkylating Agents Cyclophosphamide | Bladder malignancy | HISTORY  
Hematuria  
Urinary urgency/frequency  
Urinary incontinence/retention  
Dysuria  
Nocturia  
Abnormal urinary stream  
Yearly | HEALTH LINKS  
Bladder Health  
COUNSELING  
Promptly seek medical attention for dysuria or gross hematuria.  
POTENTIAL CONSIDERATIONS FOR FURTHER TESTING AND INTERVENTION  
Urinalysis, urine culture, spot urine calcium/creatinine ratio for patients with positive history.  
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.  
Urology referral for patients with culture-negative macroscopic hematuria. | SYSTEM = SMN  
SCORE = 2A |

### Additional Information

Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.
- Cancer/Treatment factors: Combination with pelvic radiation
- Health behaviors: Alcohol use, smoking

### References

Ifosfamide-related renal toxicity typically occurs during the acute treatment phase and improves or progresses over time. Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.

- **Patient factors:** Younger age at treatment, especially age <4 years
- **Cancer/Treatment factors:** Tumor infiltration of kidney(s), nephrectomy, higher cumulative dose, especially ifosfamide dose ≥60 grams/m², combination with other nephrotoxic agents (e.g., cisplatin, carboplatin, aminoglycosides, amphotericin, immunosuppressants, methotrexate, radiation impacting the kidney), renal radiation dose ≥15 Gy
- **Pre-morbid/Co-morbid medical conditions:** Pre-existing renal impairment, congenital absence of kidney

**References**


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<th><strong>Periodic Evaluation</strong></th>
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| 22 | Heavy Metals  
Carboplatin (myeloablative doses)  
Cisplatin | Otoxicity  
Sensorineural hearing loss  
Tinnitus  
Vertigo | **HISTORY**  
Hearing difficulties (with/without background noise)  
Tinnitus  
Vertigo  
Yearly  
**PHYSICAL**  
Otoscopic exam  
Yearly  
**SCREENING**  
Complete audiological evaluation by audiologist  
Yearly, for patients ages ≤5 years  
Pure tone audiometry testing at 1000-8000 Hz  
Every 2 years, for patients ages 6-12 years, then every 5 years beginning at age 13 years | **HEALTH LINKS**  
Hearing Loss  
School After Treatment  
**POTENTIAL CONSIDERATIONS FOR FURTHER TESTING AND INTERVENTION**  
Additional testing with high frequency audiometry at >8000 Hz is recommended if equipment is available.  
Audiology consultation for any survivor who has symptoms suggestive of hearing loss, tinnitus, or abnormal pure tone audiometry results showing a loss of more than 15 dB absolute threshold level (1000-8000 Hz).  
Ongoing follow-up with audiology for patients with hearing loss.  
Otolaryngology consultation in patients with chronic infection, cerumen impaction, or other anatomical problems exacerbating or contributing to hearing loss.  
Speech and language therapy for patients with hearing loss.  
Refer patients with auditory deficits to school liaison in community or cancer center (psychologist, social worker, school counselor) to facilitate acquisition of educational resources.  
Specialized evaluation for specific needs and/or preferential classroom seating, FM amplification system, and other educational assistance as indicated. |

### Additional Information

Myeloablative doses of carboplatin are given as conditioning for HCT and are typically ≥1500 mg/m². A “complete audiological evaluation” includes pure tone air and bone conduction, speech audiometry, and tympanometry for both ears. Frequency-specific auditory brainstem response can be performed if the above is inconclusive.

Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.

- **Patient factors:** Age <4 years at treatment
- **Cancer/Treatment factors:** CNS neoplasm, cumulative cisplatin dose ≥360 mg/m², high dose cisplatin (i.e., 40 mg/m² per day x 5 days per course), carboplatin conditioning for HCT, combination with cranial/ear radiation or ototoxic drugs (e.g., aminoglycosides, loop diuretics), cisplatin administered AFTER cranial/ear radiation, combination with radiation involving ear ≥30 Gy
- **Pre-morbid/Co-morbid medical conditions:** Chronic otitis, cerumen impaction, renal dysfunction, cerebrospinal fluid shunt

### References

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<tr>
<td>23</td>
<td>Heavy Metals</td>
<td>Carboplatin</td>
<td>Peripheral sensory neuropathy</td>
<td>HISTORY</td>
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<td></td>
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<td>Cisplatin</td>
<td>Paresthesias</td>
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<td>Yearly, until 2 to 3 years after therapy, monitor yearly if symptoms persist</td>
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<td></td>
<td>Neurologic exam</td>
<td>Yearly, until 2 to 3 years after therapy, monitor yearly if symptoms persist</td>
</tr>
</tbody>
</table>

**HEALTH LINKS**
Peripheral Neuropathy

**POTENTIAL CONSIDERATIONS FOR FURTHER TESTING AND INTERVENTION**
Physical therapy referral for patients with symptomatic neuropathy.
Physical and occupational therapy assessment of hand function.
Treat with effective agent for neuropathic pain (e.g., gabapentin or amitriptyline).
SYSTEM = PNS
SCORE = 2A

**Additional Information**
Acute toxicities most commonly occur and usually improve or resolve prior to patients entry to long-term follow-up.
Neuropathy can persist after treatment and is typically not late in onset.
Studies of adults treated during childhood support higher prevalence of deficits than previously appreciated.
Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.
- Cancer/Treatment factors: Cumulative cisplatin dose ≥300 mg/m², combination with vincristine, taxanes, gemcitabine

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<td>Heavy Metals</td>
<td>Renal toxicity</td>
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<td>HEAL TH LINKS</td>
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<td></td>
<td>Carboplatin</td>
<td>Glomerular injury</td>
<td>Blood pressure</td>
<td>Kidney Health</td>
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<td>Cisplatin</td>
<td>Renal insufficiency</td>
<td>Yearly</td>
<td>Cardiovascular Risk Factors</td>
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<td>Hypertension</td>
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<td>Tubular injury</td>
<td>SCREENING</td>
<td>COUNSELING</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(renal tubular</td>
<td>BUN</td>
<td>In patients with salt-wasting</td>
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<tr>
<td></td>
<td></td>
<td>acidosis, Fanconi</td>
<td>Creatinine</td>
<td>tubular dysfunction, educate that low</td>
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<td></td>
<td></td>
<td>syndrome, hypophosphatemic rickets)</td>
<td>Na, K, Cl, CO₂, Ca, Mg, PO₄</td>
<td>magnesium levels potentiate coronary</td>
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<td></td>
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<td></td>
<td></td>
<td>atherosclerosis.</td>
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<td>Baseline at entry into long-term follow-up,</td>
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<td>repeat as clinically indicated</td>
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</tbody>
</table>

**Additional Information**

Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.

- Cancer/Treatment factors: Nephrectomy, combination with other nephrotoxic agents (e.g., aminoglycosides, amphotericin, immunosuppressants, methotrexate, radiation impacting the kidney), cisplatin dose ≥200 mg/m², renal radiation dose ≥15 Gy
- Pre-morbid/Co-morbid medical conditions: Diabetes mellitus, hypertension, congenital absence of kidney

**References**

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<td>Antimetabolites</td>
<td>Cytarabine (high dose IV)</td>
<td>Neurocognitive deficits</td>
<td>EDUCATIONAL AND/OR VOCATIONAL PROGRESS</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Functional deficits in:</td>
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<td></td>
<td></td>
<td></td>
<td>• Executive function (planning and organization)</td>
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<tr>
<td></td>
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<td></td>
<td>• Sustained attention</td>
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<td></td>
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<td>• Memory (particularly visual, sequencing, temporal memory)</td>
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<td></td>
<td>• Processing speed</td>
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<td>• Visual-motor integration</td>
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<td>• Fine motor dexterity</td>
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<td></td>
<td>Learning deficits in math and reading (particularly reading comprehension)</td>
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<td>Diminished IQ</td>
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<td></td>
<td>Behavioral change</td>
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</tr>
</tbody>
</table>

**HISTORY**

Educational and/or vocational progress

**SCREENING**

Referral for formal neuropsychological evaluation

Baseline at entry into long-term follow-up, then periodically as clinically indicated for patients with evidence of impaired educational or vocational progress

**HEALTH LINKS**

School After Treatment

POTENTIAL CONSIDERATIONS FOR FURTHER TESTING AND INTERVENTION

Referral to school liaison in community or cancer center (psychologist, social worker, school counselor) to facilitate acquisition of educational resources and/or social skills training.

Psychotropic medication (e.g., stimulants) or evidence-based rehabilitation training. Caution—lower starting dose and assessment of increased sensitivity when initiating therapy is recommended.

Referral to community services for vocational rehabilitation or for services for developmentally disabled.

**SYSTEM = CNS**

**SCORE = 2A**

### Additional Information

Formal neuropsychological evaluation includes tests of processing speed, computer-based attention, visual motor integration, memory, comprehension of verbal instructions, verbal fluency, executive function and planning.

Neurocognitive deficits in survivors of leukemia and lymphoma are more frequently related to information processing (e.g., slow processing speed, attention problems). Extent of deficit depends on age at treatment, intensity of treatment, and time since treatment. New and progressive deficits may emerge over time.

Acute toxicity predominates if cytarabine is administered systemically as a single agent. Cytarabine may contribute to late neurotoxicity if combined with high dose or intrathecal methotrexate and/or cranial radiation.

Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.

- Patient factors: Younger age at treatment, especially age <3 years, female sex, family history of learning or attention problems
- Cancer/Treatment factors: CNS leukemia/lymphoma, relapsed leukemia/lymphoma treated with CNS-directed therapy, longer elapsed time since therapy, combination with corticosteroids, methotrexate (IT, IO, high dose IV), radiation dose ≥24 Gy, TBI, especially single fraction TBI (10 Gy), cranial radiation
- Pre-morbid/Co-morbid medical conditions: Pre-morbid learning or attention problems

### References


### Additional Information

Acute toxicities predominate, from which the majority of patients recover without sequelae.
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<tr>
<td>27</td>
<td>Antimetabolites</td>
<td>Hepatic dysfunction</td>
<td>PHYSICAL</td>
<td>HEALTH LINKS</td>
</tr>
<tr>
<td></td>
<td>Mercaptopurine (6MP)</td>
<td>Sinusoidal obstruction syndrome (SOS)</td>
<td>Scleral icterus</td>
<td>Liver Health</td>
</tr>
<tr>
<td></td>
<td>Thioguanine (6TG)</td>
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<td>Jaundice</td>
<td>POTENTIAL CONSIDERATIONS FOR FURTHER TESTING AND INTERVENTION</td>
</tr>
<tr>
<td></td>
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<td></td>
<td>Ascites</td>
<td>Platelet count for evaluation of hypersplenism and prothrombin time for evaluation of hepatic synthetic function in patients with abnormal liver screening tests.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Hepatomegaly</td>
<td>Screen for viral hepatitis in patients with persistently abnormal liver function or any patient transfused prior to 1993.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Splenomegaly</td>
<td>Gastroenterology/Hepatology consultation in patients with persistent liver dysfunction.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Yearly</td>
<td>Hepatitis A and B immunization in at-risk patients lacking immunity.</td>
</tr>
</tbody>
</table>

### Additional Information

Acute toxicities predominate from which the majority of patients recover without sequelae.

Delayed hepatic dysfunction may occur after a history of acute SOS, presenting as portal hypertension with liver biopsy indicating nodular regenerative hyperplasia, fibrosis, or siderosis.

Patients treated on CCG-1952, Regimens B1 and B2, received 6TG in place of 6MP during maintenance therapy.

Acute hepatotoxicity (manifesting as SOS) occurred in about 25% of patients.

Portal hypertension was identified as a late complication of 6TG in a small subset of patients (see Broxson et al., 2005).

Outcomes are detailed in Stork et al., 2010.

Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.

- Pre-morbid/co-morbid medical conditions: Viral hepatitis (especially chronic viral hepatitis), previous SOS, siderosis

### References

<table>
<thead>
<tr>
<th>Sec #</th>
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<th>Potential Late Effects</th>
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<th>Health Counseling/ Further Considerations</th>
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<tbody>
<tr>
<td>28</td>
<td><strong>Antimetabolites</strong></td>
<td>No known bone mineral density (BMD) late effects</td>
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<td>SYSTEM = No Known BMD Late Effects</td>
</tr>
<tr>
<td></td>
<td>Methotrexate (high dose IV)</td>
<td></td>
<td></td>
<td>SCORE = 2B</td>
</tr>
<tr>
<td></td>
<td>Methotrexate (low dose IV)</td>
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<tr>
<td></td>
<td>Methotrexate IM</td>
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<tr>
<td></td>
<td>Methotrexate PO</td>
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**References**


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<th>Potential Late Effects</th>
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<th>Health Counseling/ Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>29</td>
<td>Antimetabolites</td>
<td>No known renal late effects</td>
<td></td>
<td>SYSTEM = No Known Renal Late Effects SCORE = 2A</td>
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</tbody>
</table>

### Antimetabolites
- Methotrexate (high dose IV)
- Methotrexate (low dose IV)
- Methotrexate IM
- Methotrexate PO

### Additional Information
Acute toxicities predominate, from which the majority of patients recover without sequelae. Renal injury from other events (aminoglycoside exposure, tumor lysis) may make patients more vulnerable.

### References
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<td>30</td>
<td>Antimetabolites</td>
<td>Hepatic dysfunction</td>
<td>PHYSICAL</td>
<td>HEALTH LINKS</td>
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<td>Methotrexate (high dose IV)</td>
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<td>Scleral icterus</td>
<td>Liver Health</td>
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<td>Methotrexate (low dose IV)</td>
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<td>Jaundice</td>
<td>PONTENTIAL CONSIDERATIONS FOR FURTHER TESTING AND INTERVENTION</td>
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<td>Methotrexate PO</td>
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<td>Screen for viral hepatitis in patients with persistently abnormal liver function or any patient transfused prior to 1993.</td>
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<td>Splenomegaly</td>
<td>Gastroenterology/hepatology consultation in patients with persistent liver dysfunction.</td>
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<td>Yearly</td>
<td>Hepatitis A and B immunization in at-risk patients lacking immunity.</td>
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<td>SCREENING</td>
<td>SYSTEM = Gi/Hepatic</td>
</tr>
<tr>
<td></td>
<td></td>
<td>ALT</td>
<td>System at entry into long-term follow-up, repeat as clinically indicated.</td>
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<td></td>
<td></td>
<td>AST</td>
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<td></td>
<td></td>
<td>Bilirubin</td>
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</table>

**Additional Information**

Acute toxicities predominate from which the majority of patients recover without sequelae. Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.

- Cancer/Treatment factors: Abdominal radiation, treatment before 1970
- Pre-morbid/Co-morbid medical conditions: Viral hepatitis (especially chronic viral hepatitis)

**References**

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<tr>
<td>31</td>
<td>Antimetabolites Methotrexate (high dose IV) Methotrexate IO Methotrexate IT</td>
<td>Neurocognitive deficits Functional deficits in: • Executive function (planning and organization) • Sustained attention • Memory (particularly visual, sequencing, temporal memory) • Processing speed • Visual-motor integration • Fine motor dexterity Learning deficits in math and reading (particularly reading comprehension) Diminished IQ Behavioral change</td>
<td>HISTORY Educational and/or vocational progress Yearly SCREENING Referral for formal neuropsychological evaluation Baseline at entry into long-term follow-up, then periodically as clinically indicated for patients with evidence of impaired educational or vocational progress</td>
<td>HEALTH LINKS School After Treatment POTENTIAL CONSIDERATIONS FOR FURTHER TESTING AND INTERVENTION Referral to school liaison in community or cancer center (psychologist, social worker, school counselor) to facilitate acquisition of educational resources and/or social skills training. Psychotropic medication (e.g., stimulants) or evidence-based rehabilitation training. Caution—lower starting dose and assessment of increased sensitivity when initiating therapy is recommended. Referral to community for vocational rehabilitation or for services for developmentally disabled.</td>
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</table>

**Additional Information**

Formal neuropsychological evaluation includes tests of processing speed, computer-based attention, visual motor integration, memory, comprehension of verbal instructions, verbal fluency, executive function and planning. Neurocognitive deficits in survivors of leukemia and lymphoma are more frequently related to information processing (e.g., slow processing speed, attention problems). Extent of deficit depends on age at treatment, intensity of treatment, and time since treatment. New and progressive deficits may emerge over time.

Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.
- Patient factors: Younger age at treatment, especially age <3 years, female sex, family history of learning or attention problems
- Cancer/Treatment factors: CNS leukemia/lymphoma, relapsed leukemia/lymphoma treated with CNS-directed therapy, longer elapsed time since therapy, combination with corticosteroids, cytarabine (high dose IV), TBI, especially single fraction TBI (10 Gy), or CRT especially ≥24 Gy
- Pre-morbid/Co-morbid medical conditions: Pre-morbid learning or attention problems

**References**


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<tr>
<td>32</td>
<td>Antimetabolites</td>
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<tr>
<td></td>
<td>Methotrexate (high dose IV)</td>
<td>Clinical leukoencephalopathy</td>
<td>HISTORY</td>
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<tr>
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<td>Methotrexate IO</td>
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<tr>
<td></td>
<td>Methotrexate IT</td>
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</table>

**HISTORY**

- Cognitive, motor and/or sensory deficits
- Seizures
- Other neurologic symptoms

**PHYSICAL**

- Neurologic exam

**Yearly**

**POTENTIAL CONSIDERATIONS FOR FURTHER TESTING AND INTERVENTION**

- Brain CT or Brain MRI with MRA as clinically indicated with preferred study based on intracranial lesion to be evaluated:
  - Calcifications: CT
  - White matter: MRI with DTI
  - Microvascular injury: Gadolinium-enhanced MRI with DWI

Neurology consultation and follow-up as clinically indicated.

**SYSTEM = CNS**

**SCORE = 1**

---

### Additional Information

Clinical leukoencephalopathy may present with or without imaging abnormalities (e.g., leukoencephalopathy, cerebral lacunes, cerebral atrophy, dystrophic calcifications, mineralizing microangiopathy).

Transient white matter anomalies may follow radiotherapy and high dose chemotherapy for medulloblastoma/PNET, may mimic tumor recurrence, and signify risk of persistent neurologic sequelae.

Neuroimaging changes do not always correlate with degree of cognitive dysfunction.

Prospective studies are needed to define the dose/effect relationship of neurotoxic agents.

New deficits may emerge over time.

Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.

- Patient factors: Younger age at treatment
- Cancer/Treatment factors: CNS leukemia/lymphoma, relapsed leukemia/lymphoma treated with CNS-directed therapy, combination with cytarabine (high dose IV), dexamethasone, CRT especially ≥24 Gy

### References

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### ANTHRACYCLINE ANTIBIOTICS

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<td>Anthracycline Antibiotics</td>
<td>Acute myeloid leukemia</td>
<td>HISTORY</td>
<td>HEALTH LINKS</td>
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<tr>
<td></td>
<td>Daunorubicin</td>
<td></td>
<td>Fatigue</td>
<td>Reducing the Risk of Subsequent Cancers</td>
</tr>
<tr>
<td></td>
<td>Doxorubicin</td>
<td></td>
<td>Bleeding</td>
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<td></td>
<td>Epirubicin</td>
<td></td>
<td>Easy bruising</td>
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<td></td>
<td>Idarubicin</td>
<td></td>
<td>Yearly, up to 10 years after exposure to agent</td>
<td>COUNSELING</td>
</tr>
<tr>
<td></td>
<td>Mitoxantrone</td>
<td></td>
<td>Dermatologic exam (pallor, petechiae, purpura)</td>
<td>Promptly seek medical attention for fatigue, pallor, petechiae or bone pain.</td>
</tr>
</tbody>
</table>

**Additional Information**

Although mitoxantrone technically belongs to the anthraquinone class of anti-tumor antibiotics, it is related to the anthracycline family. There is negligible benefit to obtaining a screening CBC in the absence of clinical signs and symptoms of AML.

Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.

- **Cancer/Treatment factors:** Less than 5 years since exposure to agent, autologous HCT
- **Pre-morbid/Co-morbid medical conditions:** Evidence is conflicting that splenectomy modifies risk for AML

**References**


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<th>Potential Late Effects</th>
<th>Periodic Evaluation</th>
<th>Health Counseling/ Further Considerations</th>
</tr>
</thead>
</table>
| 34    | Anthracycline Antibiotics | Daunorubicin, Doxorubicin, Epirubicin, Idarubicin, Mitoxantrone | Cardiac toxicity, Cardiomyopathy, Subclinical left ventricular dysfunction, Congestive heart failure, Arrhythmia | HISTORY  
Shortness of breath  
Dyspnea on exertion  
Orthopnea  
Chest pain  
Palpitations  
If under 25 yrs: nausea, vomiting  
Yearly  
PHYSICAL  
Blood pressure  
Cardiac exam  
Yearly  
SCREENING  
Echo (or comparable imaging to evaluate cardiac function)  
*RECOMMENDED FREQUENCY OF ECHOCARDIOGRAM*  
| Anthracycline Dose*  
<100 mg/m²  
≥100 mg/m²  
≥250 mg/m²  
Any  
≥250 mg/m²  
Any  
**Based on radiation dose with potential impact to heart (radiation to chest, abdomen, spine [thoracic, whole], TBI). See section 77.  
**Recommended Frequency  
<150y  
Every 5 years  
Every 2 years  |
| HEALTH LINKS  
Heart Health  
Cardiovascular Risk Factors  
Nutrition and Physical Activity  
COUNSELING  
Traditional CVRFs significantly increase survivors’ risk of cardiomyopathy. Counsel regarding the importance of maintaining blood pressure, BMI, lipids, and glucose levels within goal ranges per general population guidelines.  
Regarding exercise:  
• Exercise is generally safe and encouraged for patients with normal LV systolic function  
• Consult cardiology for survivors with asymptomatic cardiomyopathy to define physical activity limits and precautions.  
• Consider cardiology consultation to define physical activity limits and precautions for high risk survivors (i.e., those requiring an echo every 2 years) who plan to participate in intensive exercise.  
If QTc interval is prolonged: Caution use of QTc prolonging medications (e.g., tricyclic anti-depressants, antifungals, macrolide antibiotics, metronidazole).  
| POTENTIAL CONSIDERATIONS FOR FURTHER TESTING AND INTERVENTION  
Cardiac MRI as an adjunct imaging modality when echo images are suboptimal.  
Cardiology consultation in patients with subclinical abnormalities on screening evaluations, LV dysfunction, dysrhythmia, or prolonged QTc interval.  
For patients who are pregnant or planning to become pregnant, additional cardiology evaluation is indicated in patients who received:  
• ≥250 mg/m² anthracyclines  
• ≥30 Gy chest radiation, or  
• Anthracycline (any dose) combined with chest radiation (≥15 Gy)  
• Evaluation should include a baseline echo (pre- or early-pregnancy). For those without prior abnormalities and with normal pre- or early-pregnancy baseline echos, follow-up echos may be obtained at the provider’s discretion. Those with a history of systolic dysfunction or with pre- or early-pregnancy systolic dysfunction are at highest risk for pregnancy-associated cardiomyopathy, and should be monitored periodically during pregnancy, labor and delivery due to increased risk for heart failure.  
SYSTEM = Cardiovascular  
SCORE = 1

### Dose Conversion

Use the following formulas to convert to doxorubicin isotoxic equivalents prior to calculating total cumulative anthracycline dose.

### To estimate cumulative anthracycline dose in doxorubicin isotoxic equivalents

1.0 x (daunorubicin total dose) + 0.67 x (epirubicin total dose) + 0.5 x (daunorubicin total dose) + 5.0 x (idarubicin total dose) + 10.0 x (mitoxantrone total dose)

### Additional Information

Although mitoxantrone is an anthraquinone, it is related to the anthracycline family and is included in this section because of its cardiotoxic potential.

Childhood cancer survivors exhibit clinical and subclinical toxicity at lower levels than adults. In patients with abnormal LV systolic function, certain conditions (such as isometric exercise and viral infections) have been anecdotally reported to precipitate cardiac decompensation. Prospective studies are needed to better define the contribution of these factors to cardiac disease risk.

Abdominal symptoms (nausea, emesis) may be seen more frequently than exertional dyspnea or chest pain in younger patients.
Exertional intolerance is an uncommon presentation of left ventricular dysfunction in patients <25 years old. Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.

- **Patient factors:** Age <5 years at time of treatment, genetic variants associated with increased anthracycline-induced cardiotoxicity
- **Cancer/Treatment factors:** Combined with radiation involving the heart, higher cumulative anthracycline doses (≥550 mg/m² in patients ≥18 years at time of treatment, ≥250 mg/m² in patients <18 years at time of treatment), chest radiation >15 Gy chest radiation combined with ≥100 mg/m² anthracycline, longer time since treatment
- **Pre-morbid/Co-morbid medical conditions:** Obesity, congenital heart disease, hypertension, diabetes mellitus, dyslipidemia. For female patients, pregnancy if systolic function is abnormal pre-pregnancy
- **Health behaviors:** Smoking, drug use (e.g., cocaine, diet pills, ephedra, mahuang)

**References**


CHEMOTHERAPY

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<tbody>
<tr>
<td>35</td>
<td>Anti-Tumor Antibiotics Bleomycin</td>
<td>Pulmonary toxicity Pulmonary fibrosis Interstitial pneumonitis Acute respiratory distress syndrome (very rare)</td>
<td>HISTORY History Cough Wheezing Shortness of breath Dyspnea on exertion Yearly PHYSICAL Pulmonary exam Yearly SCREENING PFTs (including DLCO and spirometry Baseline at entry into long-term follow-up, repeat as clinically indicated in patients with abnormal results or progressive pulmonary dysfunction</td>
<td>HEALTH LINKS Pulmonary Health Bleomycin Alert RESOURCES <a href="http://www.smokefree.gov">www.smokefree.gov</a> COUNSELING Notify healthcare providers of history of bleomycin therapy and risk of worsening fibrosis with high oxygen exposure such as during general anesthesia. Administration of high concentrations of oxygen may result in chronic progressive pulmonary fibrosis. Tobacco avoidance/smoking cessation/environmental tobacco smoke. Influenza and Pneumococcal vaccinations. POTENTIAL CONSIDERATIONS FOR FURTHER TESTING AND INTERVENTION Repeat PFTs prior to general anesthesia. Pulmonary consultation for patients with symptomatic pulmonary dysfunction. Pulmonary consultation for survivors who desire to SCUBA dive (due to potential undiagnosed pulmonary toxicities, and limited data to guide safe diving recommendations for individuals treated with pulmonary toxic therapy). SYSTEM = Pulmonary SCORE ARDS = 2B All Else = 1</td>
</tr>
</tbody>
</table>

Additional Information

Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.

- Patient factors: Pulmonary toxicity
- Cancer/Treatment factors: Higher cumulative dose, especially bleomycin dose >400 U/m² (pulmonary function deficits observed at doses as low as 60-100 U/m² in children on formal pulmonary function testing), combination with busulfan, carmustine (BCNU), or lomustine (CCNU), combination with chest radiation, or TBI
- Pre-morbid/Co-morbid medical conditions: Renal dysfunction, high dose oxygen support such as during general anesthesia
- Health behaviors: Smoking, inhaled illicit drug use

References

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</thead>
<tbody>
<tr>
<td>36</td>
<td>Anti-Tumor Antibiotics</td>
<td>No known late effects</td>
<td></td>
<td>SYSTEM = No Known Late Effects SCN = 1</td>
</tr>
</tbody>
</table>

**Additional Information**
Dactinomycin has been associated with acute SOS, from which the majority of patients recover without sequelae.

**References**
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<tr>
<td>37</td>
<td>Corticosteroids</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Dexamethasone</td>
<td>Reduced bone mineral density (BMD)</td>
<td>SCREENING</td>
<td>HEALTH LINKS</td>
</tr>
<tr>
<td></td>
<td>Prednisone</td>
<td>Defined as Z-score &gt;2 SD below the mean in male survivors &lt;50 years old and premenopausal women or T-score &gt;1 SD below the mean in male survivors &gt;50 years old and postmenopausal women</td>
<td>Bone density evaluation (DXA)</td>
<td>Bone Health</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Adjust for height-age Z-score in survivors &lt;age 20 years*</td>
<td>RESOURCES</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Baseline BMD at entry into long-term follow-up (2 to 5 years after completion of therapy) with the following recommended actions:</td>
<td>National Osteoporosis Foundation: <a href="http://www.nof.org">www.nof.org</a></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• If Z-score &gt;1 SD above the mean (normal), repeat at 25 years of age when peak bone mass should be achieved</td>
<td>POTENTIAL CONSIDERATIONS FOR FURTHER TESTING AND INTERVENTION</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Between these two measurements and thereafter, screen as clinically indicated based on BMD and ongoing risk assessment</td>
<td>Ensure the AAP recommended minimum daily intake of vitamin D (400 IU/day) for infants &lt;12 months, 600 IU/day for those age 12 months through age 70 years, 800 IU/day for those &gt;70 years</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• If Z-score &gt;2 SD below the mean, referral to (or consultation of) a bone health specialist</td>
<td>Ensure adequate dietary calcium (see table in the “Bone Health” Health Link for age-appropriate recommendations). Supplements may be necessary if there are dietary restrictions.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• If Z-score &gt;1 and &lt;2 SD below the mean, evaluation for endocrine defects (e.g., hypogonadism or GH deficiency) and consultation with a bone health specialist for further evaluation and interpretation of findings as clinically indicated. Repeat DXA after 2 years and thereafter as clinically indicated based on BMD change (i.e., BMD decline is greater than the DXA least significant change) and ongoing risk assessment</td>
<td>Use caution regarding calcium supplementation in patients with history of renal lithiasis. Advocate for regular weight-bearing exercises such as running and jumping.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>*Pediatric Z-score calculator adjusted for height age: <a href="https://zscore.research.chop.edu/calcpedbonedens.php">https://zscore.research.chop.edu/calcpedbonedens.php</a></td>
<td>Treat exacerbating or predisposing conditions (e.g., hormonal replacement therapy for hypogonadism, GH deficiency, correction of chronic metabolic acidosis that could accelerate bone loss).</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Endocrine consultation for patients with osteoporosis or history of multiple fractures for pharmacologic interventions (e.g., bisphosphonates, calcitonin, selective estrogen receptor modulators).</td>
</tr>
</tbody>
</table>

**SYSTEM = Musculoskeletal**

**SCORE = 2B**

### Additional Information

The World Health Organization definition of osteoporosis in adults is based on comparison of a measured BMD of young adults at peak bone age and defined as a T-score. A T-score is the number of standard deviations the BMD measurement is above or below the mean. Current definitions of osteopenia (T-scores between 1.0 and 2.5 SD below the mean) and osteoporosis (T-scores >2.5 SD below the mean) were developed primarily in the context of postmenopausal women. In this population, T-scores have a well-validated correlation with fracture risk that increases with age. The fracture risk associated with T-scores in younger populations, including cancer survivors with treatment-related hypogonadism, has not been established. T-scores are not appropriate to assess skeletal health in pediatric patients who have not achieved peak adult bone mass. Pediatric BMD reference data sets calculate Z-scores based on age and gender. A Z-score is the number of standard deviations the measurement is above or below the age-matched mean BMD. The fracture risk in pediatric patients with low BMD for chronologic age based on Z-scores has not been established. There are no defined standards for referral or treatment of low BMD in children.
Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.

- Patient factors: Caucasian race, lower weight/BMI. Both genders are at risk.
- Cancer/Treatment factors: Corticosteroids (especially prolonged therapy, e.g., for cGVHD), higher cumulative corticosteroid dose (especially ≥9 gm/m²), cranial/craniospinal radiation, HCT, or TBI.
- Pre-morbid/Co-morbid medical conditions: GH deficiency, hypogonadism/delayed puberty, hyperthyroidism
- Health behaviors: Intake of calcium and vitamin D, intake of alcohol and carbonated beverages, weight bearing exercise, smoking

References

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<tbody>
<tr>
<td>38</td>
<td>Corticosteroids</td>
<td>Osteonecrosis (avascular necrosis)</td>
<td>HISTORY&lt;br&gt;&lt;br&gt;Joint pain&lt;br&gt;Swelling&lt;br&gt;Immobility&lt;br&gt;Limited range of motion&lt;br&gt;Yearly&lt;br&gt;&lt;br&gt;PHYSICAL&lt;br&gt;Musculoskeletal exam&lt;br&gt;Yearly</td>
<td>HEALTH LINKS&lt;br&gt;Osteonecrosis&lt;br&gt;POTENTIAL CONSIDERATIONS FOR FURTHER TESTING AND INTERVENTION&lt;br&gt;MRI as clinically indicated. Orthopedic consultation in patients with positive imaging and/or symptoms of osteonecrosis. Physical therapy evaluation (for non-pharmacologic pain management, range of motion, strengthening, stretching, functional mobility).&lt;br&gt;&lt;br&gt;SYSTEM = Musculoskeletal&lt;br&gt;SCORE = 1</td>
</tr>
</tbody>
</table>

### Additional Information

Osteonecrosis typically occurs during the acute treatment phase; may progress over time or resolve. Multifocal osteonecrosis is significantly more common (3:1) than unifocal. Symptomatic lesions confer the greatest risk for collapse. Dexamethasone is associated with a greater risk than prednisone, especially for patients with ALL ≥10 years of age at time of exposure. Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.

- Patient factors: Being pubertal or post-pubertal at time of treatment, genetic polymorphisms
- Cancer/Treatment factors: High dose radiation to any bone, orthovoltage radiation (commonly used before 1970) due to delivery of greater dose to skin and bones, TBI, prolonged immunosuppression (e.g., for cGVHD)
- Pre-morbid/Co-morbid medical conditions: Sickle cell disease, cGVHD

### References

### CHEMOTHERAPY

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<tbody>
<tr>
<td>39</td>
<td>Corticosteroids</td>
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<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Dexamethasone</td>
<td>Cataracts</td>
<td></td>
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<tr>
<td></td>
<td>Prednisone</td>
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</tbody>
</table>

#### HISTORY
- Visual changes (decreased acuity, halos, diplopia)
- Yearly

#### PHYSICAL
- Visual acuity
- Funduscopic exam
- Yearly

#### SCREENING
- Evaluation by ophthalmologist or optometrist
- Yearly

### HEALTH LINKS

#### Cataracts

### POTENTIAL CONSIDERATIONS FOR FURTHER TESTING AND INTERVENTION
- Ophthalmology consultation as clinically indicated.
- Refer patients with visual deficits to school liaison in community or cancer center (psychologist, social worker, school counselor) to facilitate acquisition of educational resources.

### SYSTEM = Ocular
### SCORE = 1

### Additional Information
Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.
- Cancer/Treatment factors: Combination with busulfan, combination with TBI, cranial, orbital or eye radiation, longer interval since treatment

### References
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<tbody>
<tr>
<td>40</td>
<td>Enzymes Asparaginase</td>
<td>No known late effects</td>
<td></td>
<td>SYSTEM = No Known Late Effects SCORE = 1</td>
</tr>
</tbody>
</table>

**Additional Information**
Acute toxicities predominate, from which the majority of patients recover without sequelae.

**References**
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</thead>
</table>
| 41    | **Plant Alkaloids**  | **Peripheral sensory or motor neuropathy** | HISTORY  
Areflexia  
Weakness  
Foot drop  
Paresthesias  
Dysesthesias  
PHYSICAL  
Neurologic exam  
Yearly, until 2 to 3 years after therapy, monitor yearly if symptoms persist | HEALTH LINKS  
Peripheral Neuropathy  
POTENTIAL CONSIDERATIONS FOR FURTHER TESTING AND INTERVENTION  
Physical therapy referral for patients with symptomatic neuropathy.  
Physical and occupational therapy assessment of hand function.  
Treat with effective agent for neuropathic pain (e.g., gabapentin or amitriptyline).  
SYSTEM = PNS  
SCORE = 2A |

**Additional Information**

Acute toxicities most commonly occur and usually improve or resolve prior to patients entering long-term follow-up.

Neuropathy can persist after treatment and is typically not late in onset.

Studies of adults treated during childhood support higher prevalence of deficits than previously appreciated.

Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.

- Cancer/Treatment factors: Combination with platinum chemotherapy, gemcitabine, taxanes
- Pre-morbid/Co-morbid medical conditions: Anorexia, severe weight loss, Charcot-Marie-Tooth disease

**References**


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</thead>
<tbody>
<tr>
<td>42</td>
<td>Plant Alkaloids</td>
<td>Vinblastine Vincristine</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Vasospastic attacks</td>
<td>HISTORY</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>(Raynaud’s phenomenon)</td>
<td>Vasospasms of hands, feet, nose, lips, cheeks, or earlobes related to stress or cold temperatures</td>
<td>HEALTH LINKS</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Yearly</td>
<td>Raynaud’s Phenomenon</td>
</tr>
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<td></td>
<td></td>
<td></td>
<td>PHYSICAL</td>
<td>COUNSELING</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Physical exam of affected area</td>
<td>Wear appropriate protective clothing in cold environments.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Symptoms may be exacerbated by medications/chemicals that cause vasoconstriction (e.g., pseudoephedrine, stimulants), illicit drugs (e.g., cocaine), and nicotine.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>POTENTIAL CONSIDERATIONS FOR FURTHER TESTING AND INTERVENTION</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Vasodilating medications (calcium-channel blockers, alpha blockers) for patients with frequent, severe vasospastic attacks unresponsive to behavioral management.</td>
</tr>
</tbody>
</table>

**SYSTEM = PNS**

**SCORE = 2A**

**Additional Information**

Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.
- Pre-morbid/Co-morbid medical conditions: Smoking, illicit drug use, use of vasoconstricting medications/substances, exposure to repetitive vibration

**References**

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<td>43</td>
<td>Epipodophyllotoxins</td>
<td>Acute myeloid leukemia (AML)</td>
<td>HISTORY</td>
<td>HEALTH LINKS</td>
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<tr>
<td></td>
<td>Etoposide (VP16)</td>
<td></td>
<td>Fatigue</td>
<td>Reducing the Risk of Subsequent Cancers</td>
</tr>
<tr>
<td></td>
<td>Teniposide (VM26)</td>
<td></td>
<td>Bleeding</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Easy bruising</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Yearly, up to 10 years after exposure to agent</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Dermatologic exam (pallor, petechiae, purpura)</td>
<td>PHYSICAL</td>
<td>COUNSELING</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Yearly, up to 10 years after exposure to agent</td>
<td>Promptly seek medical attention for fatigue, pallor, petechiae or bone pain.</td>
</tr>
<tr>
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</tbody>
</table>

**Additional Information**

Epipodophyllotoxin administration schedules have been modified since approximately 1990 to reduce the risk of AML. There is negligible benefit to obtaining a screening CBC in the absence of clinical signs and symptoms for AML.

Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.
- Cancer/Treatment factors: Weekly or twice weekly administration, <5 years since exposure to agent, autologous HCT
- Pre-morbid/Co-morbid medical conditions: Evidence is conflicting that splenectomy modifies risk for AML

**References**

Determining Applicability of Radiation Sections for Specific Patients Based on Exposure

The radiation sections of the COG Long-Term Follow-Up Guidelines (Sections 44-98) are organized by anatomic region from the head downward. In this current version of the COG LTFU Guidelines, the radiation fields are still simplified and categorized by anatomic region, as follows:

- Head/Brain
- Neck
- Chest
- Axilla
- Abdomen
- Pelvis
- Testicular
- Spine (cervical, thoracic, lumbar, sacral, whole)
- Skin/soft tissues/bones/extremities
- TBI

The Guideline sections applicable to each radiation field are listed on the accompanying diagram.

Traditional and combined radiation fields (e.g., mantle, mediastinal, para-aortic, etc.) are defined in Appendix I and mapped to the anatomic fields specified above, as follows:

- Radiation Fields Defined, Table: Appendix I, pages 6-7
- Radiation Fields Defined, Diagram: Appendix I, page 8

Five sections of these Guidelines (Sections 60, 63, 66, 77, 78) include minimum dose specifications. These five Guideline sections are applicable only to patients who received radiation to any of the relevant fields at a total dose higher than the specified minimum dose. Instructions regarding calculating combined radiation doses are available as follows:

- Radiation Dose Calculations: Appendix I, page 9

Further details regarding radiation impact by organ systems, with associated potential late effects, are also available in Appendix I, as follows:

- Guideline Radiation Sections by Potential Impact, Table: Appendix I, pages 11-12
- Guideline Radiation Sections by Potential Impact, Diagram: Appendix I, page 13
- Total Body Irradiation (TBI) Related Potential Late Effects: Appendix I, page 14

Use the “Patient-Specific Guideline Identification Tool” in Appendix I (pages 32-37) to determine specific screening guidelines by section number for individual patients.
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</thead>
<tbody>
<tr>
<td>44</td>
<td>Any Radiation (Including TBI)</td>
<td>Subsequent benign or malignant neoplasm occurring in or near radiation field</td>
<td>HISTORY</td>
<td>HEALTH LINKS</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Such as dysplastic nevi, skin cancer (basal cell carcinoma, squamous cell carcinoma), bone malignancies, oral cancer</td>
<td>Skin lesions</td>
<td>Reducing the Risk of Subsequent Cancers</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Changing moles (asymmetry, bleeding, increasing size, indistinct borders)</td>
<td>Skin Health</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Bone pain (especially in irradiated field)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Persistent thickening or lump of soft tissue or bone</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>每年</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>PHYSICAL</td>
<td>COUNSELING</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Skin self exam</td>
<td>Promptly seek medical attention for symptoms (e.g., bone pain, bone mass, persistent fevers).</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Monthly</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Inspection and palpation of skin and soft tissues in irradiated field(s)</td>
<td>POTENTIAL CONSIDERATIONS FOR FURTHER TESTING AND INTERVENTION</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Dermatologic exam of irradiated fields</td>
<td>See relevant guideline sections to determine screening for specific radiation fields.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Palpation of bones in irradiated field</td>
<td>Dermatology consultation for evaluation and monitoring of atypical nevi.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>每年</td>
<td>Diagnostic imaging in patients as clinically indicated.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Surgical and/or oncology consultation as clinically indicated.</td>
</tr>
</tbody>
</table>

**Additional Information**

Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.

- **Patient factors:** Younger age at treatment, adolescent at treatment (bone malignancies)
- **Cancer/Treatment factors:** Higher radiation dose, especially ≥30 Gy (bone malignancies), large radiation treatment volumes, alkylating agent exposure, orthovoltage radiation (commonly used before 1970) due to delivery of greater dose to skin and bones
- **Pre-morbid/Co-morbid medical conditions:** Predisposing mutation (e.g., \( p53 \), \( NF1 \)), bilateral or familial retinoblastoma (implying \( RB1 \) likely pathogenic variant), Gorlin syndrome (nevoid basal cell carcinoma syndrome)
- **Health behaviors:** Sun exposure, tanning booths

**References**


### RADIATION

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</tr>
</thead>
</table>
| 45    | Any Radiation (Including TBI) | Dermatologic toxicity other than neoplasms  
Permanent alopecia  
Altered skin pigmentation  
Telangiectasias  
Fibrosis | PHYSICAL  
Dermatologic exam of irradiated fields  
Yearly | HEALTH LINKS  
Skin Health  
SYSTEM = Dermatologic  
SCORE = 1 |

#### Additional Information

Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.

- **Patient factors:** Younger age at treatment
- **Cancer/Treatment factors:** Total radiation dose ≥40 Gy, especially ≥50 Gy, large dose fractions (e.g., ≥2 Gy per fraction), orthovoltage radiation (commonly used before 1970) due to delivery of greater dose to skin and bones

#### References


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<tr>
<td>46</td>
<td>Head/Brain TBI</td>
<td>Brain tumor (benign or malignant)</td>
<td><strong>HISTORY</strong>&lt;br&gt;Headaches&lt;br&gt;Vomiting&lt;br&gt;Cognitive, motor or sensory deficits&lt;br&gt;Seizures and other neurologic symptoms&lt;br&gt;Yearly&lt;br&gt;<strong>PHYSICAL</strong>&lt;br&gt;Neurologic exam&lt;br&gt;Yearly</td>
<td><strong>POTENTIAL CONSIDERATIONS FOR FURTHER TESTING AND INTERVENTION</strong>&lt;br&gt;Brain MRI as clinically indicated for symptomatic patients.&lt;br&gt;Brain MRI every other year for patients with neurofibromatosis beginning 2 years after radiation therapy.&lt;br&gt;Neurosurgical consultation for tissue diagnosis and/or resection.&lt;br&gt;Neuro-oncology consultation for medical management.</td>
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<tr>
<td>47</td>
<td>Head/Brain TBI</td>
<td>Neurocognitive deficits</td>
<td>HISTORY</td>
<td>HEALTH LINKS</td>
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<td></td>
<td></td>
<td>Functional deficits in:</td>
<td>Educational and/or vocational progress</td>
<td>School After Treatment</td>
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<td></td>
<td></td>
<td>• Executive function (planning and organization)</td>
<td>Yearly</td>
<td>POTENTIAL CONSIDERATIONS FOR FURTHER TESTING AND INTERVENTION</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Sustained attention</td>
<td></td>
<td>Referral to school liaison in community or cancer center (psychologist, social worker, school counselor) to facilitate acquisition of educational resources and/ or social skills training.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Memory (particularly visual, sequencing, temporal memory)</td>
<td></td>
<td>Psychotropic medication (e.g., stimulants) or evidence-based rehabilitation training. Caution—lower starting dose and assessment of increased sensitivity when initiating therapy is recommended.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Processing speed</td>
<td></td>
<td>Referral to community services for vocational rehabilitation or for services for developmentally disabled.</td>
</tr>
<tr>
<td></td>
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<td>• Visual–motor integration</td>
<td>SCREENING</td>
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<tr>
<td></td>
<td></td>
<td>• Fine motor dexterity</td>
<td></td>
<td>Referral for formal neuropsychological evaluation</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Language</td>
<td>Baseline at entry into long-term follow-up, then periodically as clinically indicated for patients with evidence of impaired educational or vocational progress</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>• Academic fluency</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>Learning deficits in math and reading (particularly reading comprehension)</td>
<td></td>
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<td></td>
<td></td>
<td>Diminished IQ</td>
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<td></td>
<td>Behavioral change</td>
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</table>

### Additional Information

Formal neuropsychological evaluation includes tests of processing speed, computer-based attention, visual motor integration, memory, comprehension of verbal instructions, verbal fluency, executive function and planning. Neurocognitive deficits in survivors of leukemia and lymphoma are more frequently related to information processing (e.g., slow processing speed, attention problems). Neurocognitive deficits in brain tumor survivors treated with higher doses of cranial radiation are more global (significant decline in IQ). Extent of deficit depends on age at treatment, intensity of treatment, and time since treatment. New or progressive deficits may emerge over time. Note: academic fluency is defined as the ability to correctly complete multiple simple academic problems (e.g., reading words, simple math equations) within a limited amount of time.

Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.

- Patient factors: Younger age at treatment, especially age <3 years, female sex, family history of learning or attention problems
- Cancer/Treatment factors: Primary CNS tumor, CNS leukemia/lymphoma, relapsed leukemia/lymphoma treated with CNS-directed therapy, head/neck tumors with brain in radiation field, temporal lobe field including hippocampus (without hippocampal sparing), higher radiation dose, larger radiation field, greater cortical volumes, cranial radiation in combination with TBI, lack of volume-sparing radiation techniques (e.g., proton beam therapy), combination with corticosteroids, methotrexate (IT, IO, high dose IV), cytarabine (high dose IV), longer elapsed time since therapy
- Pre-morbid/Co-morbid medical conditions: Pre-morbid learning or attention problems, sleep disturbance, seizures, hydrocephalus, CRT-induced ototoxicity, chronic conditions (e.g., endocrine, cardiopulmonary, frailty)

### References

Brinkman TM, Krasin MJ, Liu W, et al: Long-term neurocognitive functioning and social attainment in adult survivors of pediatric CNS tumors treated with CNS-directed therapy, head/neck tumors with brain in radiation field, temporal lobe field including hippocampus (without hippocampal sparing), higher radiation dose, larger radiation field, greater cortical volumes, cranial radiation in combination with TBI, lack of volume-sparing radiation techniques (e.g., proton beam therapy), combination with corticosteroids, methotrexate (IT, IO, high dose IV), cytarabine (high dose IV), longer elapsed time since therapy


**Sec #** | **Therapeutic Exposure** | **Potential Late Effects** | **Periodic Evaluation** | **Health Counseling/ Further Considerations**
---|---|---|---|---
48 | Head/Brain TBI | Clinical leukoencephalopathy  
Spasticity  
Ataxia  
Dysarthria  
Dysphagia  
Hemiparesis  
Seizures | HISTORY  
Cognitive, motor and/or sensory deficits  
Seizures  
Other neurologic symptoms  
Yearly  
PHYSICAL: Neurologic exam  
Yearly | POTENTIAL CONSIDERATIONS FOR FURTHER TESTING AND INTERVENTION  
Brain CT or Brain MRI with MRA as clinically indicated with preferred study  
Based on intracranial lesion to be evaluated:  
- Calcifications: CT  
- White matter: MRI with DTI  
- Microvascular injury: Gadolinium-enhanced MRI with DWI  
Neurology consult and follow-up as clinically indicated.

**SYSTEM = CNS**

**SCORE = 1**

---

**Additional Information**
Clinical leukoencephalopathy may present with or without imaging abnormalities (e.g., leukoencephalopathy, cerebral lacunes, cerebral atrophy, dystrophic calcifications, mineralizing microangiopathy). Transient white matter anomalies may follow radiotherapy and high dose chemotherapy for medulloblastoma/PNET, may mimic tumor recurrence, and signify risk of persistent neurologic sequelae. Neuroimaging changes do not always correlate with degree of cognitive dysfunction. Prospective studies are needed to define the dose/effect relationship of neurotoxic agents. New deficits may emerge over time.

Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.

- Patient factors: Younger age at treatment
- Cancer/Treatment factors: CNS leukemia/lymphoma, relapsed leukemia/lymphoma treated with CNS-directed therapy, longer elapsed time since therapy, higher radiation dose, especially ≥24 Gy or fraction dose ≥3 Gy, larger radiation field, greater cortical volumes, combination with dexamethasone, methotrexate (IT, IO, high dose IV), cytarabine (high dose IV)

---

**References**
## RADIATION

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<td>Cerebrovascular</td>
<td>HISTORY</td>
<td>COUNSELING</td>
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<tr>
<td></td>
<td></td>
<td>complications</td>
<td>Hemiparesis</td>
<td>Importance of controlling health conditions known to increase cardiovascular and stroke risk (e.g., hypertension, diabetes, dyslipidemia).</td>
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<tr>
<td></td>
<td></td>
<td>Stroke</td>
<td>Hemiplegia</td>
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<td>Moyamoya</td>
<td>Weakness</td>
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<td>Occlusive cerebral</td>
<td>Aphasia</td>
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<td></td>
<td>vasculopathy</td>
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<td>Cavernomas</td>
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<td>Neurologic exam</td>
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<td>Yearly</td>
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</table>

### SYSTEM = CNS

**SCORE = 1**

### Additional Information

Moyamoya syndrome is the complete occlusion of ≥1 of the three major cerebral vessels with the development of small, immature collateral vessels, and reflects an attempt to revascularize the ischemic portion of the brain.

Cavernomas are a common late effect of cranial radiation, but the majority of patients with cavernomas are asymptomatic.

Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.

- Cancer/Treatment factors: Parasellar tumor, radiation dose ≥18 Gy, especially ≥50 Gy, supra-sellar radiation, circle of Willis in radiation field

- Pre-morbid/Co-morbid medical conditions: Down syndrome, sickle cell disease, neurofibromatosis

### References

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<td>50</td>
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<td>Craniofacial abnormalities</td>
<td>HISTORY</td>
<td>RESOURCES</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Psychosocial assessment with attention to:</td>
<td>FACES—The National Craniofacial Association: <a href="http://www.faces-cranio.org">www.faces-cranio.org</a></td>
</tr>
<tr>
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<td></td>
<td></td>
<td>• Educational and/or vocational progress</td>
<td>POTENTIAL CONSIDERATIONS FOR FURTHER TESTING AND INTERVENTION</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Depression</td>
<td>Reconstructive craniofacial surgical consultation.</td>
</tr>
<tr>
<td></td>
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<td></td>
<td>• Anxiety</td>
<td>Consultation with psychologist in patients with adjustment disorders related to facial asymmetry/deformity.</td>
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<td></td>
<td>• Post-traumatic stress</td>
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<td></td>
<td>• Social withdrawal</td>
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<td>Yearly</td>
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<td>PHYSICAL</td>
<td>SYSTEM = Musculoskeletal</td>
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<td>Craniofacial abnormalities</td>
<td>SCORE = 1</td>
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<td></td>
<td>Yearly</td>
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</tbody>
</table>

**Additional Information**

Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.

- Patient factors: Younger age at treatment, especially age <5 years
- Cancer/Treatment factors: Higher radiation dose, especially dose ≥30 Gy

**References**

Frascino AV, Fava M, Collassanti MDS, Odone-Filho V. Impact of Pediatric Hematopoietic Stem-Cell Transplantation on Craniofacial Growth. Clinics 75, 2020


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<td>Chronic sinusitis</td>
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<td>POTENTIAL CONSIDERATIONS FOR FURTHER TESTING AND INTERVENTION</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Rhinorrhea, postnasal discharge</td>
<td>CT scan of sinuses as clinically indicated.</td>
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<td></td>
<td>History of URIs</td>
<td>Otolaryngology consultation as clinically indicated.</td>
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<td></td>
<td>Yearly</td>
<td>System = Immune</td>
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<td>PHYSICAL</td>
<td>Score = 1</td>
</tr>
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<td></td>
<td>Nasal and sinus exam</td>
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<td></td>
<td></td>
<td>Yearly</td>
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</tbody>
</table>

**Additional Information**

Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.

- Cancer/Treatment factors: Radiation dose to sinuses ≥30 Gy, radiomimetic chemotherapy (e.g., doxorubicin, dactinomycin)
- Pre-morbid/Co-morbid medical conditions: Atopic history, hypogammaglobulinemia, underlying immunodeficiency

**References**

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<td>52</td>
<td>Head/Brain</td>
<td>Overweight Obesity</td>
<td>PHYSICAL</td>
<td>HEALTH LINKS</td>
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<td></td>
<td></td>
<td>Nutrition and Physical Activity</td>
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<td>Cardiovascular Risk Factors</td>
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<td></td>
<td></td>
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<td></td>
<td>Obesity-related health risks.</td>
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<td>POTENTIAL CONSIDERATIONS FOR FURTHER TESTING AND INTERVENTION</td>
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<td></td>
<td>Evaluate for other co-morbid conditions, including dyslipidemia, hypertension, and impaired glucose metabolism. Refer to dietitian for nutrition education and weight management.</td>
</tr>
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<td></td>
<td>SYSTEM = Endocrine/Metabolic \nSCORE = 1</td>
</tr>
</tbody>
</table>

### Additional Information

**Definition of Overweight:** Age 2-20 years BMI for age ≥85th to <95th percentile. Age ≥21 years BMI ≥25-29.9.

**Definition of Obesity:** Age 2-20 years BMI for age ≥95th percentile. Age ≥21 years BMI ≥30.


Overweight/Obesity may occur in a constellation of conditions known as metabolic syndrome.

Definitions of metabolic syndrome generally include a combination of central (abdominal) obesity with at least 2 or more of the following: elevated blood pressure, atherogenic dyslipidemia (elevated triglycerides, reduced HDL cholesterol), and abnormal glucose metabolism.

Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.

- Patient factors: Younger age at treatment, especially age <4 years, female sex
- Cancer/Treatment factors: Higher cranial radiation dose (especially ≥18 Gy), surgery in supra-sellar region, corticosteroids (especially prolonged therapy, e.g., for cGVHD)
- Pre-morbid/Co-morbid medical conditions: GH deficiency, hypothyroidism, hypogonadism, inability to exercise

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<td>Growth hormone deficiency</td>
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<tr>
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<td>Assessment of nutritional status</td>
<td>Growth Hormone Deficiency</td>
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<td></td>
<td></td>
<td></td>
<td>Every 6 months until growth is completed, then yearly</td>
<td>Hypopituitarism</td>
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<td>RESOURCES</td>
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<td></td>
<td>Tanner staging</td>
<td>Magic Foundation for Children's Growth: <a href="http://www.magicfoundation.org">www.magicfoundation.org</a></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Every 6 months until sexually mature</td>
<td>POTENTIAL CONSIDERATIONS FOR FURTHER TESTING AND INTERVENTION</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Height</td>
<td>Growth velocity can be assessed using dedicated charts or electronic medical record tools if available.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Weight</td>
<td>Consider bone density testing in patients who are GH deficient.</td>
</tr>
<tr>
<td></td>
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<td></td>
<td>BMI</td>
<td>Evaluate thyroid function in any poorly growing child.</td>
</tr>
<tr>
<td></td>
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<td></td>
<td>Every 6 months until growth is completed, then yearly</td>
<td>Endocrine consultation for:</td>
</tr>
</tbody>
</table>

- Dose ≥30 Gy
- Poor growth for age or stage of puberty as evidenced by persistent decline in growth velocity and change in percentile rankings on growth chart, weight <3rd percentile on growth chart
- Discuss risks/benefits of adult GH replacement

SYSTEM = Endocrine/Metabolic
SCORE = 1

Additional Information

Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.
- Patient factors: Younger age at treatment
- Cancer/Treatment factors: Surgery in supra-sellar region, higher radiation dose (especially ≥18 Gy), pretransplant radiation (especially CRT), ≥12 Gy fractionated, TBI given in single fraction (especially ≥ 10Gy)

References

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<td>Precocious puberty</td>
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<td>HEALTH LINKS</td>
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<td><strong>Height</strong></td>
<td>Precocious Puberty</td>
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<td></td>
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<td><strong>Testicular volume by Prader orchidometer</strong></td>
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<td>Yearly until sexually mature</td>
<td>Magic Foundation for Children's Growth: <a href="http://www.magicfoundation.org">www.magicfoundation.org</a></td>
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<td>FSH, LH, testosterone, as clinically indicated in patients with signs of accelerated pubertal progression and growth.</td>
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<td>X-ray for bone age in rapidly growing children.</td>
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<td>Growth velocity can be assessed using dedicated charts or electronic medical record tools if available.</td>
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<td>Endocrine consultation for suspected precocious puberty (males &lt;9 years).</td>
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</tbody>
</table>

**SYSTEM = Endocrine/Metabolic**  
**SCORE = 1**

### Additional Information

Testicular volume is not a reliable indicator of pubertal onset/stage in boys treated with alkylating agents and/or direct testicular radiotherapy. Affected children may present with accelerated linear growth but this could mask co-existing GH deficiency.

Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.

- Patient factors: Younger age at treatment
- Cancer/Treatment factors: Tumor near hypothalamus and/or optic pathways, radiation doses ≥18 Gy
- Pre-morbid/Co-morbid medical conditions: History of hydrocephalus

### References


Ogilvy-Stuart AL, Clayton PE, Shalet SM: Cranial irradiation and early puberty. J Clin Endocrinol Metab 78:1282-6, 1994


### RADIATION

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</table>

**Additional Information**

Affected children may present with accelerated linear growth but this could mask co-existing GH deficiency.

Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.

- Patient factors: Younger age at treatment
- Cancer/Treatment factors: Tumor near hypothalamus and/or optic pathways, radiation doses ≥18 Gy
- Pre-morbid/Co-morbid medical conditions: History of hydrocephalus

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<td>Galactorrhea</td>
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</table>

**HEALTH LINKS**
- Hyperprolactinemia

**RESOURCES**
- Magic Foundation for Children's Growth: [www.magicfoundation.org](http://www.magicfoundation.org)

**POTENTIAL CONSIDERATIONS FOR FURTHER TESTING AND INTERVENTION**
- Prolactin level in patients with galactorrhea or decreased libido, or in females with amenorrhea.
- CT evaluation of sella turcica for pituitary adenoma in patients with hyperprolactinemia.
- Endocrine consultation for patients with hyperprolactinemia or galactorrhea.

**SYSTEM** = Endocrine/Metabolic
**SCORE** = 1

### Additional Information
Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.

- **Cancer/Treatment factors:** Higher radiation dose (≥40 Gy, especially ≥50 Gy), surgery or tumor in hypothalamic area

### References
## RADIATION

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<td>Head/Brain</td>
<td>Central hypothyroidism</td>
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<td>Cold intolerance</td>
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<td>Constipation</td>
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<td>Dry skin</td>
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<td>Brittle hair</td>
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<td>Depressed mood</td>
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<td>Yearly, consider more frequent screening during periods of rapid growth</td>
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<td>Skin</td>
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<td>Thyroid exam</td>
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<td>Yearly, consider more frequent screening during periods of rapid growth</td>
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<td>Free T4</td>
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<td>Yearly, consider more frequent screening during periods of rapid growth</td>
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</table>

### Additional Information

Central hypothyroidism includes thyroid-releasing and TSH deficiency.
Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.
- Cancer/Treatment factors: Higher radiation dose, especially ≥30 Gy, may occur at lower doses with longer follow-up, surgery or tumor in supra-sellar area.

### References


RADIATION

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<tr>
<td>58 (male)</td>
<td>Head/Brain TBI</td>
<td>Gonadotropin deficiency LH and FSH deficiency</td>
<td>HISTORY</td>
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<td>Onset and tempo of puberty</td>
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<td>Sexual function (erections, nocturnal emissions, libido)</td>
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<td>Medication use Yearly</td>
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<td>Tanner staging until sexually mature</td>
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<td>Testicular volume by Prader orchidometer Yearly</td>
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<td>Monitor growth until mature Yearly</td>
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<td>RESOURCES</td>
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<td>American Society for Reproductive Medicine: <a href="http://www.asrm.org">www.asrm.org</a></td>
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<td>Alliance for Fertility Preservation: <a href="http://www.allianceforfertilitypreservation.org">www.allianceforfertilitypreservation.org</a></td>
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<td>COUNSELING</td>
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<td>Need for contraception.</td>
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<td>Spermatogenesis can be induced with gonadotropins in men with hypogonadotropic hypogonadism.</td>
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<td>POTENTIAL CONSIDERATIONS FOR FURTHER TESTING AND INTERVENTION</td>
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<td></td>
<td></td>
<td>FSH, LH, testosterone as clinically indicated in patients with delayed/arrested puberty and/or clinical signs and symptoms of testosterone deficiency.</td>
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<td></td>
<td></td>
<td>If dose ≥30 Gy refer to endocrinologist for ongoing management, given risk of multiple hormone deficiencies. If endocrinology care is not readily available, screen as indicated, and refer to endocrinologist for hormone replacement.</td>
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<td>Hormonal replacement therapy for hypogonadal patients.</td>
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<td>Refer to reproductive endocrinology as clinically indicated for infertility evaluation and consultation regarding assisted reproductive technologies.</td>
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<td>BMD testing in patients who are gonadotropin deficient.</td>
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</table>

Additional Information
Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.

- Cancer/Treatment factors: Higher radiation dose, especially ≥30 Gy, may occur at lower doses with longer follow-up, surgery or tumor in supra-sellar area

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<td>Head/Brain TBI</td>
<td>Gonadotropin deficiency LH and FSH deficiency</td>
<td>HISTORY</td>
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<td>Sexual function (vaginal dryness, libido)</td>
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<td>PHYSICAL</td>
<td>American Society for Reproductive Medicine: <a href="http://www.asrm.org">www.asrm.org</a></td>
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<td></td>
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<td>Tanner staging until sexually mature Yearly</td>
<td>Alliance for Fertility Preservation: <a href="http://www.allianceforfertilitypreservation.org">www.allianceforfertilitypreservation.org</a></td>
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<td>Monitor growth until mature Yearly</td>
<td>COUNSELING</td>
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**POTENTIAL CONSIDERATIONS FOR FURTHER TESTING AND INTERVENTION**

FSH, LH, estradiol as clinically indicated in patients with delayed or arrested puberty, irregular menses, primary or secondary amenorrhea, or clinical signs and symptoms of estrogen deficiency.

If dose ≥30 Gy refer to endocrinologist for ongoing management, given risk of multiple hormone deficiencies. If endocrinology care is not readily available, screen as indicated, and refer to endocrinologist for hormone replacement.

Hormonal replacement therapy for hypogonadal patients.

Refer to reproductive endocrinology as clinically indicated for infertility evaluation and consultation regarding assisted reproductive technologies.

BMD testing in patients who are gonadotropin deficient.

**SYSTEM = Reproductive (Female)**

**SCORE = 1**

### Additional Information

Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.

- Cancer/Treatment factors: Higher radiation dose, especially ≥30 Gy, may occur at lower doses with longer follow-up, surgery or tumor in supra-sellar area

### References


### Radiation

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<td>60</td>
<td>Head/Brain TBI</td>
<td>Central adrenal insufficiency</td>
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</table>

#### History

- If dose ≥30 Gy:
  - Failure to thrive
  - Anorexia
  - Dehydration
  - Hypoglycemia
  - Lethargy
  - Unexplained hypotension

#### Screening

- If dose ≥30 Gy:
  - 8 AM cortisol

Yearly, refer to endocrinology for further testing if level <13 mcg/dL or <365 nmol/L

#### Health Links

- Central Adrenal Insufficiency
- Hypopituitarism

#### Resources

- Magic Foundation for Children’s Growth: [www.magicfoundation.org](http://www.magicfoundation.org)

#### Counseling

- Need for corticosteroid replacement therapy and stress dosing.
- Obtain medical alert bracelet or card.

#### Potential Considerations for Further Testing and Intervention

If dose ≥30 Gy refer to endocrinologist for ongoing management, given risk of multiple hormone deficiencies. If endocrinology care is not readily available, screen as indicated, and refer to endocrinologist for hormone replacement.

**SYSTEM = Endocrine/Metabolic**

**SCORE = 1**

### Additional Information

Cortisol secretion follows a circadian rhythm. Levels should be drawn as close as possible to 8AM and before 9 AM.

Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.

- **Cancer/Treatment factors**: Higher radiation dose, especially ≥30 Gy, may occur at lower doses with longer follow-up, surgery or tumor in supra-sellar area
- **Pre-morbid/Co-morbid medical conditions**: History of another hypothalamic-pituitary endocrinopathy

### References

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<td>61</td>
<td>Head/Brain TBI</td>
<td>Cataracts</td>
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**HISTORY**
- Visual changes (decreased acuity, halos, diplopia)
- Yearly

**PHYSICAL**
- Visual acuity
- Funduscopic exam
- Yearly

**SCREENING**
- Evaluation by ophthalmologist or optometrist
- Yearly

**HEALTH LINKS**
Cataracts

**POTENTIAL CONSIDERATIONS FOR FURTHER TESTING AND INTERVENTION**
Refer patients with visual deficits to school liaison in community or cancer center (psychologist, social worker, school counselor) to facilitate acquisition of educational resources.

**SYSTEM = Ocular**
**SCORE = 1**

### Additional Information

Radiation-related ocular complications other than cataracts are generally associated only with orbital/eye radiation or higher dose CRT. Patients with a history of an ocular tumor (e.g., retinoblastoma) are at higher risk for late-onset ocular complications and should receive ongoing follow-up by an ophthalmologist at least annually, and more frequently if clinically indicated.

Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.

- **Cancer/Treatment factors:** Radiation dose ≥10 Gy, especially ≥15 Gy, radiation fraction dose ≥2 Gy, TBI dose ≥2 Gy in single fraction, TBI dose ≥5 Gy fractionated, especially ≥10 Gy, cranial/orbital/eye radiation combined with TBI, radiation combined with corticosteroids or busulfan, longer interval since treatment

### References

## RADIATION

### Therapeutic Exposure

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<th>Sec #</th>
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### Potential Late Effects

| Ocular toxicity | Orbital hypoplasia | Lacrimal duct atrophy | Xerophthalmia (keratoconjunctivitis sicca) | Keratitis | Telangiectasias | Retinopathy | Optic chiasm neuropathy | Enophthalmos | Chronic painful eye | Maculopathy | Papillopathy | Glaucoma |

### Periodic Evaluation

**HISTORY**
- Visual changes (decreased acuity, halos, diplopia)
- Dry eye
- Persistent eye irritation
- Excessive tearing
- Light sensitivity
- Poor night vision
- Painful eye

**YEARLY**

**PHYSICAL**
- Visual acuity
- Funduscopic exam

**SCREENING**
- Evaluation by ophthalmologist or optometrist

### Health Counseling/Further Considerations

**HEALTH LINKS**
- Eye Health

**RESOURCES**
- FACES—The National Craniofacial Association: www.faces-cranio.org

### POTENTIAL CONSIDERATIONS FOR FURTHER TESTING AND INTERVENTION

Refer patients with visual deficits to school liaison in community or cancer center (psychologist, social worker, school counselor) to facilitate acquisition of educational resources.

### SYSTEM = Ocular

### SCORE = 1

### Additional Information

Radiation-related ocular complications other than cataracts are generally associated only with orbital/eye radiation or higher dose CRT.

Patients with a history of an ocular tumor (e.g., retinoblastoma) are at higher risk for late-onset ocular complications and should receive ongoing ophthalmology follow-up at least annually, and more frequently if clinically indicated.

Reduced visual acuity may be associated with cataracts, retinal damage, and optic nerve damage.

Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.

- Cancer/Treatment factors: Higher radiation dose, especially ≥30 Gy, higher daily fraction dose, especially fraction dose ≥2 Gy, radiomimetic chemotherapy (e.g., doxorubicin, dactinomycin), problems related to tearing
- Pre-morbid/Co-morbid medical conditions: cGVHD (xerophthalmia only)

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<td>Head/Brain TBI</td>
<td>Ototoxicity</td>
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<td>(TBI is included for cumulative dose calculation purposes only; this section is not applicable to patients who received TBI alone.)</td>
<td>Tymanosclerosis, Otosclerosis, Eustachian tube dysfunction, Conductive hearing loss, Sensorineural hearing loss, Tinnitus, Vertigo</td>
<td>If dose ≥30 Gy: Hearing difficulties (with/without background noise)</td>
<td><strong>POTENTIAL IMPACT TO EAR</strong></td>
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<td>Tinnitus</td>
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<td>School After Treatment</td>
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<td>If dose ≥30 Gy:</td>
<td>POTENTIAL CONSIDERATIONS FOR FURTHER TESTING AND INTERVENTION</td>
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<td>Otoscopic exam</td>
<td>Additional testing with high frequency audiometry at &gt;8000 Hz is recommended if equipment is available.</td>
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<td>Yearly</td>
<td>Audiology consultation for any survivor who has symptoms suggestive of hearing loss, tinnitus, or abnormal pure tone audiometry results showing a loss of more than 15 dB absolute threshold level (1000-8000 Hz). Ongoing follow-up with audiology for patients with hearing loss. Otolaryngology consultation in patients with chronic infection, cerumen impaction, or other anatomical problems exacerbating or contributing to hearing loss. Speech and language therapy for patients with hearing loss. Refer patients with auditory deficits to school liaison in community or cancer center (psychologist, social worker, school counselor) to facilitate acquisition of educational resources. Specialized evaluation for specific needs and/or preferential classroom seating, FM amplification system, and other educational assistance as indicated.</td>
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<td>SCREENING</td>
<td><strong>SYSTEM = Auditory</strong></td>
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<td>If dose ≥30 Gy:</td>
<td><strong>SCORE = 1</strong></td>
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<td>Complete audiological evaluation by audiologist</td>
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<td>Yearly, for patients ages ≤5 years</td>
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<td>Pure tone audiometry testing at 1000-8000 Hz</td>
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<td>Every 2 years, for patients ages 6-12, then every 5 years beginning at age 13 years</td>
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</table>

**Additional Information**

A "complete audiological evaluation" includes pure tone air and bone conduction, speech audiometry, and tympanometry for both ears. Frequency-specific auditory brainstem response can be performed if the above is inconclusive.

Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.

- **Patient factors:** Younger age at treatment
- **Cancer/Treatment factors:** All hearing loss types: higher radiation dose; sensorineural hearing loss/tinnitus: CNS neoplasm, conventional (non-conformal) radiation, combination with other ototoxic agents (cisplatin, carboplatin, aminoglycosides, loop diuretics), radiation administered prior to platinum chemotherapy
- **Pre-morbid/Co-morbid medical conditions:** All hearing loss types: chronic otitis, chronic cerumen impaction; sensorineural hearing loss/tinnitus: cerebrospinal fluid shunt

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<tr>
<td>64</td>
<td>Head/Brain Neck Spine (cervical, whole) TBI</td>
<td>Xerostomia Salivary gland dysfunction</td>
<td><strong>HISTORY</strong>&lt;br&gt; Xerostomia (dry mouth)&lt;br&gt;Yearly&lt;br&gt;&lt;br&gt;<strong>PHYSICAL</strong>&lt;br&gt;Oral exam&lt;br&gt;Yearly&lt;br&gt;&lt;br&gt;<strong>SCREENING</strong>&lt;br&gt;Dental exam and cleaning&lt;br&gt;Every 6 months</td>
<td><strong>HEALTH LINKS</strong>&lt;br&gt;Dental Health&lt;br&gt;&lt;br&gt;POTENTIAL CONSIDERATIONS FOR FURTHER TESTING AND INTERVENTION&lt;br&gt;Supportive care with saliva substitutes, moistening agents, and sialagogues (e.g., pilocarpine).&lt;br&gt;Regular dental care including fluoride applications.&lt;br&gt;&lt;br&gt;<strong>SYSTEM = Dental</strong>&lt;br&gt;<strong>SCORE = 1</strong></td>
</tr>
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</table>

**Additional Information**

Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.
- Cancer/Treatment factors: Head and neck radiation involving the parotid gland, higher proportion of one gland or both salivary glands in the radiation field, higher radiation doses, radiomimetic chemotherapy (e.g., doxorubicin, dactinomycin)
- Pre-morbid/Co-morbid medical conditions: cGVHD

**References**


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<td>65</td>
<td>Head/Brain Neck Spine (cervical, whole) TBI</td>
<td>Dental abnormalities&lt;br&gt; Tooth/root agenesis&lt;br&gt; Root thinning/shortening&lt;br&gt; Enamel dysplasia&lt;br&gt; Microodontia&lt;br&gt; Ectopic molar eruption&lt;br&gt; Dental caries&lt;br&gt; Periodontal disease&lt;br&gt; Malocclusion&lt;br&gt; Temporomandibular joint dysfunction</td>
<td><strong>PHYSICAL</strong>&lt;br&gt; Oral exam&lt;br&gt; Yearly&lt;br&gt; <strong>SCREENING</strong>&lt;br&gt; Dental exam and cleaning&lt;br&gt; Every 6 months</td>
<td><strong>HEALTH LINKS</strong>&lt;br&gt; Dental Health&lt;br&gt; <strong>POTENTIAL CONSIDERATIONS FOR FURTHER TESTING AND INTERVENTION</strong>&lt;br&gt; Regular dental care including fluoride applications.&lt;br&gt; Baseline panorex prior to dental procedures to evaluate root development.&lt;br&gt; Consultation with orthodontist experienced in management of irradiated childhood cancer survivors.</td>
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</table>

**SYSTEM = Dental**<br> **SCORE**<br> Ectopic Molar Eruption = 2A<br> All Else = 1

### Additional Information

Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.

- **Patient factors:** Younger age at treatment, especially age <5 years, Gorlin syndrome (nevoid basal cell carcinoma syndrome)
- **Cancer/Treatment factors:** Higher radiation dose (especially ≥10 Gy)

### References

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</table>
| 66    | Head/Brain Neck Spine (cervical, whole) TBI (TBI is included for cumulative dose calculation purposes only; this section is not applicable to patients who received TBI alone.) | Osteoradionecrosis of the jaw | **HISTORY**  
If dose ≥40 Gy:  
Impaired or delayed healing following dental work  
Persistent jaw pain or swelling  
Trismus  
Yearly  
**PHYSICAL**  
If dose ≥40 Gy:  
Impaired wound healing  
Jaw swelling  
Trismus  
As clinically indicated | **HEALTH LINKS**  
Osteoradionecrosis  
**POTENTIAL CONSIDERATIONS FOR FURTHER TESTING AND INTERVENTION**  
Imaging studies (x-ray, CT scan and/or MRI) may assist in making diagnosis.  
Biopsy may be needed to confirm diagnosis.  
Hyperbaric oxygen treatments pre- or post-mandibular surgery to facilitate healing.  
**SYSTEM = Dental**  
**SCORE = 1** |

**Additional Information**
Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.
- Cancer/Treatment factors: Radiation dose ≥40 Gy (especially ≥50 Gy)

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<tr>
<td>67</td>
<td><strong>Head/Brain</strong>&lt;br&gt;Neck&lt;br&gt;Spine (cervical, whole)&lt;br&gt;TBI</td>
<td>Thyroid nodules</td>
<td><strong>PHYSICAL</strong>&lt;br&gt;Thyroid exam&lt;br&gt;Yearly</td>
<td><strong>HEALTH LINKS</strong>&lt;br&gt;Thyroid Problems&lt;br&gt;POTENTIAL CONSIDERATIONS FOR FURTHER TESTING AND INTERVENTION&lt;br&gt;Ultrasound for evaluation of palpable nodule(s).&lt;br&gt;FNA as clinically indicated.&lt;br&gt;Endocrine and/or surgical consultation for further management.</td>
</tr>
</tbody>
</table>

### Additional Information

Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.

- Patient factors: Younger age at treatment, female sex
- Cancer/Treatment factors: Thyroid gland directly in radiation field, TBI

### References

## RADIATION

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<tr>
<td>68</td>
<td>Head/Brain Neck Spine (cervical, whole) TBI</td>
<td>Thyroid cancer</td>
<td>PHYSICAL Thyroid exam Yearly</td>
<td>HEALTH LINKS Thyroid Problems POTENTIAL CONSIDERATIONS FOR FURTHER TESTING AND INTERVENTION Ultrasound for evaluation of palpable nodule(s). FNA as clinically indicated. Endocrine and/or surgical consultation for further management.</td>
</tr>
</tbody>
</table>

### Additional Information

Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.

- **Patient factors:** Younger age at treatment
- **Cancer/Treatment factors:** >5 years after irradiation, highest risk is between 10-30 Gy, thyroid gland directly in radiation field, TBI, alkylating agents

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<tr>
<td>69</td>
<td>Head/Brain Neck Spine (cervical, whole) TBI</td>
<td>Hypothyroidism</td>
<td><strong>HISTORY</strong>&lt;br&gt;• Fatigue&lt;br&gt;• Weight gain&lt;br&gt;• Cold intolerance&lt;br&gt;• Constipation&lt;br&gt;• Dry skin&lt;br&gt;• Brittle hair&lt;br&gt;• Depressed mood&lt;br&gt;• Menstrual irregularity&lt;br&gt;Yearly, consider more frequent screening during periods of rapid growth</td>
<td><strong>HEALTH LINKS</strong>&lt;br&gt;Thyroid Problems&lt;br&gt;&lt;br&gt;<strong>COUNSELING</strong>&lt;br&gt;For females, thyroid levels prior to attempting pregnancy and periodically throughout pregnancy.&lt;br&gt;&lt;br&gt;<strong>POTENTIAL CONSIDERATIONS FOR FURTHER TESTING AND INTERVENTION</strong>&lt;br&gt;Endocrine consultation for thyroid hormone replacement.</td>
</tr>
</tbody>
</table>

**Additional Information**
Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.

- Patient factors: Female sex
- Cancer/Treatment factors: Radiation dose ≥10 Gy (especially radiation dose ≥20 Gy), thyroid gland directly in radiation field, TBI

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</thead>
</table>
| 70    | Head/Brain Neck Spine (cervical, whole) | Hyperthyroidism | HISTORY  
Heat intolerance  
Tachycardia  
Palpitations  
Weight loss  
Emotional lability  
Muscular weakness  
Hyperphagia  
Yearly  
PHYSICAL  
Eyes  
Skin  
Thyroid  
Cardiac  
Neurologic  
Yearly  
SCREENING  
TSH  
Free T4  
Yearly | HEALTH LINKS  
Thyroid Problems  
POTENTIAL CONSIDERATIONS FOR FURTHER TESTING AND INTERVENTION  
Endocrine consultation for medical management.  
SYSTEM = Endocrine/Metabolic  
SCORE = 1 |

**Additional Information**

Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.

- Cancer/Treatment factors: Higher radiation dose, especially ≥30 Gy

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<tr>
<td>71</td>
<td>Head/Brain Neck</td>
<td>Carotid artery disease</td>
<td>HISTORY</td>
<td>HEALTH LINKS</td>
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<tr>
<td></td>
<td>Spine (cervical, whole)</td>
<td></td>
<td>Memory impairment</td>
<td>Cardiovascular Risk Factors</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Yearly</td>
<td>Nutrition and Physical Activity</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>PHYSICAL</td>
<td>POTENTIAL CONSIDERATIONS FOR FURTHER TESTING AND INTERVENTION</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Blood pressure</td>
<td>Optimize CVRFs, including blood pressure, lipid profile, and blood glucose.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Diminished carotid pulses</td>
<td>Doppler ultrasound of carotid vessels as clinically indicated. Refer to cardiology if abnormal.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Carotid bruits</td>
<td>MRI with DWI with MRA and cardiovascular surgery consultation as clinically indicated.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Abnormal neurologic exam (compromise of blood flow to brain)</td>
<td>For survivors who received ≥40 Gy radiation to the neck: Color Doppler ultrasound 10 years after completion of radiation therapy as a baseline. Refer to cardiologist if abnormal.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Yearly</td>
<td></td>
</tr>
</tbody>
</table>

**SYSTEM = Cardiovascular**

**SCORE = 2A**

### Additional Information
Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.
- Cancer/Treatment factors: ≥40 Gy radiation dose
- Pre-morbid/Co-morbid medical conditions: Hypertension, diabetes mellitus, hypercholesterolemia, smoking

### References
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<tr>
<td>72</td>
<td>Neck Chest Spine (thoracic, whole)</td>
<td>Subclavian artery disease</td>
<td><strong>PHYSICAL</strong>&lt;br&gt;Blood pressure in both arms (checking for wide blood pressure variation)&lt;br&gt;Diminished brachial and radial pulses&lt;br&gt;Pallor of upper extremities&lt;br&gt;Coolness of skin&lt;br&gt;Yearly</td>
<td><strong>HEALTH LINKS</strong>&lt;br&gt;Cardiovascular Risk Factors&lt;br&gt;Nutrition and Physical Activity&lt;br&gt;<strong>POTENTIAL CONSIDERATIONS FOR FURTHER TESTING AND INTERVENTION</strong>&lt;br&gt;Optimize CVRFs, including blood pressure, lipid profile, and blood glucose.&lt;br&gt;Doppler ultrasound of carotid vessels as clinically indicated. Refer to cardiology if abnormal.&lt;br&gt;MRI with DWI with MRA and cardiovascular surgery consultation as clinically indicated.&lt;br&gt;For survivors who received ≥40 Gy radiation to the neck: Color Doppler ultrasound 10 years after completion of radiation therapy as a baseline. Refer to cardiologist if abnormal.</td>
</tr>
</tbody>
</table>

**SYSTEM = Cardiovascular**<br>**SCORE = 2A**

### Additional Information
Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.
- Cancer/Treatment factors: ≥40 Gy radiation dose
- Pre-morbid/Co-morbid medical conditions: Hypertension, diabetes mellitus, hypercholesterolemia

### References
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<tr>
<td>73</td>
<td>Chest Axilla TBI</td>
<td>Breast cancer</td>
<td>PHYSICAL</td>
<td>HEALTH LINKS</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Clinical breast exam</td>
<td>Breast Cancer</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Yearly, beginning at puberty until age 25, then every 6 months</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>SCREENING</td>
<td>POTENTIAL CONSIDERATIONS FOR FURTHER TESTING AND INTERVENTION</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Mammogram</td>
<td>Surgery and/or oncology consultation as clinically indicated.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Yearly, beginning 8 years after radiation or at age 25, whichever occurs last</td>
<td>SYSTEM = SMN</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Breast MRI</td>
<td>SCORE = 1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Yearly, as an adjunct to mammography beginning 8 years after radiation or at age 25, whichever occurs last</td>
<td></td>
</tr>
</tbody>
</table>

**Additional Information**

Mammography is limited in its ability to evaluate the premenopausal breast.

MRI is now recommended as an adjunct to mammography in women treated with chest radiation for childhood cancer, similar to screening of other populations at high risk for breast cancer (e.g., premenopausal known or likely carriers of pathogenic or likely pathogenic variant of known penetrance).

The upper age limit at which mammography and breast MRI should be used for breast cancer surveillance has not been established.

Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.

- Patient factors: Family history of breast cancer
- Cancer/Treatment factors: Higher radiation dose, especially ≥10 Gy, longer time since radiation (>5 years). Note decreased risk in women treated with alkylating agents of sufficient dose to ablate ovarian function, although annual surveillance is still recommended.
- Pre-morbid/Co-morbid medical conditions: Personal history of BRCA1, BRCA2, ATM or p53 mutation or in absence of personal genetic testing, known BRCA mutation in first degree relative

**References**

### RADIATION

#### SYSTEM = Reproductive (Female)

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<tr>
<td>74 (female)</td>
<td>Chest Axilla TBI</td>
<td>Breast tissue hypoplasia</td>
<td>PHYSICAL Clinical breast exam Yearly</td>
<td>POTENTIAL CONSIDERATIONS FOR FURTHER TESTING AND INTERVENTION Surgical consultation for breast reconstruction after completion of growth.</td>
</tr>
</tbody>
</table>

### Additional Information

Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.
- Patient factors: Prepubertal at time of treatment
- Cancer/Treatment factors: Radiation dose ≥10 Gy to prepubertal breast bud (especially dose ≥20 Gy)

### References

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<tr>
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</thead>
<tbody>
<tr>
<td>75</td>
<td>Chest Axilla TBI</td>
<td>Pulmonary toxicity</td>
<td>HISTORY</td>
<td>HEALTH LINKS</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Pulmonary fibrosis</td>
<td>Cough</td>
<td>Pulmonary Health</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Interstitial pneumonitis</td>
<td>Wheezing</td>
<td>RESOURCES</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Restrictive lung disease</td>
<td>Shortness of breath</td>
<td><a href="http://www.smokefree.gov">www.smokefree.gov</a></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Obstructive lung disease</td>
<td>Dyspnea on exertion</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Yearly</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>PHYSICAL</td>
<td>Pulmonary exam</td>
<td>COUNSELING</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Yearly</td>
<td>Tobacco and environmental tobacco smoke avoidance/Smoking cessation.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>SCREENING</td>
<td>PFTs (including DLCO and spirometry)</td>
<td>Influenza and Pneumococcal vaccinations.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Baseline at entry into long-term follow-up, repeat as clinically indicated in patients with abnormal results or progressive pulmonary dysfunction</td>
<td>POTENTIAL CONSIDERATIONS FOR FURTHER TESTING AND INTERVENTION</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Repeat PFTs prior to general anesthesia.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Pulmonary consultation for patients with symptomatic pulmonary dysfunction.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Pulmonary consultation for survivors who desire to SCUBA dive (due to potential undiagnosed pulmonary toxicities, and limited data to guide safe diving recommendations for individuals treated with pulmonary toxic therapy).</td>
</tr>
</tbody>
</table>

**Additional Information**

Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.

- Patient factors: Younger age at irradiation
- Cancer/Treatment factors: Radiation dose $>10$ Gy, especially $\geq 15$ Gy, TBI $\geq 6$ Gy in single fraction, TBI $\geq 12$ Gy fractionated, chest radiation combined with TBI, radiation combined with bleomycin, busulfan, carmustine (BCNU), or tomustine (CCNU), radiomimetic chemotherapy (e.g., doxorubicin, dactinomycin)
- Pre-morbid/Co-morbid medical conditions: Atopic history
- Health behaviors: Smoking, inhaled illicit drug use

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<tr>
<td>76</td>
<td>Chest Axilla TBI</td>
<td>Lung cancer</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**HISTORY**
- Cough
- Wheezing
- Shortness of breath
- Dyspnea on exertion
  - Yearly

**PHYSICAL**
- Pulmonary Exam
  - Yearly

**SCREENING**
- Spiral CT Scan
  - Discuss the benefits and risks/harms of spiral CT scanning for patients at highest risk (i.e., smokers)

**HEALTH LINKS**
- Reducing the Risk of Subsequent Cancers

**POTENTIAL CONSIDERATIONS FOR FURTHER TESTING AND INTERVENTION**
- Imaging and surgery and/or oncology consultation as clinically indicated.

**SYSTEM = SMN**
**SCORE = 1**

---

**Additional Information**
Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.
- **Patient factors:** Workplace exposure to asbestos, arsenic, radiation, second hand smoke (in non-smokers)
- **Health behaviors:** Smoking, especially 30 pack-years or more

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<td>77</td>
<td>Chest Abdomen Spine (thoracic, whole) TBI</td>
<td>Cardiac toxicity Cardiomyopathy Subclinical left ventricular dysfunction Congestive heart failure Pericarditis Pericardial fibrosis Valvular disease Atherosclerotic heart disease Myocardial infarction Arrhythmia</td>
<td>HISTORY If dose ≥ 15 Gy: Shortness of breath Dyspnea on exertion Orthopnea Chest pain Palpitations If under 25 yrs: abdominal symptoms (nausea, vomiting)</td>
<td>HEALTH LINKS Heart Health Cardiovascular Risk Factors Nutrition and Physical Activity Dental Health</td>
</tr>
</tbody>
</table>

### SCREENING
- Echo (or comparable imaging to evaluate cardiac anatomy and function)

### RECOMMENDED FREQUENCY OF ECHOCARDIOGRAM

<table>
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<tr>
<th>Anthracycline Dose*</th>
<th>Radiation Dose**</th>
<th>Recommended Frequency</th>
</tr>
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<tbody>
<tr>
<td>&lt;100 mg/m²</td>
<td>&lt;15 Gy</td>
<td>No screening</td>
</tr>
<tr>
<td>≥100 to &lt;250 mg/m²</td>
<td>150 to &lt;300 mg/m²</td>
<td>Every 5 years</td>
</tr>
<tr>
<td>≥250 mg/m²</td>
<td>≥15 Gy</td>
<td>Every 2 years</td>
</tr>
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</table>

*Based on doxorubicin isotonic equivalent dose. See dose conversion instructions in section 34.

**Based on radiation dose with potential impact to heart (radiation to chest, abdomen, spine [thoracic, whole], TBI). If dose ≥ 15 Gy: EKG (include evaluation of QTc interval) Baseline at entry into long-term follow-up, repeat as clinically indicated

### POTENTIAL CONSIDERATIONS FOR FURTHER TESTING AND INTERVENTION
Cardiac MRI as an adjunct imaging modality when echo images are suboptimal. Cardiology consultation in patients with subclinical abnormalities on screening evaluations, LV dysfunction, dysrhythmia, or prolonged QTc interval.

Cardiology consultation (5 to 10 years after radiation) may be reasonable to evaluate risk for coronary artery disease in survivors who received ≥ 30 Gy chest radiation alone or ≥ 15 Gy chest radiation plus anthracycline.

In survivors with valvular disorders: Consult cardiologist to advise regarding need for endocarditis prophylaxis.

Female patients only: For patients who are pregnant or planning to become pregnant, additional cardiology evaluation is indicated in patients who received:
- ≥ 250 mg/m² anthracyclines
- ≥ 30 Gy chest radiation, or
- Anthracycline (any dose) combined with chest radiation (≥ 15 Gy)
- Evaluation should include a baseline echo (pre- or early-pregnancy). For those without prior abnormalities and with normal pre- or early-pregnancy baseline echos, follow-up echos may be obtained at the provider’s discretion. Those with a history of systolic dysfunction or with pre- or early-pregnancy systolic dysfunction are at highest risk for pregnancy-associated cardiomyopathy, and should be monitored periodically during pregnancy and during labor and delivery due to increased risk for heart failure.

**SYSTEM = Cardiovascular SCORE = 1**
Exertional intolerance is an uncommon presentation of LV dysfunction in patients <25 years old.

Abdominal symptoms (nausea, emesis) may be observed more frequently than exertional dyspnea or chest pain in younger patients.

The AHA now limits their recommendation regarding endocarditis 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) valvulopathy 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.

Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.

- Patient factors: Younger age at irradiation, especially age <5 years, family history of dyslipidemia, CAD
- Cancer/Treatment factors: Radiation dose ≥20 Gy to chest, TBI, anteriorly-weighted radiation fields, lack of subcarinal shielding, combined with radiomimetic chemotherapy (e.g., doxorubicin, daunomycin), doses ≥15 Gy in patients who have received ≥100 mg/m² of anthracyclines, doses ≥30 Gy in patients who have not received anthracyclines, longer time since treatment
- Pre-morbid/Co-morbid medical conditions: Obesity, congenital heart disease, hypertension, diabetes mellitus, dyslipidemia. For female patients, premature ovarian failure (untreated), pregnancy if systolic function is abnormal pre-pregnancy
- Health behaviors: Smoking, drug use (e.g., cocaine, diet pills, ephedra, mahuang)

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<td>78</td>
<td>Abdomen TBI</td>
<td>Functional asplenia</td>
<td>PHYSICAL</td>
<td>HEALTH LINKS Splenic Precautions</td>
</tr>
<tr>
<td></td>
<td>(TBI is included for cumulative dose calculation purposes only; this section is not applicable to patients who received TBI alone.)</td>
<td>At risk for life-threatening infection with encapsulated organisms (e.g., Haemophilus influenzae, Streptococcus pneumoniae, meningococcus)</td>
<td>If radiation dose ≥40 Gy: Physical exam at time of febrile illness to evaluate degree of illness and potential source of infection When febrile T ≥101°F (38.3°C)</td>
<td>SCREENING If dose ≥40 Gy: Blood culture When febrile T ≥101°F (38.3°C)</td>
</tr>
</tbody>
</table>

Additional Information

Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.
- **Cancer/Treatment factors:** Higher radiation dose, larger volume of spleen in treatment field, include documentation of splenic radiation dose exposure in the survivor’s treatment summary.

References


SYSTEM = Immune
SCORE = 1

POTENTIAL IMPACT TO SPLEEN
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<tr>
<td>79</td>
<td>Neck Chest Abdomen Spine (cervical, thoracic, whole)</td>
<td>Esophageal stricture</td>
<td>HISTORY Dysphagia Heartburn Yearly</td>
<td>HEALTH LINKS Gastrointestinal Health POTENTIAL CONSIDERATIONS FOR FURTHER TESTING AND INTERVENTION Surgery and/or gastroenterology consultation for symptomatic patients. SYSTEM = GI/Hepatic SCORE = 1</td>
</tr>
</tbody>
</table>

**Additional Information**

Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.

- Cancer/Treatment factors: Radiation dose ≥30 Gy (increased risk with higher radiation dose, especially ≥40 Gy)
- Pre-morbid/Co-morbid medical conditions: Gastroesophageal reflux, history of Candida esophagitis, gut GVHD

**References**

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<tbody>
<tr>
<td>80</td>
<td>Abdomen TBI</td>
<td>Impaired glucose metabolism/Diabetes mellitus</td>
<td>SCREENING Fasting blood glucose OR HbA1c Every 2 years</td>
<td>HEALTH LINKS Nutrition and Physical Activity Cardiovascular Risk Factors COUNSELING Obesity-related health risks. POTENTIAL CONSIDERATIONS FOR FURTHER TESTING AND INTERVENTION Endocrine consultation Evaluate for other co-morbid conditions, including dyslipidemia, hypertension, and overweight/obesity. Refer to dietitian for blood sugar management.</td>
</tr>
</tbody>
</table>

**Additional Information**

Impaired glucose metabolism may occur as a part of a constellation of conditions known as metabolic syndrome.

Definitions of metabolic syndrome generally include a combination of central (abdominal) obesity and ≥2 of the following: elevated blood pressure, atherogenic dyslipidemia (elevated triglycerides, reduced HDL cholesterol), abnormal glucose metabolism.

Note: Patients who received TBI may develop features of metabolic syndrome without associated obesity.

Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.

- Patient factors: Family history of diabetes mellitus, pregnancy
- Cancer/Treatment factors: Prolonged corticosteroid therapy (e.g., for cGVHD)
- Pre-morbid/Co-morbid medical conditions: Obesity

**References**


Shalitin S, Phillip M, Stein J, et al: Endocrine dysfunction and parameters of the metabolic syndrome after bone marrow transplantation during childhood and adolescence. Bone Marrow Transplant 37:1109-17, 2006

<table>
<thead>
<tr>
<th>Sec #</th>
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</thead>
<tbody>
<tr>
<td>81</td>
<td>Abdomen TBI</td>
<td>Dyslipidemia</td>
<td>SCREENING Fasting lipid profile Every 2 years</td>
<td>HEALTH LINKS Nutrition and Physical Activity Cardiovascular Risk Factors POTENTIAL CONSIDERATIONS FOR FURTHER TESTING AND INTERVENTION Evaluate for other co-morbid conditions, including hypertension, impaired glucose metabolism, and overweight/obesity. Refer to dietitian. SYSTEM = Endocrine/Metabolic SCORE Abdominal Radiation = 2A TBI = 1</td>
</tr>
</tbody>
</table>

**Additional Information**

Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.

- **Patient factors:** Family history of dyslipidemia
- **Cancer/Treatment factors:** Prolonged corticosteroid therapy (e.g., for cGVHD)

**References**

Shalitin S, Phillip M, Stein J, et al: Endocrine dysfunction and parameters of the metabolic syndrome after bone marrow transplantation during childhood and adolescence. Bone Marrow Transplant 37:1109-17, 2006
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<tr>
<td>82</td>
<td>Abdomen</td>
<td>Hepatic toxicity</td>
<td>PHYSICAL</td>
<td>HEALTH LINKS</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Scleral icterus</td>
<td>Liver Health</td>
</tr>
<tr>
<td></td>
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<td></td>
<td>Jaundice</td>
<td>POTENTIAL CONSIDERATIONS FOR FURTHER TESTING AND INTERVENTION</td>
</tr>
<tr>
<td></td>
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<td></td>
<td>Ascites</td>
<td>Platelet count for evaluation of hypersplenism and prothrombin time for evaluation of hepatic synthetic function in patients with abnormal liver screening tests.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Hepatomegaly</td>
<td>Screen for viral hepatitis in patients with persistently abnormal liver function or any patient transfused prior to 1993.</td>
</tr>
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<td></td>
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<td></td>
<td>Splenomegaly</td>
<td>Gastroenterology/Hepatology consultation in patients with persistent liver dysfunction.</td>
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<tr>
<td></td>
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<td></td>
<td>Yearly</td>
<td>Hepatitis A and B immunization in at-risk patients lacking immunity.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>SCREENING</td>
<td>ALT</td>
<td>SYSTEM = GI/Hepatic</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>AST</td>
<td>SCORE = 1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Bilirubin</td>
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<tr>
<td></td>
<td></td>
<td>Baseline at entry into long-term follow-up, repeat as clinically indicated</td>
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</tbody>
</table>

**Additional Information**

FNH is a benign change that represents a scar in the liver.
FNH is usually an asymptomatic finding noted on MRI or ultrasound of the liver.
Continued observation or biopsy may be indicated depending on individual patient factors and imaging features.
Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.
- Cancer/Treatment factors: Higher radiation dose to liver, especially ≥30 Gy, or to larger volume
- Pre-morbid/Co-morbid medical conditions: Chronic hepatitis, history of SOS
- Health behaviors: Alcohol use (in relation to hepatic fibrosis and cirrhosis)

**References**


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</thead>
<tbody>
<tr>
<td>83</td>
<td>Abdomen</td>
<td>Cholelithiasis</td>
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<td></td>
</tr>
</tbody>
</table>

**HISTORY**
- Colicky abdominal pain related to fatty food intake
- Excessive flatulence
- Yearly

**PHYSICAL**
- Epigastric or RUQ tenderness
- Positive Murphy’s sign
- As clinically indicated

**HEALTH LINKS**
- Gastrointestinal Health

**POTENTIAL CONSIDERATIONS FOR FURTHER TESTING AND INTERVENTION**
- Gallbladder ultrasound in patients with chronic abdominal pain.

**SYSTEM = GI/Hepatic**
- **SCORE = 2B**

---

### Additional Information

Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.

- **Patient factors:** Family history of cholelithiasis
- **Cancer/Treatment factors:** Radiation dose ≥30 Gy, abdominal surgery, abdominal radiation, TPN, HCT
- **Pre-morbid/Co-morbid medical conditions:** Ileal conduit, obesity, pregnancy

### References


## RADIATION

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<tbody>
<tr>
<td>84</td>
<td>Abdomen Pelvis Spine (lumbar, sacral, whole)</td>
<td>Bowel obstruction</td>
<td><strong>HISTORY</strong> Abdominal pain Distension Vomiting Constipation Yearly <strong>PHYSICAL</strong> Tenderness Abdominal guarding Distension Yearly</td>
<td><strong>HEALTH LINKS</strong> Gastrointestinal Health <strong>POTENTIAL CONSIDERATIONS FOR FURTHER TESTING AND INTERVENTION</strong> Imaging as clinically indicated for suspected obstruction. Surgical consultation in patients unresponsive to medical management. <strong>SYSTEM = GI/Hepatic</strong> <strong>SCORE = 1</strong></td>
</tr>
</tbody>
</table>

### Additional Information

Bowel obstruction is rarely seen in individuals treated with abdominal radiation who have not had abdominal surgery.

Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.

- Cancer/Treatment factors: Abdominal surgery, radiation dose $\geq 20$ Gy (especially $\geq 45$ Gy). Obstruction may occur in people who received lower doses of abdominal radiation during childhood.

### References

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<tr>
<td>85</td>
<td>Abdomen Pelvis Spine (lumbar, sacral, whole)</td>
<td>Chronic enterocolitis Fistula Strictures</td>
<td>HISTORY Nausea Vomiting Abdominal pain Diarrhea Yearly</td>
<td>HEALTH LINKS Gastrointestinal Health POTENTIAL CONSIDERATIONS FOR FURTHER TESTING AND INTERVENTION Serum protein and albumin in patients with chronic diarrhea or fistula. Surgical and/or gastroenterology consultation. SYSTEM = GI/Hepatic SCORE = 1</td>
</tr>
</tbody>
</table>

**Additional Information**

Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.

- Cancer/Treatment factors: Abdominal surgery, radiation dose ≥30 Gy (particularly radiation dose ≥45 Gy), higher radiation dose to bowel

**References**


### RADIATION

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<tr>
<td>86</td>
<td>Abdomen Pelvis Spine (lumbar, sacral, whole) TBI</td>
<td>Colorectal cancer</td>
<td>SCREENING</td>
<td>HEALTH LINKS</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Regular screening selected from the options below based on informed decision-making between patient and provider</td>
<td>Colorectal Cancer</td>
</tr>
<tr>
<td></td>
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<td></td>
<td>Beginning 5 years after radiation or at age 30 years (whichever occurs last)</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Radiation-Related Colorectal Cancer Screening Options</td>
<td>SYSTEM = SMN</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Test</td>
<td>Frequency</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Multitarget stool DNA test*</td>
<td>Every 3 years</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Colonoscopy</td>
<td>Every 5 years</td>
</tr>
<tr>
<td></td>
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<td></td>
<td>*Positive result should be followed up with timely colonoscopy.</td>
<td>Note: Colonoscopy is considered the gold standard for colorectal cancer screening in high-risk populations; however, recognizing that not all survivors are willing or able to undergo colonoscopy, multitarget stool DNA testing is deemed a reasonable alternative. Alternative stool-based testing (i.e., annual fecal immunochemical testing [FIT] or high-sensitivity guaiac-based fecal occult blood testing) or alternative structural examination (i.e., every 5 year CT colonography or flexible sigmoidoscopy) may also be considered if colonoscopy or multitarget stool DNA testing are not feasible or acceptable to the survivor. All positive results from these alternative testing methods should be followed up with timely colonoscopy.</td>
</tr>
</tbody>
</table>

### Additional Information

Participation in screening remains poor in the cancer survivor population, with >70% of at-risk survivors unscreened (see Daniel et al. 2015); thus it is important for clinicians to engage survivors in informed decision-making, weighing risks and benefits of the available options, and selecting an option that is acceptable to the survivor and likely to result in successful completion of timely periodic screening.

For patients at high risk due to personal or family history or hereditary syndromes predisposing to colorectal cancer, more intensive and earlier screening is recommended (see Giardiello et al. 2014, Kahl et al. 2016, Lieberman et al. 2012, and Syngal et al. 2015).

Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.

- Patient factors: Current age ≥45 years, family history of colorectal cancer or polyps in first degree relative
- Cancer/Treatment factors: Hepatoblastoma, gastrointestinal malignancy, higher radiation dose, especially ≥20 Gy, combination with chemotherapy (especially alkylators)
- Pre-morbid/Co-morbid medical conditions: Obesity, ulcerative colitis, adenomatous polyps, familial polyposis
- Health behaviors: High fat/low fiber diet

### References

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<tbody>
<tr>
<td>87</td>
<td>Abdomen TBI</td>
<td>Renal toxicity</td>
<td>PHYSICAL</td>
<td>HEALTH LINKS</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Glomerular injury</td>
<td>Blood pressure</td>
<td>Kidney Health</td>
</tr>
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<td></td>
<td></td>
<td>Renal insufficiency</td>
<td>Yearly</td>
<td>Cardiovascular Risk Factors</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Hypertension</td>
<td>SCREENING</td>
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</tr>
<tr>
<td></td>
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<td></td>
<td>BUN</td>
<td>POTENTIAL CONSIDERATIONS FOR FURTHER TESTING AND INTERVENTION</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Creatinine</td>
<td>Nephrology consultation for patients with hypertension or progressive renal insufficiency.</td>
</tr>
<tr>
<td></td>
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<td></td>
<td>Na, K, Cl, CO₂, Ca, Mg, PO₄ Baseline at entry into long-term follow-up, repeat as clinically indicated</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>SYSTEM = Urinary</td>
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<td></td>
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<td></td>
<td></td>
<td>SCORE = 1</td>
</tr>
</tbody>
</table>

**Additional Information**

Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.

- **Cancer/Treatment factors**: Bilateral Wilms tumor, nephrectomy, radiomimetic chemotherapy (e.g., doxorubicin, dactinomycin), combination with other nephrotoxic agents (e.g., cisplatin, carboplatin, ifosfamide, aminoglycosides, amphotericin, immunosuppressants), radiation dose ≥10 Gy, especially dose ≥15 Gy, TBI ≥6 Gy in single fraction, TBI ≥12 Gy fractionated, TBI combined with radiation to the kidney

- **Pre-morbid/Co-morbid medical conditions**: Diabetes mellitus, hypertension, congenital absence of kidney

**References**

<table>
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</thead>
</table>
| 88    | Pelvis Spine (sacral, whole) | Urinary tract toxicity  
Hemorrhagic cystitis  
Bladder fibrosis  
Dysfunctional voiding  
Vesicoureteral reflux  
Hydronephrosis | **HISTORY**  
Hematuria  
Urinary urgency/frequency  
Urinary incontinence/retention  
Dysuria  
Nocturia  
Abnormal urinary stream  
Yearly | **HEALTH LINKS**  
Bladder Health  
**COUNSELING**  
Promptly report dysuria or gross hematuria.  
**POTENTIAL CONSIDERATIONS FOR FURTHER TESTING AND INTERVENTION**  
Urinalysis, urine culture, spot urine calcium/creatinine ratio for patients with positive history.  
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, incontinence, or dysfunctional voiding.  
**SYSTEM = Urinary**  
**SCORE**  
Hemorrhagic cystitis = 2A  
All Else = 1 |
<table>
<thead>
<tr>
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<th>Potential Late Effects</th>
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</thead>
<tbody>
<tr>
<td>89</td>
<td>Pelvis Spine (sacral, whole)</td>
<td>Bladder malignancy</td>
<td>HISTORY: Hematuria, Urinary urgency/frequency, Urinary incontinence/retention, Dysuria, Nocturia, Abnormal urinary stream</td>
<td>Yearly evaluation: Urinalysis, urine culture, spot urine calcium/creatinine ratio for patients with positive history. Ultrasound of kidneys and bladder for patients with microscopic hematuria (defined as &gt;5 RBC/HPF on at least 2 occasions). Nephrology or urology referral for patients with culture-negative microscopic hematuria AND abnormal ultrasound. Urology referral for patients with culture-negative macroscopic hematuria.</td>
</tr>
</tbody>
</table>

**Health Links:**
- Bladder Health

**Counseling:**
Promptly seek medical attention for dysuria or gross hematuria.

**Potential Considerations for Further Testing and Intervention:**
- Urinalysis, urine culture, spot urine calcium/creatinine ratio for patients with positive history.
- 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.
- Urology referral for patients with culture-negative macroscopic hematuria.

**Additional Information:**
The bladder is included in the left and right flank/hemiabdomen treatment fields only if the fields extended below iliac crest. Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.
- Cancer/Treatment factors: Combination with cyclophosphamide or ifosfamide
- Health behaviors: Alcohol use, smoking

**References:**
### RADIATION

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<tr>
<td>90 (male)</td>
<td>Testes</td>
<td>Testicular hormonal dysfunction</td>
<td>HISTORY</td>
<td>HEALTH LINKS</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Testosterone deficiency/insufficiency</td>
<td>Onset and tempo of puberty</td>
<td>Testicular and Reproductive Health</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Delayed/Arrested puberty</td>
<td>Sexual function (erections, nocturnal emissions, libido)</td>
<td>POTENTIAL CONSIDERATIONS FOR FURTHER TESTING AND INTERVENTION</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Medication use</td>
<td>Testosterone insufficiency or deficiency requiring hormone replacement after alkylating agents only is rare.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Yearly</td>
<td>Endocrine referral for the following:</td>
</tr>
<tr>
<td></td>
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<td></td>
<td>Monitor growth until mature</td>
<td>• No signs of puberty by age 14 years</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>• Failure of pubertal progression</td>
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<td></td>
<td></td>
<td>Adults with low AM testosterone levels</td>
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<tr>
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<td>SCREENING</td>
<td>Periodic re-evaluation of testosterone in males with low normal testosterone as they age or if they become symptomatic.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>AM testosterone in high risk patients starting at 18 years</td>
<td>HEALTH LINKS</td>
<td>Bone density evaluation in androgen deficient patients.</td>
</tr>
<tr>
<td></td>
<td></td>
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<td></td>
<td>Consider assessment of fertility status prior to initiation of testosterone replacement therapy.</td>
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<td>SYSTEM = Reproductive (Male)</td>
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<td></td>
<td>SCORE = 1</td>
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</tbody>
</table>

### Additional Information

Testicular volume is not a reliable indicator of pubertal onset/stage in boys treated with alkylating agents and/or direct testicular radiotherapy.

Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.

- Cancer/Treatment factors: Testicular cancer, testicular irradiation combined with head/brain irradiation, testicular dose ≥12 Gy, combination with alkylating agents, combination with cyclophosphamide conditioning for HCT, combination with unilateral orchietomy

### References

<table>
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<tr>
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</tr>
</thead>
</table>
| **91** (male) | Testes TBI | Impaired spermatogenesis  
Reduced fertility  
Oligospermia  
Azoospermia  
Infertility | HISTORY  
Onset and tempo of puberty  
Sexual function (erections, nocturnal emissions, libido)  
Medication use  
Yearly | HEALTH LINKS  
Testicular and Reproductive Health |
| **SYSTEM** | Reproductive (Male) | **SCORE = 1** | RESOURCES  
American Society for Reproductive Medicine: [www.asrm.org](http://www.asrm.org)  
Alliance for Fertility Preservation: [www.allianceforfertilitypreservation.org](http://www.allianceforfertilitypreservation.org) | COUNSELING  
Need for contraception.  
Review previous fertility preservation counseling/interventions.  
Fertility recovery can be seen in the early years after completion of therapy and occasionally thereafter. |
| **POTENTIAL CONSIDERATIONS FOR FURTHER TESTING AND INTERVENTION** | For sexually mature patients who desire information about potential future fertility:  
semen analysis (optimal) and/or FSH and inhibin B (alternative if unable or unwilling to provide semen sample).  
Reproductive endocrinology/urology referral for infertility evaluation and consultation regarding assisted reproductive technologies. | | | |

**Additional Information**

Testicular volume is not a reliable indicator of pubertal onset/stage in boys treated with alkylating agents and/or direct testicular radiotherapy.

Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.

- Patient factors: Medications (anabolic steroids, testosterone), occupational exposures (pesticides, heavy metals, solvents)
- Cancer/Treatment factors: Testicular cancer, fractionated small doses greater risk than single large doses, radiation dose to testes (up to 6 Gy azoospermia may be transient, ≥6 Gy azoospermia likely permanent and especially testicular dose ≥20 Gy), combination with alkylating agents, genitourinary surgery
- Pre-morbid/Co-morbid medical conditions: Obesity, ejaculatory dysfunction, history of sexually transmitted infections, cGVHD
- Health behaviors: Tobacco/Marijuana use

**References**

Grigg AP, McLachlan R, Zaja J, et al: Reproductive status in long-term bone marrow transplant survivors receiving busulfan-cyclophosphamide (120 mg/kg). Bone Marrow Transplant 26:1089-95, 2000
### System = Reproductive (Female)

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<tr>
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</tr>
</thead>
</table>
| 92 (female) | Pelvis Spine (sacral, whole) TBI | Ovarian hormone deficiencies Delayed puberty Arrested puberty Premature ovarian insufficiency/Premature menopause | **HISTORY** <br> Onset and tempo of puberty Menstrual history Sexual function (vaginal dryness, libido) Menopausal symptoms Medication use Yearly<br><br>**PHYSICAL**<br>Tanner staging until sexually mature Yearly<br>Monitor growth until mature Yearly | **HEALTH LINKS**<br>Ovarian and Reproductive Health<br><br>**COUNSELING**<br>Review previous fertility preservation counseling/interventions. Higher cumulative doses of alkylating agents with or without radiation may increase risk. Dose can be estimated using CED dose calculation located in section 14. Adverse impact of ovarian hormone deficiencies on growth, bone mineralization, cardiovascular disease and sexual dysfunction.<br><br>**POTENTIAL CONSIDERATIONS FOR FURTHER TESTING AND INTERVENTION**<br>FSH and estradiol and/or endocrine/gynecology referral for patients with:<br>- No signs of puberty by age 13 years<br>- Failure of pubertal progression<br>- Abnormal menstrual patterns or menopausal symptoms<br>- Ovarian hormone deficiency/insufficiency to weigh risks and benefits of hormonal replacement therapy<br> Bone density evaluation in patients with ovarian hormone deficiencies.<br><br>**SYSTEM** = Reproductive (Female)<br>**SCORE** = 1

#### Additional Information

The ovaries are included in the left and right flank/hemiabdomen treatment fields only if the fields extended below the iliac crest. Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.

- **Patient factors:** Older age at irradiation
- **Cancer/Treatment factors:** Radiation dose ≥5 Gy if pubertal (especially ≥10 Gy), dose ≥10 Gy if prepubertal (especially ≥15 Gy), combination with alkylating agent chemotherapy, longer time since treatment, combination with cyclophosphamide conditioning for HCT
- **Health behaviors:** Smoking

#### References

## RADIATION

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<tr>
<td>93</td>
<td>Pelvis</td>
<td>Diminished Ovarian Reserve (DOR)</td>
<td>HISTORY</td>
</tr>
<tr>
<td></td>
<td>(female)</td>
<td>Infertility</td>
<td>Menstrual and pregnancy history</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Hormonal Therapy</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Yearly</td>
</tr>
<tr>
<td></td>
<td>Spine (sacral, whole)</td>
<td></td>
<td>PHYSICAL</td>
</tr>
<tr>
<td></td>
<td>TBI</td>
<td></td>
<td>Tanner staging until sexually mature</td>
</tr>
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<td></td>
<td></td>
<td></td>
<td>Yearly</td>
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</tbody>
</table>

### Health Counseling/Further Considerations

**HEALTH LINKS**
- Ovarian and Reproductive Health

**RESOURCES**
- American Society for Reproductive Medicine: [www.asrm.org](http://www.asrm.org)
- Alliance for Fertility Preservation: [www.allianceforfertilitypreservation.org](http://www.allianceforfertilitypreservation.org)
- Livestrong Foundation: [www.livestrong.org/what-we-do/program/fertility](http://www.livestrong.org/what-we-do/program/fertility)
- Oncofertility Consortium: [https://oncofertility.msu.edu](https://oncofertility.msu.edu)

**COUNSELING**
Need for contraception.
Review previous fertility preservation counseling/interventions.
Fertility recovery can be seen in the early years after the completion of therapy and occasionally thereafter.
Potential for shorter period of fertility in family planning. Those with DOR should consider discussing reproductive health options with a reproductive endocrinologist or fertility specialist.
Higher cumulative doses of alkylating agents with or without radiation may increase risk.
Dose can be estimated using CED dose calculation located in section 15.

**POTENTIAL CONSIDERATIONS FOR FURTHER TESTING AND INTERVENTION**
- FSH and estradiol for patients with menstrual cycle dysfunction suggestive of premature ovarian insufficiency or those who desire information about potential for future fertility.
- AMH to assess for diminished ovarian reserve.
- Reproductive endocrinology referral for antral follicle count, ovarian reserve evaluation and consultation regarding assisted reproductive technologies in at-risk patients who desire information about potential fertility and interventions to preserve future fertility.

**SYSTEM = Reproductive (Female)**
**SCORE = 1**

### Additional Information
The ovaries are included in the left and right flank/abdomen treatment fields only if the fields extended below the iliac crest.
AMH may be low in the presence of normal FSH. AMH should be interpreted relative to age-specific reference ranges. FSH is lowered and AMH may be lowered by concurrent hormonal contraceptive use.
Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.
- Patient factors: Older age at irradiation
- Cancer/Treatment factors: Radiation dose ≥5 Gy if pubertal (especially ≥10 Gy), radiation dose ≥10 Gy if prepubertal (especially ≥15 Gy), combination with alkylating agent chemotherapy, longer time since treatment, combination with cyclophosphamide conditioning for HCT
- Health behaviors: Smoking

### References
Section 93 References (cont)

**SYSTEM = Reproductive (Female)**  
**SCORE = 2B**

### Table of Contents

- Radiation
- Potential Impact to Female Reproductive System (Cont)

---

**Sec #**

**Therapeutic Exposure**

**Potential Late Effects**

**Periodic Evaluation**

**Health Counseling/ Further Considerations**

---

**94 (female)**

**Pelvis**  
**Spine (sacral, whole)**  
**TBI**

**Uterine vascular insufficiency**

Resulting in adverse pregnancy outcomes such as:
- Spontaneous abortion  
- Neonatal death  
- Low-birth weight infant  
- Fetal malposition  
- Premature labor

**HISTORY**

- Pregnancy  
- Childbirth history

**Yearly for women of reproductive age**

**HEALTH LINKS**

- Ovarian and Reproductive Health

**RESOURCES**

- American Society for Reproductive Medicine: [www.asrm.org](http://www.asrm.org)  
- Alliance for Fertility Preservation: [www.allianceforfertilitypreservation.org](http://www.allianceforfertilitypreservation.org)

**POTENTIAL CONSIDERATIONS FOR FURTHER TESTING AND INTERVENTION**

- High-level ultrasound evaluation of genitourinary tract after pubertal development as clinically indicated in patients contemplating pregnancy.  
- High-risk obstetrical care during pregnancy.

---

### Additional Information

The uterus is included in the left and right flank/hemiabdomen treatment fields only if the fields extended below iliac crest.

10% of girls with Wilms tumor have congenital uterine anomalies.

Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.

- Patient factors: Wilms tumor and associated Mullerian anomalies (i.e., agenesis, hypoplasia), prepubertal at time of treatment  
- Cancer/Treatment factors: TBI, higher radiation dose to pelvis, radiation dose ≥30 Gy

### References

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</table>
| 95    | Pelvis (female)      | Vaginal fibrosis/stenosis | HISTORY: <br>Psychosocial assessment <br>Dyspareunia <br>Post-coital bleeding <br>Difficulty with tampon insertion <br>Vaginal dryness <br>Vulvar pain/tenderness <br>Vulvovaginal burning or pruritus <br>Dysuria <br>Yearly<br>PHYSICAL: <br>Exam of external genitalia <br>Yearly | COUNSELING: <br>Avoid frequent contact with irritants (e.g., bubble bath, wet wipes and soaps). <br>POTENTIAL CONSIDERATIONS FOR FURTHER TESTING AND INTERVENTION: <br>Gynecologic consultation for management. Psychological consultation in patients with emotional difficulties. | SYSTEM = Reproductive (Female)  
SCORE = 2A |

**Additional Information**

The vagina is included in the left and right flank/hemiabdomen treatment fields only if the fields extended below iliac crest. Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.

- Cancer/Treatment factors: Vaginal tumor or pelvic tumor adjacent to vagina, radiation dose ≥50 Gy if postpubertal (especially dose ≥55 Gy), radiation dose ≥25 Gy if prepubertal (especially dose ≥35 Gy)
- Pre-morbid/Co-morbid medical conditions: cGVHD

**References**

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</thead>
</table>
| 96    | Any Radiation (Including TBI) | Musculoskeletal growth problems  
Hypoplasia  
Fibrosis  
Reduced or uneven growth  
Shortened trunk height (trunk radiation)  
Limb length discrepancy (extremity radiation) | PHYSICAL  
Height  
Weight  
Yearly  
Sitting height  
Yearly for patients who had trunk radiation  
Limb lengths  
Yearly for patients who had extremity radiation | SYSTEM = Musculoskeletal  
SCORE = 1  
COUNSELING  
Increased risk of fractures in weight-bearing irradiated bones.  
**POTENTIAL CONSIDERATIONS FOR FURTHER TESTING AND INTERVENTION**  
Orthopedic consultation for any deficit noted in growing child.  
Plastic surgery consult for reconstruction. |

**Additional Information**
Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.

- **Patient factors:** Younger age at treatment, especially prepubertal at treatment
- **Cancer/Treatment factors:** Higher cumulative radiation dose, especially dose ≥20 Gy, larger radiation treatment field, higher radiation dose per fraction, orthovoltage radiation (commonly used before 1970) due to delivery of greater dose to skin and bones, epiphysis in treatment field

**References**
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</thead>
</table>
| 97    | Chest Abdomen Spine (thoracic, lumbar, whole) | Scoliosis/Kyphosis | **PHYSICAL**
Exam of back/spine
Yearly until growth completed, may need more frequent assessment during puberty or if curve detected | **HEALTH LINKS**
Scoliosis and Kyphosis

**POTENTIAL CONSIDERATIONS FOR FURTHER TESTING AND INTERVENTION**
Spine films in patients with clinically apparent curve. Orthopedic consultation as indicated based on physical and/or radiographic exam.

**SYSTEM = Musculoskeletal **
**SCORE = 1**

---

**Additional Information**

With contemporary treatment approaches, scoliosis is infrequently seen as a consequence of radiation unless the patient has also undergone surgery to the hemithorax, abdomen or spine. Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.

- Patient factors: Younger age at irradiation
- Cancer/Treatment factors: Paraspinal malignancies, hemithoracic, abdominal or spinal surgery, hemithoracic or abdominal radiation, radiation of only a portion of (rather than whole) vertebral body, radiation doses ≥20 Gy (lower doses for infants), orthovoltage radiation (commonly used before 1970)
- Pre-morbid/Co-morbid medical conditions: Neurofibromatosis

**References**

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<tr>
<td>98</td>
<td>Any Radiation (not including TBI)</td>
<td>Radiation-induced fracture</td>
<td>PHYSICAL: Pain, swelling, deformity of bone As clinically indicated</td>
<td>POTENTIAL CONSIDERATIONS FOR FURTHER TESTING AND INTERVENTION: Radiograph of affected bone as clinically indicated. Orthopedic evaluation as clinically indicated. SYSTEM = Musculoskeletal SCORE = 1</td>
</tr>
</tbody>
</table>

**Additional Information**

Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.
- Cancer/Treatment factors: History of surgery to cortex of bone, radiation dose ≥40 Gy, radiation dose ≥50 Gy to bone

**References**

Hematopoietic Cell Transplant Introductory Information

- Complications after HCT have multifactorial etiologies, including prior therapy for primary malignancy, intensity of transplant conditioning, stem cell product (e.g., marrow, cord blood, peripheral stem cells), donor (e.g., autologous, allogeneic, unrelated), quality of donor to recipient match, complications of the transplant process (immunosuppression and GVHD), complications in the post-transplant period, underlying disease, host genetic factors, and lifestyle behaviors.

- This section includes late treatment complications that may be observed in hematopoietic cell transplant recipients not covered elsewhere in these guidelines.

- Refer to other sections of these guidelines for specific details related to late complications of radiation and of specific chemotherapeutic agents.


**Total Body Irradiation (TBI) Related Potential Late Effects**

- The complete list of potential late effects and associated Guideline section numbers are included on the accompanying table for clinician convenience when evaluating patients who received TBI. For details regarding each potential late effect and indicated screening, please refer to the relevant section within the Guidelines.

<table>
<thead>
<tr>
<th>Section Number</th>
<th>Sex</th>
<th>Potential Late Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>44</td>
<td>Both</td>
<td>Subsequent benign or malignant neoplasm occurring in or near radiation field</td>
</tr>
<tr>
<td>45</td>
<td>Both</td>
<td>Dermatologic toxicity</td>
</tr>
<tr>
<td>46</td>
<td>Both</td>
<td>Brain tumor (benign or malignant)</td>
</tr>
<tr>
<td>47</td>
<td>Both</td>
<td>Neurocognitive deficits</td>
</tr>
<tr>
<td>48</td>
<td>Both</td>
<td>Clinical leukoencephalopathy</td>
</tr>
<tr>
<td>53</td>
<td>Both</td>
<td>Growth hormone deficiency</td>
</tr>
<tr>
<td>58</td>
<td>Male</td>
<td>Gonadotropin deficiency</td>
</tr>
<tr>
<td>59</td>
<td>Female</td>
<td>Gonadotropin deficiency</td>
</tr>
<tr>
<td>61</td>
<td>Both</td>
<td>Cataracts</td>
</tr>
<tr>
<td>64</td>
<td>Both</td>
<td>Xerostomia; Salivary gland dysfunction</td>
</tr>
<tr>
<td>65</td>
<td>Both</td>
<td>Dental abnormalities; Temporomandibular joint dysfunction</td>
</tr>
<tr>
<td>67</td>
<td>Both</td>
<td>Thyroid nodules</td>
</tr>
<tr>
<td>68</td>
<td>Both</td>
<td>Thyroid cancer</td>
</tr>
<tr>
<td>69</td>
<td>Both</td>
<td>Hypothyroidism</td>
</tr>
<tr>
<td>73</td>
<td>Female</td>
<td>Breast cancer</td>
</tr>
<tr>
<td>74</td>
<td>Female</td>
<td>Breast tissue hypoplasia</td>
</tr>
<tr>
<td>75</td>
<td>Both</td>
<td>Pulmonary toxicity</td>
</tr>
<tr>
<td>76</td>
<td>Both</td>
<td>Lung cancer</td>
</tr>
<tr>
<td>80</td>
<td>Both</td>
<td>Impaired glucose metabolism/diabetes mellitus</td>
</tr>
<tr>
<td>81</td>
<td>Both</td>
<td>Dyslipidemia</td>
</tr>
<tr>
<td>86</td>
<td>Both</td>
<td>Colorectal cancer</td>
</tr>
<tr>
<td>87</td>
<td>Both</td>
<td>Renal toxicity</td>
</tr>
<tr>
<td>91</td>
<td>Male</td>
<td>Impaired spermatogenesis</td>
</tr>
<tr>
<td>92</td>
<td>Female</td>
<td>Ovarian hormone deficiencies</td>
</tr>
<tr>
<td>93</td>
<td>Female</td>
<td>Diminished ovarian reserve</td>
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<tr>
<td>94</td>
<td>Female</td>
<td>Uterine vascular insufficiency</td>
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<tr>
<td>96</td>
<td>Both</td>
<td>Musculoskeletal growth problems</td>
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</table>
### Hematopoietic Cell Transplant (HCT)

<table>
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<tr>
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</thead>
<tbody>
<tr>
<td>99</td>
<td>Autologous Hematopoietic Cell Transplant (HCT)</td>
<td>Acute myeloid leukemia (AML) Myelodysplasia (MDS)</td>
<td><strong>HISTORY</strong>&lt;br&gt;Fatigue&lt;br&gt;Bleeding&lt;br&gt;Easy bruising&lt;br&gt;Yearly, up to 10 years after transplant</td>
<td><strong>HEALTH LINKS</strong>&lt;br&gt;Reducing the Risk of Subsequent Cancers&lt;br&gt;<strong>COUNSELING</strong>&lt;br&gt;Promptly seek medical attention for fatigue, pallor, petechiae or bone pain. <strong>POTENTIAL CONSIDERATIONS FOR FURTHER TESTING AND INTERVENTION</strong>&lt;br&gt;CBC and bone marrow exam as clinically indicated.</td>
</tr>
</tbody>
</table>

### Additional Information

There is negligible benefit to obtaining a screening CBC in the absence of clinical signs and symptoms for AML/MDS. Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.

- Patient factors: Older age at transplant
- Cancer/Treatment factors: Radiation therapy, alkylating agent chemotherapy, epipodophyllotoxins, anthracyclines, history of non-Hodgkin and Hodgkin lymphoma, peripheral blood stem cells as the stem cell source
- Pre-morbid/Co-morbid medical conditions: Evidence is conflicting that splenectomy modifies risk for AML/MDS

### References


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<th>Periodic Evaluation</th>
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</tr>
</thead>
</table>
| 100   | Hematopoietic Cell Transplant (HCT) | Solid tumors Such as basal cell carcinoma, melanoma, liver cancer | **PHYSICAL**  
Skin self exam  
Monthly  
Dermatologic exam  
Abdominal exam  
Yearly | **HEALTH LINKS**  
Reducing the Risk of Subsequent Cancers  
COUNSELING  
Importance of sun protection measures.  
**POTENTIAL CONSIDERATIONS FOR FURTHER TESTING AND INTERVENTION**  
Dermatology and/or oncology consultation as clinically indicated.  
SYSTEM = SMN  
SCORE = 1 |

**Additional Information**
Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.
- Patient factors: Younger age at transplant
- Cancer/Treatment factors: Radiation therapy (especially TBI), second HCT, umbilical cord blood HCT, haploidentical HCT, unrelated donor transplant, HLA mismatch, T-cell depletion, ATG
- Pre-morbid/Co-morbid medical conditions: Hepatitis C infection, cGVHD, Fanconi anemia, primary immune deficiency

**References**
HEMATOPOIETIC CELL TRANSPLANT (CONT)

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<th>Periodic Evaluation</th>
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</thead>
</table>
| 101 (female) | Hematopoietic Cell Transplant (HCT) | Solid tumors Such as basal cell carcinoma, melanoma, liver cancer, cervical cancer | PHYSICAL
Skin self exam Monthly |
Dermatologic exam Abdominal exam Yearly |
Pelvic exam Every 3-5 years beginning at age 21 years (see “Screening” below for specific recommendations) |
SCREENING
Cervical PAP smear Cervical cancer screening should begin at age 21 years Women: 21 to 29 years: PAP test every 3 years. Women: 30 to 65 years: HPV and PAP test every 5 years (optimal), or PAP test alone every 3 years (alternative). Women: >65 years: No testing for cervical cancer if normal screening results in past 10 years. |

HEALTH LINKS
Reducing the Risk of Subsequent Cancers

COUNSELING
Importance of sun protection measures. Safer sexual practices to reduce HPV transmission. Importance of HPV vaccination.

POTENTIAL CONSIDERATIONS FOR FURTHER TESTING AND INTERVENTION
Dermatology, gynecology and/or oncology consultation as clinically indicated. HPV vaccination per current recommendations.

SYSTEM = SMN
SCORE = 1

Additional Information
Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.

- Patient factors: Younger age at transplant
- Cancer/Treatment factors: Radiation therapy (especially TBI), second HCT, umbilical cord blood HCT, haploidentical HCT, unrelated donor transplant, HLA mismatch, T-cell depletion, ATG
- Pre-morbid/Co-morbid medical conditions: Hepatitis C infection, HPV infection, cGVHD, Fanconi anemia, primary immune deficiency

References
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<tbody>
<tr>
<td>102</td>
<td>Hematopoietic Cell Transplant (HCT)</td>
<td>Hepatic toxicity Chronic hepatitis Cirrhosis Iron overload Cholelithiasis FNH</td>
<td>PHYSICAL Scleral icterus Jaundice Ascites Hepatomegaly Splenomegaly Yearly SCREENING ALT AST Bilirubin Ferritin Base line at entry into long-term follow-up, repeat as clinically indicated</td>
<td>HEALTH LINKS Liver Health Gastrointestinal Health POTENTIAL CONSIDERATIONS FOR FURTHER TESTING AND INTERVENTION Platelet count to evaluate hypersplenism and prothrombin time to evaluate hepatic synthetic function in patients with abnormal liver screening tests. Screen for viral hepatitis in patients with persistently abnormal liver function or any patient transfused prior to 1993. PCR testing for HCV in immunosuppressed patients negative for antibody. Gastroenterology/Hepatology consultation in patients with persistent liver dysfunction or known hepatitis. Hepatitis A and B immunization in at-risk patients lacking immunity. T2* MRI for evaluation of liver iron content. Liver biopsy in patients with evidence of excessive liver iron content (based on clinical context and magnitude of elevation). Phlebotomy or chelation therapy for treatment of iron overload.</td>
</tr>
</tbody>
</table>

**Additional Information**

FNH is a benign change that represents a scar in the liver. FNH is usually an asymptomatic finding noted on MRI or ultrasound of the liver. Continued observation or biopsy may be indicated depending on individual patient factors and imaging features. Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.
- Cancer/Treatment factors: History of multiple transfusions, radiation to the liver, antimetabolite therapy
- Pre-morbid/Co-morbid medical conditions: cGVHD, viral hepatitis, history of SOS, chronic hepatitis C with siderosis, steatosis, cholelithiasis
- Health behaviors: Alcohol use (in relation to hepatic fibrosis and cirrhosis)

**References**

McDonald GB: Hepatobiliary complications of hematopoietic cell transplantation, 40 years on. Hepatology 51:1450-60, 2010
McKay PJ, Murphy JA, Cameron S, et al: Iron overload and liver dysfunction after allogeneic or autologous bone marrow transplantation. Bone Marrow Transplant 17:63-6, 1996
## Hematopoietic Cell Transplant (HCT)

### Osteonecrosis (Avascular Necrosis)

#### History
- Joint pain
- Swelling
- Immobility
- Limited range of motion
- Yearly

#### Physical
- Musculoskeletal exam
- Yearly

### Health Counseling/Further Considerations

**Health Links**
- Osteonecrosis

**Potential Considerations for Further Testing and Intervention**
- MRI as clinically indicated.
- Orthopedic consultation in patients with positive imaging and/or symptoms of osteonecrosis.
- Physical therapy evaluation (for non-pharmacologic pain management, range of motion, strengthening, stretching, functional mobility).

**System = Musculoskeletal**
**Score = 1**

### Additional Information

Osteonecrosis typically occurs during the acute treatment phase, may progress over time or resolve.

Multifocal osteonecrosis is significantly more common (3:1) than unifocal.

Symptomatic lesions confer the greatest risk for collapse.

Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.

- **Patient factors:** Being pubertal or post-pubertal at time of transplant
- **Cancer/Treatment factors:** Corticosteroids (dexamethasone effect is more potent than prednisone), other immunosuppressants, prolonged immunosuppressive therapy (e.g., for cGVHD), TBI, high dose radiation to any bone, allogeneic HCT > autologous HCT
- **Pre-morbid/Co-morbid medical conditions:** Sickle cell disease, cGVHD, pre-transplant osteonecrosis

### References


### Hematopoietic Cell Transplant (HCT)

#### Reduced bone mineral density (BMD)

Defined as Z-score >2 SD below the mean in male survivors <50 years old and premenopausal women or T-score >1 SD below the mean in male survivors >50 years old and postmenopausal women

### Screening

**Bone density evaluation (DXA)**

Adjust for height-age Z-score in survivors < age 20 years

- Baseline BMD at entry into long-term follow-up (2 to 5 years after completion of therapy) with the following recommended actions:
  - If Z-score >1 SD above the mean (normal), repeat at 25 years of age when peak bone mass should be achieved
  - Between these two measurements and thereafter, screen as clinically indicated based on BMD and ongoing risk assessment
  - If Z-score >2 SD below the mean, referral to (or consultation of) a bone health specialist
  - If Z-score >1 and <2 SD below the mean, evaluation for endocrine defects (e.g., hypogonadism or GH deficiency) and consultation with a bone health specialist for further evaluation and interpretation of findings as clinically indicated. Repeat DXA after 2 years and thereafter as clinically indicated based on BMD change (i.e., BMD decline is greater than the DXA least significant change) and ongoing risk assessment

*Pediatric Z-score calculator adjusted for height age: [https://zscore.research.chop.edu/calcedbonedens.php](https://zscore.research.chop.edu/calcedbonedens.php)*

### Health Counseling/Further Considerations

#### Health Links

**Bone Health**

**Resources**

- National Osteoporosis Foundation: [www.noof.org](http://www.noof.org)

#### Potential Considerations for Further Testing and Intervention

Ensure the AAP recommended minimum daily intake of vitamin D (400 IU/day) for infants <12 months, 600 IU/day for those aged 12 months through aged 70 years, 800 IU/day for those >70 years

Ensure adequate dietary calcium (see table in the “Bone Health” Health Link for age-appropriate recommendations). Supplements may be necessary if there are dietary restrictions.

Use caution regarding calcium supplementation in patients with history of renal lithiasis. Advocate for regular weight-bearing exercises such as running and jumping. Treat exacerbating or predisposing conditions (e.g., hormonal replacement therapy for hypogonadism, GH deficiency, correction of chronic metabolic acidosis that could accelerate bone loss). Endocrine consultation for patients with osteoporosis or history of multiple fractures for pharmacologic interventions (e.g., bisphosphonates, calcitonin, selective estrogen receptor modulators).

### System = Musculoskeletal

**Score = 2B**

### Additional Information

The World Health Organization definition of osteoporosis in adults is based on comparison of a measured BMD of young adults at peak bone age and defined as a T-score. A T-score is the number of standard deviations the BMD measurement is above or below the mean.

Current definitions of osteopenia (T-scores between 1.0 and 2.5 SD below the mean) and osteoporosis (T-scores >2.5 SD below the mean) were developed primarily in the context of postmenopausal women. In this population, T-scores have a well-validated correlation with fracture risk that increases with age.

The fracture risk associated with T-scores in younger populations, including cancer survivors with treatment-related hypogonadism, has not been established.

T-scores are not appropriate to assess skeletal health in pediatric patients who have not achieved peak adult bone mass.

Pediatric BMD reference data sets calculate Z-scores based on age and gender.

A Z-score is the number of standard deviations the measurement is above or below the age-matched mean BMD.

The fracture risk in pediatric patients with low bone density for chronologic age based on Z-scores has not been established.

There are no defined standards for referral or treatment of low BMD in children.
Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.

- **Patient factors:** Caucasian race, lower weight/BMI.
- **Cancer/Treatment factors:** Corticosteroids (especially prolonged therapy, e.g., for cGVHD), CRT, craniospinal radiation, HCT/TBI.
- **Pre-morbid/Co-morbid medical conditions:** GH deficiency, hypogonadism/delayed puberty, hyperthyroidism, central and primary hypogonadism.
- **Health behaviors:** Intake of calcium and vitamin D, intake of alcohol and carbonated beverages, lack of weight bearing exercise, smoking.

References


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<th>Health Counseling/Further Considerations</th>
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<tbody>
<tr>
<td>105</td>
<td>Hematopoietic Cell Transplant (HCT)</td>
<td>Renal toxicity Glomerular injury Renal insufficiency Hypertension Tubular injury (renal tubular acidosis, Fanconi syndrome, hypophosphatemic rickets)</td>
<td>PHYSICAL Blood pressure Yearly SCREENING BUN Creatinine Na, K, Cl, CO₂, Ca, Mg, PO₄ Baseline at entry into long-term follow-up, repeat as clinically indicated</td>
<td>HEALTH LINKS Kidney Health Cardiovascular Risk Factors COUNSELING In patients with salt-wasting tubular dysfunction, educate that low magnesium levels potentiate coronary atherosclerosis. POTENTIAL CONSIDERATIONS FOR FURTHER TESTING AND INTERVENTION Electrolyte supplements for patients with persistent electrolyte wasting. Nephrology consultation for patients with hypertension or progressive renal insufficiency.</td>
</tr>
</tbody>
</table>

**Additional Information**
Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.
- Patient factors: Older age
- Cancer/Treatment factors: Chronic cyclosporine use, TBI
- Pre-morbid/Co-morbid medical conditions: Acute kidney injury within 6 months of HCT, history of cGVHD

**References**
## Hematopoietic Cell Transplant (HCT) with any history of cGVHD

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</thead>
<tbody>
<tr>
<td>106</td>
<td>Hematopoietic Cell Transplant (HCT) with any history of cGVHD</td>
<td>Dermatologic toxicity</td>
<td>PHYSICAL</td>
<td>HEALTH LINKS</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Permanent alopecia</td>
<td>Skin self exam</td>
<td>Skin Health</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Nail dystrophy</td>
<td>Every 3 months</td>
<td>POTENTIAL CONSIDERATIONS FOR FURTHER TESTING AND INTERVENTION</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Vitiligo</td>
<td>Hair (alopecia)</td>
<td>Surgery, dermatology, and/or oncology consultation as clinically indicated.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Sclerodermatous changes</td>
<td>Nails (dystrophy)</td>
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<tr>
<td></td>
<td></td>
<td>Squamous cell carcinoma of the skin</td>
<td>Vitiligo, atypical and changing skin lesions, sclerodermatous changes)</td>
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<td></td>
<td>Melanoma</td>
<td>Yearly</td>
<td>SYSTEM = Dermatologic</td>
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<td></td>
<td>Altered skin pigmentation</td>
<td></td>
<td>SCORE = 1</td>
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### Additional Information

Dermatologic toxicity is more common in presence of active cGVHD; effects may persist after cGVHD resolves.

### References


### Hematopoietic Cell Transplant (HCT) with any history of cGVHD

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| 107   | Hematopoietic Cell Transplant (HCT) with any history of cGVHD | Xerophthalmia (keratoconjunctivitis sicca) | HISTORY  
Dry eyes (burning, itching, foreign body sensation, inflammation)  
Yearly  
PHYSICAL  
Eye exam  
Yearly  
SCREENING  
Evaluation by ophthalmologist or optometrist  
Yearly | HEALTH LINKS  
Eye Health  
POTENTIAL CONSIDERATIONS FOR FURTHER TESTING AND INTERVENTION  
Supportive care with artificial tears.  
SYSTEM = Ocular  
SCORE = 1 |

#### Additional Information

Xerophthalmia is more common in presence of active cGVHD; effects may persist after cGVHD resolves.

Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.

- Cancer/Treatment factors: Cranial radiation, higher radiation dose, especially ≥30 Gy, radiation fraction ≥2 Gy, radiomimetic chemotherapy (e.g., doxorubicin, dactinomycin)

#### References


HEMATOPOIETIC CELL TRANSPLANT WITH CHRONIC GVHD (CONT)

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<td>Dental caries</td>
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<td></td>
<td></td>
<td>Periodontal disease</td>
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<td></td>
<td></td>
<td>Oral cancer (squamous cell carcinoma)</td>
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**SYSTEM = Dental **

**SCORE = 1**

**HEALTH LINKS**
Dental Health

**COUNSELING**

Safer sexual practices to reduce HPV transmission.
Importance of HPV vaccination.

**POTENTIAL CONSIDERATIONS FOR FURTHER TESTING AND INTERVENTION**

Supportive care with saliva substitutes, moistening agents, and sialagogues (pilocarpine).
Regular dental care including fluoride applications and intraoral malignancy screening.
Head and neck/otolaryngology consultation as indicated.

HPV vaccination per current recommendations.

**Additional Information**

Oral-dental late effects are more common in presence of active cGVHD; effects may persist after cGVHD resolves.
Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.

- Cancer/Treatment factors: Use of azathioprine for cGVHD management, head and neck radiation involving the parotid gland, higher radiation dose, especially ≥30 Gy, radiomimetic chemotherapy (e.g., doxorubicin, daclintomycin)
- Pre-morbid/Co-morbid medical conditions: High grade of cGVHD, Fanconi anemia, dyskeratosis congenita, HPV infection

**References**


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<td></td>
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<td>Bronchiectasis</td>
<td>Shortness of breath</td>
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<td>Dyspnea on exertion</td>
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<td>PHYSICAL</td>
<td>Pulmonary exam</td>
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<td>SCREENING</td>
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<td></td>
<td></td>
<td>PFTs (including DLCO and spirometry)</td>
<td>Baseline at entry into long-term follow-up, repeat as clinically indicated in patients with abnormal results or progressive pulmonary dysfunction</td>
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**SYSTEM = Pulmonary SCORE = 1**

**Additional Information**

Pulmonary late effects are more common in presence of active cGVHD; effects may persist after cGVHD resolves.

- Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.
  - Cancer/Treatment factors: Prolonged immunosuppression related to cGVHD, chest radiation, TBI, pulmonary toxic chemotherapy (e.g., busulfan, bleomycin, carmustine [BCNU], lomustine [CCNU])
  - Health behaviors: Smoking, inhaled illicit drug use

**References**


HEMATOPOIETIC CELL TRANSPLANT

110 Hematopoietic Cell Transplant (HCT) with any history of cGVHD

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<td>Immunologic complications</td>
<td>HISTORY</td>
<td>POTENTIAL CONSIDERATIONS FOR FURTHER TESTING AND INTERVENTION</td>
</tr>
<tr>
<td>Secretory IgA deficiency</td>
<td></td>
<td>Administer pneumocystis jirovecii pneumonia prophylaxis, consider antibiotic prophylaxis for encapsulated organisms, and anti-viral and anti-fungal prophylaxis in patients with active cGVHD for duration of immunosuppressive therapy.</td>
</tr>
<tr>
<td>Hypogammaglobulinemia</td>
<td></td>
<td>Immunize with inactivated vaccines for all patients according to published guidelines; postponing vaccination in patients with GVHD is not recommended with the exception of live vaccines.</td>
</tr>
<tr>
<td>Decreased B cells</td>
<td></td>
<td>Immunology or infectious diseases consultation for assistance with management of infections.</td>
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<tr>
<td>T cell dysfunction</td>
<td></td>
<td>Some patients with hypogammaglobulinemia require lifelong IgG replacement.</td>
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<td>Chronic infections (e.g., conjunctivitis, sinusitis, and bronchitis)</td>
<td>PHYSICAL</td>
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<tr>
<td>Eye exam</td>
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<td>Yearly</td>
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<td>Nasal exam</td>
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<td>Pulmonary exam</td>
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</table>

SYSTEM = Immune SCORE = 1

Additional Information

Immunologic complications related to cGVHD may persist or resolve over time. Immunologic abnormalities may persist for up to 20 years post transplant. Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.

- Pre-morbid/Co-morbid medical conditions: Active cGVHD, prolonged immunosuppression related to cGVHD and its treatment

References


Mordv T, Kolstad A, Endresen P, et al: Persistent changes in the immune system 4-10 years after ABMT. Bone Marrow Transplant 24:873-8, 1999


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<tr>
<td>111</td>
<td>Hematopoietic Cell Transplant (HCT) with CURRENTLY ACTIVE cGVHD</td>
<td>Functional asplenia At risk for life-threatening infection with encapsulated organisms (e.g., Haemophilus influenzae, Streptococcus pneumoniae, meningococcus)</td>
<td>PHYSICAL Physical exam at time of febrile illness to evaluate degree of illness and potential source of infection When febrile T ≥101°F (38.3°C) as indicated for patients with active cGVHD</td>
<td>HEALTH LINKS Splenic Precautions</td>
</tr>
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</table>

**COUNSELING**
Risk of life-threatening infections with encapsulated organisms.
Risk associated with malaria and tick-borne diseases if living in or visiting endemic areas.
Obtain medical alert bracelet/card noting functional asplenia.
Discuss importance of immunization with Pneumococcal, Meningococcal (including serotype B), Influenza and Hib vaccines according to current ACIP recommendations.
For further details regarding antibiotic prophylaxis and immunizations, see current edition of AAP Red Book.

**POTENTIAL CONSIDERATIONS FOR FURTHER TESTING AND INTERVENTION**
Antibiotic prophylaxis for encapsulated organisms and bacteremia/endocarditis prophylaxis for duration of immunosuppressive therapy for cGVHD (see: American Academy of Pediatric Dentistry, Guideline on Antibiotic Prophylaxis for Dental Patients at Risk for Infection).
Administer a long-acting, broad-spectrum parenteral antibiotic (e.g., ceftriaxone) in patients with T ≥101°F (38.3°C) or other signs of serious illness and continue close medical monitoring while awaiting blood culture results.
Hospitalize and broaden antimicrobial coverage (e.g., addition of vancomycin) under certain circumstances, such as the presence of marked leukocytosis, neutropenia, or significant change from baseline CBC, toxic clinical appearance, fever ≥104°F (40°C), meningitis, pneumonia, or other serious focus of infection, signs of septic shock, or previous history of serious infection.

**SYSTEM = Immune**
**SCORE = 1**

**Additional Information**
Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.
- Cancer/Treatment factors: Splenic radiation, ongoing immunosuppression
- Pre-morbid/Co-morbid medical conditions: Hypogammaglobulinemia

**References**


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**Additional Information**

Esophageal stricture related to cGVHD is generally not reversible over time.
Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.

- Cancer/Treatment factors: Radiation involving the esophagus, radiation dose ≥30 Gy (increased risk with higher radiation dose, particularly dose ≥40 Gy)
- Pre-morbid/Co-morbid medical conditions: Gastroesophageal reflux, candida esophagitis, gut GVHD

**References**

Williams M: Gastrointestinal manifestations of graft-versus-host disease: diagnosis and management. AACN Clin Issues 10:500-6, 1999
### Hematopoietic Cell Transplant (HCT) with any history of cGVHD

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<td>COUNSELING</td>
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<td></td>
<td>Vaginal fibrosis/stenosis</td>
<td>Psychosocial assessment</td>
<td>Avoid frequent contact with irritants (bubble bath, wet wipes and soaps).</td>
</tr>
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<td></td>
<td>Dyspareunia</td>
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<td>Post-coital bleeding</td>
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<td></td>
<td>Difficulty with tampon insertion</td>
<td>Psychological consultation in patients with emotional difficulties.</td>
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<tr>
<td></td>
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<td></td>
<td>Vaginal dryness</td>
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<td></td>
<td></td>
<td></td>
<td>Vulvar pain/tenderness</td>
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<td></td>
<td>Vulvovaginal burning or pruritus</td>
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<td></td>
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<td></td>
<td>Dysuria</td>
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<td>Yearly</td>
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<td>PHYSICAL</td>
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<td></td>
<td></td>
<td>Exam of genitalia for lichen planus-like features, erosions, fissures, ulcers</td>
<td>Yearly</td>
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</table>

### Additional Information

Vulvovaginal cGVHD is rare before the onset of puberty, but should be considered beyond thelarche. Estrogen deficiency and infection (HPV/HSV, yeast, bacteria and other recognized gynecological pathogens) should be ruled out before a diagnosis of genital cGVHD is made. Vaginal fibrosis/stenosis related to cGVHD is generally not reversible over time. Physical examination should be done with each assessment for cGVHD to detect vulvar lesions before vaginal stenosis develops.

Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.

- Cancer/Treatment factors: Pelvic radiation

### References


### Hematopoietic Cell Transplant (HCT) with any history of cGVHD

**Joint contractures**

**Periodic Evaluation**

**Physical**
- Musculoskeletal exam
- Yearly

**Potential Considerations for Further Testing and Intervention**
- Consultation with physical therapy, rehabilitation medicine/physiatrist.

**System = Musculoskeletal**

**Score = 1**

### Additional Information

Joint contractures related to cGVHD are generally not reversible over time.

### References

## SURGERY

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| 115   | Amputation           | Amputation-related complications  
Impaired cosmesis  
Functional and activity limitations  
Residual limb integrity problems  
Pain  
Increased energy expenditure  
Impaired quality of life  
Psychological maladjustment | HISTORY  
Phantom pain  
Functional, activity, and fitness limitations  
Yearly | HEALTH LINKS  
Amputation | COUNSELING  
Skin checks  
Signs of poor prosthetic fit  
Residual limb and prosthetic hygiene  
Physical fitness  
Importance of maintaining a healthy weight and lifestyle. |
|       |                      | PHYSICAL               | RESIDUAL LIMB INTEGRITY | FUTURE TESTING AND INTERVENTION |
|       |                      | SCREENING              | Prosthetic evaluation |  
Every 6 months until skeletally mature, then yearly |  
Physical therapy consultation as needed per changing physical status such as weight gain or gait training with a new prosthesis, and for non-pharmacological pain management.  
Occupational therapy consultation as needed to assist with activities of daily living.  
Psychological/social work consultation to assist with emotional difficulties related to body image, marriage, pregnancy, parenting, employment, insurance, depression, sexual health, or high-risk behaviors (e.g., alcohol or tobacco use).  
Vocational counseling/training to identify vocations that will not produce/exacerbate functional limitations. |

### Additional Information
Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.
- Patient factors: Skeletally immature/growing children
- Cancer/Treatment factors: Hemipelvectomy site of amputation (trans-femur amputation, trans-tibia amputation)
- Pre-morbid/Co-morbid medical conditions: Obesity, diabetes, poor residual limb healing

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| 116   | Central venous catheter | Thrombosis, Vascular insufficiency, Infection of retained cuff or line tract, Post-thrombotic syndrome | **HISTORY**  
Tenderness or swelling at previous catheter site  
Yearly  
**PHYSICAL**  
Venous stasis  
Swelling  
Tenderness at previous catheter site  
Yearly | SYSTEM = Cardiovascular  
SCORE = 2A |

**References**

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| 117  | Cystectomy           | Cystectomy-related complications  
Asymptomatic bacteriuria  
Chronic urinary tract infection  
Renal dysfunction  
Vesicoureteral reflux  
Hydronephrosis  
Reservoir calculi  
Spontaneous neobladder perforation  
Vitamin B12/Folate/Carotene deficiency (patients with ileal enterocystoplasty only) | SCREENING  
Vitamin B12 level  
Yearly, starting 5 years after cystectomy  
(patients with ileal enterocystoplasty only)  
Evaluation by urologist  
Yearly | HEALTH LINKS  
Cystectomy  
Kidney Health  
SYSTEM = Urinary  
SCORE  
Reservoir calculi = 2A  
Vitamin B12/folate/carotene deficiency = 2B  
All Else = 1 |

**Additional Information**

All potential late effects for pelvic surgery apply to cystectomy (see also sections 141-145).
Reservoir calculi are stones in the neobladder (a reservoir for urine usually constructed of ileum/colon).

**References**

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<td>Yearly</td>
<td>Vocational rehabilitation referral as clinically indicated.</td>
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</table>

**SYSTEM = Ocular**  
**SCORE = 1**

**Additional Information**  
Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.
- **Patient factors:** Younger age at enucleation
- **Cancer/Treatment factors:** Combination with radiation

**References**
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<td>Pelvic floor dysfunction, Urinary incontinence, Sexual dysfunction</td>
<td>HISTORY&lt;br&gt;Psychosocial assessment&lt;br&gt;Urinary leakage&lt;br&gt;Abdominal pain&lt;br&gt;Dyspareunia&lt;br&gt;Yearly</td>
<td>HEALTH LINKS&lt;br&gt;Ovarian and Reproductive Health&lt;br&gt;COUNSELING&lt;br&gt;Potential for biologic parenthood using gestational surrogate.&lt;br&gt;POTENTIAL CONSIDERATIONS FOR FURTHER TESTING AND INTERVENTION&lt;br&gt;Reproductive endocrinology consultation for patients wishing to pursue pregnancy via gestational surrogate.&lt;br&gt;Female pelvic medicine and reconstructive surgery consultation for patients with urinary complaints after hysterectomy.</td>
</tr>
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**Additional Information**

For patients who also underwent oophorectomy, see also: sections 136-137 (unilateral oophorectomy) or section 138 (bilateral oophorectomy).

Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.

- Cancer/Treatment factors: Pelvic radiation

**References**


### Laparotomy

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<td><strong>PHYSICAL</strong></td>
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</table>

**SYSTEM = GI/Hepatic**  
**SCORE = 1**

---

**Additional Information**

Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.

- Cancer/Treatment factors: Combined with radiation

**References**

### LIMB SPARING PROCEDURE

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<th>Health Counseling/ Further Considerations</th>
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<tbody>
<tr>
<td>121</td>
<td>Limb sparing procedure</td>
<td>Conditions related to limb sparing procedure</td>
<td>HISTORY Functional and activity limitations Yearly PHYSICAL Residual limb integrity Yearly SCREENING Radiograph of affected limb Yearly</td>
<td>HEALTH LINKS Limb Sparring Procedures COUNSELING Potential need to discuss antibiotic prophylaxis prior to dental and invasive procedures with their treating dentist/orthopedic surgeon. POTENTIAL CONSIDERATIONS FOR FURTHER TESTING AND INTERVENTION Physical therapy consultation as needed per changes in functional status (such as post-lengthening, revisions, life changes such as pregnancy), and for non-pharmacological pain management. Psychological consultation as needed to assist with emotional difficulties related to body image, marriage, pregnancy, parenting, employment, insurance, depression or sexual health. Vocational counseling/training to identify vocations that will not produce/ exacerbate functional limitations. SYSTEM = Musculoskeletal SCORE = 1</td>
</tr>
</tbody>
</table>

### Additional Information

Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.
- Patient factors: Younger age at surgery, being skeletally immature, rapid growth spurt
- Cancer/Treatment factors: Tibial endoprosthesis, use of biologic material (allograft or autograft) for reconstruction, radiation to extremity
- Pre-morbid/Co-morbid medical conditions: Obesity, endoprosthetic infection, history of poor healing, infection of reconstruction
- Health behaviors: High level of physical activity (associated with higher risk loosening), low level of physical activity (associated with higher risk of contractures or functional limitations)

### References

### Surgeries

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<tbody>
<tr>
<td>122</td>
<td>Nephrectomy (male)</td>
<td>Hydrocele</td>
<td>PHYSICAL</td>
<td>HEALTH LINKS</td>
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<tr>
<td></td>
<td></td>
<td>Renal toxicity</td>
<td>Height</td>
<td>Single Kidney Health</td>
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<td></td>
<td></td>
<td>Proteinuria</td>
<td>Weight</td>
<td>Kidney Health</td>
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<td></td>
<td>Hyperfiltration</td>
<td>BMI</td>
<td>Cardiovascular Risk Factors</td>
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<tr>
<td></td>
<td></td>
<td>Renal insufficiency</td>
<td>Blood pressure</td>
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<td></td>
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<td>Hypertension</td>
<td>Yearly</td>
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<td><strong>SCREENING</strong></td>
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<td>Na, K, Cl, CO₂, Ca, Mg, PO₄</td>
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<td>Baseline at entry into long-term follow-up, repeat as clinically indicated</td>
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<td>Urine dipstick for protein</td>
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<td></td>
<td>Creatinine with calculated eGFR*</td>
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<td>Yearly</td>
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### Additional Information

Surgery-induced renal atrophy (vanishing kidney) is a rare complication reported in survivors who have undergone retroperitoneal tumor resections. Once this diagnosis is established, annual screening should include evaluations recommended for children treated with nephrectomy.


Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.

- Cancer/Treatment factors: Bilateral Wilms tumor, other nephrotoxic therapy (e.g., cisplatin, carboplatin, ifosfamide, aminoglycosides, amphotericin, immunosuppressants, methotrexate, radiation impacting the kidneys)
- Pre-morbid/Co-morbid medical conditions: Denys-Drash syndrome, WAGR syndrome, hypospadias, cryptorchidism

### References

### Surgery - Nephrectomy (Cont)

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<tr>
<td>123</td>
<td>Nephrectomy</td>
<td>Renal toxicity</td>
<td>PHYSICAL</td>
<td>HEALTH LINKS</td>
</tr>
<tr>
<td></td>
<td>(female)</td>
<td>Proteinuria</td>
<td>Height</td>
<td>Single Kidney Health</td>
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<td>Hyperfiltration</td>
<td>Weight</td>
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<td>Renal insufficiency</td>
<td>BMI</td>
<td>Cardiovascular Risk Factors</td>
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<td>Hypertension</td>
<td>Blood pressure</td>
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#### Additional Information

Surgery-induced renal atrophy (vanishing kidney) is a rare complication reported in survivors who have undergone retroperitoneal tumor resections. Once this diagnosis is established, annual screening should include evaluations recommended for children treated with nephrectomy.


Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.

- Cancer/Treatment factors: Bilateral Wilms tumor, other nephrotoxic therapy (e.g., cisplatin, carboplatin, ifosfamide, aminoglycosides, amphotericin, immunosuppressants, methotrexate, radiation impacting the kidneys)
- Pre-morbid/Co-morbid medical conditions: Denys-Drash syndrome, WAGR syndrome

#### References

**SURGERY**

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<td>124</td>
<td>Neurosurgery-Brain</td>
<td>Neurocognitive deficits Functional deficits in:</td>
<td>HEALTH LINKS&lt;br&gt;<strong>School After Treatment</strong>&lt;br&gt;POTENTIAL CONSIDERATIONS FOR FURTHER TESTING AND INTERVENTION&lt;br&gt;Referral to school liaison in community or cancer center (psychologist, social worker, school counselor) to facilitate acquisition of educational resources and/or social skills training. Psychotropic medication (e.g., stimulants) or evidence-based rehabilitation training. Caution—lower starting dose and assessment of increased sensitivity when initiating therapy is recommended. Referral to community services for vocational rehabilitation or for services for developmentally disabled.</td>
<td><strong>SYSTEM = CNS</strong> <strong>SCORE = 1</strong></td>
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<td></td>
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<td>• Executive function (planning and organization)</td>
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<td>• Sustained attention</td>
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<td>• Memory (particularly visual, sequencing, temporal memory)</td>
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<td>• Processing speed</td>
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<td>• Visual-motor integration</td>
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<td>Learning deficits in math and reading (particularly reading comprehension)</td>
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<td>Diminished IQ</td>
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<td>Behavioral change</td>
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**HISTORY**<br>**Educational and/or vocational progress**<br>Yearly

**SCREENING**<br>**Referral for formal neuropsychological evaluation**<br>Baseline at entry into long-term follow-up, then periodically as clinically indicated for patients with evidence of impaired educational or vocational progress

**Additional Information**

Formal neuropsychological evaluation includes tests of processing speed, computer-based attention, visual motor integration, memory, comprehension of verbal instructions, verbal fluency, executive function and planning.

Neurocognitive deficits vary with extent of surgery, postoperative complications and location. Neurosensory deficits (i.e., vision, hearing) due to tumor or its therapy may complicate neurocognitive outcomes. Extent of deficit depends on age at treatment, intensity of treatment, and time since treatment. New and progressive deficits may emerge over time.

Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.

- **Patient factors:** Younger age at treatment, especially age <3 years, family history of learning or attention problems
- **Cancer/Treatment factors:** Primary CNS tumor, extent and location of resection, longer elapsed time since therapy, combination with methotrexate (IT, IO, high dose IV), cytarabine (high dose IV), radiation dose ≥24 Gy to whole brain, radiation dose ≥40 Gy to local fields, TBI, CRT
- **Pre-morbid/Co-morbid medical conditions:** Pre-morbid learning or attention problems, hydrocephalus/history of shunt placement, seizures, posterior fossa syndrome, CNS infection, neurologic and pulmonary conditions

**References**


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### Additional Information

Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.
- Cancer/Treatment factors: Primary CNS tumor, skull base tumors, optic pathway tumor, hypothalamic tumor, supra-sellar tumor (eye problems)
- Pre-morbid/Co-morbid medical conditions: Hydrocephalus

### References

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<thead>
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<tr>
<td>126</td>
<td>Neurosurgery-Brain</td>
<td>Seizures</td>
<td>HISTORY</td>
<td>POTENTIAL CONSIDERATIONS FOR FURTHER TESTING AND INTERVENTION</td>
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<td>Seizures</td>
<td>Evaluation by neurologist as clinically indicated.</td>
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<td>Yearly</td>
<td>SYSTEM = CNS</td>
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<td>PHYSICAL</td>
<td>SCORE = 1</td>
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<td>Neurologic exam</td>
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<td>Yearly</td>
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</table>

### Additional Information

Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.
- Cancer/Treatment factors: Primary CNS tumor, methotrexate (IV, IT, IO)

### References

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<td>Shunt malfunction</td>
<td>Headaches</td>
<td>Educate patient/family regarding potential symptoms of shunt malfunction.</td>
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<td></td>
<td>Nausea/Vomiting</td>
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<td>Ataxia</td>
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<td>Irritability</td>
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<td>Drowsiness</td>
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<td>Neurologic exam</td>
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<td>SCREENING</td>
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<td>Abdominal x-ray</td>
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<td></td>
<td>After pubertal growth spurt for patients with shunts to assure distal shunt tubing in peritoneum</td>
<td>POTENTIAL CONSIDERATIONS FOR FURTHER TESTING AND INTERVENTION</td>
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<td>Evaluation by neurosurgeon for patients with shunts.</td>
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<td></td>
<td>Per the American Academy of Pediatric Dentistry endocarditis prophylaxis guidelines, antibiotic prophylaxis prior to dental work is indicated for survivors with V-A and V-V shunts, but not for survivors with V-P shunts.</td>
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</table>

**SYSTEM = CNS**

**SCORE = 1**

**Additional Information**

Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.

- Cancer/Treatment factors: Primary CNS tumor

**References**


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<tr>
<td>128</td>
<td>Neurosurgery-Brain (applies only to neurosurgery with potential to affect the hypothalamic-pituitary axis)</td>
<td>Overweight Obesity</td>
<td>PHYSICAL</td>
<td>HEALTH LINKS</td>
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<td></td>
<td>Height</td>
<td>Nutrition and Physical Activity</td>
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<td></td>
<td>Weight</td>
<td>Cardiovascular Risk Factors</td>
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<td>BMI</td>
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<td></td>
<td>COUNSELING</td>
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<td>Obesity-related health risks.</td>
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<td>POTENTIAL CONSIDERATIONS FOR FURTHER TESTING AND INTERVENTION</td>
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<td>Evaluate for central endocrinopathies, including GH deficiency, central hypothyroidism, central adrenal insufficiency, precocious puberty, and gonadotropin deficiency. Refer to endocrine for management of hormonal dysfunction. Evaluate for other co-morbid conditions, including dyslipidemia, hypertension, and impaired glucose metabolism. Refer to dietitian for weight management.</td>
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<td>SYSTEM = Endocrine/Metabolic</td>
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<td>SCORE = 2A</td>
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**Additional Information**

Definition of Overweight: Age 2-20 years BMI for age >85th to <95th percentile. Age ≥21 years BMI ≥25-29.9.

Definition of Obesity: Age 2-20 years BMI for age >95th percentile. Age ≥21 years BMI ≥30.


Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.

- Cancer/Treatment factors: Craniopharyngioma, tumor extension to hypothalamus, surgery in supra-sellar region
- Pre-morbid/Co-morbid medical conditions: Pre-treatment obesity

**References**


### SURGERY

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<td>Neurosurgery-Brain</td>
<td>Diabetes insipidus</td>
<td>HISTORY</td>
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<td>(applies only to</td>
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<td>Assessment of</td>
<td>Hypopituitarism</td>
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<td>neurosurgery with</td>
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<td>excessive thirst/polyuria</td>
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<td>potential to affect</td>
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<td>POTENTIAL CONSIDERATIONS FOR FURTHER TESTING AND INTERVENTION</td>
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<td></td>
<td>the hypothalamic-pituitary axis)</td>
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<td>Na, K, Cl, CO₂, serum osmolality, and urine osmolality as clinically indicated if history consistent with excessive thirst and/or polyuria.</td>
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<td>Evaluation for other central endocrinopathies, including GH deficiency, central hypothyroidism, central adrenal insufficiency, precocious puberty, and gonadotropin deficiency.</td>
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<td>Refer to endocrine to manage hormonal dysfunction.</td>
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<td>Diabetes insipidus is unlikely to occur as a late effect past two years from therapeutic exposure, other causes should be considered in the presence of symptoms.</td>
</tr>
</tbody>
</table>

**SYSTEM = Endocrine/Metabolic**  
**SCORE = 1**

### Additional Information

Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.

- Cancer/Treatment factors: Craniopharyngioma, extension of tumor into hypothalamus, surgery in supra-sellar region, reoperation for recurrent tumor

### References

### SURGERY

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<td>Neurosurgery–Spinal cord</td>
<td>Neurogenic bladder Urinary incontinence</td>
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<td>Urinary urgency/frequency</td>
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<td>Abnormal urinary stream</td>
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<td>Importance of adequate fluid intake, regular voiding, and seeking medical attention for symptoms of voiding dysfunction or urinary tract infection.</td>
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<td>Importance of compliance with recommended bladder catheterization regimen.</td>
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<td>POTENTIAL CONSIDERATIONS FOR FURTHER TESTING AND INTERVENTION</td>
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<td>Urologic consultation for patients with dysfunctional voiding or recurrent urinary tract infections.</td>
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**SYSTEM = CNS**  
**SCORE = 1**

### Additional Information

Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.

- Cancer/Treatment factors: Tumor adjacent to or compressing spinal cord or cauda equina, injury above the level of the sacrum, radiation dose ≥45 Gy to lumbar and/or sacral spine and/or cauda equina, especially radiation dose ≥50 Gy

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<td>Chronic constipation</td>
<td>Benefits of adherence to bowel regimen, including adequate hydration, fiber, laxatives/enemas as clinically indicated.</td>
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<td>POTENTIAL CONSIDERATIONS FOR FURTHER TESTING AND INTERVENTION</td>
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<td>Rectal exam</td>
<td>GI consultation to establish bowel regimen for patients with chronic impaction or fecal soiling.</td>
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</table>

**SYSTEM = CNS**  
**SCORE = 1**

**Additional Information**
Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.
- Cancer/Treatment factors: Tumor adjacent to or compressing spinal cord or cauda equina, injury above the level of the sacrum, radiation dose ≥50 Gy to bladder, pelvis, or spine

**References**
### SURGERY

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<td>Use of assisted reproductive technology for sperm retrieval.</td>
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**Additional Information**

Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.

- Cancer/Treatment factors: Tumor adjacent to or compressing spinal cord or cauda equina, radiation to bladder, pelvis, or spine, radiation dose $\geq 55$ Gy to penile bulb in adult, $\geq 45$ Gy in prepubertal child
- Pre-morbid/Co-morbid medical conditions: Testosterone deficiency/insufficiency, injury above the level of the sacrum

**References**


**SYSTEM = Reproductive (Male)  
SCORE = 2A**
## Surgically Endangered Sexual Functions

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<td>Altered or diminished sensation, loss of sensation</td>
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<td>SYSTEM = Reproductive (Female)</td>
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<td>Medication use</td>
<td>SCORE = 2A</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Yearly</td>
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</tbody>
</table>

### Additional Information

Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.

- Cancer/Treatment factors: Tumor adjacent to or compressing spinal cord or cauda equina, radiation to bladder, pelvis, or spine
- Pre-morbid/Co-morbid medical conditions: Hypogonadism, vaginal fibrosis/stenosis, cGVHD, injury above the level of the sacrum

### References


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<tr>
<td>134</td>
<td>Neurosurgery-Spinal cord Laminectomy Laminoplasty</td>
<td>Scoliosis/Kyphosis</td>
<td><strong>PHYSICAL</strong>&lt;br&gt;Exam of back/spine&lt;br&gt;Yearly until growth completed, may need more frequent assessment during puberty or if curve detected</td>
<td><strong>HEALTH LINKS</strong>&lt;br&gt;Scoliosis and Kyphosis&lt;br&gt;POTENTIAL CONSIDERATIONS FOR FURTHER TESTING AND INTERVENTION&lt;br&gt;Spine films in patients with clinically apparent curve. Orthopedic consultation as indicated based on physical and/or radiographic exam.&lt;br&gt;SYSTEM = Musculoskeletal&lt;br&gt;SCORE = 1</td>
</tr>
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</table>

### Additional Information

Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.

- **Patient factors:** Young age (deformity can still develop even if skeletally mature at time of surgery)
- **Cancer/Treatment factors:** Radiation to the spine, increasing number of laminae removed, especially >3 laminae removed, facetectomy, laminectomy (versus laminotomy), laminectomy without fusion, increasing number of resections, surgery of thoracolumbar junction
- **Pre-morbid/Co-morbid medical conditions:** Preoperative deformity

### References


### SURGERY

#### OOPHOROPEXY

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<td>135 (female)</td>
<td>Oophoropexy</td>
<td>Oophoropexy-related complications</td>
<td>HISTORY&lt;br&gt;Inability to conceive&lt;br&gt;Dyspareunia&lt;br&gt;Abdominal pain&lt;br&gt;Pelvic pain&lt;br&gt;Yearly</td>
<td>POTENTIAL CONSIDERATIONS FOR FURTHER TESTING AND INTERVENTION&lt;br&gt;Gynecologic consultation for patients with positive history.&lt;br&gt;SYSRIA = Reproductive (Female)&lt;br&gt;SCORE = 2A</td>
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</table>

### Additional Information

Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.

- Cancer/Treatment factors: Ovarian radiation, tubo-ovarian dislocation (especially with lateral ovarian transposition)

### References


### Surgeries

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</table>
| 136 (female) | Oophorectomy unilateral | Ovarian hormone deficiencies Delayed puberty Arrested puberty Premature ovarian insufficiency/Premature menopause | HISTORY
Onset and tempo of puberty Menstrual history Sexual function (vaginal dryness, libido) Menopausal symptoms Medication use Yearly
PHYSICAL
Tanner staging until sexually mature Yearly
Monitor growth until mature Yearly | HEALTH LINKS
Ovarian and Reproductive Health
COUNSELING
Adverse impact of ovarian hormone deficiencies on growth, bone mineralization, cardiovascular disease and sexual dysfunction.
POTENTIAL CONSIDERATIONS FOR FURTHER TESTING AND INTERVENTION
FSH and estradiol and/or endocrine/gynecology referral for patients with:
- No signs of puberty by age 13 years
- Failure of pubertal progression
- Abnormal menstrual patterns or menopausal symptoms
- Ovarian hormone deficiency/insufficiency to weigh risks and benefits of hormonal replacement therapy
Bone density evaluation in patients with ovarian hormone deficiencies. | SYSTEM = Reproductive (Female)  
SCORE = 2A |

### Additional Information

Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.

- Cancer/Treatment factors: Combination with pelvic radiation, TBI, or alkylating agents
- Health behaviors: Smoking

### References


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</table>
| 137  | Oophorectomy unilateral | Diminished Ovarian Reserve (DOR) Infertility | HISTORY  
Menstrual and pregnancy history  
Hormonal therapy  
Yearly  
PHYSICAL  
Tanner staging until sexually mature  
Yearly | HEALTH LINKS  
Ovarian and Reproductive Health  
RESOURCES  
American Society for Reproductive Medicine: www.asrm.org  
Alliance for Fertility Preservation: www.allianceforfertilitypreservation.org  
Livestrong Foundation: www.livestrong.org/what-we-do/program/fertility  
Oncofertility Consortium: https://oncofertility.msu.edu  
COUNSELING  
Potential for shorter period of fertility in family planning. Those with DOR should consider discussing reproductive health options with a reproductive endocrinologist or fertility specialist.  
Review previous fertility preservation counseling/interventions.  
Need for contraception.  
POTENTIAL CONSIDERATIONS FOR FURTHER TESTING AND INTERVENTION  
FSH and estradiol for patients with menstrual cycle dysfunction suggestive of premature ovarian insufficiency or those who desire information about potential for future fertility.  
AMH to assess for DOR.  
Reproductive endocrinology referral for antral follicle count, ovarian reserve evaluation and consultation regarding assisted reproductive technologies in at-risk patients who desire information about potential fertility and interventions to preserve future fertility. |

**Additional Information**

AMH may be low in the presence of normal FSH. AMH should be interpreted relative to age-specific reference ranges. FSH is lowered and AMH may be lowered by concurrent hormonal contraceptive use.

Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.

- Cancer/Treatment factors: Combination with pelvic radiation, TBI, or alkylating agents
- Health behaviors: Smoking

**References**


### Oophorectomy (Bilateral)

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</table>
| 138   | Oophorectomy bilateral | Ovarian hormone deficiencies  
Absence of puberty  
Loss of ovarian follicular pool  
Infertility | **SCREENING**  
Endocrinologic or gynecologic consultation for initiation of hormonal replacement therapy  
At age 11 years or immediately for post-pubertal patients | **HEALTH LINKS**  
Ovarian and Reproductive Health |
|       |                      |                        |                     | **RESOURCES**  
American Society for Reproductive Medicine: [www.asrm.org](http://www.asrm.org)  
Alliance for Fertility Preservation: [www.allianceforfertilitypreservation.org](http://www.allianceforfertilitypreservation.org)  
Livestrong Foundation [www.livestrong.org/what-we-do/program/fertility](http://www.livestrong.org/what-we-do/program/fertility)  
Oncofertility Consortium [https://oncofertility.msu.edu](https://oncofertility.msu.edu) |
|       |                      |                        |                     | **COUNSELING**  
Benefits of hormone replacement therapy in promoting pubertal progression, bone and cardiovascular health.  
Counsel women regarding pregnancy potential with donor eggs (if intact uterus).  
Review previous fertility preservation counseling/interventions. |
|       |                      |                        |                     | **POTENTIAL CONSIDERATIONS FOR FURTHER TESTING AND INTERVENTION**  
Reproductive endocrinology referral regarding assisted reproductive technologies.  
BMD evaluation. |

**SYSTEM = Reproductive (Female)  
SCORE = 1**

### References

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</table>
| 139 (male) | Orchiectomy unilateral partial | Testicular hormonal dysfunction Testosterone deficiency/insufficiency Delayed/Arrested puberty | HISTORY  
Onset and tempo of puberty  
Sexual function (erections, nocturnal emissions, libido)  
Medication use  
Yearly  
PHYSICAL  
Tanner staging until sexually mature  
Testicular volume by Prader orchidometer  
Yearly  
Monitor growth until mature  
Yearly | HEALTH LINKS  
Testicular and Reproductive Health  
COUNSELING  
Wear athletic supporter with protective cup during athletic activities.  
POTENTIAL CONSIDERATIONS FOR FURTHER TESTING AND INTERVENTION  
Testosterone insufficiency or deficiency requiring hormone replacement after alkylating agents only is rare.  
Endocrine referral for the following:  
- No signs of puberty by age 14 years  
- Failure of pubertal progression  
- Adults with low AM testosterone levels  
Periodic re-evaluation of testosterone in males with low-normal testosterone as they age or if they become symptomatic.  
Bone density evaluation in androgen deficient patients.  
Surgical placement of testicular prosthesis and ongoing monitoring for surgical complications after prosthesis placement.  
Psychology referral (because orchiectomy can be associated with psychological distress related to altered body image).  

**SYSTEM = Reproductive (Male)  
SCORE = 2A**

### Additional Information

Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.  
- Patient factors: Medications (anabolic steroids, testosterone), occupational exposures (pesticides, heavy metals, solvents)  
- Cancer/Treatment factors: Testicular cancer, unilateral orchiectomy combined with pelvic or testicular radiation and/or alkylating agents, higher cumulative dose platinum chemotherapy, infradiaphragmatic radiation  
- Pre-morbid/Co-morbid medical conditions: Obesity, ejaculatory dysfunction, history of sexually transmitted infections  
- Health behaviors: Tobacco/Marijuana use

### References

### ORCHIECTOMY (UNILATERAL, PARTIAL) (CONT)

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<td>Orchiectomy (male)</td>
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<td>Reduced fertility</td>
<td>Sexual function (erections, nocturnal emissions, libido)</td>
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<td></td>
<td></td>
<td>Oligospermia</td>
<td>Medication use</td>
<td>American Society for Reproductive Medicine: <a href="http://www.asrm.org">www.asrm.org</a></td>
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<tr>
<td></td>
<td></td>
<td>Azoospermia</td>
<td>Yearly</td>
<td>Alliance for Fertility Preservation: <a href="http://www.allianceforfertilitypreservation.org">www.allianceforfertilitypreservation.org</a></td>
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<tr>
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<td></td>
<td>Infertility</td>
<td>PHYSICAL</td>
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<td>Tanner staging until sexually mature</td>
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<td>Testicular volume by Prader orchidometer</td>
<td>Review previous fertility preservation counseling/interventions.</td>
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<td>Yearly</td>
<td>Wear athletic supporter with protective cup during athletic activities.</td>
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**POTENTIAL CONSIDERATIONS FOR FURTHER TESTING AND INTERVENTION**

- For sexually mature patients who desire information about potential future fertility: semen analysis (optimal) and/or FSH and inhibin B (alternative if unable or unwilling to provide semen sample).
- Reproductive endocrinology/urology referral for infertility evaluation and consultation regarding assisted reproductive technologies.
- Surgical placement of testicular prosthesis and ongoing monitoring for surgical complications after prosthesis placement.
- Psychology referral (because orchiectomy can be associated with psychological distress related to altered body image).

**SYSTEM = Reproductive (Male)**

**SCORE = 2A**

## Additional Information

Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.

- Patient factors: Medications (anabolic steroids, testosterone), occupational exposures (pesticides, heavy metals, solvents).
- Cancer/Treatment factors: Testicular cancer, unilateral orchiectomy combined with pelvic or testicular radiation and/or alkylating agents, higher cumulative dose platinum chemotherapy, infradiaphragmatic radiation.
- Pre-morbid/Co-morbid medical conditions: Obesity, ejaculatory dysfunction, history of sexually transmitted infections.
- Health behaviors: Tobacco/Marijuana use.

## References

### Orthoectomy (Bilateral)

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</table>
| 141 (male) | Orchiectomy bilateral | Testosterone deficiency  
Absence of puberty  
Azoospermia  
Infertility | PHYSICAL  
Exam of testicular prostheses  
Yearly  
SCREENING  
Endocrinologic consultation for initiation of hormonal replacement therapy  
At age 11 years or immediately for post-pubertal patients | HEALTH LINKS  
Testicular and Reproductive Health  
COUNSELING  
Review previous fertility preservation counseling/interventions.  
POTENTIAL CONSIDERATIONS FOR FURTHER TESTING AND INTERVENTION  
Surgical placement of testicular prostheses and ongoing monitoring for surgical complications after prostheses placement.  
Psychology referral (because orchiectomy can be associated with psychological distress related to altered body image).  
Bone density evaluation. |

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**PELVIC SURGERY**

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<td>142</td>
<td>Pelvic surgery Cystectomy</td>
<td>Urinary incontinence Urinary tract obstruction</td>
<td>HISTORY: Urinary urgency/frequency Urinary incontinence/retention Dysuria Nocturia Abnormal urinary stream Yearly</td>
<td>COUNSELING: Importance of adequate fluid intake, regular voiding, and seeking medical attention for symptoms of voiding dysfunction or urinary tract infection. Importance of compliance with recommended bladder catheterization regimen. POTENTIAL CONSIDERATIONS FOR FURTHER TESTING AND INTERVENTION: Urologic consultation for patients with dysfunctional voiding or recurrent urinary tract infections.</td>
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</table>

**Additional Information**

For patients with cystectomy, see also section 117.

Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.

- Pre-morbid/Co-morbid medical conditions: Tumor adjacent to or compressing spinal cord or cauda equina, retroperitoneal node dissection, extensive pelvic dissection (e.g., bilateral ureteral re-implantation, retroperitoneal tumor resection), radiation to the bladder, pelvis, and/or lumbar-sacral spine

**References**


**SYSTEM = Urinary**

**SCORE = 1**
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<tr>
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<td>Cystectomy</td>
<td></td>
<td>Chronic constipation</td>
<td>Benefits of adherence to bowel regimen, including adequate hydration, fiber, laxatives/enemas as clinically indicated.</td>
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<td>Fecal soiling</td>
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<td></td>
<td></td>
<td>PHYSICAL</td>
<td>POTENTIAL CONSIDERATIONS FOR FURTHER TESTING AND INTERVENTION</td>
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<td>Rectal exam</td>
<td>GI consultation to establish bowel regimen for patients with chronic impaction or fecal soiling.</td>
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**SYSTEM = GI/Hepatic**
**SCORE = 1**

**Additional Information**
Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.
- Cancer/Treatment factors: Tumor adjacent to or compressing spinal cord or cauda equina, radiation to bladder, pelvis, or spine

**References**
## SURGERY

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</table>
| 144 (male) | Pelvic surgery Cystectomy | Psychosexual dysfunction Erectile dysfunction | HISTORY  
Sexual function (erections, nocturnal emissions, libido)  
Medication use  
Yearly | HEALTH LINKS  
Testicular and Reproductive Health  
POTENTIAL CONSIDERATIONS FOR FURTHER TESTING AND INTERVENTION  
Urologic consultation in patients with positive history.  
SYSTEM = Reproductive (Male)  
SCORE = 2A |

### Additional Information

Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.

- Cancer/Treatment factors: Tumor adjacent to spine, retroperitoneal node dissection, retroperitoneal tumor resection, extensive presacral tumor resection, cystectomy, radical prostatectomy, radiation to bladder, pelvis, or spine, or dissection, radiation dose ≥55 Gy to penile bulb in adult, ≥45 Gy in prepubertal child
- Pre-morbid/Co-morbid medical conditions: Hypogonadism

### References

**SURGERY**

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<tr>
<td>145 (male)</td>
<td>Pelvic surgery</td>
<td>Sexual dysfunction (anatomic)</td>
<td><strong>HISTORY</strong> Quality of ejaculate (frothy white urine with first void after intercourse suggests retrograde ejaculation)</td>
<td><strong>HEALTH LINKS</strong> Testicular and Reproductive Health <strong>COUNSELING</strong> Use of assisted reproductive technology for sperm retrieval. <strong>POTENTIAL CONSIDERATIONS FOR FURTHER TESTING AND INTERVENTION</strong> Urologic consultation in patients with positive history. <strong>SYSTEM = Reproductive (Male) SCORE = 2A</strong></td>
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</table>

**Additional Information**

Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.

- Cancer/Treatment factors: Tumor adjacent to spine, retroperitoneal node dissection, retroperitoneal tumor resection, extensive presacral tumor resection, cystectomy, radical prostatectomy, radiation to bladder, pelvis, or spine, or dissection, radiation dose ≥55 Gy to penile bulb in adult, ≥45 Gy in prepubertal child

- Pre-morbid/Co-morbid medical conditions: Hypogonadism

**References**


## PELVIC SURGERY (CONT)

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<tr>
<td>146</td>
<td>Pelvic surgery Cystectomy</td>
<td>Sexual dysfunction</td>
<td>HISTORY: Altered or diminished sensation, loss of sensation, Dyspareunia, Medication use</td>
<td>SYSTEM = Reproductive (Female)</td>
</tr>
</tbody>
</table>

### Additional Information

Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.

- Cancer/Treatment factors: Tumor adjacent to spine, radiation to bladder, pelvis or spine
- Pre-morbid/Co-morbid medical conditions: cGVHD, hypogonadism

### References


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<td>147</td>
<td>Splenectomy</td>
<td>Asplenia</td>
<td>PHYSICAL</td>
<td>HEALTH LINKS</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td><strong>Physical exam at time of febrile illness to evaluate degree of illness and potential source of infection</strong></td>
<td>Splenic Precautions</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>When febrile T ≥101°F (38.3°C)</td>
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<td></td>
<td>SCREENING</td>
<td>Counseling</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Blood culture</td>
<td>Risk of life-threatening infections with encapsulated organisms.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>When febrile T ≥101°F (38.3°C)</td>
<td>Risk of malaria and tick-borne diseases if living in or visiting endemic areas.</td>
</tr>
<tr>
<td></td>
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<td>Obtain medical alert bracelet/card noting asplenia.</td>
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<td></td>
<td>Discuss importance of immunization with Pneumococcal, Meningococcal (including serotype B), Influenza and HIB vaccines according to current ACIP recommendations. For further details regarding antibiotic prophylaxis and immunizations, see current edition of AAP Red Book.</td>
</tr>
<tr>
<td></td>
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<td></td>
<td><strong>POTENTIAL CONSIDERATIONS FOR FURTHER TESTING AND INTERVENTION</strong></td>
</tr>
<tr>
<td></td>
<td></td>
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<td></td>
<td>Administer a long-acting, broad-spectrum parenteral antibiotic (e.g., ceftaroline) in patients with T ≥101°F (38.3°C) or other signs of serious illness and continue close medical monitoring while awaiting blood culture results.</td>
</tr>
<tr>
<td></td>
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<td></td>
<td>Hospitalize and broaden antimicrobial coverage (e.g., addition of vancomycin) under certain circumstances, such as the presence of marked leukocytosis, neutropenia, or significant change from baseline CBC, toxic clinical appearance, fever ≥104°F (40°C), meningitis, pneumonia, or other serious focus of infection, signs of septic shock, or previous history of serious infection. Discuss with dental provider potential need for antibiotic prophylaxis based on planned procedure.</td>
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<td></td>
<td><strong>SYSTEM = Immune</strong></td>
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<td></td>
<td></td>
<td></td>
<td><strong>SCORE = 2A</strong></td>
</tr>
</tbody>
</table>

**References**

- Newland A, Provan D, Myint S: Preventing severe infection after splenectomy - Patients should know the risks, be immunised, and take prophylactic antibiotics. BMJ 331:417-418, 2005
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<td>148</td>
<td>Thoracic surgery</td>
<td>Pulmonary dysfunction</td>
<td>HISTORY</td>
<td>HEALTH LINKS</td>
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<td>Cough</td>
<td>Pulmonary Health</td>
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<td></td>
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<td>Wheezing</td>
<td>RESOURCES</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Shortness of breath</td>
<td><a href="http://www.smokefree.gov">www.smokefree.gov</a></td>
</tr>
<tr>
<td></td>
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<td></td>
<td>Dyspnea on exertion</td>
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<td></td>
<td></td>
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<td>Yearly</td>
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<td></td>
<td>PHYSICAL</td>
<td>COUNSELING</td>
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<td></td>
<td></td>
<td></td>
<td>Pulmonary exam</td>
<td>Tobacco and Environmental tobacco smoke avoidance/Smoking cessation.</td>
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<tr>
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<td></td>
<td>Yearly</td>
<td>Influenza and Pneumococcal vaccinations.</td>
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<td>SCREENING</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>PFTs (including DLCO and spirometry)</td>
<td>POTENTIAL CONSIDERATIONS FOR FURTHER TESTING AND INTERVENTION</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Baseline at entry into long-term follow-up, repeat as clinically indicated in patients with abnormal results or progressive pulmonary dysfunction</td>
<td>Repeat PFTs prior to general anesthesia.</td>
</tr>
<tr>
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<td></td>
<td>Pulmonary consultation for patients with symptomatic pulmonary dysfunction.</td>
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<td></td>
<td>Pulmonary consultation for survivors who desire to SCUBA dive (due to potential undiagnosed pulmonary toxicities, and limited data to guide safe diving recommendations for individuals treated with pulmonary toxic therapy).</td>
</tr>
</tbody>
</table>

**Additional Information**

Thoracic surgery includes thoractomy, chest wall surgery, rib resection, pulmonary lobectomy, pulmonary metastasectomy and pulmonary wedge resection.

Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.

- Cancer/Treatment factors: Combination with pulmonary toxic therapy (e.g., bleomycin, busulfan, carmustine [BCNU], lomustine [CCNU]), combination with chest radiation and TBI
- Pre-morbid/Co-morbid medical conditions: Atopic history
- Health behaviors: Smoking, inhaled illicit drug use

**References**


## Thoracic Surgery

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</table>
| 149   | Thoracic surgery     | Scoliosis/Kyphosis     | PHYSICAL Exam of back/spine | **SYSTEM = Musculoskeletal**  
*SCORE = 2A*  
**HEALTH LINKS**  
Scoliosis and Kyphosis  
**POTENTIAL CONSIDERATIONS FOR FURTHER TESTING AND INTERVENTION**  
Spine films in patients with clinically apparent curve.  
Orthopedic consultation as indicated based on physical and/or radiographic exam. |

### Additional Information

Thoracic surgery includes thoractomy, chest wall surgery, rib resection, pulmonary lobectomy, pulmonary metastasectomy and pulmonary wedge resection.

Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.  
- Patient factors: Young age (deformity can still develop even if skeletally mature at time of surgery)  
- Cancer/Treatment factors: Radiation to the spine, greater number of ribs resected  
- Pre-morbid/Co-morbid medical conditions: Preoperative deformity

### References

### SURGERY

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<td>Thyroidectomy</td>
<td>Hypothyroidism</td>
<td>SCREENING</td>
<td>HEALTH LINKS</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Endocrine consultation for initiation of thyroid hormone replacement Immediately</td>
<td>Thyroid Problems</td>
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<td>COUNSELING</td>
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<td></td>
<td>For females, thyroid levels prior to attempting pregnancy and periodically throughout pregnancy.</td>
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<td></td>
<td></td>
<td>SYSTEM = Endocrine/Metabolic SCORE = 1</td>
</tr>
</tbody>
</table>

### Additional Information

Total thyroidectomy is associated with the risk of hypoparathyroidism. This complication generally occurs in the early postoperative period and may persist. Patients with a history of total thyroidectomy should be monitored for signs and symptoms of hypoparathyroidism (e.g., paresthesias, muscle cramping, altered mental status, hyperreflexia, tetany, hypocalcemia, and hyperphosphatemia).

### References

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<tr>
<td>151</td>
<td>Thyroidectomy partial</td>
<td>Hypothyroidism</td>
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</table>

**HISTORY**
- Fatigue
- Weight gain
- Cold intolerance
- Constipation
- Dry skin
- Brittle hair
- Depressed mood

Yearly, consider more frequent screening during periods of rapid growth

**PHYSICAL**
- Height
- Weight
- Hair
- Skin
- Thyroid exam

Yearly, consider more frequent screening during periods of rapid growth

**SCREENING**
- TSH
- Free T4

Yearly, consider more frequent screening during periods of rapid growth

**HEALTH LINKS**
- Thyroid Problems

**COUNSELING**
For females, thyroid levels prior to attempting pregnancy and periodically throughout pregnancy.

**POSSIBLE CONSIDERATIONS FOR FURTHER TESTING AND INTERVENTION**
Endocrine consultation for thyroid hormone replacement.

**SYSTEM = Endocrine/Metabolic**
**SCORE = 1**

**Additional Information**
Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.

- Cancer/Treatment factors: Thyroid gland in radiation field

**References**


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<tr>
<td>152</td>
<td>Radioiodine therapy (I-131 thyroid ablation)</td>
<td>Lacrimal duct atrophy</td>
<td>HISTORY Excessive tearing Yearly</td>
<td>POTENTIAL CONSIDERATIONS FOR FURTHER TESTING AND INTERVENTION Ophthalmology consultation as clinically indicated. SYSTEM = Ocular SCORE = 2A</td>
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**References**


### OTHER THERAPEUTIC MODALITIES

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<tr>
<td>153</td>
<td>Radioiodine therapy (I-131 thyroid ablation)</td>
<td>Hypothyroidism</td>
<td>HISTORY&lt;br&gt;Fatigue&lt;br&gt;Weight gain&lt;br&gt;Cold intolerance&lt;br&gt;Constipation&lt;br&gt;Dry skin&lt;br&gt;Brittle hair&lt;br&gt;Depressed mood&lt;br&gt;Yearly, consider more frequent screening during periods of rapid growth</td>
<td>HEALTH LINKS&lt;br&gt;Thyroid Problems&lt;br&gt;COUNSELING&lt;br&gt;For females, thyroid levels prior to attempting pregnancy and periodically throughout pregnancy. &lt;br&gt;POTENTIAL CONSIDERATIONS FOR FURTHER TESTING AND INTERVENTION&lt;br&gt;Endocrine consultation for thyroid hormone replacement.</td>
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<td></td>
<td>PHYSICAL&lt;br&gt;Height&lt;br&gt;Weight&lt;br&gt;Hair&lt;br&gt;Skin&lt;br&gt;Thyroid exam&lt;br&gt;Yearly, consider more frequent screening during periods of rapid growth</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>SCREENING&lt;br&gt;TSH&lt;br&gt;Free T4&lt;br&gt;Yearly, consider more frequent screening during periods of rapid growth</td>
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**References**


**SYSTEMIC RADIATION (CONT)**
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<tr>
<td>154</td>
<td>Radioiodine therapy (I-131 thyroid ablation)</td>
<td>Xerostomia, Salivary gland dysfunction, Chronic sialadenitis</td>
<td>HISTORY</td>
<td>HEALTH LINKS</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Xerostomia</td>
<td>Dental Health</td>
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<td></td>
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<td>Yearly</td>
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<td></td>
<td></td>
<td></td>
<td>PHYSICAL</td>
<td>POTENTIAL CONSIDERATIONS FOR FURTHER TESTING AND INTERVENTION</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Oral Exam</td>
<td>Supportive care with saliva substitutes, moistening agents, and sialagogues (pilocarpine).</td>
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<td></td>
<td></td>
<td>Yearly</td>
<td>Regular dental care including fluoride applications.</td>
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<td></td>
<td>SCREENING</td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td>Dental Exam and Cleaning</td>
<td>SYSTEM = Oral/Dental</td>
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<td></td>
<td></td>
<td></td>
<td>Every 6 months</td>
<td>SCORE</td>
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References


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<th>Health Counseling/ Further Considerations</th>
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</table>
| 155   | Systemic MIBG (in therapeutic doses) | Hypothyroidism | HISTORY  
Fatigue  
Weight gain  
Cold intolerance  
Constipation  
Dry skin  
Brittle hair  
Depressed mood  
Yearly, consider more frequent screening during periods of rapid growth  
PHYSICAL  
Height  
Weight  
Hair  
Skin  
Thyroid exam  
Yearly, consider more frequent screening during periods of rapid growth  
SCREENING  
TSH  
Free T4  
Yearly, consider more frequent screening during periods of rapid growth | HEALTH LINKS  
Thyroid Problems  
COUNSELING  
For females, thyroid levels prior to attempting pregnancy and periodically throughout pregnancy.  
POTENTIAL CONSIDERATIONS FOR FURTHER TESTING AND INTERVENTION  
Endocrine consultation for thyroid hormone replacement.  
SYSTEM = Endocrine/Metabolic  
SCORE = 1 |

### Additional Information

MIBG used for diagnostic purposes (i.e., MIBG scanning) does NOT put patients at risk for hypothyroidism.

### References

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<tr>
<td>156</td>
<td>Systemic MIBG (in therapeutic doses)</td>
<td>Thyroid nodules</td>
<td>PHYSICAL</td>
<td>HEALTH LINKS</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Thyroid exam</td>
<td>Thyroid Problems</td>
</tr>
<tr>
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<td></td>
<td>Yearly</td>
<td>POTENTIAL CONSIDERATIONS FOR FURTHER TESTING AND INTERVENTION</td>
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<td></td>
<td></td>
<td>Ultrasound for evaluation of palpable nodule(s).</td>
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<td>FNA as clinically indicated.</td>
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<td></td>
<td>Endocrine and/or surgical consultation for further management.</td>
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SYSTEM = SMN
SCORE = 2A

References
### OTHER THERAPEUTIC MODALITIES

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<th>Health Counseling/ Further Considerations</th>
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<tbody>
<tr>
<td>157</td>
<td>Systemic MIBG (in therapeutic doses)</td>
<td>Thyroid cancer</td>
<td>PHYSICAL Thyroid exam Yearly</td>
<td>HEALTH LINKS Thyroid Problems POTENTIAL CONSIDERATIONS FOR FURTHER TESTING AND INTERVENTION Ultrasound for evaluation of palpable nodule(s). FNA as clinically indicated. Endocrine and/or surgical consultation for further management. SYSTEM = SMN SCORE = 2A</td>
</tr>
</tbody>
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### References
### OTHER THERAPEUTIC MODALITIES

#### BIOIMMUNOTHERAPY

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<th>Periodic Evaluation</th>
<th>Health Counseling/ Further Considerations</th>
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</table>
| 158   | Bioimmunotherapy     | Insufficient information currently available regarding late effects | | SYSTEM = No Known Late Effects  
SCORE = N/A |
### OTHER THERAPEUTIC MODALITIES

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<td>159</td>
<td>BCR-ABL tyrosine kinase inhibitors (e.g., imatinib, dasatinib, nilotinib)</td>
<td>Growth attenuation</td>
<td><strong>HISTORY</strong>&lt;br&gt;Parental heights at baseline&lt;br&gt;Growth rate&lt;br&gt;Signs of puberty&lt;br&gt;Yearly&lt;br&gt;<strong>PHYSICAL</strong>&lt;br&gt;Tanner staging every 6 months until sexually mature&lt;br&gt;Height and weight measured at every visit, at least every 6 months&lt;br&gt;Plot growth velocity</td>
<td><strong>POTENTIAL CONSIDERATIONS FOR FURTHER TESTING AND INTERVENTION</strong>&lt;br&gt;Endocrine consultation for poor growth for age or stage of puberty as evidenced by decline in growth velocity and change in percentile rankings on growth chart.&lt;br&gt;Need for systematic study of the use of GH in children on chronic TKI therapy.&lt;br&gt;&lt;br&gt;<strong>SYSTEM = Endocrine/Metabolic</strong>&lt;br&gt;<strong>SCORE = 2A</strong></td>
</tr>
</tbody>
</table>

### Additional Information

Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.

- Cancer/Treatment factors: Cranial/CRT, HCT, chronic steroid treatment

### References


## OTHER THERAPEUTIC MODALITIES

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<th>Health Counseling/ Further Considerations</th>
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<tr>
<td>160</td>
<td>BCR-ABL tyrosine kinase inhibitors (e.g., imatinib, dasatinib, nilotinib)</td>
<td>Hypothyroidism</td>
<td>HISTORY&lt;br&gt;Fatigue&lt;br&gt;Weight gain&lt;br&gt;Cold intolerance&lt;br&gt;Constipation&lt;br&gt;Dry skin&lt;br&gt;Brittle hair&lt;br&gt;Depressed mood&lt;br&gt;Yearly, consider more frequent screening during periods of rapid growth</td>
<td>HEALTH LINKS&lt;br&gt;Thyroid Problems&lt;br&gt;COUNSELING&lt;br&gt;For females, thyroid levels prior to attempting pregnancy and periodically throughout pregnancy. POTENTIAL CONSIDERATIONS FOR FURTHER TESTING AND INTERVENTION&lt;br&gt;Other forms of thyroid dysfunction (hyperthyroidism) may occur. Endocrine consultation for thyroid hormone replacement.</td>
</tr>
</tbody>
</table>

### HEALTH LINKS

**Thyroid Problems**

### COUNSELING

For females, thyroid levels prior to attempting pregnancy and periodically throughout pregnancy.

### POTENTIAL CONSIDERATIONS FOR FURTHER TESTING AND INTERVENTION

Other forms of thyroid dysfunction (hyperthyroidism) may occur. Endocrine consultation for thyroid hormone replacement.

**SYSTEM = Endocrine/Metabolic**<br>**SCORE = 2B**

### Additional Information

Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.

- Cancer/Treatment factors: Thyroid gland in radiation field

### References


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<th>Health Counseling/ Further Considerations</th>
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<tr>
<td>161</td>
<td>Other targeted biologic therapies</td>
<td>Insufficient information currently available regarding late effects</td>
<td></td>
<td>SYSTEM = No Known Late Effects SCORE = N/A</td>
</tr>
</tbody>
</table>
### OTHER THERAPEUTIC MODALITIES

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<tr>
<td>162</td>
<td>B-cell directed antibody-based therapies (rituximab)</td>
<td>Immunologic complications Hypogammaglobulinemia</td>
<td>HISTORY Recurrent unusual infections SCREENING Serum quantitative immunoglobulins Baseline at entry into long-term follow-up, repeat as clinically indicated in patients with abnormal results</td>
<td>POTENTIAL CONSIDERATIONS FOR FURTHER TESTING AND INTERVENTION Immunology or infectious diseases consultation for assistance with management of infections. Some patients with hypogammaglobulinemia require lifelong IgG replacement. SYSTEM = Immune SCORE = 2A</td>
</tr>
</tbody>
</table>

### Additional Information

Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.
- Cancer/Treatment factors: Prior HCT
- Pre-morbid/Co-morbid medical conditions: Underlying primary immunodeficiency

### References

### OTHER THERAPEUTIC MODALITIES

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| 163   | Other antibody-based immune therapies, including antibody drug conjugates (e.g., blinatumomab, brentuximab vedotin, inotuzumab, gemtuzumab ozogamicin, dinutuximab, naxitamab, pembrolizumab, ipilimumab, nivolumab, atezolizumab) | Insufficient information currently available regarding late effects                  |                     | SYSTEM = No Known Late Effects
<p>|       |                                                                                      |                                                                                        |                     | SCORE = N/A                               |</p>
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<tr>
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</table>
| 164   | **SCREENING**
Refer to the Centers for Disease Control and Prevention recommendations for screening, vaccines, and healthy choices: [www.cdc.gov/cancer/dcpc/prevention](http://www.cdc.gov/cancer/dcpc/prevention) |

<table>
<thead>
<tr>
<th></th>
<th>Health Counseling/ Further Considerations</th>
</tr>
</thead>
</table>
| | **COUNSELING**
Importance of general health maintenance based on age and gender, including all recommended immunizations and cancer screening. |

**POTENTIAL CONSIDERATIONS FOR FURTHER TESTING AND INTERVENTION**

General health maintenance and screening per standard recommendations for age. Screening for hypertension, obesity, depression, tobacco use, alcohol misuse.

Certain subpopulations require screening for lipid disorders, sexually transmitted infections, and diabetes mellitus. Others require counseling regarding the prevention of cardiovascular disease, osteoporosis, and other disorders.

See [www.ahrq.gov/clinic/uspstfix.htm](http://www.ahrq.gov/clinic/uspstfix.htm) for specific recommendations.

Follow preventive screening recommendations for common adult-onset cancers for average risk individuals.

**References**


### GENERAL HEALTH SCREENING

**Screening**

- Review age-appropriate vaccination history yearly

### HEALTH LINKS

- Vaccines after Treatment for Cancer Survivors Treated with HCT
- Vaccines after Treatment for Cancer Survivors Treated with Chemotherapy and/or Radiation (Non-HCT)

### COUNSELING

**For survivors who have NOT received HCT:**

- At entry into long-term follow-up, confirm survivors have been offered catch-up vaccinations for any that were missed during therapy according to national or regional guidelines

**For survivors who have received HCT:**

- Revaccinate allogeneic and autologous HCT survivors per international guidelines and after discussing with primary HCT team

### POTENTIAL_considerations_for_further_testing_and_intervention

All cancer survivors: screen for HPV vaccination - all cancer survivors should receive the 3-dose series regardless of age at first HPV vaccine dose.

Regarding all other immunizations, reimmunize as indicated below:

- HCT patients consider current recommendations (Tomblyn et al, 2009: [https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3103296](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3103296))
- Non-HCT patients, some survivors treated with conventional therapy may lose vaccine-related immunity. Shared decision-making regarding revaccinations/boosters for previously received vaccines may include any of the following approaches:
  - Give boosters for all routine vaccinations
  - Measure antibody titres (serology check) to assess for seroprotection and boosting as needed
  - Observe and manage as needed. See [https://www.cdc.gov/vaccines/schedules/index.html](https://www.cdc.gov/vaccines/schedules/index.html) for current immunization schedules

### Additional Information

Testing of immune function and referral to immunology in survivors (other than allogeneic HCT survivors) should be considered only if there is clinical suspicion of immune dysfunction.

Allogeneic HCT recipients undergo testing of immune reconstitution at some centers, but there are no universal standards.

New therapies (eg immunotherapy such as chimeric antigen receptor T-cell therapy) may impact immunologic function in both the short and long term; challenges exist in recommending standard testing or re-vaccination in survivors due to paucity of long-term data.

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# Abbreviations

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<tr>
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<tbody>
<tr>
<td>AAP</td>
<td>American Academy of Pediatrics</td>
</tr>
<tr>
<td>ABR</td>
<td>Auditory brainstem response</td>
</tr>
<tr>
<td>ACIP</td>
<td>Advisory Committee on Immunization Practices</td>
</tr>
<tr>
<td>ACS</td>
<td>American Cancer Society</td>
</tr>
<tr>
<td>AHA</td>
<td>American Heart Association</td>
</tr>
<tr>
<td>ALL</td>
<td>Acute lymphoblastic leukemia</td>
</tr>
<tr>
<td>ALT</td>
<td>Alanine aminotransferase</td>
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<td>AMH</td>
<td>Anti-Mullerian hormone</td>
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<tr>
<td>AML</td>
<td>Acute myeloid leukemia</td>
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<td>AST</td>
<td>Aspartate aminotransferase</td>
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<td>ATG</td>
<td>Anti-thymocyte globulin</td>
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<tr>
<td>ATM</td>
<td>Ataxia telangiectasia cancer susceptibility gene (located on chromosome 11)</td>
</tr>
<tr>
<td>AVN</td>
<td>Avascular necrosis</td>
</tr>
<tr>
<td>BMD</td>
<td>Bone mineral density</td>
</tr>
<tr>
<td>BMI</td>
<td>Body mass index</td>
</tr>
<tr>
<td>BRCA1</td>
<td>Breast cancer susceptibility gene 1 (located on chromosome 17)</td>
</tr>
<tr>
<td>BRCA2</td>
<td>Breast cancer susceptibility gene 2 (located on chromosome 13)</td>
</tr>
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<td>BUN</td>
<td>Blood urea nitrogen</td>
</tr>
<tr>
<td>Ca</td>
<td>Calcium</td>
</tr>
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<td>CAD</td>
<td>Coronary artery disease</td>
</tr>
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<td>CBC</td>
<td>Complete blood count</td>
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<tr>
<td>CCG</td>
<td>Children’s Cancer Group</td>
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<tr>
<td>CDC</td>
<td>Centers for Disease Control</td>
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<tr>
<td>cGVHD</td>
<td>Chronic graft versus host disease</td>
</tr>
<tr>
<td>CI</td>
<td>Chloride</td>
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<tr>
<td>CNS</td>
<td>Central nervous system</td>
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<td>CO₂</td>
<td>Carbon dioxide</td>
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<tr>
<td>COG</td>
<td>Children’s Oncology Group</td>
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<td>CRT</td>
<td>Cranial radiation</td>
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<td>dB</td>
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<td>DES</td>
<td>Diethylstilbestrol</td>
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<tr>
<td>DI</td>
<td>Diabetes Insipidus</td>
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<td>DLCO</td>
<td>Diffusion capacity of carbon monoxide</td>
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<td>DOR</td>
<td>Diminished ovarian reserve</td>
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<tr>
<td>DTI</td>
<td>Diffusion-tensor imaging</td>
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<tr>
<td>DWI</td>
<td>Diffusion-weighted imaging</td>
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<td>DXA</td>
<td>Dual energy x-ray absorptiometry</td>
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<td>Echocardiogram</td>
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<td>Electrocardiogram</td>
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<tr>
<td>EIA</td>
<td>Enzyme immunoassay</td>
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<tr>
<td>FAP</td>
<td>Familial adenomatous polyposis</td>
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<tr>
<td>FM</td>
<td>Frequency modulated</td>
</tr>
<tr>
<td>FNA</td>
<td>Fine needle aspirate</td>
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<tr>
<td>FNH</td>
<td>Focal nodular hyperplasia</td>
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<td>Follicle stimulating hormone</td>
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<td>G-CSF</td>
<td>Granulocyte colony stimulating factor</td>
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<td>GH</td>
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<td>Gastrointestinal</td>
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<td>Graft versus host disease</td>
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<td>HBsAg</td>
<td>Hepatitis B surface antigen</td>
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<tr>
<td>HCT</td>
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<td>HIB</td>
<td>Haemophilus influenzae type B</td>
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<td>HIV</td>
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<td>HLA</td>
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<td>HNPCC</td>
<td>Hereditary nonpolyposis colorectal cancer</td>
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<td>HPF</td>
<td>High power field</td>
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<td>HPV</td>
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<td>ht</td>
<td>Height</td>
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<td>Hertz</td>
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<td>IBD</td>
<td>Inflammatory bowel disease</td>
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<td>I-131</td>
<td>Iodine 131 radioisotope</td>
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<td>IgA</td>
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<td>IL-2</td>
<td>Interleukin-2</td>
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<td>Intramuscular</td>
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<td>IMRT</td>
<td>Intensity-modulated radiation therapy</td>
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<tr>
<td>IO</td>
<td>Intra-Ommaya</td>
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<tr>
<td>IQ</td>
<td>Intelligence quotient</td>
</tr>
<tr>
<td>IT</td>
<td>Intrathecal</td>
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<tr>
<td>IU</td>
<td>International unit</td>
</tr>
<tr>
<td>IV</td>
<td>Intravenous</td>
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<tr>
<td>IVIG</td>
<td>Intravenous immunoglobulin</td>
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<tr>
<td>kg</td>
<td>Kilogram</td>
</tr>
<tr>
<td>KUB</td>
<td>Kidneys, ureters, bladder radiograph</td>
</tr>
<tr>
<td>LH</td>
<td>Luteinizing hormone</td>
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<tr>
<td>LV</td>
<td>Left ventricular</td>
</tr>
<tr>
<td>m²</td>
<td>Square meter</td>
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<td>MDS</td>
<td>Myelodysplastic syndrome</td>
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<td>MIBG</td>
<td>Iodine-131-meta-iodobenzylguanidine</td>
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<tr>
<td>mg</td>
<td>Milligram</td>
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<tr>
<td>Mg</td>
<td>Magnesium</td>
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<td>MMF</td>
<td>Mycophenolate mofetil</td>
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<tr>
<td>MOPP</td>
<td>Mechlorethamine, Oncovin, Procarbazine, Prednisone</td>
</tr>
<tr>
<td>MR</td>
<td>Magnetic resonance</td>
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<tr>
<td>MRA</td>
<td>Magnetic resonance angiography</td>
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<td>Magnetic resonance imaging</td>
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<tr>
<td>Na</td>
<td>Sodium</td>
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<tr>
<td>NF1</td>
<td>Neurofibromin 1 (neurofibromatosis) cancer susceptibility gene (located on chromosome 17)</td>
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<tr>
<td>NHL</td>
<td>Non-Hodgkin lymphoma</td>
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<tr>
<td>NSAIDs</td>
<td>Non-steroidal anti-inflammatory drugs</td>
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<td>p53</td>
<td>Cancer susceptibility gene associated with familial cancers (located on chromosome 17)</td>
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<td>PAP</td>
<td>Papanicolaou</td>
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<tr>
<td>PCR</td>
<td>Polymerase chain reaction</td>
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<td>PFTs</td>
<td>Pulmonary function tests</td>
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<td>PNET</td>
<td>Primitive neuroectodermal tumor</td>
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<td>PNS</td>
<td>Peripheral nervous system</td>
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<tr>
<td>PO</td>
<td>By mouth</td>
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<tr>
<td>PO₄³⁻</td>
<td>Phosphate</td>
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<tr>
<td>PSA</td>
<td>Prostate specific antigen</td>
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<td>PUVA</td>
<td>Psoralen plus ultraviolet-A radiation</td>
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<td>QTc</td>
<td>Corrected QT interval</td>
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<td>RB1</td>
<td>Retinoblastoma cancer susceptibility gene (located on chromosome 13)</td>
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<tr>
<td>RBC</td>
<td>Red blood cell</td>
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<tr>
<td>RUQ</td>
<td>Right upper quadrant</td>
</tr>
<tr>
<td>SCUBA</td>
<td>Self-contained underwater breathing apparatus</td>
</tr>
<tr>
<td>SD</td>
<td>Standard deviation</td>
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<tr>
<td>SOS</td>
<td>Sinusoidal obstruction syndrome</td>
</tr>
<tr>
<td>SQ</td>
<td>Subcutaneous</td>
</tr>
<tr>
<td>STLTI</td>
<td>Subtotal lymphoid irradiation</td>
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<tr>
<td>T4</td>
<td>Thyroxine</td>
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<td>TBI</td>
<td>Total body irradiation</td>
</tr>
<tr>
<td>TLI</td>
<td>Total lymphoid irradiation</td>
</tr>
<tr>
<td>TPN</td>
<td>Total parenteral nutrition</td>
</tr>
<tr>
<td>TSH</td>
<td>Thyroid stimulating hormone</td>
</tr>
<tr>
<td>U</td>
<td>Units</td>
</tr>
<tr>
<td>USPSTF</td>
<td>United States Preventive Services Task Force</td>
</tr>
<tr>
<td>V-A</td>
<td>Ventriculointeral</td>
</tr>
<tr>
<td>V-P</td>
<td>Ventriculoperitoneal</td>
</tr>
<tr>
<td>V-V</td>
<td>Ventriculovenous</td>
</tr>
<tr>
<td>VZIG</td>
<td>Varicella zoster immunoglobulin</td>
</tr>
<tr>
<td>WAGR</td>
<td>Wilms’ tumor, aniridia, genitourinary anomalies, range of developmental delays</td>
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<td>wt</td>
<td>Weight</td>
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## Chemotherapy Agents

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<th>Generic Name</th>
<th>Additional Name(s)</th>
<th>Classification</th>
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<tbody>
<tr>
<td>Asparaginase</td>
<td>Elspar®, Erwinia asparaginase, L-asparaginase</td>
<td>Enzyme</td>
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<tr>
<td></td>
<td>Oncaspar®, PEG-asparaginase</td>
<td></td>
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<tr>
<td>Bleomycin</td>
<td>Blenoxane®</td>
<td>Anti-tumor antibiotic</td>
</tr>
<tr>
<td>Busulfan</td>
<td>Busulfex®, Busulphan, Myleran®</td>
<td>Alkylating agent</td>
</tr>
<tr>
<td>Carboplatin</td>
<td>CBDCA, Paraplatin®</td>
<td>Heavy metal</td>
</tr>
<tr>
<td>Carmustine</td>
<td>BCNU, BiCNU®</td>
<td>Alkylating agent</td>
</tr>
<tr>
<td>Chlorambucil</td>
<td>Leukeran®</td>
<td>Alkylating agent</td>
</tr>
<tr>
<td>Cisplatin</td>
<td>CDDP, Cisplatinum, Platinol®</td>
<td>Heavy metal</td>
</tr>
<tr>
<td>Cyclophosphamide</td>
<td>CPM, Cytoxan®, Neosar®, Procytox®</td>
<td>Alkylating agent</td>
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<tr>
<td>Cytarabine</td>
<td>Ara-C, Cytosar®, Cytosar-U®, Cytosine arabinoside</td>
<td>Antimetabolite</td>
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<tr>
<td>Dacarbazine</td>
<td>DTIC, DTIC-Dome®</td>
<td>Non-classical alkylation</td>
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<tr>
<td>Dactinomycin</td>
<td>Actinomycin-D Cosmegen®</td>
<td>Anti-tumor antibiotic</td>
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<td>Daunorubicin</td>
<td>Cerubidine®, Daunomycin, DaunoXome®</td>
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<td>Dexamethasone</td>
<td>Decadron®</td>
<td>Corticosteroid</td>
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<td>Adriamycin®, Doxil®, Rubex®</td>
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<td>Ellence®, Pharmorubicin PFS®</td>
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<td>VePesid®, VP16</td>
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<td>Mustargen®, Nitrogen Mustard</td>
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<td>Alkeran®</td>
<td>Alkylating agent</td>
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<td>Mercaptopurine</td>
<td>6-Mercaptopurine, 6MP, Purinethol®</td>
<td>Antimetabolite</td>
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<td>Methotrexate</td>
<td>Amethopterin, Folex®, Mexate®, Trexall®</td>
<td>Antimetabolite</td>
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<td>Mitoxantrone</td>
<td>Novantrone®</td>
<td>Anthracycline antibiotic</td>
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<td>Deltasone®, Methylprednisolone, Prednisolone</td>
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<td>Matulane®, Natulan®</td>
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<td>Temozolomide</td>
<td>Temodal®, Temodar®</td>
<td>Non-classical alkylation</td>
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<td>VM26, Vumon®</td>
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<td>Antimetabolite</td>
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<td>Vinblastine</td>
<td>VBL, Velban®, Velbe®</td>
<td>Plant alkaloid</td>
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<tr>
<td>Vincristine</td>
<td>Oncovin®, VCR, Vincasar®, Vincres®</td>
<td>Plant alkaloid</td>
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## Radiation Fields Defined

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<tr>
<th>Traditional Radiation Field</th>
<th>Definition</th>
<th>Corresponding Version 5.0 Fields</th>
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</thead>
<tbody>
<tr>
<td>Total body irradiation (TBI)</td>
<td>Entire body; encompassing all radiation fields</td>
<td>TBI</td>
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<tr>
<td>Cranial</td>
<td>Any field involving the cranium, head, brain and/or face</td>
<td>Head/brain</td>
</tr>
<tr>
<td>Waldeyer’s ring</td>
<td>Nasopharyngeal and oropharyngeal (tonsils and adenoids)</td>
<td>Head/brain</td>
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<tr>
<td>Spine-cervical</td>
<td>Including some or all of the cervical spine (C1–C7)</td>
<td>Spine (cervical)</td>
</tr>
<tr>
<td>Spine-thoracic</td>
<td>Including some or all of the thoracic spine (T1–T12)</td>
<td>Spine (thoracic)</td>
</tr>
<tr>
<td>Spine-lumbar</td>
<td>Including some or all of the lumbar spine (L1–L5)</td>
<td>Spine (lumbar)</td>
</tr>
<tr>
<td>Spine-sacral</td>
<td>Including some or all of the sacral spine (S1–S5)</td>
<td>Spine (sacral)</td>
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<tr>
<td>Spine-whole</td>
<td>Including the cervical, thoracic, lumbar and sacral spine</td>
<td>Spine (whole)</td>
</tr>
<tr>
<td>Mini-mantle</td>
<td>Bilateral cervical (neck), supraclavicular and axillary fields (excludes mediastinal and lung)</td>
<td>Neck and Axilla</td>
</tr>
<tr>
<td>Mantle</td>
<td>Bilateral cervical (neck), supraclavicular, mediastinal, hilar, and axillary fields</td>
<td>Neck, Axilla, and Chest</td>
</tr>
<tr>
<td>Extended mantle</td>
<td>Mantle and paraaortic fields</td>
<td>Neck and Axilla, and Chest</td>
</tr>
<tr>
<td>Subtotal lymphoid irradiation (STLI)</td>
<td>Mantle + paraaortic + splenic</td>
<td>Neck, Axilla, and Abdomen</td>
</tr>
<tr>
<td>Inverted Y</td>
<td>Paraaortic + pelvic ± splenic</td>
<td>Abdomen and Pelvis</td>
</tr>
<tr>
<td>Total lymphoid irradiation (TLI)</td>
<td>Mantle + inverted Y (paraaortic/pelvic) + splenic</td>
<td>Neck, Axilla, and Abdomen, Pelvis</td>
</tr>
<tr>
<td>Chest (thorax)</td>
<td>May include any of the following: Mediastinal, hilar, whole lung, chest wall</td>
<td>Chest</td>
</tr>
<tr>
<td>Mediastinal</td>
<td>Mediastinum and bilateral hilar fields</td>
<td>Chest</td>
</tr>
<tr>
<td>Abdomen (also commonly referred to as “upper abdomen”)</td>
<td>Top of diaphragm to iliac crests (bilaterally), including the following fields: • Hepatic • Upper quadrant (right, left) • Renal/Renal bed • Paraaortic • Spleen (partial, entire) • Flank/Hemiabdomen (right, left)</td>
<td>Abdomen</td>
</tr>
<tr>
<td>Paraaortic</td>
<td>Paraaortic lymph nodes (generally from T10 to L4 cephalad-caudad, and the transverse processes laterally) ± splenic</td>
<td>Abdomen</td>
</tr>
<tr>
<td>Renal</td>
<td>Renal bed</td>
<td>Abdomen</td>
</tr>
</tbody>
</table>
## Radiation Fields Defined (cont)

<table>
<thead>
<tr>
<th>Traditional Radiation Field</th>
<th>Definition</th>
<th>Corresponding Version 5.0 Fields</th>
</tr>
</thead>
</table>
| Flank/Hemiabdomen           | Top of diaphragm to iliac crest (unilateral; medial border along contralateral vertebral bodies)  
**Note:** Most hemiabdominal fields do not extend beyond the iliac crest; however, in some cases, depending on tumor location, the hemiabdominal field may have extended into the pelvis. If the hemiabdominal field extended below the iliac crest, exposure to pelvic fields should be considered in assessing risk for late sequelae. | Abdomen ± Pelvis |
| Whole abdomen                | Includes all abdominal and pelvic fields | Abdomen Pelvis |
| Pelvis                      | Iliac crest to 3 cm below ischium, including the following fields:  
- Pelvic  
- Iliac  
- Vaginal  
- Inguinal  
- Prostate  
- Femoral  
- Bladder | Pelvis |
| Extremities                 | Including some or all of the arm(s), leg(s), feet or hand(s) | Extremities |
Radiation Fields Defined (cont)

Version 6.0 fields shown in black boxes.
Radiation Dose Calculations

Instructions for Radiation Dose Calculation:
Five sections of the COG Long-Term Follow-Up Guidelines (sections 60, 63, 66, 77, 78) include radiation dose specifications. These specifications indicate the minimum dose of radiation that is believed (based on available evidence and the recommendations of the expert panel) to place patients sufficiently at risk of the referenced late effect to recommend screening. For guideline sections that have a minimum specified dose, the following considerations apply in determining the applicability of the section for a patient based on his/her radiation exposure.

Sections with minimum dose specifications are applicable to a patient only if:
1. Patient received radiation to any field(s) relevant to the particular guideline section at ≥ the specified minimum dose†
OR
2. Patient received a combination of radiation to any relevant field(s)† plus relevant spinal radiation‡ and/or TBI, the sum of which is ≥ the specified minimum dose

†Total dose to each field should include boost dose, if given. If patient received radiation to more than one field relevant to a particular guideline section during a single planned course of radiation treatment (excluding spinal radiation and TBI), the field that received the largest radiation dose should be used in making the determination as to the applicability of the indicated guideline section(s). Exception: If patient received radiation to the same field at different times (e.g., at time of diagnosis AND at relapse), these doses should be added together when considering the applicability of the indicated guideline section.
‡Use the largest dose of radiation delivered to the spinal field(s) specified in the guideline section.

Examples of Radiation Dose Calculations:
Step 1: If radiation was given to more than one field relevant to the guideline (not including spine, TBI), select the largest dose received
Step 2: If patient received radiation to the same field at different times (e.g., at time of diagnosis AND at relapse), add these doses together
Step 3: If patient received relevant spinal field radiation, add the largest relevant spinal dose
Step 4: If patient received TBI, add TBI dose

Example #1

<table>
<thead>
<tr>
<th>Guideline Information</th>
<th>Patient Information</th>
</tr>
</thead>
<tbody>
<tr>
<td>Guideline section</td>
<td>Minimum dose</td>
</tr>
<tr>
<td></td>
<td>specification</td>
</tr>
<tr>
<td></td>
<td>for screening</td>
</tr>
<tr>
<td></td>
<td>Relevant radiation fields</td>
</tr>
<tr>
<td>Section 66, osteoradionecrosis of the jaw</td>
<td>≥40 Gy</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Example #2

<table>
<thead>
<tr>
<th>Guideline Information</th>
<th>Patient Information</th>
</tr>
</thead>
<tbody>
<tr>
<td>Guideline section</td>
<td>Minimum dose</td>
</tr>
<tr>
<td></td>
<td>specification</td>
</tr>
<tr>
<td></td>
<td>for screening</td>
</tr>
<tr>
<td></td>
<td>Relevant radiation fields</td>
</tr>
<tr>
<td>Section 77, cardiac toxicity</td>
<td>≥15 Gy</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>
*Minimum dose specifications apply. For instructions and examples regarding radiation dose calculations, refer to "Radiation Dose Calculations" in COG Long-Term Follow-Up Guidelines Appendix I Reference Materials.
## Guideline Radiation Sections by Potential Impact

Applicable guideline sections indicated in bold/dark blue; M=Male; F=Female

<table>
<thead>
<tr>
<th>Potential Impact</th>
<th>Fields</th>
<th>Dose</th>
<th>Section Numbers</th>
<th>Potential Late Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Fields</td>
<td>Any radiation</td>
<td>Any</td>
<td>44*</td>
<td>Subsequent benign or malignant neoplasm</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>45*</td>
<td>Dermatologic toxicity</td>
</tr>
<tr>
<td>Brain/Cranium</td>
<td>Head/Brain</td>
<td>Any</td>
<td>46*</td>
<td>Brain tumor (benign or malignant)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>47*</td>
<td>Neurocognitive deficits</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>48*</td>
<td>Clinical leukoencephalopathy</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>49</td>
<td>Cerebrovascular complications</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>50</td>
<td>Craniofacial abnormalities</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>51</td>
<td>Chronic sinusitis</td>
</tr>
<tr>
<td>Neuroendocrine Axis</td>
<td>Head/Brain</td>
<td>Any</td>
<td>52</td>
<td>Overweight; Obesity</td>
</tr>
<tr>
<td>Eye</td>
<td>Head/Brain</td>
<td>Any</td>
<td>53*</td>
<td>Growth hormone deficiency</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>54M</td>
<td>Precocious puberty (male)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>55F</td>
<td>Precocious puberty (female)</td>
</tr>
<tr>
<td>Oral Cavity</td>
<td>Head/Brain</td>
<td>Any</td>
<td>56</td>
<td>Hyperprolactinemia</td>
</tr>
<tr>
<td></td>
<td>Neck</td>
<td></td>
<td>57</td>
<td>Central hypothyroidism</td>
</tr>
<tr>
<td></td>
<td>Spine (cervical, whole)</td>
<td></td>
<td>58M*</td>
<td>Gonadotropin deficiency (male)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>59F*</td>
<td>Gonadotropin deficiency (female)</td>
</tr>
<tr>
<td>Neck/Thyroid</td>
<td>Head/Brain</td>
<td>Any</td>
<td>59</td>
<td>Hypothyroidism</td>
</tr>
<tr>
<td></td>
<td>Neck</td>
<td></td>
<td>60</td>
<td>Central adrenal insufficiency</td>
</tr>
<tr>
<td></td>
<td>Spine (cervical, whole)</td>
<td></td>
<td>61*</td>
<td>Cataracts</td>
</tr>
<tr>
<td></td>
<td>Neck</td>
<td></td>
<td>62</td>
<td>Ocular toxicity</td>
</tr>
<tr>
<td></td>
<td>Spine (cervical, whole)</td>
<td></td>
<td>63</td>
<td>Ototoxicity</td>
</tr>
<tr>
<td></td>
<td>Neck</td>
<td></td>
<td>64*</td>
<td>Xerostomia; Salivary gland dysfunction</td>
</tr>
<tr>
<td></td>
<td>Neck</td>
<td></td>
<td>65*</td>
<td>Dental abnormalities; Temporomandibular joint dysfunction</td>
</tr>
<tr>
<td></td>
<td>Spine (cervical, whole)</td>
<td></td>
<td>66</td>
<td>Osteoradionecrosis of the jaw</td>
</tr>
<tr>
<td></td>
<td>Neck</td>
<td></td>
<td>67*</td>
<td>Thyroid nodules</td>
</tr>
<tr>
<td></td>
<td>Neck</td>
<td></td>
<td>68*</td>
<td>Thyroid cancer</td>
</tr>
<tr>
<td></td>
<td>Spine (cervical, whole)</td>
<td></td>
<td>69*</td>
<td>Hypothyroidism</td>
</tr>
<tr>
<td></td>
<td>Neck</td>
<td></td>
<td>70</td>
<td>Hyperthyroidism</td>
</tr>
<tr>
<td></td>
<td>Chest</td>
<td></td>
<td>71</td>
<td>Carotid artery disease</td>
</tr>
<tr>
<td></td>
<td>Spine (thoracic, whole)</td>
<td></td>
<td>72</td>
<td>Subclavian artery disease</td>
</tr>
</tbody>
</table>

*Patients who received TBI are at risk for this late effect. For a full list of TBI related sections, refer to "Total Body Irradiation Related Potential Late Effects" in COG Long-Term Follow-Up Guidelines Appendix I Reference Materials.

**TBI should be included for dose calculation purposes only
# Guideline Radiation Sections by Potential Impact (cont)

Applicable guideline sections indicated in bold/dark blue; M=Male; F=Female

<table>
<thead>
<tr>
<th>Potential Impact</th>
<th>Fields</th>
<th>Dose</th>
<th>Potential Late Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Breast</strong></td>
<td>Chest</td>
<td>Any</td>
<td>73F* Breast cancer</td>
</tr>
<tr>
<td></td>
<td>Axilla</td>
<td></td>
<td>74F* Breast tissue hypoplasia</td>
</tr>
<tr>
<td><strong>Lungs</strong></td>
<td>Chest</td>
<td>Any</td>
<td>75* Pulmonary toxicity</td>
</tr>
<tr>
<td></td>
<td>Axilla</td>
<td></td>
<td>76* Lung cancer</td>
</tr>
<tr>
<td><strong>Heart</strong></td>
<td>Chest</td>
<td>≥15 Gy**</td>
<td>77 Cardiac toxicity</td>
</tr>
<tr>
<td></td>
<td>Abdomen</td>
<td>Any</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Spine (thoracic, whole)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Spleen</strong></td>
<td>Abdomen</td>
<td>≥40 Gy**</td>
<td>78 Functional asplenia</td>
</tr>
<tr>
<td><strong>GI/Hepatic System</strong></td>
<td>Neck</td>
<td>Any</td>
<td>79 Esophageal stricture</td>
</tr>
<tr>
<td></td>
<td>Chest</td>
<td>Any</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Abdomen</td>
<td>Any</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Spine (cervical, thoracic, whole)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Abdomen</strong></td>
<td>Any</td>
<td>80*</td>
<td>Impaired glucose metabolism/Diabetes mellitus</td>
</tr>
<tr>
<td><strong>Pelvis</strong></td>
<td>Any</td>
<td>81*</td>
<td>Dyslipidemia</td>
</tr>
<tr>
<td><strong>Spine (lumbar, sacral, whole)</strong></td>
<td>Any</td>
<td>82</td>
<td>Hepatic toxicity</td>
</tr>
<tr>
<td><strong>83</strong></td>
<td></td>
<td></td>
<td>Cholelithiasis</td>
</tr>
<tr>
<td><strong>Urinary Tract</strong></td>
<td>Abdomen</td>
<td>Any</td>
<td>84 Bowel obstruction</td>
</tr>
<tr>
<td></td>
<td>Pelvis</td>
<td>Any</td>
<td>85 Chronic enterocolitis; Fistula; Strictures</td>
</tr>
<tr>
<td></td>
<td>Spine (sacral, whole)</td>
<td>Any</td>
<td>86* Colorectal cancer</td>
</tr>
<tr>
<td><strong>Male Reproductive System</strong></td>
<td>Testes</td>
<td>Any</td>
<td>90M Testicular hormonal dysfunction</td>
</tr>
<tr>
<td></td>
<td>Any</td>
<td>91M*</td>
<td>Impaired spermatogenesis</td>
</tr>
<tr>
<td><strong>Female Reproductive System</strong></td>
<td>Pelvis</td>
<td>Any</td>
<td>92F* Ovarian hormone deficiencies</td>
</tr>
<tr>
<td></td>
<td>Spine (sacral, whole)</td>
<td>Any</td>
<td>93F* Diminished ovarian reserve (DOR)</td>
</tr>
<tr>
<td></td>
<td>Any</td>
<td>94F*</td>
<td>Uterine vascular insufficiency</td>
</tr>
<tr>
<td><strong>Musculoskeletal System</strong></td>
<td>Pelvis</td>
<td>Any</td>
<td>95F Vaginal fibrosis/stenosis</td>
</tr>
<tr>
<td></td>
<td>Any radiation</td>
<td>Any</td>
<td>96* Musculoskeletal growth problems</td>
</tr>
<tr>
<td></td>
<td>Chest</td>
<td>Any</td>
<td>97 Scoliosis/Kyphosis</td>
</tr>
<tr>
<td></td>
<td>Abdomen</td>
<td>Any</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Spine (thoracic, lumbar, whole)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Any radiation</strong></td>
<td>Any</td>
<td>98</td>
<td>Radiation-induced fracture</td>
</tr>
</tbody>
</table>

* Patients who received TBI are at risk for this late effect. For a full list of TBI related sections, refer to “Total Body Irradiation Related Potential Late Effects” in COG Long-Term Follow-Up Guidelines Appendix I Reference Materials.

**TBI should be included for dose calculation purposes only.
Guideline Radiation Sections by Potential Impact (cont)

Applicable guideline sections indicated in bold/dark blue; M=Male; F=Female

*Minimum dose specifications apply. For instructions and examples regarding radiation dose calculations, refer to "Radiation Dose Calculations" in COG Long-Term Follow-Up Guidelines Appendix I Reference Materials.

Note: Oral cavity, neck/thyroid, heart, esophagus, and bowel are affected by multiple anatomic regions.
# Total Body Irradiation (TBI) Related Potential Late Effects

The complete list of potential late effects and associated Guideline section numbers are included here for clinician convenience when evaluating patients who received TBI. For details regarding each potential late effect and indicated screening, please refer to the relevant section within the Guidelines.

<table>
<thead>
<tr>
<th>Section Number</th>
<th>Sex</th>
<th>Potential Late Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>44</td>
<td>Both</td>
<td>Subsequent benign or malignant neoplasm occurring in or near radiation field</td>
</tr>
<tr>
<td>45</td>
<td>Both</td>
<td>Dermatologic toxicity</td>
</tr>
<tr>
<td>46</td>
<td>Both</td>
<td>Brain tumor (benign or malignant)</td>
</tr>
<tr>
<td>47</td>
<td>Both</td>
<td>Neurocognitive deficits</td>
</tr>
<tr>
<td>48</td>
<td>Both</td>
<td>Clinical leukoencephalopathy</td>
</tr>
<tr>
<td>53</td>
<td>Both</td>
<td>Growth hormone deficiency</td>
</tr>
<tr>
<td>58</td>
<td>Male</td>
<td>Gonadotropin deficiency</td>
</tr>
<tr>
<td>59</td>
<td>Female</td>
<td>Gonadotropin deficiency</td>
</tr>
<tr>
<td>61</td>
<td>Both</td>
<td>Cataracts</td>
</tr>
<tr>
<td>64</td>
<td>Both</td>
<td>Xerostomia; Salivary gland dysfunction</td>
</tr>
<tr>
<td>65</td>
<td>Both</td>
<td>Dental abnormalities; Temporomandibular joint dysfunction</td>
</tr>
<tr>
<td>67</td>
<td>Both</td>
<td>Thyroid nodules</td>
</tr>
<tr>
<td>68</td>
<td>Both</td>
<td>Thyroid cancer</td>
</tr>
<tr>
<td>69</td>
<td>Both</td>
<td>Hypothyroidism</td>
</tr>
<tr>
<td>73</td>
<td>Female</td>
<td>Breast cancer</td>
</tr>
<tr>
<td>74</td>
<td>Female</td>
<td>Breast tissue hypoplasia</td>
</tr>
<tr>
<td>75</td>
<td>Both</td>
<td>Pulmonary toxicity</td>
</tr>
<tr>
<td>76</td>
<td>Both</td>
<td>Lung cancer</td>
</tr>
<tr>
<td>80</td>
<td>Both</td>
<td>Impaired glucose metabolism/Diabetes mellitus</td>
</tr>
<tr>
<td>81</td>
<td>Both</td>
<td>Dyslipidemia</td>
</tr>
<tr>
<td>86</td>
<td>Both</td>
<td>Colorectal cancer</td>
</tr>
<tr>
<td>87</td>
<td>Both</td>
<td>Renal toxicity</td>
</tr>
<tr>
<td>91</td>
<td>Male</td>
<td>Impaired spermatogenesis</td>
</tr>
<tr>
<td>92</td>
<td>Female</td>
<td>Ovarian hormone deficiencies</td>
</tr>
<tr>
<td>93</td>
<td>Female</td>
<td>Diminished ovarian reserve</td>
</tr>
<tr>
<td>94</td>
<td>Female</td>
<td>Uterine vascular insufficiency</td>
</tr>
<tr>
<td>96</td>
<td>Both</td>
<td>Musculoskeletal growth problems</td>
</tr>
</tbody>
</table>
Appeal Letter Following Denial of Insurance Claims

Version 6.0
October 2023
Instructions:

Appeal Letter Following Denial of Insurance Claims for Survivorship Care

Not all insurance companies recognize the need for ongoing long-term follow-up care for survivors of childhood, adolescent, and young adult cancers. As with any medical care, it is prudent for the survivor to determine coverage for anticipated screening tests that may be recommended as part of their long-term follow-up care, and to work with the survivorship provider to obtain any pre-authorizations that may be necessary.

Nevertheless, we recognize that some essential services may be denied from time to time. The letters on the following pages are designed for use as templates to appeal denial letters from insurance companies, should the need arise. One letter is designed to be completed and submitted to the insurance company by the patient (or his/her parent). The other letter is designed to be completed and submitted to the insurance company by the patient's survivorship care provider. Although neither letter can guarantee insurance coverage, we are hopeful that these letters may be helpful in securing the indicated coverage for tests recommended as part of routine long-term follow-up care after the completion of cancer-directed therapy.

These templates were developed by Kristy Sharif and Alison Olig, COG Patient Advocacy Committee, 2018.
Appeal Letter Following Denial of Insurance Claims for Survivorship Care: Template for Letter from Patient, Parent or Guardian

(Date)

(Name)
(Insurance Company Name)
(Address)
(City, State ZIP)

Re: (Patient's Name)
(Type of Coverage)
(Group number/Policy number)

Dear (name of contact person at insurance company),

Please accept this letter as (patient's name)'s appeal to (insurance company name)'s decision to deny coverage for (name of test). It is my understanding based on your letter of denial dated (date) that (name of test) has been denied because:

(Quote the specific reason for the denial stated in denial letter)

It is possible that you did not have all the necessary information at the time of your initial review. (Patient's name) was diagnosed with (disease) on (date). Currently (name of long-term follow-up clinician) from (name of treating facility), a specialist in long-term follow-up after therapy for cancer during childhood, adolescence, and young adulthood, has indicated that (patient's name) requires (name of test) in order to monitor for long-term complications related to (patient's name) cancer treatment. Please see the enclosed letter from (name of long-term follow-up clinician) that discusses (patient's name)'s medical history and provides justification for this testing in more detail. Also included are medical records and support documentation explaining the evidence-based recommendations for this required monitoring.

Based on this information, (patient's name) is asking that you reconsider your previous decision and allow coverage for the procedure Dr. (name) outlines in the enclosed letter. (Name of test) is recommended to be completed by (date). Should you require additional information, please do not hesitate to contact me at (phone number). I look forward to hearing from you in the near future.

Sincerely,

(Patient, parent or guardian name)
Appeal Letter Following Denial of Insurance Claims for Survivorship Care: Template for Letter from Long-Term Follow-Up Clinician

(Date)

(Name)
(Insurance Company Name)
(Address)
(City, State ZIP)

Re:  
(Patient's Name)
(Type of Coverage)
(Group number/Policy number)

Dear (name of contact person at insurance company),

This letter is written in support of (patient's name)'s appeal to (insurance company name)'s decision to deny coverage for (name of test). I am the clinician who is currently providing long-term follow-up care for this patient. Based on your letter of denial dated (date), it is my understanding that (name of test) has been denied because:

(Quote the specific reason for the denial stated in denial letter)

(Patient's name) is a (age) year old (male/female) who was diagnosed with (disease) on (date) and began treatment on (date). Treatment was completed on (date).

The treatments that (patient's name) received for (disease) were lifesaving, however, this treatment has the potential to cause significant long-term complications (late effects) that can negatively impact (patient's name)'s health. Ongoing monitoring is required so that any long-term complications of cancer therapy can be identified and treated in a timely fashion in order to optimize (patient's name)'s health and prevent a decline in health status.

Because (patient's name) received (name of relevant therapeutic exposures/doses) as part of (his/her) cancer therapy, (he/she) is at risk for (relevant late effect(s)). The Children's Oncology Group (COG) Long-Term Follow-Up Guidelines, which set the standard of care for the ongoing follow-up of survivors of childhood, adolescent, and young adult cancers, provide specific follow-up recommendations related to (patient's name)'s treatment, including (name of test denied). These evidence-based guidelines are based on the known long-term risks associated with cancer therapy delivered during childhood, adolescence, and young adulthood. The recommendations within the COG Long-Term Follow-Up Guidelines represent the consensus of experts in the late effects of pediatric cancer treatment.

I have attached documentation that supports the recommended testing in more detail [attach relevant sections from COG LTFU Guidelines and any additional supportive materials such as journal articles], along with (patient's name)'s relevant medical records. Additional information is available from the Children's Oncology Group at www.survivorshipguidelines.org.

Based on this information, as the clinician providing (patient's name)'s long-term follow-up care, I am asking that you reconsider your previous decision and allow coverage for (name of test). (Name of test) is recommended to be completed by (date). Should you require additional information, please do not hesitate to contact me at (phone number). I look forward to hearing from you.

Sincerely,

(Name of long-term follow-up clinician)
Importance of a Comprehensive Cancer Treatment Summary

The Children’s Oncology Group Long-Term Follow-Up Guidelines for Survivors of Childhood, Adolescent, and Young Adult Cancers are based on therapeutic exposures received during cancer treatment. Availability of a comprehensive treatment summary, including all therapeutic agents received by the survivor, is presumed. Patients who do not have a comprehensive treatment summary should be instructed to obtain one from the institution(s) where they received their treatment.

The following table outlines:

1. The minimum information necessary to generate patient-specific guidelines (i.e., an abbreviated treatment summary).
2. The ideal information included in the comprehensive treatment summary. We strongly advise that a comprehensive treatment summary be prepared for each childhood cancer survivor when feasible.

<table>
<thead>
<tr>
<th>At Minimum</th>
<th>Additional Information - Strongly Advised if Feasible</th>
</tr>
</thead>
<tbody>
<tr>
<td>Demographics</td>
<td>Demographics</td>
</tr>
<tr>
<td>Name</td>
<td>Race/Ethnicity</td>
</tr>
<tr>
<td>Sex</td>
<td>Social security number, if available</td>
</tr>
<tr>
<td>Date of birth</td>
<td>COG registration number, if available</td>
</tr>
<tr>
<td>Race/Ethnicity</td>
<td>Contact information</td>
</tr>
<tr>
<td>Social security number, if available</td>
<td></td>
</tr>
<tr>
<td>COG registration number, if available</td>
<td></td>
</tr>
<tr>
<td>Contact information</td>
<td></td>
</tr>
<tr>
<td>Cancer Diagnosis</td>
<td>Cancer Diagnosis</td>
</tr>
<tr>
<td>Diagnosis</td>
<td>Diagnosis, including date, site/stage, laterality, and relapse(s) if any</td>
</tr>
<tr>
<td>Date of diagnosis</td>
<td>Pertinent hereditary conditions, past medical history and subsequent neoplasms</td>
</tr>
<tr>
<td>Date cancer therapy was completed</td>
<td>Treating institution and team</td>
</tr>
<tr>
<td>Cancer Treatment: Protocols</td>
<td>Cancer Treatment: Protocols</td>
</tr>
<tr>
<td>N/A</td>
<td>Treatment protocol information, if applicable</td>
</tr>
<tr>
<td>Cancer Treatment: Chemotherapy</td>
<td>Cancer Treatment: Chemotherapy</td>
</tr>
<tr>
<td>Names of all chemotherapy agents received</td>
<td>Cumulative doses for all other agents should be provided if available, particularly for alkylators and bleomycin.</td>
</tr>
<tr>
<td>– For a list of chemotherapy agents addressed by these guidelines (Sections 11-43), see the “Chemotherapy” portion of the Patient-Specific Guideline Identification Tool in Appendix I.</td>
<td>– For doses in mg/kg, multiply by 30 to obtain equivalent dosing in mg/m² (example: 2 mg/kg = 60 mg/m²).</td>
</tr>
<tr>
<td>– For generic and brand names of chemotherapy agents, see Chemotherapy Agents in Appendix I.</td>
<td>– Route of administration for all other agents</td>
</tr>
<tr>
<td>Cumulative dose of all anthracycline chemotherapy received (i.e., doxorubicin, daunorubicin, idarubicin, mitoxantrone and epirubicin)</td>
<td></td>
</tr>
<tr>
<td>– See Section 34 of Guidelines for anthracycline isotoxic dose-equivalent conversion.</td>
<td></td>
</tr>
<tr>
<td>– For doses in mg/kg, multiply by 30 to obtain equivalent dosing in mg/m² (example: 2 mg/kg = 60 mg/m²).</td>
<td></td>
</tr>
<tr>
<td>For carboplatin, whether any dose was myeloablative (i.e., given as conditioning for HCT)</td>
<td></td>
</tr>
<tr>
<td>For cytarabine and methotrexate:</td>
<td></td>
</tr>
<tr>
<td>– Route of administration (i.e., IV, IM, SQ, PO, IT, IO)</td>
<td></td>
</tr>
<tr>
<td>– If IV, designation of “high dose” (any single dose ≥ 1000 mg/m²) versus “standard dose” (all single doses &lt; 1000 mg/m²)</td>
<td></td>
</tr>
</tbody>
</table>
## Instructions:
### Summary of Cancer Treatment (cont)

<table>
<thead>
<tr>
<th>At Minimum</th>
<th>Additional Information- Strongly Advised if Feasible</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cancer Treatment: Radiation</strong></td>
<td><strong>Cancer Treatment: Radiation</strong></td>
</tr>
<tr>
<td>• Names of all radiation field(s) treated</td>
<td>• Laterality (if applicable), start/stop dates, radiation type, number of fractions, dose per fraction, boost dose/location (if applicable)</td>
</tr>
<tr>
<td>– For list of radiation fields addressed by these guidelines (Sections 44-98), see “Radiation” portion of the Patient-Specific Guideline Identification Tool in Appendix I</td>
<td>• Total dose (in Gy) for all other fields</td>
</tr>
<tr>
<td>– For definition of radiation fields, see “Radiation Fields Defined” in Appendix I</td>
<td>– Should include boost dose if given</td>
</tr>
<tr>
<td>• For head/brain, neck, chest, abdomen, spine (whole, cervical, thoracic) radiation and TBI, total dose (in Gy):</td>
<td>– To convert cGy or rads to Gy, divide dose by 100 (example: 2400 cGy = 2400 rads = 24 Gy)</td>
</tr>
<tr>
<td>– Total radiation dose to each field (should include boost dose, if given)</td>
<td>• Treating institution and radiation oncologist</td>
</tr>
<tr>
<td>– To convert cGy or rads to Gy, divide dose by 100 (example: 2400 cGy = 2400 rads = 24 Gy)</td>
<td></td>
</tr>
<tr>
<td><strong>Cancer Treatment: Hematopoietic Cell Transplant(s)</strong></td>
<td><strong>Cancer Treatment: Hematopoietic Cell Transplant(s)</strong></td>
</tr>
<tr>
<td>• Whether or not the survivor underwent a hematopoietic cell transplant (HCT), and if so:</td>
<td>• Type(s), source(s), date(s), conditioning regimen(s), GVHD prophylaxis and/or treatment</td>
</tr>
<tr>
<td>– Transplant type (autologous vs allogeneic)</td>
<td>• Treating institution and transplant physician</td>
</tr>
<tr>
<td>– Chronic graft-versus-host disease (cGVHD) status (no history of chronic GVHD, history of chronic GVHD, currently active chronic GVHD)</td>
<td></td>
</tr>
<tr>
<td><strong>Cancer Treatment: Surgery</strong></td>
<td><strong>Cancer Treatment: Surgery</strong></td>
</tr>
<tr>
<td>• Names of all surgical procedures.</td>
<td>• Dates, site (if applicable), laterality (if applicable)</td>
</tr>
<tr>
<td>– For list of surgical procedures addressed by these guidelines (Sections 115–151), see “Surgery” portion of the Patient-Specific Guideline Identification Tool in Appendix I</td>
<td>• Treating institution and surgeon</td>
</tr>
<tr>
<td><strong>Cancer Treatment: Other Therapeutic Modalities</strong></td>
<td><strong>Cancer Treatment: Other Therapeutic Modalities</strong></td>
</tr>
<tr>
<td>• Whether or not the survivor received radioiodine therapy (I-131 thyroid ablation), systemic MIBG (in therapeutic doses), or a novel therapy</td>
<td>• Names, routes and cumulative doses of all other therapeutic modalities received</td>
</tr>
<tr>
<td><strong>Additional Clinical Information</strong></td>
<td><strong>Additional Clinical Information</strong></td>
</tr>
<tr>
<td>N/A</td>
<td>• Significant complications/late effects with dates of onset/resolution</td>
</tr>
<tr>
<td></td>
<td>• Adverse drug reactions/allergies</td>
</tr>
<tr>
<td></td>
<td>• Additional information/comments</td>
</tr>
</tbody>
</table>

### Templates for Summary of Cancer Treatment

Two templates for summarizing cancer treatment are included in Appendix I (also available in electronic format at www.survivorshipguidelines.org). These templates were originally developed by the COG Nursing Clinical Practice Subcommittee under the leadership of Lisa Bashore, MS, RN, CPNP, CPON® and Lori Boucher, RN, CRA. The templates were subsequently pilot tested and revised, then further refined based on feedback from the Late Effects Committee and a working group from the National Cancer Institute.

The abbreviated form contains all data elements currently necessary for generation of patient-specific recommendations from the COG LTFU Guidelines, and meets the minimum data requirements for initial use of the “Passport for Care” web-based guideline interface. However, the COG Long-Term Follow-Up Guidelines Core Committee recognizes that as new evidence becomes available and these guidelines are updated, additional details regarding the childhood cancer survivor’s therapeutic exposures may be required in order to generate comprehensive recommendations. Therefore, we strongly advise that a comprehensive treatment summary be prepared for each childhood cancer survivor when feasible, including a record of all therapeutic exposures with applicable dates, details of administration, and cumulative doses of all agents, including those not currently addressed by these guidelines.

In addition to the treatment summary templates, a “key” for completing the comprehensive version of the treatment summary is also included in Appendix I.
# Summary of Cancer Treatment (Abbreviated)

## Demographics

<table>
<thead>
<tr>
<th>Name</th>
<th>Sex</th>
<th>Date of birth</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>M</td>
<td></td>
</tr>
<tr>
<td></td>
<td>F</td>
<td></td>
</tr>
</tbody>
</table>

## Cancer Diagnosis

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Date of diagnosis</th>
<th>Date therapy completed</th>
</tr>
</thead>
</table>

## Chemotherapy

- **Yes**
- **No**

**If yes, provide information below**

<table>
<thead>
<tr>
<th>Drug name</th>
<th>Additional information†</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

†**Anthracyclines**: Include cumulative dose in mg/m² (see section 34 of Guidelines for isotoxic dose conversion);

**Carboplatin**: Indicate if dose was myeloablative

**Methotrexate and Cytarabine**: Indicate route of administration (i.e., IV, IM, SQ, PO, IT, IO);

**IV Methotrexate and Cytarabine**: Indicate if “high dose” (any single dose ≥ 1000 mg/m²) or “standard dose” (all single doses < 1000 mg/m²)

**Note**: Cumulative doses, if known, should be recorded for all agents, particularly for alkylators and bleomycin.

## Radiation

- **Yes**
- **No**

**If yes, provide information below**

<table>
<thead>
<tr>
<th>Site/Field</th>
<th>Total dose* (including boost) (Gy)**</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*For head/brain, neck, chest, abdomen, spine (whole, cervical, thoracic) radiation and TBI, include total doses (including boost dose, if given)

**To convert cGy or rads to Gy, divide dose by 100 (example: 2400 cGy = 2400 rads = 24 Gy)

## Hematopoietic Cell Transplant

- **Yes**
- **No**

**If yes, provide information below**

<table>
<thead>
<tr>
<th>Transplant type</th>
<th>Autologous</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Allogeneic</td>
<td>Yes</td>
<td>No</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Chronic graft-versus-host disease (cGVHD)</th>
<th>Ever diagnosed?</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Currently active?</td>
<td>Yes</td>
<td>No</td>
</tr>
</tbody>
</table>

## Surgery

- **Yes**
- **No**

**If yes, provide information below**

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Site (if applicable)</th>
<th>Laterality (if applicable)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

## Other Therapeutic Modalities

- **Yes**
- **No**

**If yes, provide information below**

- Did the patient receive radioiodine therapy (I-131 thyroid ablation)?
- Did the patient receive systemic MIBG (in therapeutic doses)?
- Did the patient receive any other novel therapy from Sections 158-163 (in therapeutic doses)?

## Summary prepared by:

<table>
<thead>
<tr>
<th>Date prepared:</th>
<th></th>
</tr>
</thead>
</table>
# Summary of Cancer Treatment (Comprehensive)

Superscript numbers correspond with lists in "Key for Completing Summary of Cancer Treatment Form"

## Demographics

<table>
<thead>
<tr>
<th>Name</th>
<th>Sex</th>
<th>Date of birth</th>
<th>Race/Ethnicity</th>
<th>SS#</th>
<th>COG Reg #</th>
<th>Address</th>
<th>Phone</th>
<th>Alternate contact</th>
<th>Relationship</th>
<th>Phone</th>
</tr>
</thead>
</table>

## Cancer Diagnosis

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Date of diagnosis</th>
<th>Age at diagnosis</th>
<th>Date therapy completed</th>
<th>Laterality</th>
<th>Right</th>
<th>Left</th>
<th>NA</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Sites involved/Stage/Diagnostic details</th>
<th>Laterality</th>
<th>Right</th>
<th>Left</th>
<th>NA</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Hereditary/Congenital history</th>
<th></th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Pertinent past medical history</th>
<th></th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Institution</th>
<th>MD/APN</th>
<th>Medical record #</th>
</tr>
</thead>
</table>

## Relapse(s)

<table>
<thead>
<tr>
<th>Date of diagnosis</th>
<th>Age at diagnosis</th>
<th>Date therapy completed</th>
<th>Laterality</th>
<th>Right</th>
<th>Left</th>
<th>NA</th>
</tr>
</thead>
</table>

## Subsequent malignant neoplasm(s)

<table>
<thead>
<tr>
<th>Date of diagnosis</th>
<th>Age at diagnosis</th>
<th>Date therapy completed</th>
<th>Laterality</th>
<th>Right</th>
<th>Left</th>
<th>NA</th>
</tr>
</thead>
</table>

## Cancer Treatment Summary

<table>
<thead>
<tr>
<th>Protocol(s)</th>
<th>Acronym/Number</th>
<th>Title/Description</th>
<th>Initiated</th>
<th>Completed</th>
<th>On-study</th>
</tr>
</thead>
</table>

## Chemotherapy

<table>
<thead>
<tr>
<th>Drug name</th>
<th>Route</th>
<th>Additional information</th>
</tr>
</thead>
</table>

---

1. **Anthracyclines**: Include cumulative dose in mg/m² and age at first dose (see section 34 of Guidelines for isotoxic dose conversion);
2. **Carboplatin**: Indicate if dose was myeloablative
3. **IV Methotrexate and Cytarabine**: Indicate if “high dose” (any single dose ≥ 1000 mg/m²) or “standard dose” (all single doses < 1000 mg/m²);
4. **Note**: Cumulative doses, if known, should be recorded for all agents, particularly for alkylators and bleomycin.
## Summary of Cancer Treatment (Comprehensive) (cont)

### Cancer Treatment Summary (cont)

<table>
<thead>
<tr>
<th>Radiation</th>
<th>☐ Yes</th>
<th>☐ No</th>
<th>If yes, provide information below</th>
</tr>
</thead>
<tbody>
<tr>
<td>Site/Field</td>
<td>Laterality</td>
<td>Start/Stop dates</td>
<td>Type</td>
</tr>
<tr>
<td>Institution</td>
<td>Radiation oncologist</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Note: To convert cGy or rads to Gy, divide dose by 100 (example: 2400 cGy = 2400 rads = 24 Gy)*

### Hematopoietic Cell Transplant

<table>
<thead>
<tr>
<th>Type</th>
<th>Tandem?</th>
<th>Source</th>
<th>Date of infusion</th>
<th>Conditioning regimen</th>
</tr>
</thead>
<tbody>
<tr>
<td>☐ Yes</td>
<td>☐ No</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Institution Transplant physician

### Graft-Versus-Host Disease (GVHD) Prophylaxis/Treatment (for transplant patients only)

<table>
<thead>
<tr>
<th>Type</th>
<th>First dose</th>
<th>Last dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>☐ Yes</td>
<td>☐ No</td>
<td></td>
</tr>
</tbody>
</table>

Was the patient ever diagnosed with chronic GVHD? | ☐ Yes | ☐ No | Does the patient currently have active chronic GVHD? | ☐ Yes | ☐ No

### Surgery

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Date</th>
<th>Site (if applicable)</th>
<th>Laterality (if applicable)</th>
<th>Institution/Surgeon</th>
</tr>
</thead>
<tbody>
<tr>
<td>☐ Yes</td>
<td>☐ No</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Other Therapeutic Modalities

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Route</th>
<th>Cumulative dose (if known)</th>
</tr>
</thead>
<tbody>
<tr>
<td>☐ Yes</td>
<td>☐ No</td>
<td></td>
</tr>
</tbody>
</table>

### Additional Clinical Information

#### Complications/Late Effects

<table>
<thead>
<tr>
<th>Problem</th>
<th>Date onset</th>
<th>Date resolved</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>☐ Active</td>
<td>☐ Resolved</td>
<td></td>
<td></td>
</tr>
<tr>
<td>☐ Active</td>
<td>☐ Resolved</td>
<td></td>
<td></td>
</tr>
<tr>
<td>☐ Active</td>
<td>☐ Resolved</td>
<td></td>
<td></td>
</tr>
<tr>
<td>☐ Active</td>
<td>☐ Resolved</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

#### Adverse Drug Reactions/Allergies

<table>
<thead>
<tr>
<th>Drug</th>
<th>Reaction</th>
<th>Date</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>☐ Active</td>
<td>☐ Resolved</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

#### Additional Information/Comments

<table>
<thead>
<tr>
<th>☐ Yes</th>
<th>☐ No</th>
<th>If yes, provide information below</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Summary prepared by: Date prepared: Date updated:
## Key for Completing Summary of Cancer Treatment (Comprehensive)

### #1: Race/Ethnicity
- Asian
- Black/African American
- Caucasian (non-Hispanic/non-Latino)
- Hispanic or Latino
- Native American/Alaskan Native
- Native Hawaiian/Pacific Islander
- Multi-racial/multi-ethnic
- Race/ethnicity, other, specify:

### #2: Cancer Diagnosis
#### Central Nervous System Tumor
- Astrocytoma
- Cerebellar astrocytoma
- Supratentorial astrocytoma
- Brainstem glioma
- Choroid plexus neoplasm
- Craniopharyngioma
- Ependymoma
- Germ cell tumor, intracranial
- Optic glioma
- Pineal tumor
- PNET
  - Cerebellar (medulloblastoma)
  - Supratentorial PNET
- Spinal cord tumor, intramedullary
- CNS tumor, other, specify:

#### Endocrine tumor
- Adrenal tumor (non-neuroblastoma)
- Thyroid tumor
- Parathyroid tumor
- Gastroenteropancreatic tumor
- Multiple endocrine neoplasia syndrome
- Endocrine tumor, other, specify:

#### Germ cell tumor (extracranial)
- Seminoma
- Germinoma
- Dyserminoma
- Non-seminomas
- Yolk sac tumor
- Embryonal carcinoma
- Choriocarcinoma
- Teratoma
- Mature
- Immature
- With malignant transformation

#### #2: Cancer Diagnosis (cont)
- Germ cell tumor (extracranial) (cont)
  - Germ cell tumor, other, specify:
  - Langerhans cell histiocytosis
  - Leukemia
    - Acute lymphoblastic leukemia
    - Acute myeloid leukemia
    - Chronic myeloid leukemia
    - Myelodysplastic syndrome
    - Myeloproliferative disorder
  - Leukemia, other, specify:
  - Liver tumor
    - Hepatoblastoma
    - Hepatocellular carcinoma
    - Liver tumor, other, specify:

#### Lymphoma
- Hodgkin lymphoma
- Non-Hodgkin lymphoma
- Lymphoblastic lymphoma
- Burkitt's lymphoma
- Large cell lymphoma
- Anaplastic large cell lymphoma
- Diffuse large B-cell lymphoma
- Lymphoma, other, specify:

#### Nasopharyngeal carcinoma
- Neuroblastoma
- Ganglioneuroblastoma

#### Renal tumor
- Wilms tumor
- Clear cell sarcoma
- Renal cell carcinoma
- Renal tumor, other, specify:

#### Retinoblastoma
- Sarcoma
  - Ewing's sarcoma/peripheral PNET
  - Osteogenic sarcoma
  - Rhabdomyosarcoma
  - Soft tissue sarcoma (nonrhabdomyosarcomatous)
  - Alveolar soft part sarcoma
  - Fibrosarcoma
  - Leiomyosarcoma
  - Liposarcoma
  - Malignant fibrous histiocytoma
  - Malignant peripheral nerve sheath tumor
  - Neurofibrosarcoma

#### Sarcoma
- Soft tissue sarcoma (nonrhabdomyosarcomatous) (cont)
- Synovial sarcoma
- Undifferentiated sarcoma
- Sarcoma, other, specify:

#### Skin cancer
- Basal cell carcinoma
- Malignant melanoma
- Squamous cell carcinoma
- Skin cancer, other, specify:

#### Malignancy, other, specify:
- Diagnosis, other, specify:

#### #3: Hereditary/Congenital History
- Congenital heart disease
- Congenital disease, other, specify:
- Hemi-hypertrophy
- Neurofibromatosis
  - Type I
  - Type II
- Down syndrome
- Syndrome, other, specify:
- Hereditary condition, other, specify:
  - None
  - Unknown

#### #4: Subsequent Malignancy Diagnosis
- Bladder cancer
- Breast cancer
- Central nervous system tumor
- Malignant, specify type and location:
  - Meningioma, specify location:
  - CNS tumor, other, specify type:
- Cervical cancer
- Gastrointestinal cancer
- Esophageal cancer
- Stomach cancer
- Colorectal cancer
- Hepatocellular carcinoma
- Pancreatic cancer
- GI cancer, other, specify:

#### Leukemia
- Acute lymphoblastic leukemia
- Acute myeloid leukemia
- Chronic myeloid leukemia
- Myelodysplastic syndrome
- Myeloproliferative disorder
## Key for Completing Summary of Cancer Treatment (Comprehensive) (cont)

<table>
<thead>
<tr>
<th>#4 Subsequent Malignancy Diagnosis (cont)</th>
<th>#5: Chemotherapy (cont)</th>
<th>#6: Route</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Leukemia (cont)</strong></td>
<td>Cyclophosphamide</td>
<td>PO</td>
</tr>
<tr>
<td>Leukemia, other, specify:</td>
<td></td>
<td>IM</td>
</tr>
<tr>
<td><strong>Lung cancer</strong></td>
<td>Cytarabine</td>
<td>IV</td>
</tr>
<tr>
<td><strong>Lymphoma</strong></td>
<td>If IV: any single dose ≥ 1000 mg/m²? □ Yes □ No</td>
<td>SQ</td>
</tr>
<tr>
<td>Hodgkin lymphoma</td>
<td>Dacarbazine (DTIC)</td>
<td>IT</td>
</tr>
<tr>
<td>Non-Hodgkin lymphoma</td>
<td>Daunorubicin</td>
<td>IO</td>
</tr>
<tr>
<td>Lymphoblastic lymphoma</td>
<td>Dexamethasone</td>
<td>Route, other, specify:</td>
</tr>
<tr>
<td>Burkitt lymphoma</td>
<td>Docetaxel</td>
<td>Unknown</td>
</tr>
<tr>
<td>Large cell lymphoma</td>
<td>Doxorubicin</td>
<td></td>
</tr>
<tr>
<td>Post-transplant lymphoproliferative disorder (PTLD)</td>
<td>Epirubicin</td>
<td></td>
</tr>
<tr>
<td>Lymphoma, other, specify:</td>
<td>Etoposide (VP-16)</td>
<td></td>
</tr>
<tr>
<td><strong>Peripheral nerve sheath tumor/ Schwanoma/Acoustic neuroma</strong></td>
<td>Fludarabine</td>
<td></td>
</tr>
<tr>
<td><strong>Renal cancer</strong></td>
<td>Fluorouracil</td>
<td></td>
</tr>
<tr>
<td>Renal cell carcinoma</td>
<td>Gemcitabine</td>
<td></td>
</tr>
<tr>
<td>Clear cell sarcoma</td>
<td>Hydrocortisone</td>
<td></td>
</tr>
<tr>
<td>Renal cancer, other, specify:</td>
<td>Hydroxyurea</td>
<td></td>
</tr>
<tr>
<td><strong>Sarcoma</strong></td>
<td>Idoxuridine</td>
<td></td>
</tr>
<tr>
<td>Ewing’s sarcoma/peripheral PNET</td>
<td>Imitinib Mesylate</td>
<td></td>
</tr>
<tr>
<td>Osteogenic sarcoma</td>
<td>Irinotecan</td>
<td></td>
</tr>
<tr>
<td>Rhabdomyosarcoma</td>
<td>Lomustine (CCNU)</td>
<td></td>
</tr>
<tr>
<td>Soft tissue sarcoma (nonrhabdomyosarcomatous)</td>
<td>Mechlorethamine</td>
<td></td>
</tr>
<tr>
<td>Undifferentiated sarcoma</td>
<td>Melphalan</td>
<td></td>
</tr>
<tr>
<td>Sarcoma, other, specify:</td>
<td>Mercapturine</td>
<td></td>
</tr>
<tr>
<td><strong>Skin cancer</strong></td>
<td>Methotrexate</td>
<td></td>
</tr>
<tr>
<td>Basal cell carcinoma</td>
<td>If IV: Any single dose ≥ 1000 mg/m²? □ Yes □ No</td>
<td>Head/brain</td>
</tr>
<tr>
<td>Malignant melanoma</td>
<td>Mitoxantrone</td>
<td>Cranial</td>
</tr>
<tr>
<td>Squamous cell carcinoma</td>
<td>Oxaliplatin</td>
<td>Orbital/Eye</td>
</tr>
<tr>
<td><strong>Thyroid cancer</strong></td>
<td>Paclitaxel</td>
<td>Specify:</td>
</tr>
<tr>
<td>Malignancy, other, specify:</td>
<td>Prednisone</td>
<td>□ Right □ Left □ Bilateral</td>
</tr>
<tr>
<td>None</td>
<td>Procarbazine</td>
<td>Ear/Infratemporal</td>
</tr>
<tr>
<td>Unknown</td>
<td>Temozolomide</td>
<td>Specify:</td>
</tr>
<tr>
<td>#5: Chemotherapy</td>
<td>Teniposide (VM-26)</td>
<td>□ Right □ Left □ Bilateral</td>
</tr>
<tr>
<td>Asparaginase</td>
<td>Thioguanine (6-TG)</td>
<td>Nasopharyngeal</td>
</tr>
<tr>
<td>Bleomycin</td>
<td>Thiopeta</td>
<td>Oropharyngeal</td>
</tr>
<tr>
<td>Busulfan</td>
<td>Topotecan</td>
<td>Waldeyer's ring</td>
</tr>
<tr>
<td>Carboplatin</td>
<td>Trimetrexate</td>
<td>Head/brain radiation, other, specify:</td>
</tr>
<tr>
<td>Myeloblastic dose? □ Yes □ No</td>
<td>Vinorelbine</td>
<td></td>
</tr>
<tr>
<td>Carmustine (BCNU)</td>
<td>Vinblastine</td>
<td></td>
</tr>
<tr>
<td>Chlorambucil</td>
<td>Vinristine</td>
<td></td>
</tr>
<tr>
<td>Cisplatin</td>
<td>Chemotherapy, other, specify:</td>
<td></td>
</tr>
<tr>
<td>Cladribine</td>
<td>None</td>
<td></td>
</tr>
<tr>
<td>Clofarabine</td>
<td>Unknown</td>
<td></td>
</tr>
<tr>
<td><strong>Unknown</strong></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>#7: Cumulative Dose (Note: this is a required field for anthracyclines and optional but suggested for all others)</th>
<th>#8: Radiation Site/Field</th>
</tr>
</thead>
<tbody>
<tr>
<td>mg/m²</td>
<td>Head/brain</td>
</tr>
<tr>
<td>units/m²</td>
<td>Cranial</td>
</tr>
<tr>
<td>mg/kg</td>
<td>Orbital/Eye</td>
</tr>
<tr>
<td>(Note: computer will multiply mg by 30 and display as mg/m²)</td>
<td>Specify: □ Right □ Left □ Bilateral</td>
</tr>
<tr>
<td>Not available</td>
<td>Ear/Infratemporal</td>
</tr>
<tr>
<td>Not applicable</td>
<td>Specify: □ Right □ Left □ Bilateral</td>
</tr>
<tr>
<td>Cumulative dose, other, specify:</td>
<td>Nasopharyngeal</td>
</tr>
<tr>
<td>Unknown</td>
<td>Oropharyngeal</td>
</tr>
<tr>
<td></td>
<td>Waldeyer's ring</td>
</tr>
<tr>
<td></td>
<td>Head/brain radiation, other, specify:</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>#8: Radiation Site/Field</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Head/brain</strong></td>
</tr>
<tr>
<td>Cervical (neck)</td>
</tr>
<tr>
<td>Supraclavicular</td>
</tr>
<tr>
<td>Spine</td>
</tr>
<tr>
<td>Spine – cervical</td>
</tr>
<tr>
<td>Spine – thoracic</td>
</tr>
<tr>
<td>Spine – lumbar</td>
</tr>
<tr>
<td>Spine – sacral</td>
</tr>
<tr>
<td>Spine – whole</td>
</tr>
<tr>
<td><strong>Axilla</strong></td>
</tr>
<tr>
<td>Specify: □ Right □ Left □ Bilateral</td>
</tr>
</tbody>
</table>
### #8: Radiation Site/Field (cont)

#### Chest
- Chest (thorax)
- Whole lung
  - Specify: □ Right  □ Left  □ Bilateral
- Mediastinal
- Chest, other, specify:

#### Abdomen
- Hepatic
- Renal
  - Specify: □ Right  □ Left  □ Bilateral
- Upper quadrant
  - Specify: □ Right  □ Left  □ Bilateral
- Spleen
  - Specify: □ Partial  □ Entire
- Paraortic
- Flank/hemiabdomen
  - Specify: □ Right  □ Left
  - Specify: Extended below iliac crest: □ Yes  □ No

#### Pelvis
- Pelvic
- Vaginal
- Prostate
- Bladder
- Iliac
- Inguinal
- Femoral

#### Testicular
- Specify: □ Right  □ Left  □ Bilateral

#### Extremity
- Upper
  - Specify: □ Right  □ Left  □ Bilateral
  - Specify: □ Proximal  □ Distal  □ Entire
- Lower
  - Specify: □ Right  □ Left  □ Bilateral
  - Specify: □ Proximal  □ Distal  □ Entire

#### Total Body Irradiation (TBI)

### #9: Radiation Type

#### Brachytherapy
#### Conformal
#### External beam (conventional)
#### Intensity-modulated radiation therapy (IMRT)
#### Proton beam
#### Stereotactic

### #8: Radiation Site/Field (cont)

#### Radiation site/field, other, specify:
- None
- Unknown

### #10: Radiation Boost

#### Tumor bed, specify location:
- None
- Unknown

### #11: Hematopoietic Cell Transplant (HCT) – Type

#### Autologous
#### Matched related
#### Mismatched related
#### Haploidentical related
#### Syngeneic
#### Matched unrelated
#### HCT type, other, specify:
- Unknown

### #12: Hematopoietic Cell Transplant – Source

#### Bone marrow
#### Peripheral blood stem cells
#### Cord blood
#### HCT source, other, specify:
- Unknown

### #13: Hematopoietic Cell Transplant – Conditioning Regimen

#### Anti-thymocyte globulin (ATG)
#### Busulfan
#### Carmustine (BCNU)
#### Cyclophosphamide
#### Etoposide
#### Fludarabine

### #14: Graft versus host disease (GVHD) – Prophylaxis/Treatment

#### Anti-thymocyte globulin (ATG)
#### Cyclosporine
#### Methotrexate
#### Myophenolate mofetil (MMF)
#### Prednisone
#### Psoralen plus ultraviolet-A radiation (PUVA)
#### Sirolimus
#### Tacrolimus

### #15: Surgery

#### Amputation, specify site:
- Specify: □ Right  □ Left  □ Bilateral
- Central venous catheter
- Cystectomy
- Enucleation
  - Specify: □ Right  □ Left  □ Bilateral
- Hysterectomy
- Laparotomy
- Limb sparing procedure, specify site:
  - Specify: □ Right  □ Left  □ Bilateral
- Nephrectomy
  - Specify: □ Right  □ Left  □ Bilateral
- Neurosurgery – brain
  - Potential to affect hypothalamic-pituitary axis?
    - □ Yes  □ No
- Neurosurgery – spinal cord
- Oophoropexy
- Oophorectomy
  - Specify: □ Right  □ Left  □ Bilateral
  - If partial or unilateral, specify: □ Right  □ Left
- Orchiectomy
  - Specify: □ Partial  □ Unilateral  □ Bilateral
  - If partial or unilateral, specify: □ Right  □ Left
- Pelvic surgery
- Thoracic surgery*
- Splenectomy
### Key for Completing Summary of Cancer Treatment (Comprehensive) (cont)

#### #15: Surgery (cont)
- **Thyroidectomy**
- Surgery, other, specify:
  - None
  - Unknown
- Add comment:
  - *Thoracic surgery includes: thoracotomy, chest wall surgery, rib resection, pulmonary lobectomy, pulmonary metastasectomy, and pulmonary wedge resection*

#### #16: Other Therapeutic Modalities

**Systemic Radiation**
- Radiolodine therapy (I-131 thyroid ablation)
- Systemic iodine metaiodobenzylguanidine (MIBG) (in therapeutic doses)
- Systemic radiation, other, specify:

**Bioimmunootherapy**
- Hematopoietic growth factors:
  - Granulocyte colony stimulating factor (G-CSF)
  - Erythropoietin
  - Thrombopoietin
- Interferon:
  - Alpha interferon
  - Gamma interferon
- Interleukin (IL):
  - IL-2
  - IL-11
- Other, specify:
- Monoclonal antibody, specify type:
- Retinoid acid, specify type:
- Bioimmunootherapy, other, specify:

**Other therapeutic modality, specify:**
- None
- Unknown

#### #17: Complications/Late Effects (by system)

**Cardiovascular (cont)**
- Atherosclerotic heart disease
- Cardiomyopathy
- Carotid artery disease
- Congestive heart failure
- Infection of retained cuff or line tract
- Myocardial infarction
- Pericardial fibrosis
- Pericarditis
- Post-thrombotic syndrome
- Subclavian artery disease
- Subclinical left ventricular dysfunction
- Thrombosis
- Valvular disease
- Vascular insufficiency
- Cardiovascular complication, other, specify:

**Central Nervous System (CNS)**
- Ataxia
- Cavernomas
- Chronic pain, central neuropathic
- Clinical leukoencephalopathy
- Dysarthria
- Dysphagia
- Hemiparesis
- Hydrocephalus
- Movement disorders
- Moyamoya
- Neurocognitive deficits
- Academic fluency
- Behavioral change
- Diminished IQ
- Executive function (planning and organization)
- Fine motor dexterity
- Language
- Learning deficits in math and reading (particularly reading comprehension)
- Memory (particularly visual, sequencing, temporal memory)
- Processing speed
- Sustained attention
- Visual-motor integration
- Neurogenic bladder
- Neurogenic bowel

**Central Nervous System (CNS) (cont)**
- Occlusive cerebral vasculopathy
- Paralysis
- Seizures
- Shunt malfunction
- Spasticity
- Stroke
- CNS complication, other, specify:

**Dental**
- Dental caries
- Ectopic molar eruption
- Enamel dysplasia
- Malocclusion
- Microdonta
- Osteoradionecrosis of the jaw
- Periodontal disease
- Root thinning/shortening
- Salivary gland dysfunction
- Temporomandibular joint dysfunction
- Tooth/root agenesis
- Xerostomia
- Dental complication, other, specify:

**Dermatologic**
- Altered skin pigmentation
- Nail dystrophy
- Permanent alopecia
- Scleroderma changes
- Skin fibrosis
- Telangiectasias
- Vitiligo
- Dermatologic complication, other, specify:

**Endocrine/Metabolic**
- Central adrenal insufficiency
- Diabetes insipidus
- Dyslipidemia
- Gonadotropin deficiency (LH/FSH deficiency)
- Growth hormone (GH) deficiency
- Hyperprolactinemia
- Hyperthyroidism
- Hypothyroidism, primary (thyroid gland failure)
- Hypothyroidism, central/secondary (T4/TSH deficiency)
#17: Complications/Late Effects (by system)

## Endocrine/Metabolic (cont)

- Impaired glucose metabolism/diabetes mellitus
- Overweight [Body Mass Index (BMI)]
  - Age 2–20 yrs: BMI for age ≥ 85 – <95%ile
  - Age > 20 yrs: BMI 25 to 29.9
- Obesity
  - Age 2–20 yrs: BMI for age ≥ 95%ile
  - Age > 20 yrs, BMI ≥ 30
- Precocious puberty
- Thyroid nodule
- Endocrine/metabolic complication, other, specify:

## Gastrointestinal/Hepatic

- Abdominal adhesions
- Bowel obstruction
- Cholelithiasis
- Chronic enterocolitis
- Cirrhosis
- Esophageal stricture
- Fecal incontinence
- Fistula
- Focal nodular hyperplasia
- Hepatic dysfunction
- Hepatic fibrosis
- Iron overload
- Sinusoidal obstruction syndrome (SOS) [previously known as veno-occlusive disease (VOD)]
- Strictures
- Vitamin B12/folate/carotene deficiency
- Gastrointestinal/hepatic complication, other, specify:

## Immune

- Asplenia - functional
- Asplenia - surgical
- Chronic hepatitis B
- Chronic hepatitis C
- Chronic graft-versus-host disease (cGVHD)
- Chronic infection
- Chronic sinusitis
- Decreased B cells
- HIV infection
- Hypogammaglobulinemia
- Secretory IgA deficiency
- T cell dysfunction

## Immune (cont)

- Immune complication, other, specify:

## Musculoskeletal

- Chronic pain, musculoskeletal
- Contractures
- Fibrosis
- Functional and activity limitations
- Hypoplasia
- Increased energy expenditure (related to amputation/limb salvage)
- Kyphosis
- Limb length discrepancy
- Osteonecrosis (avascular necrosis)
- Prosthetic malfunction (loosening, non-union, fracture) requiring revision, replacement or amputation
- Radiation-induced fracture
- Reduced bone mineral density (BMD)
- Reduced or uneven growth
- Residual limb integrity problems
- Scoliosis
- Shortened trunk height
- Musculoskeletal complication, other, specify:

## Ocular

- Cataract
- Chronic painful eye
- Gaze paresis
- Glaucoma
- Keratitis
- Lacrimal duct atrophy
- Maculopathy
- Nystagmus
- Ocular nerve palsy
- Optic atrophy
- Optic chiasm neuropathy
- Orbital hypoplasia
- Papilledema
- Papillopathy
- Poor prosthetic fit (related to enucleation)
- Retinopathy
- Telangiectasias

## Pulmonary

- Acute respiratory distress syndrome
- Bronchiectasis
- Bronchiolitis obliterans
- Chronic bronchitis
- Interstitial pneumonitis
- Obstructive lung disease
- Pulmonary fibrosis
- Restrictive lung disease
- Pulmonary complication, other, specify:
#17: Complications/Late Effects (by system) (cont)

## Reproductive – Female
- Adverse pregnancy outcome
- Delivery complications
- Fetal malposition
- Adverse pregnancy outcome (cont)
- Low-birth weight infant
- Neonatal death
- Premature labor
- Pregnancy complications
- Spontaneous abortion
- Breast tissue hypoplasia
- Dyspareunia
- Infertility
- Pelvic adhesions
- Pelvic floor dysfunction
- Premature ovarian insufficiency/premature menopause
- Psychosexual/sexual dysfunction
- Puberty - absence
- Puberty - delayed/arrested
- Reduced fertility
- Symptomatic ovarian cysts
- Uterine vascular insufficiency
- Vaginal fibrosis/stenosis
- Vulvar scarring
- Adverse pregnancy outcome (cont)
- Delivery complications
- Fetal malposition
- Adverse pregnancy outcome (cont)
- Low-birth weight infant
- Neonatal death
- Premature labor
- Pregnancy complications
- Spontaneous abortion
- Breast tissue hypoplasia
- Dyspareunia
- Infertility
- Pelvic adhesions
- Pelvic floor dysfunction
- Premature ovarian insufficiency/premature menopause
- Psychosexual/sexual dysfunction
- Puberty - absence
- Puberty - delayed/arrested
- Reduced fertility
- Symptomatic ovarian cysts
- Uterine vascular insufficiency
- Vaginal fibrosis/stenosis
- Vulvar scarring

## Reproductive – Male
- Anejaculation
- Azospermia
- Ejaculatory dysfunction
- Erectile dysfunction
- Infertility
- Oligospermia
- Puberty - absence
- Puberty - delayed/arrested
- Reduced fertility
- Retrograde ejaculation
- Testosterone deficiency/insufficiency
- Reproductive – male complication, other, specify:

## Urinary
- Asymptomatic bacteriuria
- Bladder fibrosis
- Chronic urinary tract infection
- Dysfunctional voiding
- Fanconi syndrome
- Glomerular injury
- Hemorrhagic cystitis
- Hydrocele
- Hydronephrosis
- Hyperfiltration
- Hypertension
- Hypophosphatemic rickets
- Proteinuria
- Renal dysfunction
- Renal insufficiency
- Renal tubular acidosis
- Reservoir calculi
- Spontaneous neobladder perforation
- Urinary incontinence
- Urinary tract obstruction
- Vesicoureteral reflux
- Urinary complication, other, specify:
- Other, specify:
- No late effects identified
- Unknown
Instructions:
Patient-Specific Guideline Identification Tool (Version 6.0)

To determine Long-Term Follow-Up Guideline sections relevant to an individual patient:

1. Place a check mark in the “Mark if Patient Received” column for each chemotherapy agent, radiation field, transplant type, surgery, or other therapeutic modality that the patient received.

2. Compile a list of all section numbers generated during step 1. Include the following sections as applicable:
   - Sections 1 - 7 Applicable to all patients
   - Section 8 Patients diagnosed before 1972
   - Section 9 Patients diagnosed before 1993
   - Section 10 Patients diagnosed between 1977 and 1985
   - Section 11 All patients who received chemotherapy
   - Sections 44, 45, 96 All patients who received radiation
   - Sections 100 - 105 All patients who underwent hematopoietic cell transplant
     - Section 100 is for males only
     - Section 101 is for females only
   - Section 164-165 Applicable to all patients

3. For patients who received radiation for which a minimum dose specification is indicated, follow the “Instructions for Radiation Dose Calculation” in Appendix I. Delete from your list those radiation section(s) for which the patient did not receive the minimum radiation exposure at which the section(s) become applicable.

4. You now have a finalized list of all guideline sections applicable to this patient.
### Patient-Specific Guideline Identification Tool

Applicable guideline sections indicated in bold/dark blue; M=Male; F=Female

<table>
<thead>
<tr>
<th>Name</th>
<th>Sex</th>
<th>Date of Birth</th>
<th>Cancer Diagnosis</th>
<th>Date of Diagnosis</th>
<th>End Therapy Date</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- **Sections 1–7 applicable to all patients**
- Prior to 1972: □ Section 8
- Prior to 1993: □ Section 9
- 1977–1985: □ Section 10

LTFU guidelines are applicable to patients who are ≥ 2 years following completion of cancer therapy.

#### CHEMOTHERAPY

- □ Yes  □ No

If yes: □ Section 11 and applicable guidelines for specific chemotherapy agents below

<table>
<thead>
<tr>
<th>Mark If Patient Received</th>
<th>Chemotherapy Agent</th>
<th>Applicable Guideline Sections</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Asparaginase</td>
<td>Section 40</td>
</tr>
<tr>
<td></td>
<td>Bleomycin</td>
<td>Section 35</td>
</tr>
<tr>
<td></td>
<td>Busulfan**</td>
<td>Sections 12M, 13M, 14F, 15F, 16, 17, 18</td>
</tr>
<tr>
<td></td>
<td>Cumulative dose = _____ mg/m²</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Cyclophosphamide isotoxic dose = _____ mg/m² = Cumulative dose x 8.823</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Carboplatin: All doses</td>
<td>Sections 12M, 13M, 14F, 15F, 16, 23, 24</td>
</tr>
<tr>
<td></td>
<td>Carboplatin: Myeloablative dose (conditioning for HCT)</td>
<td>Section 22</td>
</tr>
<tr>
<td></td>
<td>Carmustine (BCNU)**</td>
<td>Sections 12M, 13M, 14F, 15F, 16, 17</td>
</tr>
<tr>
<td></td>
<td>Cumulative dose = _____ mg/m²</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Cyclophosphamide isotoxic dose = _____ mg/m² = Cumulative dose x 15</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Chlorambucil**</td>
<td>Sections 12M, 13M, 14F, 15F, 16</td>
</tr>
<tr>
<td></td>
<td>Cumulative dose = _____ mg/m²</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Cyclophosphamide isotoxic dose = _____ mg/m² = Cumulative dose x 14.286</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Cisplatin</td>
<td>Sections 12M, 13M, 14F, 15F, 16, 22, 23, 24</td>
</tr>
<tr>
<td></td>
<td>Cyclophosphamide**</td>
<td>Sections 12M, 13M, 14F, 15F, 16, 19, 20</td>
</tr>
<tr>
<td></td>
<td>Cumulative dose = _____ mg/m²</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Cyclophosphamide isotoxic dose = _____ mg/m² = Cumulative dose x 1</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Cytarabine: Low dose IV (all single doses &lt;1000 mg/m²), IO, IT, SQ</td>
<td>Section 26</td>
</tr>
<tr>
<td></td>
<td>Cytarabine: High dose IV (any single dose ≥1000 mg/m²)</td>
<td>Section 25</td>
</tr>
<tr>
<td></td>
<td>Dacarbazine (DTIC)</td>
<td>Sections 12M, 13M, 14F, 15F, 16</td>
</tr>
<tr>
<td></td>
<td>Daunorubicin*</td>
<td>Sections 12M, 13M, 14F, 15F, 16</td>
</tr>
<tr>
<td></td>
<td>Cumulative dose = _____ mg/m²</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Doxorubicin isotoxic dose = _____ mg/m² = Cumulative dose x 0.5</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Dexamethasone</td>
<td>Sections 37, 38, 39</td>
</tr>
<tr>
<td></td>
<td>Doxorubicin*</td>
<td>Sections 33, 34</td>
</tr>
<tr>
<td></td>
<td>Cumulative dose: _____ mg/m²</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Doxorubicin isoxic dose: _____ mg/m² = Cumulative dose x 1</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Epirubicin*</td>
<td>Sections 33, 34</td>
</tr>
<tr>
<td></td>
<td>Cumulative dose: _____ mg/m²</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Doxorubicin isoxic dose: _____ mg/m² = Cumulative dose x 0.67</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Etoposide (VP16)</td>
<td>Section 43</td>
</tr>
<tr>
<td></td>
<td>Idarubicin*</td>
<td>Sections 33, 34</td>
</tr>
<tr>
<td></td>
<td>Cumulative dose: _____ mg/m²</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Doxorubicin isoxic dose: _____ mg/m² = Cumulative dose x 5</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Ifosfamide**</td>
<td>Sections 12M, 13M, 14F, 15F, 16, 19, 21</td>
</tr>
<tr>
<td></td>
<td>Cumulative dose = _____ mg/m²</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Cyclophosphamide isoxic dose: _____ mg/m² = Cumulative dose x 0.244</td>
<td></td>
</tr>
</tbody>
</table>
### Patient-Specific Guideline Identification Tool (cont)

<table>
<thead>
<tr>
<th>Chemotherapy Agent (cont)</th>
<th>Applicable Guideline Sections (cont)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lomustine (CCNU)**</td>
<td>Sections 12M, 13M, 14F, 15F, 16, 17</td>
</tr>
<tr>
<td>Cumulative dose = _______ mg/m²</td>
<td></td>
</tr>
<tr>
<td>Cyclophosphamide isotoxic dose = _______ mg/m² = Cumulative dose x 16</td>
<td></td>
</tr>
<tr>
<td>Mechloretamine**</td>
<td>Sections 12M, 13M, 14F, 15F, 16</td>
</tr>
<tr>
<td>Cumulative dose = _______ mg/m²</td>
<td></td>
</tr>
<tr>
<td>Cyclophosphamide isotoxic dose = _______ mg/m² = Cumulative dose x 100</td>
<td></td>
</tr>
<tr>
<td>Melphalan**</td>
<td>Sections 12M, 13M, 14F, 15F, 16</td>
</tr>
<tr>
<td>Cumulative dose = _______ mg/m²</td>
<td></td>
</tr>
<tr>
<td>Cyclophosphamide isotoxic dose = _______ mg/m² = Cumulative dose x 40</td>
<td></td>
</tr>
<tr>
<td>Mercaptopurine (6MP)</td>
<td>Section 27</td>
</tr>
<tr>
<td>Methotrexate: High dose IV, Low dose IV, IM, PO</td>
<td>Sections 28, 29, 30</td>
</tr>
<tr>
<td>Methotrexate: High dose IV, IO, IT</td>
<td>Sections 31, 32</td>
</tr>
<tr>
<td>Mitoxantrone*</td>
<td>Section 33, 34</td>
</tr>
<tr>
<td>Cumulative dose: _______ mg/m²</td>
<td></td>
</tr>
<tr>
<td>Doxorubicin isotoxic dose = _______ mg/m² = Cumulative dose x 10</td>
<td></td>
</tr>
<tr>
<td>Prednisone</td>
<td>Sections 37, 38, 39</td>
</tr>
<tr>
<td>Procyclophosphamide**</td>
<td>Sections 12M, 13M, 14F, 15F, 16</td>
</tr>
<tr>
<td>Cumulative dose = _______ mg/m²</td>
<td></td>
</tr>
<tr>
<td>Cyclophosphamide isotoxic dose = _______ mg/m² = Cumulative dose x 0.857</td>
<td></td>
</tr>
<tr>
<td>Temozolomide</td>
<td>Sections 12M, 13M, 14F, 15F, 16</td>
</tr>
<tr>
<td>Teniposide (VM26)</td>
<td>Section 43</td>
</tr>
<tr>
<td>Thioguanine (6TG)</td>
<td>Section 27</td>
</tr>
<tr>
<td>Thiopeta**</td>
<td>Sections 12M, 13M, 14F, 15F, 16</td>
</tr>
<tr>
<td>Cumulative dose = _______ mg/m²</td>
<td></td>
</tr>
<tr>
<td>Cyclophosphamide isotoxic dose = _______ mg/m² = Cumulative dose x 50</td>
<td></td>
</tr>
<tr>
<td>Vinblastine</td>
<td>Sections 41, 42</td>
</tr>
<tr>
<td>Vincristine</td>
<td>Sections 41, 42</td>
</tr>
</tbody>
</table>

*Instructions for Anthracycline Dose Calculation: Use formulas below to convert to doxorubicin isotoxic equivalents prior to calculating total cumulative anthracycline dose:

- **Daunorubicin** – multiply total dose x 0.5
- **Doxorubicin** – multiply total dose x 1
- **Epirubicin** – multiply total dose x 0.67
- **Idarubicin** – multiply total dose x 5
- **Mitoxantrone** – multiply total dose x 10

**Instructions for Cyclophosphamide Dose Calculation: Use formulas below to convert to cyclophosphamide isotoxic equivalents prior to calculating total cumulative cyclophosphamide dose:

- **Busulfan** – multiply total dose x 8.823
- **BCNU** – multiply total dose x 15
- **Chlorambucil** – multiply total dose x 14.286
- **Cyclophosphamide** – multiply total dose x 1
- **Iosfamide** – multiply total dose x 0.244
- **CCNU** – multiply total dose x 16
- **Mechlorethamine** – multiply total dose x 100
- **Melphalan** – multiply total dose x 40
- **Procarbazine** – multiply total dose x 0.857
- **Thiotepa** – multiply total dose x 50

**Note:** There is a paucity of literature to support isotoxic dose conversion; however, the above conversion factors may be used for convenience in order to gauge screening frequency. Clinical judgment should ultimately be used to determine indicated screening for individual patients.

### RADIATION: ☐ Yes ☐ No
If yes: ☐ Sections 44, 45, 96 and applicable guidelines for specific radiation fields below

<table>
<thead>
<tr>
<th>Radiation Field*</th>
<th>Dose</th>
<th>Applicable Guideline Sections</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any Radiation (not including TBI)</td>
<td>Any</td>
<td>Section 98</td>
</tr>
<tr>
<td>Head/Brain</td>
<td>Any</td>
<td>Sections 46, 47, 48, 49, 50, 51, 52, 53, 54M, 55F, 56, 57, 58M, 59F, 61, 62, 64, 65, 67, 68, 69, 70, 71</td>
</tr>
<tr>
<td>Head/Brain</td>
<td>Minimum dose specifications apply**</td>
<td>Sections 60, 63, 66</td>
</tr>
</tbody>
</table>
## Patient-Specific Guideline Identification Tool (cont)

### RADIATION

**Yes** ☐ No ☐

If yes: ☐ Sections 44, 45, 96 and applicable guidelines for specific radiation fields below

<table>
<thead>
<tr>
<th>Mark If Patient Received (cont)</th>
<th>Radiation Field* (cont)</th>
<th>Dose (cont)</th>
<th>Applicable Guideline Sections (cont)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neck</td>
<td>Any</td>
<td></td>
<td>Sections 64, 65, 67, 68, 69, 70, 71, 72, 79</td>
</tr>
<tr>
<td>Neck</td>
<td>Minimum dose specifications apply**</td>
<td></td>
<td>Section 66</td>
</tr>
<tr>
<td>Axilla</td>
<td>Any</td>
<td></td>
<td>Sections 73F, 74F, 75, 76</td>
</tr>
<tr>
<td>Chest</td>
<td>Any</td>
<td></td>
<td>Sections 72, 73F, 74F, 75, 76, 79, 97</td>
</tr>
<tr>
<td>Chest</td>
<td>Minimum dose specifications apply**</td>
<td></td>
<td>Section 77</td>
</tr>
<tr>
<td>Abdomen</td>
<td>Any</td>
<td></td>
<td>Sections 79, 80, 81, 82, 83, 84, 85, 86, 87, 97</td>
</tr>
<tr>
<td>Abdomen</td>
<td>Minimum dose specifications apply**</td>
<td></td>
<td>Sections 77, 78</td>
</tr>
<tr>
<td>Pelvis</td>
<td>Any</td>
<td></td>
<td>Sections 84, 85, 86, 88, 89, 92F, 93F, 94F, 95F</td>
</tr>
<tr>
<td>Testes</td>
<td>Any</td>
<td></td>
<td>Sections 90M, 91M</td>
</tr>
<tr>
<td>Spine (whole)</td>
<td>Any</td>
<td></td>
<td>Sections 64, 65, 67, 68, 69, 70, 71, 72, 79, 84, 85, 86, 88, 89, 92F, 93F, 94F, 97</td>
</tr>
<tr>
<td>Spine (whole)</td>
<td>Minimum dose specifications apply**</td>
<td></td>
<td>Sections 66, 77</td>
</tr>
<tr>
<td>Spine (cervical)</td>
<td>Any</td>
<td></td>
<td>Sections 64, 65, 67, 68, 69, 70, 71, 79</td>
</tr>
<tr>
<td>Spine (cervical)</td>
<td>Minimum dose specifications apply**</td>
<td></td>
<td>Section 66</td>
</tr>
<tr>
<td>Spine (thoracic)</td>
<td>Any</td>
<td></td>
<td>Sections 72, 79, 97</td>
</tr>
<tr>
<td>Spine (thoracic)</td>
<td>Minimum dose specifications apply**</td>
<td></td>
<td>Section 77</td>
</tr>
<tr>
<td>Spine (lumbar)</td>
<td>Any</td>
<td></td>
<td>Sections 84, 85, 86, 97</td>
</tr>
<tr>
<td>Spine (sacral)</td>
<td>Any</td>
<td></td>
<td>Sections 84, 85, 86, 88, 89, 92F, 93F, 94F</td>
</tr>
<tr>
<td>TBI</td>
<td>Any</td>
<td></td>
<td>Sections 44, 45, 46, 47, 48, 53, 58M, 59F, 61, 64, 65, 67, 68, 69, 73F, 74F, 75, 76, 80, 81, 86, 87, 91M, 92F, 93F, 94F, 96</td>
</tr>
<tr>
<td>TBI</td>
<td>For cumulative dose calculation purposes only; these sections are not applicable to patients who received TBI alone**</td>
<td></td>
<td>Sections 60, 63, 66, 77, 78</td>
</tr>
</tbody>
</table>

*Instructions for Determining Radiation Field*

Refer to “Radiation Fields Defined” in COG Long-Term Follow-Up Guidelines Appendix I pages 6-8 to determine applicable radiation fields. Note, for patients who received radiation to the flank/hemiabdomen, include the pelvis only if the field extended below the iliac crest.

**Instructions for Radiation Dose Calculation:**

Five sections of the COG Long-Term Follow-Up Guidelines (sections 60, 63, 66, 77, 78) include radiation dose specifications. These specifications indicate the minimum dose of radiation that is believed (based on available evidence and the recommendations of the expert panel) to place patients sufficiently at risk of the referenced late effect to recommend screening. For guideline sections that have a minimum specified dose, the following considerations apply in determining the applicability of the section for a patient based on his/her radiation exposure.

Sections with minimum dose specifications are applicable to a patient only if:

1. Patient received radiation to any field(s) relevant to the particular guideline section at ≥ the specified minimum dose†

OR

2. Patient received a combination of radiation to any relevant field(s)† plus relevant spinal radiation‡ and/or TBI, the sum of which is ≥ the specified minimum dose

†Total dose to each field should include boost dose, if given. If patient received radiation to more than one field relevant to a particular guideline section during a single planned course of radiation treatment (excluding spinal radiation and TBI), the field that received the largest radiation dose should be used in making the determination as to the applicability of the indicated guideline section(s). **Exception:** If patient received radiation to the same field at different times (e.g., at time of diagnosis AND at relapse), these doses should be added together when considering the applicability of the indicated guideline section.

‡Use the largest dose of radiation delivered to the spinal field(s) specified in the guideline section.

For examples of radiation dose calculations, refer to “Radiation Dose Calculations” in COG Long-Term Follow-Up Guidelines Appendix I page 9.
## Patient-Specific Guideline Identification Tool (cont)

### Hematopoietic Cell Transplant: □ Yes □ No
If yes: □ Sections 100M, 101F, 102, 103, 104, 105 and applicable guidelines below

<table>
<thead>
<tr>
<th>Mark If Patient Received</th>
<th>Transplant Type</th>
<th>Chronic GVHD Status</th>
<th>Applicable Guideline Sections</th>
</tr>
</thead>
<tbody>
<tr>
<td>Autologous</td>
<td>N/A</td>
<td></td>
<td>Section 99</td>
</tr>
<tr>
<td>Allogeneic</td>
<td>Without history of chronic GVHD</td>
<td></td>
<td>No additional guideline sections</td>
</tr>
<tr>
<td>Allogeneic</td>
<td>With currently active chronic GVHD</td>
<td></td>
<td>Section 111</td>
</tr>
</tbody>
</table>

### Surgery: □ Yes □ No
If yes, applicable guidelines for specific surgical procedures below

<table>
<thead>
<tr>
<th>Mark If Patient Received</th>
<th>Surgical Procedure</th>
<th>Applicable Guideline Sections</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amputation</td>
<td></td>
<td>Section 115</td>
</tr>
<tr>
<td>Central venous catheter</td>
<td></td>
<td>Section 116</td>
</tr>
<tr>
<td>Cystectomy</td>
<td></td>
<td>Sections 117, 142, 143, 144M, 145M, 146F</td>
</tr>
<tr>
<td>Enucleation</td>
<td></td>
<td>Section 118</td>
</tr>
<tr>
<td>Hysterectomy</td>
<td></td>
<td>Section 119F</td>
</tr>
<tr>
<td>Laparotomy</td>
<td></td>
<td>Section 120</td>
</tr>
<tr>
<td>Limb sparing procedure</td>
<td></td>
<td>Section 121</td>
</tr>
<tr>
<td>Nephrectomy</td>
<td></td>
<td>Sections 122M, 123F</td>
</tr>
<tr>
<td>Neurosurgery – brain (all types)</td>
<td></td>
<td>Sections 124, 125, 126, 127</td>
</tr>
<tr>
<td>Neurosurgery – brain (applies only to neurosurgery with potential to affect the hypothalamic-pituitary axis)</td>
<td></td>
<td>Sections 128, 129</td>
</tr>
<tr>
<td>Neurosurgery – spinal cord</td>
<td></td>
<td>Sections 130, 131, 132M, 133F, 134</td>
</tr>
<tr>
<td>Oophoropexy</td>
<td></td>
<td>Section 135F</td>
</tr>
<tr>
<td>Oophorectomy – unilateral</td>
<td></td>
<td>Section 136F, 137F</td>
</tr>
<tr>
<td>Oophorectomy – bilateral</td>
<td></td>
<td>Section 138F</td>
</tr>
<tr>
<td>Orchietomy – unilateral/partial</td>
<td></td>
<td>Sections 139M, 140M</td>
</tr>
<tr>
<td>Orchietomy – bilateral</td>
<td></td>
<td>Section 141M</td>
</tr>
<tr>
<td>Pelvic surgery</td>
<td></td>
<td>Sections 142, 143, 144M, 145M, 146F</td>
</tr>
<tr>
<td>Splenectomy</td>
<td></td>
<td>Section 147</td>
</tr>
<tr>
<td>Thoracic surgery</td>
<td></td>
<td>Sections 148, 149</td>
</tr>
<tr>
<td>Thyroidectomy - total/partial</td>
<td></td>
<td>Sections 150, 151</td>
</tr>
</tbody>
</table>
### Other Therapeutic Modalities: □ Yes □ No

If yes, applicable guidelines for specific modalities below

<table>
<thead>
<tr>
<th>Mark If Patient Received</th>
<th>Other Therapeutic Modality</th>
<th>Applicable Guideline Sections</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Radiiodine therapy (I-131 thyroid ablation)</td>
<td>Sections 152, 153, 154</td>
</tr>
<tr>
<td></td>
<td>Systemic MIBG</td>
<td>Sections 155, 156, 157</td>
</tr>
<tr>
<td></td>
<td>Biocimmunotherapy (e.g., G-CSF, IL-2, erythropoietin)</td>
<td>Section 158</td>
</tr>
<tr>
<td></td>
<td>BCR-ABL tyrosine kinase inhibitors (e.g., imatinib, dasatinib)</td>
<td>Section 159, 160</td>
</tr>
<tr>
<td></td>
<td>Other targeted biologic therapies</td>
<td>Section 161</td>
</tr>
<tr>
<td></td>
<td>B-cell directed antibody-based therapies (e.g., rituximab)</td>
<td>Section 162</td>
</tr>
<tr>
<td></td>
<td>Other antibody-based immune therapies, including antibody drug conjugates (e.g., blinatumomab, brentuximab vedotin, inotuzumab, gemtuzumab ozogamicin, dinutuximab, naxitamab, pembrolizumab, ipilimumab, nivolumab, atezolizumab)</td>
<td>Section 163</td>
</tr>
</tbody>
</table>

### General Health Screening

All patients: □ [Section 164, 165]
## Section Number Comparison

### COG LTFU Guidelines Version 6.0 vs 5.0

<table>
<thead>
<tr>
<th>Version 6.0</th>
<th>Version 5.0</th>
<th>Potential Late Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1</td>
<td>Adverse psychosocial/quality of life effects</td>
</tr>
<tr>
<td>2</td>
<td>2</td>
<td>Mental health disorders</td>
</tr>
<tr>
<td>3</td>
<td>3</td>
<td>Risky behavior</td>
</tr>
<tr>
<td>4</td>
<td>4</td>
<td>Psychosocial disability due to pain</td>
</tr>
<tr>
<td>5</td>
<td>5</td>
<td>Fatigue; Sleep problems</td>
</tr>
<tr>
<td>6</td>
<td>6</td>
<td>Limitations in healthcare and insurance access</td>
</tr>
<tr>
<td>7</td>
<td>N/A</td>
<td>New to V6: Subsequent malignancy; Risk of malignancy in offspring</td>
</tr>
</tbody>
</table>

### Blood/Serum Products

<table>
<thead>
<tr>
<th>Version 6.0</th>
<th>Version 5.0</th>
<th>Potential Late Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>8</td>
<td>7</td>
<td>Chronic hepatitis B</td>
</tr>
<tr>
<td>9</td>
<td>8</td>
<td>Chronic hepatitis C</td>
</tr>
<tr>
<td>10</td>
<td>9</td>
<td>HIV infection</td>
</tr>
</tbody>
</table>

### Chemotherapy

<table>
<thead>
<tr>
<th>Version 6.0</th>
<th>Version 5.0</th>
<th>Potential Late Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>11</td>
<td>10</td>
<td>Dental abnormalities</td>
</tr>
<tr>
<td>12</td>
<td>11</td>
<td>Testicular hormonal dysfunction</td>
</tr>
<tr>
<td>13</td>
<td>12</td>
<td>Impaired spermatogenesis</td>
</tr>
<tr>
<td>14</td>
<td>13</td>
<td>Ovarian hormone deficiencies</td>
</tr>
<tr>
<td>15</td>
<td>14</td>
<td>Diminished ovarian reserve (DOR), previously Reduced ovarian follicular pool</td>
</tr>
<tr>
<td>16</td>
<td>15</td>
<td>Acute myeloid leukemia; Myelodysplasia</td>
</tr>
<tr>
<td>17</td>
<td>16</td>
<td>Pulmonary fibrosis</td>
</tr>
<tr>
<td>18</td>
<td>17</td>
<td>Cataracts</td>
</tr>
<tr>
<td>19</td>
<td>18</td>
<td>Urinary tract toxicity</td>
</tr>
<tr>
<td>20</td>
<td>19</td>
<td>Bladder malignancy</td>
</tr>
<tr>
<td>21</td>
<td>20</td>
<td>Renal toxicity</td>
</tr>
<tr>
<td>22</td>
<td>21</td>
<td>Ototoxicity</td>
</tr>
<tr>
<td>23</td>
<td>22</td>
<td>Peripheral sensory neuropathy</td>
</tr>
<tr>
<td>24</td>
<td>23</td>
<td>Renal toxicity</td>
</tr>
<tr>
<td>25</td>
<td>24</td>
<td>Neurocognitive deficits</td>
</tr>
<tr>
<td>26</td>
<td>25</td>
<td>No known late effects related to cytarabine (low dose IV, IO, IT, SQ)</td>
</tr>
<tr>
<td>27</td>
<td>26</td>
<td>Hepatic dysfunction; Sinusoidal obstruction syndrome (SOS)</td>
</tr>
<tr>
<td>28</td>
<td>27</td>
<td>Update in V6: No known BMD late effects related to methotrexate (IV, IM, PO)</td>
</tr>
</tbody>
</table>

### Radiation

<table>
<thead>
<tr>
<th>Version 6.0</th>
<th>Version 5.0</th>
<th>Potential Late Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>29</td>
<td>28</td>
<td>No known renal late effects related to methotrexate</td>
</tr>
<tr>
<td>30</td>
<td>29</td>
<td>Hepatic dysfunction</td>
</tr>
<tr>
<td>31</td>
<td>30</td>
<td>Neurocognitive deficits</td>
</tr>
<tr>
<td>32</td>
<td>31</td>
<td>Clinical leukoencephalopathy</td>
</tr>
<tr>
<td>33</td>
<td>32</td>
<td>Acute myeloid leukemia</td>
</tr>
<tr>
<td>34</td>
<td>33</td>
<td>Cardiac toxicity</td>
</tr>
<tr>
<td>35</td>
<td>34</td>
<td>Pulmonary toxicity</td>
</tr>
<tr>
<td>36</td>
<td>35</td>
<td>No known late effects related to dactinomycin</td>
</tr>
<tr>
<td>37</td>
<td>36</td>
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<td>Subsequent benign or malignant neoplasm occurring in or near radiation field</td>
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<td>Dermatologic toxicity other than neoplasms</td>
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<td>Impaired cosmesis; Poor prosthetic fit; Orbital hypoplasia</td>
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<td>Pelvic floor dysfunction; Urinary incontinence; Sexual dysfunction (female)</td>
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<td>Neurogenic bladder; Urinary incontinence</td>
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<td>Neurogenic bowel; Fecal incontinence</td>
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<td>Ovarian hormone deficiencies; Loss of ovarian follicular pool</td>
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<td>Testosterone deficiency; Azospermia</td>
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<td>Fecal incontinence</td>
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### Other Therapeutic Models

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Late Effects after Amputation

Treatment for a childhood bone or soft tissue tumor of the arms or legs may include an amputation (removal of a limb or part of a limb).

**What are the potential late effects of amputation?**

- Skin blisters, redness, or bruising from a poorly fitting prosthesis
- Phantom limb pain (perception of pain coming from the area where the limb used to be)
- Shooting pains, severe cramping, or a burning sensation in the amputated limb
- Skin breakdown and slow wound healing of the remaining limb
- Back or other muscle pain (due to increased use of other muscle groups and limbs to make up for decreased function in the amputated extremity)
- Emotional distress related to change in body image
- Physical fitness limitations that may result in difficulties performing daily activities and maintaining a healthy weight

**What are the follow-up recommendations for amputees?**

- Keep the residual limb clean and dry
- Check the skin daily for color changes and skin breakdown
- Regularly wash items that are used in the prosthesis (stump shrinker, elastic garments, stump socks)
- Have an evaluation of the prosthesis fit every 6 months until you are fully grown, then once a year, and if any problems arise
- Work with a physical and occupational therapist to develop a plan for gait training, activities of daily living, and an exercise plan (including range of motion, strength, agility, and balance)
- Have a yearly physical examination
- Maintain a healthy diet and activity level

**What are the signs that your prosthesis needs the attention of a prosthetist?**

- You hear noises of any kind (squeaking, popping, clicking, etc.)
- You break any part of the prosthesis
- You need new supplies
- You have outgrown the prosthesis
- You have chronic pain while wearing your prosthesis

**What other issues occur after amputation?**

- Dealing with peer pressure and body image change
- Coping with “being different”
- Feeling anxious, unsure, or sad
- Paying for a new prosthesis
Health Link

Healthy living after treatment of childhood, adolescent, and young adult cancer

- Coping with environments that may or may not be accessible
- Using public transportation (airplane, train, bus, etc.)
- In some cases, living with chronic pain (see related Health Link: Chronic Pain after Childhood Cancer)

Where can I get help?

Talk with your healthcare provider regularly to let them know of any difficulties that you may be facing. In addition, the following web sites offer resources for amputees:

- [www.amputee-coalition.org](http://www.amputee-coalition.org)
  Provides resources for education, advocacy and peer support for amputees.

Written by Victoria G. Marchese, PhD, PT, University of Maryland/Greenebaum Cancer Center, Baltimore, MD; Rajaram Nagarajan, MD, MPH, Cincinnati Children’s Hospital Medical Center, Cincinnati, OH; and Thomas R. Baker, CP (certified prosthetist), Wolfchase Limb and Brace, Jackson, TN.

Reviewed by Leeann Carmichael DNP, APN, FNP-BC; Kayla L. Foster, MD, MPH; and Melissa Acquazzino MD, MS.


Additional health information for childhood cancer survivors is available at [www.survivorshipguidelines.org](http://www.survivorshipguidelines.org)

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Bladder Health after Cancer Treatment

Certain types of cancer and certain cancer treatments can cause damage to the urinary bladder. The information in this Health Link will help you to recognize signs and symptoms of urinary bladder problems that may occur after treatment with chemotherapy or radiation for childhood cancer.

What is the urinary bladder?
The urinary bladder is a hollow organ that stores urine. It is located behind the pubic bone. The kidneys filter the blood and make urine, which enters the bladder through two tubes called “ureters.” Urine leaves the bladder through another tube, the urethra.

What are the risk factors for bladder problems?
- Chemotherapy with cyclophosphamide and/or ifosfamide
- Radiation therapy to the pelvic area
- Surgery to the pelvic area

What types of bladder problems can occur?
- Difficulty voiding or incompletely emptying the bladder
- Bleeding into the bladder (hemorrhagic cystitis)
- Scarring (fibrosis) of the bladder
- Bladder cancer
- Neurogenic bladder (see related Health Link: Neurogenic bladder after Cancer Treatment)

Hemorrhagic cystitis
- What is hemorrhagic cystitis? Hemorrhagic cystitis is a condition in which bladder irritation results in blood in the urine.
- What are the symptoms of hemorrhagic cystitis? The urine color may range from slightly pink to bright red. Some people may feel like they have to urinate urgently, or that they cannot release all the urine, but there is usually no pain. Hemorrhagic cystitis may occur off and on for months to years after completion of therapy.
- How is hemorrhagic cystitis diagnosed? Usually, blood can be seen in the urine. Sometimes, the amount of blood in the urine is so small that it is seen only during a urinalysis (lab test to examine the urine). When there is blood in the urine, a urine culture is usually done to check for infection.
- What can I do if I have hemorrhagic cystitis? Usually it is helpful to drink extra fluids to flush out the bladder. Avoid tea, coffee, cola beverages, and other fluids containing caffeine since they may worsen the sudden urge to urinate. If you have kidney or heart problems, check with your healthcare provider before drinking extra fluid.
- When should I call my healthcare provider? Call your healthcare provider any time you see blood in the urine. You should also report any fever, pain with urination, difficulty urinating, or the need to urinate urgently or frequently, because these are common symptoms of a urinary tract infection or other bladder problems.
Bladder fibrosis

- **What is bladder fibrosis?** Bladder fibrosis is scar tissue in the bladder. This may build up and cause the bladder wall to thicken. When this happens, the pressure inside the bladder increases. This may affect the bladder’s ability to store and empty urine. Over time these changes can lead to damage to the kidneys.

- **What are the symptoms of bladder fibrosis?** Problems may include difficulty emptying the bladder, leakage of urine, or blood in the urine. Sometimes, bladder fibrosis may not cause any symptoms at all.

- **How is bladder fibrosis diagnosed?** An ultrasound of the bladder may show thickening of the bladder wall. A urologist, a doctor who specializes in bladder health, may also perform a cystoscopy, a test that allows the doctor to look directly in the bladder through a thin, lighted tube.

- **What can I do if I think I have bladder fibrosis?** If you are at risk for bladder fibrosis and have any of the symptoms described above, you should ask for a referral to a urologist.

- **When should I call my healthcare provider?** Call your healthcare provider if you have symptoms of bladder fibrosis, such as difficulty emptying the bladder, leakage of urine, or blood in the urine.

Bladder cancer

- **What is bladder cancer?** Bladder cancer is a type of tumor that can develop in people who have been treated with cyclophosphamide or radiation involving the bladder. This is a rare type of subsequent cancer due to treatment.

- **What are the symptoms of bladder cancer?** The most common symptom is blood in the urine. There may also be a need to urinate urgently or frequently. If the cancer is advanced at the time of diagnosis, there may be pain over the bladder, in the genital area, or in the bones.

- **How is bladder cancer diagnosed?** The diagnosis is usually made by doing a cystoscopy to obtain a biopsy of bladder tissue. Sometimes the diagnosis can be made by finding cancer cells in the urine.

- **What can I do if I think I have bladder cancer?** If you are concerned about whether your symptoms may represent bladder cancer, ask for a referral to a urologist.

Neurogenic bladder

- **What is neurogenic bladder?** A neurogenic bladder is abnormal function of the bladder caused by damage to the nerves that control the bladder’s ability to fill, store and empty urine.

- **What are the symptoms of neurogenic bladder?** Abnormal bladder function can cause the bladder to be underactive (not emptying completely) or overactive (emptying too frequently or quickly). People with neurogenic bladders also have a higher risk of urinary tract infections (UTIs) and kidney damage. (see related Health Link: Neurogenic bladder after Cancer Treatment)

- **How is neurogenic bladder diagnosed?** Neurogenic bladder can be evaluated by a urologist. To make a diagnosis, your provider may recommend imaging or urodynamic testing.

- **What can I do if I think I have neurogenic bladder?** If you are concerned about whether your symptoms may be caused by neurogenic bladder, your provider can refer you to a urologist for additional evaluation and testing.
Health Link

Written by Patricia Shearer, MD, MS, Emory Healthcare, Johns Creek, GA; Michael L. Ritchey, MD, Phoenix Childrens Hospital, Phoenix, AZ; Fernando A. Ferrer, MD, Children’s Hospital and Medical Center of Omaha, Omaha, NE; and Sheri L. Spunt, MD, Lucile Packard Children’s Hospital Stanford University, Palo Alto, CA.

Reviewed by Linda Rivard, RN, BSN; Kayla L. Foster, MD, MPH; and Christine Yun, MSN, PNP, CPON.

Additional health information for childhood cancer survivors is available at www.survivorshipguidelines.org

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Bleomycin Alert

The lungs are very important organs that are responsible for supplying oxygen to the body and ridding it of carbon dioxide. Sometimes, treatments given for childhood cancer can cause lung damage. Because you received bleomycin during treatment for childhood cancer, it is important for you to learn about certain lung problems that can sometimes happen after treatment with bleomycin. We also suggest that you read the Health Link: Pulmonary Health, which contains more information about your lungs and how to keep them healthy.

What are the problems that can happen after treatment with bleomycin?

People who received bleomycin during treatment for childhood cancer can sometimes develop lung problems many years after their treatment has been completed. These problems may include:

- Lung inflammation (interstitial pneumonitis)
- Lung scarring (pulmonary fibrosis)
- Breathing problems associated with high levels of oxygen and/or intravenous fluids (acute respiratory distress syndrome)

What is interstitial pneumonitis?

Interstitial pneumonitis is inflammation of the thin layer of tissue between the air sacs (alveoli) in the lungs. This inflammation can worsen if a person develops lung infections, such as pneumonia. Interstitial pneumonitis that occurs as a result of therapy with bleomycin sometimes develops after exposure to toxic fumes, tobacco, or high levels of oxygen given over several hours.

What is pulmonary fibrosis?

Pulmonary fibrosis is the formation of scar tissue in the small air sacs (alveoli) of the lungs. This scarring makes the lungs stiffer and affects the exchange of oxygen and carbon dioxide in the alveoli. Pulmonary fibrosis may worsen over time and can sometimes lead to early heart failure.

What is acute respiratory distress syndrome (ARDS)?

ARDS is a serious condition that occurs when alveoli in the lungs are damaged and can no longer provide oxygen to the body. People who received bleomycin in the past may be at risk for developing ARDS, usually as a result of a combination of high levels of oxygen and large amounts of intravenous fluid given during surgery. However, the risk of developing ARDS is very low. If you need a medical procedure requiring oxygen or general anesthesia, be sure to tell your surgeon, anesthesiologist, and other healthcare providers that you have received bleomycin in the past for treatment of childhood cancer.

What are factors that increase the risk of developing lung problems after treatment with bleomycin?

- High total doses of bleomycin (400 units/m² or more in all doses combined)
- Radiation to the chest or lungs, or total body irradiation (TBI)
• Treatment with other chemotherapy drugs that can also damage the lungs (see related Health Link: Pulmonary Health)
• Exposure to high oxygen levels (such as during general anesthesia or SCUBA diving)
• Smoking
• Inhaled drugs, such as smoking marijuana, vaping, or cocaine

What monitoring is recommended for people who have received bleomycin for treatment of childhood cancer?

• A yearly medical check-up is recommended.
• Pulmonary function tests may show lung problems that are not apparent during a check-up. For this reason, it is helpful to have these tests done at least once (at least 2 years after completing cancer treatment) to find out if there are any problems. Your healthcare provider can decide if further testing is needed based on these results.
• In some cases, your healthcare provider may recommend repeating the pulmonary function tests if you are scheduled for surgery that requires general anesthesia to check for changes in the lungs that could increase the risk of breathing problems during or after anesthesia.

Are there any special precautions I should take?

If you received therapy with bleomycin, you should:

• Avoid SCUBA diving, unless you have had a complete check-up and have been advised by a pulmonologist (lung specialist) that diving is safe. During SCUBA diving, increased underwater pressures and high oxygen levels can damage the lungs.
• Tell your surgeon, anesthesiologist, and other healthcare providers about your medical history before any scheduled procedures that may require oxygen.
• Avoid breathing high concentrations of oxygen whenever possible, especially for long periods of time (such as over several hours). If you require oxygen, monitoring of your oxygen levels can usually be done so that you can receive the lowest oxygen concentration that is necessary.
• Get the pneumococcal (pneumonia) vaccine.
• Get yearly influenza (flu) vaccines.
• Don’t smoke or use inhaled drugs such as marijuana, vaping, or cocaine. If you currently smoke, talk to your healthcare provider about a program to help you quit.
Health Link
Healthy living after treatment of childhood, adolescent, and young adult cancer

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Keeping Your Bones Healthy

During childhood and into young adulthood, bone formation usually occurs faster than bone loss, causing bones to grow and become heavier (more dense). As a person gets older, the process of bone removal gradually overtakes bone formation, and bones slowly lose strength as part of the normal aging process. However, loss of bone strength may occur at earlier ages in childhood cancer survivors because of certain cancer treatments. Loss of bone strength may result in a condition known as osteoporosis, which is sometimes referred to as “low bone mineral density.”

Osteoporosis: A Silent Disease

Osteoporosis is a disorder resulting from too little new bone formation or too much bone loss, causing bones to become weak. Most people do not have symptoms, especially in the early stages. However, as bones become weaker, the risk for fractures increases. Osteoporosis may occur in any bone, but most commonly affects the wrists, hips, spine, and leg bones.

How is osteoporosis diagnosed?

Although osteoporosis may be suspected based on a patient’s symptoms and risk factors, the diagnosis is made by measuring bone density with special x-ray techniques, called DXA or bone density scans. These scans do not expose patients to large amounts of radiation, and generally take less than 20 minutes to perform.

People who have osteoporosis should discuss treatment options with their healthcare provider. Medications, such as bisphosphonates and calcitonin, are available specifically for the treatment of low bone density. In addition, if you have low levels of sex hormones, or low levels of growth hormone (GH), you may also benefit from hormone replacement therapy.

What are the risk factors for osteoporosis?

Osteoporosis is more common in people with the following characteristics:

- Female (especially after menopause)
- Family history of osteoporosis
- Caucasian or Asian race
- Small, thin frame
- Older age

The following factors may also increase the risk of osteoporosis:

- Smoking
- Diet low in calcium
- Lack of weight-bearing exercise
- Too much caffeine, alcohol, or soda
- A diet high in salt

Additional causes of osteoporosis in people who have had cancer may include:

A history of treatment with:

- Corticosteroids (such as prednisone and dexamethasone)
Conditions resulting from cancer treatment, including:

- Low levels of sex hormones
- GH deficiency
- High levels of thyroid hormone
- Chronic graft-versus-host disease requiring prolonged therapy with corticosteroids
- Prolonged periods of inactivity (bed rest)

Other medical treatments, including:

- Certain anticonvulsants (phenytoin and barbiturates)
- Aluminum-containing antacids (such as Maalox® or Amphogel®)
- Medications such as Lupron (used for treatment of early puberty and endometriosis)
- High doses of heparin (used to prevent blood clots), especially with prolonged use
- Cholestyramine (used to control blood cholesterol)

Many of the medications on this list are essential treatments for certain medical conditions. If you are taking any of these medications, do not change your dosage or stop taking your medication without consulting with your healthcare provider.

What lowers the risk of osteoporosis?

Fortunately, there are many things you can do to reduce the risk of osteoporosis. Regular weight-bearing exercise (such as brisk walking, dancing, and jogging) helps to develop and maintain healthy bones. Bicycling and swimming are excellent exercises for general fitness, but these are NOT weight-bearing exercises, and they do not help to build strong bones. Exercises that are especially good for bone health include higher-impact weight-bearing activities, such as hopping, jogging and jumping rope. Resistance exercises, such as light weightlifting, also help to build strong bones and are especially important for bones of the upper body, including the arms and shoulders. If you have problems with your heart, or have painful bones or joints, be sure to discuss your individual health status and cancer treatment history with your healthcare provider before starting any new exercise program.

A diet high in calcium also is important in preventing osteoporosis. Most healthcare professionals recommend 1000–1500 mg a day, which means a diet rich in dairy products (milk, cheese, yogurt) and leafy green vegetables. Talking with a dietitian may help you design a healthy diet. Over-the-counter calcium supplements also may be useful. See Tables 1 for recommended daily calcium intake. Additional information about calcium-rich diets is available at www.usdairy.com/dairy-nutrition/products.

Vitamin D is needed to absorb calcium. Your skin makes this vitamin naturally when exposed to sunlight. Many dairy products also contain vitamin D. In general, at least 400 units of Vitamin D is recommended daily. You should not take more than 800 units of Vitamin D per day unless your health care provider has recommended a higher dose for you. Taking too much vitamin D may be harmful, so it’s important to check with your healthcare provider before taking any vitamin D supplements.

What screening is recommended?

After reviewing your treatment history and risk factors, your healthcare provider can advise you regarding the need for bone density testing. For those at risk, a baseline bone density scan is recommended for childhood cancer survivors when they enter long-term follow-up (2 or more years after completion of therapy). Follow-up scans may be needed for ongoing...
monitoring of bone density in some patients.

Table 1: Recommendations for Adequate Dietary Calcium Intake in the United States

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<th>Age</th>
<th>Recommended Calcium Intake</th>
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<tr>
<td>1–3 years</td>
<td>700 mg per day</td>
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<td>4–8 years</td>
<td>1000 mg per day</td>
</tr>
<tr>
<td>9–18 years</td>
<td>1300 mg per day</td>
</tr>
<tr>
<td>19–50 years</td>
<td>1000 mg per day</td>
</tr>
<tr>
<td>50–70+ years</td>
<td>1000-1200 mg per day</td>
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</table>

(National Institutes of Health Office of Dietary Supplements (NIH ODS) Calcium Fact Sheet for Health Professionals)

Written by Julie Blatt, MD, UNC Lineberger Comprehensive Cancer Center, Chapel Hill, NC; and Lillian R. Meacham, MD, Children’s Healthcare of Atlanta - Egleston, Atlanta, GA.

Reviewed by Kayla L. Foster, MD, MPH; Sarah Ford, MS, PA-C; and Melissa Acquazzino, MD, MS.

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Breast Cancer: Are You at Risk?

The risk of cancer increases for everyone as they age. Depending on the specific treatment you received for childhood cancer, you may be at increased risk for developing breast cancer. It is important to understand that risk, so that you can take steps to protect your health.

What are the risk factors?
Several studies have shown that women treated with radiation to the chest for cancer during childhood, adolescence, or young adulthood have an increased risk of developing breast cancer as they get older, compared to women their same age in the general population. The risk of secondary breast cancer is related to the location and dose of radiation. People treated with higher doses of radiation have the highest risk. Researchers are studying this problem to better understand the risk factors and find ways to prevent secondary breast cancer.

When is breast cancer likely to occur?
The risk of secondary breast cancer begins to increase at about ten years following radiation therapy and continues to rise thereafter. This means that if a woman develops breast cancer following chest radiation for childhood/adolescent cancer, it usually happens at a much younger age (usually 30 to 40 years old) than in women who develop primary breast cancer (usually age 50 or older).

What can I do to protect my health?
Most women who received radiation therapy to the chest during childhood, adolescence, or young adulthood will not develop breast cancer. However, if you received radiation to the chest, it is important to understand that the risk is higher for you than it is for women your age who never received radiation. So, the best way for you to protect your health is by taking steps to closely monitor your breasts. That way, if a cancer develops, it will be detected in its earliest stages, when treatment is most effective. It is also important to tell your healthcare provider about your cancer treatment history, including the dose of chest radiation that you received. You should ask your treating oncologist or cancer center for a written summary of your cancer treatment (see related Health Link: Introduction to Long-Term Follow-Up).

What monitoring is recommended?
If you received radiation therapy to the chest, underarm (axilla), or total body irradiation (TBI) during childhood, adolescence, or young adulthood, you should:

1. Have a clinical breast exam performed by your healthcare provider—at least once a year until you reach age 25—then every 6 months thereafter.
2. Have a yearly mammogram and breast MRI (magnetic resonance imaging test) starting at age 25, or 8 years after you received radiation (whichever comes last).

If your healthcare provider is not familiar with these monitoring recommendations for women who have received chest radiation during childhood, adolescence, or young adulthood, we encourage you to share this Health Link with them, and tell them that additional information is also available at www.survivorshipguidelines.org.

Is there anything else I can do to minimize the risk?
The following lifestyle changes may help reduce the risk of developing breast cancer, and will also help you to stay as healthy as possible:

• Eat more fruits and vegetables (at least 5 servings a day are recommended).
Healthy living after treatment of childhood, adolescent, and young adult cancer

- Exercise at least 30 minutes per day on most days of the week.
- Maintain a healthy body weight.
- Limit your intake of alcohol to no more than one drink per day.
- Avoid smoking or vaping.
- If you have a baby, try to breastfeed for at least four months.
- If you need hormone replacement therapy or birth control pills, discuss the risks and benefits with your healthcare professional.

If you have questions regarding your risk of developing breast cancer, and how you can best protect your health, be sure to discuss this with your healthcare provider.

Written by Melissa M. Hudson, MD, St. Jude Children’s Research Hospital, Memphis, TN; and Wendy Landier, PhD, CPNP, Children's Hospital of Alabama, Birmingham, AL. Portions adapted from CCSS Newsletter Winter 2001, used with permission.

Reviewed by Amelia DeRosa, RN, BSN, CPON; Kayla L. Foster, MD, MPH; and Christine Yun MSN, PNP, CPON®.

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Preventing Cardiovascular Complications

As people get older, the risk for developing cardiovascular problems, such as heart attack and stroke, increases. Additional factors that increase the risk of developing cardiovascular problems include:

- Being overweight or obese
- High blood pressure
- Unhealthy cholesterol levels (high LDL, high triglycerides, or low HDL)
- Prediabetes or diabetes mellitus
- Smoking
- Excessive alcohol intake
- Family history of heart disease

Certain cancer treatments given during childhood, adolescence, or young adulthood may increase the risk of developing cardiovascular complications. It is important for you to be aware of these risks so that you can practice healthy habits that can help prevent cardiovascular problems.

What increases the risk for being overweight or obese?

Treatment factors:

- Radiation to the brain or head (especially at doses of 18 Gy or higher)
- Surgery to the brain affecting the “mid-brain” area (containing the pituitary gland)

Other known risk factors:

- Overeating
- Eating a diet that is high in fats and sugar
- Not having regular physical activity
- Having certain medical conditions, like an underactive thyroid (hypothyroidism), or low levels of GH

What increases the risk for high blood pressure?

Treatments factors:

- Ifosfamide
- Cisplatin
- Carboplatin
- Radiation involving the kidneys, including the abdomen, flank, and total body irradiation (TBI)
- Removal of one kidney (see related Health Link: Single Kidney Health)
- Hematopoietic cell transplant (particularly if complicated by chronic graft-versus-host disease)

Other known risk factors:

- Being overweight or obese
- Having a family history of high blood pressure
What increases the risk for unhealthy cholesterol levels (including high triglycerides and low HDL)?

Treatment factors:
- Total body irradiation (TBI)
- Abdominal radiation

Other known risk factors:
- Being overweight or obese
- Having a family history of unhealthy cholesterol levels
- Not getting regular physical activity
- Eating a diet high in fat

What increases the risk for high blood sugar/diabetes mellitus?

Treatment factors:
- Abdominal radiation
- Total body irradiation (TBI)
- Prolonged treatment with corticosteroids, such as prednisone or dexamethasone

Other known risk factors:
- Being overweight or obese (note that survivors who received TBI may be at increased risk even if they are not overweight or obese)
- Having a family history of diabetes

How I can I tell if I am overweight or obese?

Visit with your health care provider about your weight to determine if you are at a healthy weight for your height, age and activity level. The body mass index (BMI) is a tool your provider may use to help determine if you are at a healthy weight. BMI calculators and information on how to interpret results are available on-line at www.cdc.gov/healthyweight/assessing/bmi/.

What can I do to lower my risk of cardiovascular complications?
- Get regular check-ups and follow your health care provider’s recommendations regarding how often you need blood pressure checks and blood tests to monitor your cholesterol and/or blood sugar levels.
- Eat a healthy diet (See related Health Link: Staying Health through Nutrition and Physical Activity).
- Increase physical activity if you are able (See related Health Link: Staying Health through Nutrition and Physical Activity).
- Avoid smoking. If you are interested in quitting smoking, online assistance is available from the National Institutes of Health at www.smokefree.gov.
• If you are overweight, obese, have high blood pressure, unhealthy cholesterol levels and/or high blood sugar, see your health care provider regularly. Follow their recommendations for additional testing, if needed, and for ongoing treatment of your health condition.

• In some cases, medications may be required to treat these conditions. If you are prescribed medications, be sure to take them regularly and to carefully follow your health care provider’s instructions.

Written by Adam J. Esbenshade, MD, MSci, Vanderbilt University/Ingram Cancer Center, Nashville, TN.

Reviewed by Linda Rivard, RN, BSN, CPON; Melissa Acquazzino, MD, MS; and Kayla L. Foster, MD, MPH.

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**Cataracts after Cancer Treatment**

Childhood cancer treatment sometimes requires the use of medications or radiation that can increase the risk of developing cataracts. Because vision can have a significant impact on daily living, it is important for survivors who received these treatments to have their eyes checked regularly.

**What is a cataract?**

A cataract is clouding of the normally clear lens of the eye. Cataracts often develop slowly, but as the clouding increases, vision can be affected.

**How does a cataract affect vision?**

The eyes are remarkable organs, allowing light to be converted into impulses that are transmitted to the brain, where images are perceived. Light enters the eye through a clear layer of tissue known as the cornea. The cornea bends and focuses the light and sends it through the opening of the eye known as the pupil. The pupil controls how much light enters the eye. Behind the pupil is the lens of the eye, which focuses the light onto the retina, the membrane along the back wall of the eye. The nerve cells in the retina change the light into electrical impulses and send them through the optic nerve to the brain, where the image is perceived. When the lens becomes cloudy due to a cataract, the image delivered to the retina becomes blurry.

**What are the symptoms of a cataract?**

Common symptoms of cataracts include:

- Painless blurring of vision
- Sensitivity to light and glare
- Double vision in one eye
- Poor night vision
- Fading or yellowing of colors
- The need for frequent changes in prescriptions for glasses or contact lenses

**What cancer therapies increase the risk of developing cataracts?**

Certain chemotherapy, including:

- **Busulfan**
- **Corticosteroids**, such as prednisone and dexamethasone

Radiation therapy to the following areas:

- Eye and surrounding tissue (orbits)
- Head or brain
- Total body irradiation (TBI)

The risk for cataracts increases with:

- Higher radiation doses
- Frequent exposure to sunlight
- The passage of time (the longer off therapy the survivor is)
Health Link
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What monitoring is recommended?

- Have an eye examination every year during your regular check-up
- See an eye specialist (ophthalmologist or optometrist) for a full eye evaluation every year if you had:
  - Total body irradiation (TBI)
  - Radiation to the head, brain or eyes
  - A tumor involving the eye

How are cataracts treated?
Not all cataracts need treatment. In many cases, an ophthalmologist may monitor the vision closely over many years and will recommend treatment if and when it becomes necessary. The only treatment for cataracts is surgical removal of the lens and replacement with an artificial lens. Today, cataract surgery is a low-risk procedure that is performed on an outpatient basis and usually is successful in restoring vision.

How can I keep my eyes as healthy as possible?

- Wear sunglasses with ultraviolet (UV) protection when in bright sunlight.
- When participating in sports, be sure to select protective eyewear that is appropriate for the sport. Eyewear worn for sports should be properly fitted by an eye care professional.
- Avoid toys with sharp, protruding or projectile parts.
- Never play with fireworks or sparklers of any kind to avoid accidental injury.
- Be careful when working with hazardous household chemicals.
- Wear protective eyewear when using a lawnmower, power trimmer, or edger, and when working with dangerous equipment in the workshop.
- If you do experience an eye injury, seek medical attention promptly.

Written by Teresa Sweeney, RN, MSN, CPNP, St. Jude Children’s Research Hospital, Memphis, TN; and Wendy Landier, PhD, CPNP, Children’s Hospital of Alabama, Birmingham, AL.

Reviewed by Angela Yarbrough DNP, APRN, FNP-BC, CPON®; Kayla L. Foster, MD, MPH; and Christine Yun MSN, PNP, CPON®.

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Health Link

Healthy living after treatment of childhood, adolescent, and young adult cancer

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Central Adrenal Insufficiency after Cancer Treatment

Some people who were treated for cancer during childhood may develop endocrine (hormone) problems because of changes in the function of a complex system of glands known as the endocrine system.

What is the endocrine system?
The endocrine system is a group of glands that regulates many body functions including growth, puberty, energy level, urine production, and stress response. Glands of the endocrine system include the pituitary, hypothalamus, thyroid, pancreas, adrenals, ovaries, and testes. The hypothalamus and pituitary are sometimes called the “master glands” because they control many of the other glands in the endocrine system. Unfortunately, some treatments given for childhood cancer can damage the endocrine system, resulting in a variety of problems.

What are hormones?
Hormones are chemical messengers that carry information from the endocrine glands through the bloodstream to the body’s cells. The endocrine system makes many hormones (such as growth hormone, sex hormones, adrenal and thyroid hormones) that work together to maintain specific bodily functions.

What is central adrenal insufficiency?
Central adrenal insufficiency is caused by a deficiency of the pituitary hormone known as adrenocorticotrophic hormone (ACTH). The adrenal glands (located on top of the kidneys) are stimulated by ACTH to produce a hormone known as cortisol. If the pituitary gland doesn’t make enough ACTH, then cortisol will not be made by the adrenal gland. Cortisol is important for health because it helps to keep the blood sugar at a normal level and helps the body deal with physical stress, such as fevers or injuries.

What are the risk factors for central adrenal insufficiency?
- Radiation to the brain, especially in higher doses (30 Gy or 3000 cGy/rads or higher)
- Surgical removal of the pituitary gland

What are the symptoms of central adrenal insufficiency?
Under normal circumstances, there may be no symptoms at all, or there may be mild symptoms, such as fatigue, weakness, poor appetite, or dizziness. However, under stressful circumstances, such as fever, infection, surgery, or injury, symptoms may become severe, and may include vomiting, diarrhea, low blood sugar, low blood pressure, and dehydration.

What screening is recommended?
People who had radiation in a dose of 30 Gy (3000 cGy/rads) or higher to the central area of the brain (hypothalamic-pituitary axis) should have a yearly blood test to check the cortisol level or yearly evaluation by an endocrinologist (hormone specialist). Anyone who is having symptoms suggestive of central adrenal insufficiency should also have an evaluation by an endocrinologist.
How is central adrenal insufficiency treated?

Central adrenal insufficiency is treated with hydrocortisone, a medication that is given by mouth every day on a regular schedule. In times of increased stress, such as illness or surgery, the dose of hydrocortisone is increased, also known as stress dosing, and can be administered by injection if necessary. If you have central adrenal insufficiency, you should wear a medical alert bracelet so that in case of an accident or sudden illness, emergency medical workers will be aware of your special health needs.

Written by Debra A. Kent, RN, MSN, CPNP, Cincinnati Children’s Hospital Medical Center, Cincinnati, OH; and Wendy Landier, PhD, CPNP, Children’s Hospital of Alabama, Birmingham, AL.

Reviewed by Angela Yarbrough DNP, APRN, FNP-BC, CPON®; Christine Yun MSN, PNP, CPON®; and Kayla L. Foster, MD, MPH.

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Chronic Pain after Cancer Treatment

Pain is a common experience during cancer treatment, either from the cancer itself or from the treatment. Usually, after the treatment is finished, there is no more pain. For some people, however, pain continues to be a side effect of either the cancer or its treatment, even when the cancer is in remission and treatment has been completed. For cancer survivors, long-term pain may occur for a variety of reasons, such as damage to bones, joints, or nerves resulting from treatment with radiation, surgery, certain chemotherapy medications, or corticosteroids.

What is the difference between acute and chronic pain?

Acute pain is generally the result of illness (such as cancer), injury and/or surgery and is usually confined to a limited period of time. Acute pain has a biologic purpose, that is, it tells us that we are hurt or ill, so that we can protect ourselves.

Chronic pain lasts after the underlying illness or injury has resolved. Chronic pain is a problem because the longer the pain lasts, the more complicated it might become, particularly in the way it could affect a survivor's quality of life.

Pain is very complex

Healthcare providers used to think that the amount of pain a person had was directly related to the extent of physical damage to body tissue. Healthcare providers now know that the pain people feel is affected by many physical, emotional, and cognitive factors that are unique to everyone.

Recent studies involving new technology to study the brain are confirming that many processes are involved in chronic pain. The experience of pain is the result of a complex interchange of information from many different areas of the brain. These studies have also helped us to understand that pain can sometimes persist (even when the original injury has healed) due to changes in the way the body sends and receives pain signals.

Healthcare providers have learned that different people perceive pain in different ways. These differences can be seen in brain imaging studies as individuals rate their pain to the same source of pain, or “stimulus.” That is, some people seem to be very sensitive, whereas others may report little pain even with the same stimulus. While you might be born with some of these differences, environmental factors tend to play an important role too. Factors such as age, sex, developmental level, family and cultural traditions, prior pain experience, and circumstances surrounding the injury all contribute toward how a cancer survivor might interpret, experience, and cope with pain.

Pain and Psychological Health

Psychological factors play a role in the amount of distress that is experienced, or how upsetting the pain might be to each individual. Furthermore, other factors, such as family or work environment, can also affect the ability to cope with pain.

In the case of chronic pain that lasts for months and years, it is possible for cancer survivors to become increasingly depressed if they don’t have ways to cope with the pain in a healthy way. Survivors with pain may sometimes become frustrated and angry, especially if pain is preventing them from doing activities that they used to enjoy. If a survivor believes that pain controls his or her life, then they may begin to feel powerless, develop low self-esteem, and avoid taking on challenges and opportunities for growth. Pain can develop into a troublesome cycle. For example, a survivor might stop moving around and doing physical activities because they are afraid of triggering or worsening their pain. However, the less active they are, the weaker their muscles become, which can then worsen the pain.
Sometimes, people begin to anticipate the physical sensations of pain in a fearful way. They may withdraw from social or community activities to avoid having to deal with pain in public situations, and they may increasingly isolate themselves. Depression, anxiety, and chronic stress may follow, which can make the pain worse. This may also lead to physical changes in the body associated with stress, depression, and anxiety, which can lower the pain thresholds.

**How is Pain Treated?**

Fortunately, there are ways to manage and cope with chronic pain. Chronic pain can be treated with medicine, without medicine using behavioral treatments (such as relaxation or meditation), or by a combination of the two. Non-medicine treatments can be used along with medications to manage pain during and after cancer treatment. Studies of patients suffering from chronic pain show that training in pain-coping skills can help increase self-confidence and reduce distress from pain. Changes in how a person copes with pain and what they believe about their pain may also produce positive changes in behavior, such as increased exercise, improved pacing of activities, better results with medication, and increased participation in social activities.

Behavioral skills can be helpful in treating and coping with pain. Specific techniques include relaxation, meditation, guided imagery, distraction, and redirected thinking, as well as changing thoughts and beliefs about pain and what it means. Other effective approaches include support groups, massage, music, and counseling focused on pain management and behavioral modification.

Written by Sunita K. Patel, PhD, City of Hope Comprehensive Cancer Center, Duarte, CA.

Reviewed by Kayla L. Foster, MD, MPH; Beth Fisher, DNP, APRN, CPNP; and Melissa Acquazzino, MD, MS.

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Colorectal Cancer: Are You at Risk?

The risk of cancer increases for everyone as they age. Depending on the specific treatment you received for childhood cancer, you may be at increased risk for developing colorectal cancer (cancer of the colon or rectum). It is important to understand that risk, so that you can take steps to protect your health.

What is colorectal cancer?
Colorectal cancer is a type of cancer that occurs in the colon (large intestine) or the rectum (the last several inches of the large intestine). Colorectal cancer is the second leading cause of cancer deaths in the United States. Many of these deaths happen because the cancers are found too late to be cured. If colorectal cancer is found early enough, it can usually be cured.

What are the risk factors?
Several studies have shown those who were treated with radiation to the abdomen, pelvis, spine, or total body irradiation (TBI) during childhood, adolescence, or young adulthood have an increased risk of developing colorectal cancer. It is therefore important for you to obtain your radiation treatment records so that you know what radiation you received.

Other known risk factors for developing colorectal cancer include:
- Having had colorectal cancer or large intestinal polyps in the past
- Having a close relative (sibling, parent or child) who has had colorectal cancer before age 50
- Having ulcerative colitis or Crohn’s disease
- Having a hereditary colon cancer syndrome (such as familial adenomatous polyposis)

What are the signs of colorectal cancer?
Most colorectal cancers begin as a polyp. A polyp starts as a small, harmless growth in the wall of the colon or rectum. However, as a polyp gets larger, it can develop into a cancer that grows and spreads. During the early stage of colorectal cancer, there are rarely any outward signs or symptoms to alert you or your healthcare provider that cancer is present. This is why screening is so important. Once the cancer has become more advanced, the following signs may be evident. If you have any of these signs, you should see your healthcare provider immediately:
- Bleeding from your rectum
- Blood in your stool or in the toilet after you have a bowel movement
- A change in the shape of your stool
- Cramping pain in your lower stomach
- A feeling of discomfort or an urge to have a bowel movement when there is no need to have one
- A change in the normal frequency of your bowel movements

Other conditions can cause these same symptoms. You should be evaluated by your healthcare provider to find out the reason for your symptoms.

When is colorectal cancer likely to occur?
In the general population, colorectal cancer is most likely to occur between the ages of 45 and 65. In cancer survivors who were treated with abdominal, pelvic, spinal, or TBI radiation, it may occur earlier. The risk begins to increase around 10 years after the radiation.
What can I do to protect my health?

Most people who received radiation therapy to the abdomen, pelvis, spine, or TBI will not develop colorectal cancer. However, if you received this type of radiation, it is important to understand that the risk is higher for you than it is for other people your age who never received radiation. So, the best way for you to protect your health is by taking steps to closely monitor your colon. That way, if a cancer develops, it can be detected in its earliest stages, when treatment is most effective.

What monitoring is recommended?

If you were treated with radiation therapy to the abdomen, pelvis, spine, or TBI during childhood, adolescence, or young adulthood, you should be screened for colorectal cancer beginning 5 years after radiation or at age 30, whichever occurs last. You should talk with your healthcare provider about which screening option is best for you. These options include stool-based testing every three years or colonoscopy every five years.

What is stool-based testing?

If you choose stool-based testing, you will need to provide a stool sample, which will be sent to a laboratory to check for signs of colorectal cancer.

What is a colonoscopy?

A colonoscopy is a procedure where a thin, flexible tube connected to a video camera is inserted into your rectum and slowly guided into your colon. The doctor is able to look at the colon on a monitor, and any polyps or growths can be removed through the tube during the exam.

A colonoscopy requires a “bowel prep” the day or night before the procedure to empty the intestines. Your healthcare provider should give you instructions on how to do this.

The procedure may be uncomfortable, but it is usually not painful. Before you have this test, you will be given a medicine to make you feel relaxed and sleepy.

Is there anything else that I can do to minimize the risk?

The following lifestyle changes may help to reduce the risk of colorectal cancer and will help you stay as healthy as possible:

- Eat a variety of healthy foods, with an emphasis on grains, fruits and vegetables.
  - Eat five or more servings of a variety of vegetables and fruits each day.
  - Choose whole grains in preference to processed (refined) grains and sugars.
  - Limit consumption of red meats, especially processed meats (such as hot dogs or bologna) and those high in fat.
  - Choose foods that help you maintain a healthy weight.

- Adopt a physically active lifestyle.
  - Engage in at least moderate physical activity (such as brisk walking) for 30 minutes or more on five or more days of the week.
  - Engaging in 45 minutes or more of moderate to vigorous activity (activities such as running, in which you are not able to carry on a conversation without needing to catch your breath) on five or more days per week may further reduce your risk of colorectal cancer.
Health Link

Healthy living after treatment of childhood, adolescent, and young adult cancer

Written by Kevin C. Oeffinger, MD, Duke University Medical Center, Durham, NC.
Reviewed by Amelia DeRosa, RN, BSN, CPON; Kayla L. Foster, MD, MPH; Christine Yun, MSN, PNP, CPON.

Additional health information for childhood cancer survivors is available at www.survivorshipguidelines.org

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Late Effects after Cystectomy

The information in this Health Link will help you recognize signs and symptoms of urinary bladder problems that may occur after cystectomy.

What is a cystectomy?
A cystectomy is an operation to remove the urinary bladder.

Who needs a cystectomy?
Two groups of cancer survivors may have undergone a cystectomy during their childhood cancer treatment. The first group includes those who had a cystectomy as part of their cancer treatment. Successful treatment of rhabdomyosarcoma of the urinary bladder and prostate, Ewing's sarcoma, and other sarcomas in the pelvic area sometimes requires cystectomy. The second group includes people who required a cystectomy because of treatment complications, such as hemorrhagic cystitis (bleeding) or bladder fibrosis (scar tissue).

How does urine exit the body after a cystectomy?
After the urinary bladder is removed, a new passageway is created so that urine can leave the body. Urine is removed from the kidney in a process called “diversion.” There are three main types of diversions, based on whether urine flows from the body spontaneously (“incontinent diversion”) or is collected in a reservoir (“continent diversion”).

An “incontinent diversion” is usually made through a loop of small intestine that is separated from the rest of the bowel and called an “ileal conduit” or “urostomy.” The ileal conduit is connected to the outside of the abdomen by way of an opening called a “stoma”. Internally, the ureters empty into the conduit, which then serves as a pipeline for urine to flow directly through the stoma.

There are two types of “continent diversions.” The first is the cutaneous continent diversion. This reservoir is made from intestine and is placed within the abdomen in front of the kidneys. The ureters are then connected to this pouch. The appendix or another short piece of small intestine is used to create an extension from this pouch through the abdominal wall to the surface of the skin, often around the belly button. This opening is called a “stoma.” This design prevents urine from flowing back into the kidney (reflux) or spilling out onto the skin. Urine collects in the reservoir and is removed several times a day by insertion of a catheter (tube) into the stoma.

The second type of continent diversion is done by making a new bladder from bowel and is called an “orthotopic neobladder.” The neobladder is connected directly to the urethra. Some people with a neobladder can urinate naturally, while others may require catheterization to empty the bladder.

What problems can occur following cystectomy?
People who have an ileal conduit or ileal pouch may have leakage of urine around the stoma. This may lead to irritation of the skin and infection at the site of the stoma. Scar tissue (“strictures”) may form around the ureters or the conduit and block the flow of urine from the kidneys. Reflux of urine into the kidney may also occur, which increases the risk of a urinary tract infection or kidney stones.

Incontinence, or the inability to control passage of urine, may occur after a neobladder is formed. People with this problem may benefit from muscle re-training to control urination effectively. If there is persistent leakage of urine, pressure testing of the neobladder and urethra may help decide about treatment.
Bladder surgeries involving portions of the small intestine sometimes cause abnormal levels of chemicals and fats in the blood. These problems may result in diarrhea, kidney stones, and/or low levels of Vitamin B12.

A cystectomy may also increase the risk of sexual dysfunction in both men and women. Surgery and medications may be used to treat this complication.

What can I do if I have a problem following cystectomy?

If you have had a cystectomy, you will need life-long close follow-up by a urologist. An enterostomal nurse (“ET nurse”) can help by giving advice about skin care, appliance fitting, and supplies. The nurse can also help “troubleshoot” if there are problems with catheterization.

What monitoring is recommended?

If you had an ileal enterocystoplasty (bladder surgery involving a portion of the small intestine), you should have a yearly blood test to check your Vitamin B12 level starting 5 years after your bladder surgery.

When should I call my healthcare provider?

Call your healthcare provider whenever you have fever, pain in the midback or side, blood in the urine, or severe irritation of the skin. If you perform self-catheterization and have difficulty inserting the catheter, this is a medical emergency that needs immediate attention. This complication may mean that the pouch has ruptured, or that the pouch will rupture if the reservoir cannot be drained properly. This can result in serious infection from leakage of urine into the abdomen or pelvis. If you have had a cystectomy, contact your healthcare provider immediately if you have vomiting or abdominal pain. These symptoms may indicate a bowel blockage (obstruction) from scar tissue.
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Dental Health after Cancer Treatment

Treatment for cancer during childhood often increases the risk for dental problems. As a childhood cancer survivor, it is important for you to understand the reasons why dental care is especially important for maintaining your health.

What are the risk factors for dental problems after childhood cancer treatment?

- **Treatment with chemotherapy** before your permanent teeth were fully formed, especially if you were younger than 5 years old at the time of your treatment
- **Radiation that included the mouth and/or salivary glands**
- **Radioiodine therapy (I-131 thyroid ablation)**
- **Treatment with azathioprine** (sometimes given to patients receiving a hematopoietic cell transplant [HCT])
- **Chronic graft-versus-host disease** (cGVHD) associated with HCT

What dental problems can occur following treatment for cancer in childhood?

Chemotherapy and radiation can affect the health of the teeth. Survivors of childhood cancer may be at increased risk of developing cavities, having abnormal development of the teeth, roots of the teeth and the protective tooth enamel, as well as small or absent teeth. It is important to share a history of childhood cancer treatment with your dental health professional and attend regular dental cleanings every 6 months to preserve dental health.

In addition to affecting the teeth, cancer treatments can also affect your salivary glands, gums, taste buds, the jaw bones and the joint (called the temporomandibular joint, or “TMJ”) between the upper and lower jaw.

What can be done for these problems?

Taking care of teeth and gums is always important, and it is even more important if you have had radiation or chemotherapy at a young age. If your gums are not healthy, they can shrink away from your teeth, causing infection in the bone supporting the roots. This bone can dissolve away slowly, causing the teeth to become loose. This condition is called **periodontitis** (inflammation surrounding a tooth). Periodontitis can be prevented by proper brushing of your teeth and gums and by flossing between your teeth at least once a day. Taking good care of your teeth and gums, combined with routine visits to your dentist, can prevent the development of cavities and gum disease.

If your permanent teeth do not develop normally, you may need caps or crowns to improve your smile and the function of your teeth. Sometimes reconstructive surgery is needed to correct poor bone growth of the face or jaw. Radiation can sometimes make it difficult to open your mouth fully (trismus), or cause some scarring and hardening of the jaw muscles (fibrosis). Stretching exercises for the jaw may reduce fibrosis and improve your ability to open your mouth.

Your dentist will be able to instruct you or refer you to occupational therapy to learn these exercises. If you have crooked or small teeth, this may be improved by bonding (applying a thin coating of plastic material on the front surface of the teeth to cover any flaws). If braces are needed, your dentist will do a panorex x-ray of the teeth to see if the teeth, roots and supporting bone are strong enough for braces. If you had high doses of radiation to the face or mouth and you require dental surgery, you may be at increased risk of developing a bone-healing problem (osteoradionecrosis) after the surgery. Your dentist should discuss this potential problem with a radiation oncologist before any dental surgery. If you had an allogeneic bone marrow or stem cell transplant (from a donor other than yourself), it is important to let your dentist know, so that the dentist can check for changes indicating cGVHD.
What is xerostomia and what should I do if I have it?

Dry mouth, also called “xerostomia” can occur after radiation to the head or neck. Other problems related to xerostomia include persistent sore throat, burning sensation in the mouth and gums, problems speaking, difficulty swallowing, hoarseness, or dry nasal passages. Dryness of the mouth is a result of decreased saliva and/or thickening of the saliva, and can lead to the development of cavities.

Drinking liquids frequently and the use of artificial saliva can help relieve the symptoms of xerostomia. Sugar-free candy stimulates saliva production. Proper brushing habits are very important for people with xerostomia, as is limiting the intake of candy and other sweets. Your dentist may recommend application of a fluoride gel to your teeth at least once a day. The fluoride acts on the enamel of your teeth to make it more resistant to decay. Ask your dentist about whether you should use daily fluoride.

Should I take any special precautions when having dental work done?

Always let your dentist know if you have the following health conditions:

- **Splenectomy** (surgical removal of the spleen)
- **High doses of radiation to the spleen** (40 Gy–4000 cGy/rads or more)
- **Heart valve replacement or repair** with artificial or prosthetic material
- **Ventricular shunt** (surgical placement of a tube to drain fluid from the brain) that drains into the heart (ventriculoatrial/V-A) or venous system (ventriculovenous/V-V)
- **Currently active cGVHD** following HCT

In any of these situations, bacteria that normally enter the bloodstream during dental work may increase the risk of serious infections. As a precaution against infection, if you have any of these conditions, antibiotics may be needed before any dental work is done.

When dental work is planned, ask your dentist if you need to take antibiotics before the procedure.

What is the risk of developing oral cancer?

People who have had radiation to the head and neck during childhood, or who have cGVHD after bone marrow or stem cell transplant, may be at increased risk for oral cancers. Using tobacco in any form or using alcohol in combination with smoking greatly increases this risk. Infection with certain forms of the human papillomavirus (HPV) also increases this risk. Your dentist should perform an oral cancer screening exam during each visit.

If you notice any of the following, notify your dentist immediately:

- **A sore that does not heal** or that bleeds easily
- **A change in the color** of your mouth tissues
- **A lump, thickening or rough spot** in the mouth
- **Pain, tenderness or numbness** anywhere in the mouth or on the lips

Most of the time, these symptoms do not indicate any problem, but a dentist can tell if they are the sign of a serious problem.
What should I do to keep my teeth and mouth as healthy as possible?

Follow these recommendations (unless your dentist recommends otherwise):

- **See your dentist regularly at least every six months.** Make sure that your dentist knows your health history and the treatment you received. (Ask your oncologist for a summary of your treatment). Be sure that your visit includes an oral cancer screening, and be sure to notify your dentist if you notice any warning signs of oral cancer.

- **Have a panorex x-ray done before dental/orthodontic procedures** to evaluate the root development of your teeth and determine if any modifications need to be made to your dental treatment plan.

- **Brush your teeth at least twice a day.**
  - Use a fluoride-containing toothpaste to help prevent tooth decay.
  - Place your brush at a slight angle toward the gum when brushing along the gum line.
  - Use a soft-bristle toothbrush, as recommended by your dentist.
  - Clean all surfaces of the teeth.
  - Brush your tongue to remove bacteria that can cause bad breath.

- **Floss your teeth at least once a day.**
  - Floss carefully between teeth because brushing alone does not remove plaque between teeth.
  - Use a gentle touch to avoid injury to gums.
  - It is normal to have a small amount of bleeding when flossing, but if the bleeding increases or your gums are red and puffy, this may be a sign of infection and you should notify your dentist.

- **Use antibacterial, alcohol-free fluoride mouth rinses** (your dentist can recommend the best ones for you).

- **Drink liquids frequently and/or use artificial saliva** (available at most pharmacies without a prescription).

- **Apply fluoride frequently.** Your dentist may recommend a daily fluoride rinse or gel that you can use at home after brushing, in addition to the special fluoride application you may receive at your regular dental cleanings.

- **Limit sweets and carbohydrate-rich foods.**

- **Do not use tobacco products and use alcohol only in moderation** (check with your healthcare provider to see if you should drink alcohol at all, since alcohol may increase other problems following childhood cancer treatment).

- **Notify your dentist immediately if you develop any signs of infection** in your mouth or gums, such as redness, tenderness, excessive bleeding of gums, painful teeth, and/or increased areas of sensitivity.

**For more information** about dental health issues following childhood cancer treatment:

- American Dental Association’s dental health website at [www.mouthhealthy.org](http://www.mouthhealthy.org)

Adapted by Deborah Lafond, MS, RNCS, PNP, CPON®, Children’s National Medical Center, Washington, DC, from “Save Your Smile” by Melissa Hudson, MD, St Jude Children’s Research Hospital, After Completion of Therapy (ACT) Clinic, used with permission. Reviewed by Sarah Ford, MS, PA-C; Kayla L. Foster, MD, MPH; and Melissa Acquazzino, MD, MS.

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Health Link
Healthy living after treatment of childhood, adolescent, and young adult cancer

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Staying Healthy through Nutrition and Physical Activity

Good nutrition and regular exercise offer many benefits to childhood cancer survivors. These include:

- Promoting healing of tissues and organs affected by cancer and its treatment
- Building strength and endurance
- Reducing the risk of certain types of adult cancers and other diseases such as diabetes, high blood pressure, and obesity
- Decreasing stress and providing a feeling of well-being

Impact of Childhood Cancer on Nutrition and Physical Activity

The effects of childhood cancer on nutrition and physical activity will be different for each survivor. Cancer affects nutrition in several ways. Some survivors may have difficulty gaining weight, while others may have problems with gaining too much weight. Physical activity is an important factor in maintaining a healthy body weight. There are many factors that can influence a survivor’s ability to be physically active; however, childhood cancer and its treatment should not be used as an excuse for not eating a healthy diet or staying physically active. Many survivors, just like many people who have never experienced cancer, have poor health habits. Now is a good time to begin making healthy choices about what you eat and stay active. These choices can have a positive effect on your health for many years to come.

Developing a Healthy Nutrition Plan

Suggestions for good nutrition include:

- Choosing a variety of foods from all the food groups. Use the interactive customized guide at [www.choosemyplate.gov](http://www.choosemyplate.gov) to help develop a well-balanced diet and activity plan.
- Eating five or more servings a day of fruits and vegetables, including citrus fruits and dark-green and deep-yellow vegetables.
- Limiting juice to 4 ounces of 100% fruit or vegetable juice per day.
- Eating plenty of high-fiber foods, such as whole grain breads, rice, pasta, and cereals.
- Limiting refined carbohydrates, including pastries, sweetened cereals, soft drinks, and sugars.
- Decreasing the amount of fat in your meals by baking, broiling or boiling foods.
- Limiting intake of red meat and eating fish, poultry, or beans instead. When eating meat, select leaner and smaller portions.
- Limiting fried and high-fat foods, such as fries, snack chips, cheeseburgers, and pizza.
- Choosing low-fat milk and dairy products.
- Avoiding salt-cured, smoked, charbroiled, and pickled foods.
- For adults, limiting alcoholic drinks to less than two a day for men and one for women.

If you need to lose or gain weight, consult with your health care team and/or a nutritionist to develop a nutrition plan. Herbal or dietary supplements should be discussed with your team. There are several questions you should ask yourself to make sure your nutrition plan will be effective.

- Do you have a realistic, achievable weight goal?
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Healthy living after treatment of childhood, adolescent, and young adult cancer

- Does your plan include foods that you will enjoy eating for the rest of your life, not just a few weeks or months?
- Does your plan include a variety of foods?
- Are foods on your plan easily available at your supermarket?
- Does your plan fit into your lifestyle, daily schedule and budget?
- Does your plan include lifestyle changes that will help you maintain your weight change?

Developing a Healthy Exercise Plan

Check with your healthcare team before starting an exercise plan or taking part in new sports and recreational activities. Your healthcare provider can make you aware of the activities that you can safely take part in and those you should avoid.

When choosing an exercise plan, ask yourself these questions:

- Do you have reasonable goals based on your present strength and endurance?
- Is the activity safe for you to perform?
- Does the plan fit into your lifestyle and schedule?
- Does the activity require special equipment or protective gear and will your budget cover the expense?
- Do you need to make changes in the sport or activity based on a special need?
- Do you enjoy doing the sport or activity?

Here are a few helpful suggestions when implementing your exercise plan:

- Start out slow. Don’t try activities that are too strenuous or put you at risk for muscle strain.
- Begin your exercise plan with a warm-up program and end with a cool-down activity, such as stretching and slow easy movements.
- Use correct posture when exercising.
- Exercise until you are tired, but not in pain.
- Identify the muscles you want to strengthen and choose exercises that work on those muscles.
- Alternate exercises to work different muscles and different parts of your body.
- To avoid injury, use the right equipment and shoes. Avoid running, jogging, or aerobic dancing on hard surfaces such as asphalt or concrete.

The American Cancer Society recommends having a physically active lifestyle. Adults should get at least 150 minutes of moderate physical activity (brisk walking, bicycling, vacuuming, gardening), or 75 minutes of vigorous physical activity (running, aerobics, heavy yard work), or a combination of these each week, preferably spread throughout the week. Children and adolescents should engage in at least 60 minutes each day of moderate to vigorous physical activity each day (running, aerobics, heavy yard work), with vigorous activity at least 3 days each week. Here are some practical suggestions to try to work physical activity into your daily schedule.

- Park a good distance from your place of work and walk the extra distance each day.
- Set aside 30 minutes a day to take a brisk walk.
- Take the stairs instead of the elevator.
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• If you have a sit-down job, get up and stretch your muscles every hour and take a walk during your lunch or break.
• Ride a bike to work or for running errands.
• If you have a dog, take him/her on a brisk walk every day.
• Plant a garden, wash your car, mow the lawn, paint furniture, clean out the garage and catch up on all those chores you have been meaning to do—instead of watching TV or playing on the computer.
• Keep your body moving while watching TV or reading the newspaper on a stationary bike or treadmill.
• Plan active outings with family or friends.
• Exercise with a partner.
• Join a sports team.

Physical Activity for Survivors with Special Needs

Survivors who have special needs can take part in most activities, but the help of a physical or occupational therapist may be needed to adapt the activity for success. A social worker may be able to help find insurance coverage or other resources for special equipment. Specialized programs for individuals with special needs, organizations and other resources are often available through your healthcare center, in your local community, and at www.ncpad.org.

Adapted by Sharon A. Frierdich, RN, MS, CPNP, University of Wisconsin Hospital and Clinics, Madison, WI, from “Staying Physically Healthy, Play Safely, Play Well,” St. Jude Children’s Research Hospital, used with permission.

Reviewed by Linda Rivard, RN, BSN, CPON®; Christine S. Yun, MSN, PNP, CPON®; and Kayla L. Foster, MD, MPH.

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School after Cancer Treatment

Treatment for cancer during childhood or adolescence may affect educational progress due to prolonged absences or reduced energy levels that frequently occur during or after treatment. In addition, some types of cancer may require therapy to control or prevent spread of the disease to the brain and/or spinal cord (central nervous system). This therapy can sometimes affect memory and learning abilities. Parents and teachers should be aware of potential educational problems that may be related to cancer treatment. You/your child or teen may be eligible for special accommodations at school which may also require specialized testing.

What increases the risk of educational problems?

Factors that may place children and teens at increased risk for difficulties in school include:

- Diagnosis of cancer at a very young age
- Numerous or prolonged school absences
- A history of learning difficulties before the cancer diagnosis
- Cancer treatment that results in reduced energy levels
- Cancer treatment that affects hearing or vision
- Cancer treatment that results in physical disabilities
- Cancer therapy that includes treatment to the central nervous system (see below).

Are children and teens with certain types of cancer at higher risk of developing educational difficulties?

Yes, children and teens with the types of cancer listed below are more likely to have received treatments that may affect learning and memory. Since treatments for these types of cancer vary widely, not everyone who was treated for these cancers are at increased risk.

- Brain tumors
- Tumors involving the eye or ear
- Acute lymphoblastic leukemia (ALL)
- Non-Hodgkin lymphoma (NHL)

What types of treatment place children and teens at higher risk for learning and memory problems?

- Methotrexate—if given in high doses into the veins intravenously (IV) or injected into the spinal fluid [intrathecally (IT) or intra-omaya (IO)]
- Cytarabine—if given in high doses intravenously (IV)
- Surgery involving the brain
- Radiation to the head/brain or total body irradiation (TBI)
- Cisplatin or carboplatin (may affect hearing)
What testing is recommended?

Any young person who has had any of the above cancer treatments, or who is having difficulties in school, should undergo a specialized evaluation by a pediatric psychologist (neuropsychological testing) at the time of entry into long-term follow-up. This type of testing will measure IQ and school-based skills, along with more detailed information about how the child or teen processes and organizes information.

Even if the initial neuropsychological evaluation is normal, it is important for parents and teachers to remain watchful. Further neuropsychological evaluations may be necessary if the child or teen begins having trouble in school or develops any of the problems listed in the section below. In addition, repeat testing is often recommended at times when academic challenges are more likely to occur, such as at entry into elementary school, middle school, high school, and during pre-college planning.

What learning problems may occur?

The brain is a very complex structure that continues to grow and develop throughout childhood and adolescence. Some problems may not become apparent until years after therapy is completed. Common problem areas include:

- Handwriting
- Spelling
- Reading
- Vocabulary
- Math
- Concentration
- Attention span
- Ability to complete tasks on time
- Memory
- Processing (ability to complete assignments that require multiple steps)
- Planning
- Organization
- Problem-solving
- Social skills

What can be done to help with learning problems?

If a problem is identified, special accommodations or services can be requested to help maximize the student’s learning potential. The first step is to schedule a meeting with the school to develop a specialized educational plan, this may include a 504 plan or an individualized education plan (IEP). Examples of strategies that are often helpful for children and teens with educational problems related to cancer treatment include:

- Seating near the front of the classroom
- Minimizing the amount of written work required
- Use of tape-recorded textbooks and lectures
- Use of a computer keyboard instead of handwriting
- Use of a calculator for math
- Modification of test requirements (extra time, oral exams instead of written exams)
- Assignment of a classroom aide
- Extra help with math, spelling, reading, and organizational skills
- Access to an elevator
- Extra time for transition between classes
- Duplicate set of textbooks to keep at home
What laws protect the rights of students who have undergone treatment for cancer?

In the United States, there are three public laws that protect the rights of students with educational problems related to cancer treatment. These laws are:

**The Rehabilitation Act of 1973 – Section 504**

This legislation provides accommodations for students with a “physical or mental impairment which substantially limits one or more major life activities,” or students who have “a record of such impairment,” or who are “perceived as having such an impairment” (The Rehabilitation Act, 1973). Qualifying conditions include chronic illnesses such as cancer, as well as many other disabilities, including hearing problems, vision problems, learning disabilities, speech disorders, and orthopedic handicaps. All childhood cancer survivors in the United States are eligible for accommodations under this law, and all educational institutions receiving federal funding (including colleges and universities) are required to comply. Accommodations may include modifications in the curriculum (such as allowing the use of a calculator and extra time for assignments or test-taking) and the environment (such as seating near the front of the classroom or allowing extra time between classes).

**The Individuals with Disabilities Education Act (IDEA)**

The IDEA legislation (PL 105-17) requires that public schools provide “free and appropriate education in the least restrictive environment” for disabled students between the ages of 3 and 21 years of age. In order to qualify for special education services under IDEA, the student must meet qualifications under at least one disability outlined in the law—that most commonly apply to students treated for cancer include “specific learning disability,” “traumatic brain injury,” or “other health impairment.” To access services under the IDEA legislation, parents must initiate the process by requesting that the student be evaluated for an “Individualized Education Plan” or IEP. The student will then undergo an assessment process to determine what assistance is required. A conference is then held to discuss the results of the evaluation and, if the student qualifies, to determine an individualized plan to meet the identified specialized educational needs. Services available under the IDEA legislation include tutoring, specialized classroom placements (such as a resource room), psychological services, adaptive physical education, physical, occupational and speech/language therapy, and transportation services. All services and accommodations required by the student should be specified in the IEP (the written document describing the special education program). The IEP should be reviewed and updated on an annual basis to assure that it continues to meet the student’s educational needs.

**The Americans with Disabilities Act (ADA)**

The ADA law (PL 101-336) protects against discrimination in employment, transportation, communication, government, and public accommodations for people with disabilities. It guarantees equal access to public spaces, event, and opportunities and may be particularly helpful for students seeking higher education or employment.

Where can I get more information?

Additional information is available from the Center for Parent Information and Resources [www.parentcenterhub.org](http://www.parentcenterhub.org)
American Childhood Cancer Organization, for the free publication: Educating the Child with Cancer, a Guide for Parents and Teachers (phone: 1-855-858-2226, ext. 101) or [www.acco.org](http://www.acco.org)
US Department of Education; Office for Civil Rights. Protecting Students with Disabilities [www2.ed.gov/about/offices/list/ocr/index.html](http://www2.ed.gov/about/offices/list/ocr/index.html)
Keeping Your Eyes Healthy

Radiation to the brain, eye, or eye socket (orbit) during treatment for childhood cancer can have a long-lasting effect on the eyes. Radioiodine (I-131) treatment and chronic graft-versus-host disease (an immune response that can develop after bone marrow or stem cell transplant) can also affect the eyes. Because vision can have a significant impact on daily living, it is important for survivors who received these treatments to have their eyes checked regularly.

How do the eyes work?
The eyes are remarkable organs, allowing light to be converted into impulses that are transmitted to the brain, where images are perceived. The eyes are located in the area of the skull known as the orbit or eye socket. A thin layer of tissue called the conjunctiva covers and protects the eye and eyelids. Tears are produced in the lacrimal gland, located in the outer corner of the eye socket, above the eyeball. Tears flow over the eye, providing lubrication, and drain into a tiny canal at the inner corner of the eye, called the lacrimal duct. Light enters the eye through a clear layer of tissue known as the cornea. The cornea bends and focuses the light and sends it through the opening of the eye known as the pupil. The pupil controls how much light enters the eye. Behind the pupil is the lens of the eye, which focuses the light onto the retina, the membrane along the back wall of the eye. The nerve cells in the retina change the light into electrical impulses and send them through the optic nerve to the brain, where the image is perceived.

What eye problems can develop following treatment for childhood cancer?

**Cataracts**: Clouding of the lens of the eye. When this happens, light cannot pass through the lens easily. Common symptoms of cataracts include painless blurring of vision, sensitivity to light and glare, double vision in one eye, poor night vision, fading or yellowing of colors, and the need for frequent changes in glasses or contact lens prescriptions (see related Health Link: Cataracts).

**Xerophthalmia**: Dry eyes resulting from decreased tear production due to radiation or chronic graft-versus-host disease. Symptoms include pain at the surface of the eye and light sensitivity.

**Lacrimal duct atrophy**: Shrinking of the lacrimal duct, which drains tears from the eye. Lacrimal duct atrophy can result in problems with increased tearing. This can be caused by radiation to the eye or orbit, or by radioiodine (I-131) therapy given for treatment of thyroid cancer.

**Other eye problems:**
The following eye problems are less common and are usually seen only in survivors who had radiation doses of 30 Gy or 3000 cGy/rads or higher directed at the eye or orbit:

**Orbital hypoplasia**: Underdevelopment of the eye and surrounding tissues, caused by radiation to the eye or orbit. This can result in a small eye and orbit (orbital hypoplasia).

**Enophthalmos**: Sunken eyeball within the orbit as a result of radiation.

**Keratitis**: Inflammation of the cornea (the clear, outer surface of the eye). This can cause pain at the surface of the eye and light sensitivity.

**Telangiectasias**: Enlargement of blood vessels in the white part of the eye. These do not usually cause any symptoms.
but are sometimes bothersome because of their appearance.

**Retinopathy:** Damage to the retina (the back surface of the eye where visual information is passed from the eye to the brain). Painless vision loss is the major symptom of retinopathy.

**Maculopathy:** Damage to the macula (area of central vision within the retina), which may result in blurred vision.

**Optic chiasm neuropathy:** Damage to the nerves that send visual information from the eye to the brain. This can result in vision loss.

**Papillopathy:** Swelling of the optic disc (area where the optic nerve enters the eye).

**Glaucoma:** Increased pressure within the eye. This can damage the optic nerve and result in vision loss.

### What cancer therapies increase the risk of developing these eye complications?

- Radiation therapy at doses of 30 Gy (3000 cGy/rads) or higher to the following areas increases the risk of treatment-related eye problems:
  - Eye
  - Orbits
  - Head/Brain

- Other factors that may increase the risk for developing certain eye problems include:
  - Radioiodine (I-131) treatment for thyroid cancer (increased risk for lacrimal duct atrophy)
  - Chronic graft-versus-host disease following bone marrow, cord blood, or stem cell transplant (increased risk for xerophthalmia)
  - Diabetes mellitus (increased risk for problems involving the retina and optic nerve)
  - High blood pressure (increased risk of optic chiasm neuropathy)
  - Frequent exposure to sunlight (increased risk for cataracts)
  - Certain chemotherapy drugs, such as, actinomycin-D and doxorubicin, which can increase the risk of eye problems when given together with radiation.

### What monitoring is recommended?

- Evaluation by an eye specialist (ophthalmologist or optometrist) at least once a year is recommended for anyone who:
  - Had radiation to the head, brain, eyes, or total body irradiation (TBI)
  - Had a tumor involving the eye
  - Has graft-versus-host disease (as a result of bone marrow, cord blood, or stem cell transplant)

  **Note:** An ophthalmologist is a medical doctor (MD or DO) who specializes in eye problems—this is different from a doctor of optometry (OD), who is also a vision specialist but not a medical doctor. Examination by an eye specialist should include vision screening, examination for cataracts, and a full examination of the internal structures of the eye. People who develop vision problems should be followed regularly by an ophthalmologist.

- Evaluation by an ocularist (a trained person who makes and fits artificial eyes) at least once a year is recommended for anyone who has had:
  - An eye removed because of cancer treatment and/or complications related to treatment
  - An artificial eye (prosthesis) that does not fit well

- Evaluation by an ophthalmologist is recommended on an as-needed basis for people who had Radioiodine (I-
If you develop any of the following symptoms, seek prompt medical evaluation. In some cases, referral to an ophthalmologist may be needed:

- Blurry vision
- Double vision
- Blind spots
- Sensitivity to light
- Poor night vision
- Persistent irritation of surface of eye or eyelids
- Excessive tearing/watering of eyes
- Pain within the eye
- Dry eyes

How are eye problems treated?

**Cataracts:** Not all cataracts need treatment. In many cases, an ophthalmologist may monitor the vision closely over many years and will recommend treatment if and when it becomes necessary. The only treatment for cataracts is surgical removal of the lens and replacement with an artificial lens. Today, cataract surgery is a low-risk procedure that is performed on an outpatient basis and works well in restoring vision.

**Orbital hypoplasia:** Usually no treatment is needed for orbital hypoplasia. In severe cases, rebuilding of the bones around the eye may be possible.

**Enophthalmos:** Plastic surgery can be done to build up the orbit.

**Lacrimal duct atrophy:** A surgical procedure to widen the tear drainage system can be performed if heavy tearing is a significant problem.

**Xerophthalmia:** Treatment of dry eye includes the frequent use of artificial tears (eye drops) or ointments to moisten the surface of the eye. In severe cases, the tear drainage system can be blocked by surgery to reduce the drainage of tears from the eye.

**Keratitis:** The frequent use of artificial tears (eye drops) or ointments to moisten the surface of the eye is recommended. Patching the affected eye during sleep may also promote healing. Keratitis caused by infection is treated with antibiotic eye drops or ointment. Rarely, surgical replacement (transplant) of the cornea is necessary.

**Telangiectasias:** No treatment is necessary.

**Retinopathy and maculopathy:** Retinopathy may require laser or photocoagulation (heat) treatment of the retina. Rarely, surgery to remove the eye is necessary in severe cases.

**Optic chiasm neuropathy:** No treatment available.

What can be done if there is impaired vision?

If impaired vision is detected, it is important to follow the recommendations of your ophthalmologist regarding treatment. If vision is not correctable, services are available in most communities to assist people with visual impairments.

In addition, in the United States, services are available for people under 22 years of age through the local public school district or referral agencies (available under the Individuals with Disabilities Education Act, PL 105-17). Sometimes
Health Link

Healthy living after treatment of childhood, adolescent, and young adult cancer

It's important to protect your eyes whether or not you have treatment-related eye disorders. Precautions you can take include:

- Wear sunglasses with ultraviolet (UV) protection when in bright sunlight.
- When participating in sports, be sure to select protective eyewear that is appropriate for the sport. Eyewear worn for sports should be properly fitted by an eye care professional.
- Avoid toys with sharp, protruding, or projectile parts.
- Never play with fireworks or sparklers of any kind to avoid accidental injury.
- Be careful when working with hazardous household chemicals.
- Wear protective eyewear when using a lawnmower, power trimmer, or edger, and when working with dangerous equipment in the workshop.
- If you do experience an eye injury, seek medical attention promptly.

Written by Teresa Sweeney, RN, MSN, CPNP, St. Jude Children's Research Hospital, Memphis, TN.
Reviewed by Angela Yarbrough DNP, APRN, FNP-BC, CPON®; Kayla L. Foster, MD, MPH; and Christine Yun MSN, PNP, CPON®.

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Ovarian and Reproductive Health after Cancer Treatment

The effects of childhood cancer therapy on reproductive function depend on many factors, including age at the time of cancer therapy, the specific type and location of the cancer, and the treatment that was given. It is important to understand how the ovaries function and how they may be affected by cancer treatment.

The reproductive system

At birth, the ovaries contain all the eggs they will ever have. When the time comes to begin puberty, the pituitary gland in the brain signals the ovaries by releasing two hormones (FSH and LH). The ovaries secrete the estrogen and progesterone, which are necessary for reproductive function. Normally, during a monthly menstrual cycle, one egg matures and is released from the ovaries. If the egg is not fertilized, menstruation begins. The cycle then repeats itself about every 28 days. With each menstrual cycle, the supply of eggs decreases. When most of the eggs are depleted from the ovaries, menopause begins. During menopause, the menstrual cycles stop, the ovaries stop making hormones, and pregnancy progressively becomes less likely.

How does cancer therapy affect the ovaries?

Certain chemotherapy drugs, radiation therapy, and surgery can sometimes damage the ovaries, decreasing ovarian hormone production and reducing the reserve supply of eggs. When the ovaries are not able to produce sufficient hormones to regulate ovulation and menstruation, otherwise known as premature ovarian insufficiency (POI), an individual may not begin puberty and menstruation, may have irregular menstrual cycles or menstrual cycles may stop earlier than expected (also known as premature menopause). Additionally, when the ovaries do not function properly, this can result in infertility or difficulty becoming pregnant.

What are the causes of premature ovarian insufficiency (POI)?

Chemotherapy of the “alkylator” type (such as cyclophosphamide, thiotepa, melphalan and busulfan) is most likely to affect ovarian function. The total dose of alkylators used during cancer treatment is important in determining the likelihood of ovarian damage. With higher total doses, the likelihood of damage to the ovaries increases. Heavy metal chemotherapy (cisplatin and carboplatin) may also damage the ovaries. If treatment for childhood cancer included a combination of both radiation and these chemotherapies, the risk of POI may be higher.

Radiation therapy can affect ovarian function in two ways:

Radiation aimed at or near the ovaries. The age of the person at the time of radiation and the total radiation dose can affect whether or not POI occurs. With lower doses of radiation, younger people tend to have less damage to the ovaries than those who received equal doses but who were teenagers or young adults at the time of radiation. High doses of radiation usually result in a loss of ovarian function and infertility regardless of age.

Radiation to the hypothalamic and pituitary gland regions in the brain. The hypothalamus and pituitary gland regulate the production of two hormones (FSH and LH) needed for proper ovarian function.

Radiation to the brain at higher doses can damage to these areas of the brain leading to low levels of these hormones.

Surgery. If both ovaries were removed (bilateral oophorectomy) during cancer therapy, this always results in a loss of ovarian function and infertility. This type of POI is sometimes called “surgical menopause.” If one ovary was removed (unilateral oophorectomy), menstruation may stop earlier than it otherwise would have.
What types of cancer therapy increase the risk of POI?

Individuals who received the following therapy may be at risk for POI:

- **Chemotherapy** - the class of drugs called “alkylators” can cause POI when given in high doses. Heavy metal chemotherapy can also affect ovarian function. Examples of these drugs are:

  **Alkylating agents:**
  - Busulfan
  - Carmustine (BCNU)
  - Chlorambucil
  - Cyclophosphamide (Cytoxan®)
  - Ifosfamide

  **Heavy metals:**
  - Carboplatin
  - Cisplatin

- **Radiation therapy** to any of the following areas:
  - Pelvis
  - Lower spine (sacral area)
  - Total body irradiation (TBI)
  - Head/brain especially if dose was 30 Gy (3000 cGy/rads) or higher

- **Surgery:**
  - Removal of one or both ovaries

**Non-classical alkylators:**
- Dacarbazine (DTIC)
- Temozolomide

What are the effects of childhood cancer therapy on the female reproductive system?

1. **Failure to enter puberty.** Pre-pubertal individuals who received cancer therapy that results in ovarian failure will need hormonal therapy (hormones prescribed by a doctor) to progress through puberty. If this occurs, referral to an endocrinologist (hormone doctor) should be made for further evaluation and management.

2. **Temporary cessation of menstrual cycles.** Many who were already menstruating will stop having monthly periods during their cancer therapy. In most cases, menstrual cycles will resume sometime after cancer treatment ends, although the timing of this is unpredictable. In some cases, it may take up to several years to restart menstruation. Since eggs are released before the menstrual cycles, pregnancy can occur before the menstrual periods resume. If pregnancy is undesired, birth control (contraception) should be used, even if the menstrual cycles have not resumed.

3. **Permanent cessation of menstrual cycles (premature menopause).** Menopause (the permanent cessation of menstrual cycles) occurs at an average age of 51. People who were already menstruating prior to their cancer therapy sometimes develop ovarian failure as a result of their cancer treatment and never resume menstrual cycles. Others may resume menstrual cycles, but then stop menstruating much earlier than would normally be expected. If a person is currently having menstrual periods but received chemotherapy or radiation that can affect ovarian function or had one ovary removed, they may still be at risk for entering menopause at an early age. **If a person at risk for premature menopause desires to have children, it is best not to delay childbearing beyond the early thirties, because the period of fertility may be shortened after having cancer therapy.**
4. **Lack of sex hormones.** People with ovarian failure do not make enough estrogen. Estrogen is needed for functions other than reproduction—it is very important for maintaining strong healthy bones, a healthy heart, and overall well-being. Young people with ovarian failure should see an endocrinologist (hormone specialist) for hormone replacement therapy, which will be necessary until they reach middle age.

5. **Infertility.** Infertility is the inability to achieve a pregnancy after at least one year of unprotected intercourse. Infertility occurs when the ovaries cannot produce eggs (ovarian failure), or when the reproductive organs are unable to sustain a pregnancy. Infertility may be the result of surgery, radiation therapy, chemotherapy, or any combination of these. There may also be other reasons for infertility that are unrelated to cancer therapy.

   If a person has regular monthly menstrual periods and normal hormone levels (FSH, LH and estradiol), they are likely to be fertile and able to have a baby. If they do NOT have monthly menstrual periods, or if they have monthly menstrual periods ONLY with the use of supplemental hormones, or if they had to take hormones in order to enter or progress through puberty, they are likely to be infertile.

   People who had surgical removal of both ovaries will be infertile. Those who had surgical removal of the uterus (hysterectomy) but still have functioning ovaries can become a parent with the use of a gestational surrogate (another person who carries the pregnancy to term). People who are infertile should discuss their options with a fertility specialist and their oncologist. The use of donor eggs may be an alternative for some. Additional options may include adoption of a biologically unrelated child or child-free living.

6. **Pregnancy risks.** Certain therapies used during treatment for childhood cancer can sometimes increase the risk of problems that a person may experience during pregnancy, labor, and childbirth. The following may be at increased risk:

   - Those who had radiation to the pelvis, lower spine, or total body (TBI) may have an increased risk of miscarriage, premature delivery, or problems during labor.
   - Those who received anthracycline chemotherapy (such as doxorubicin or daunorubicin), and those who received radiation to the abdomen, chest or thoracic spine may be at risk for heart problems that can worsen with pregnancy and labor (see related Health Link: “Heart Health”).

   People with these risk factors should be followed closely by an obstetrician who is qualified to care for high-risk pregnancies.

   Fortunately, in most cases, there is no increased risk of cancer or birth defects in children born to childhood cancer survivors. In rare cases, if the type of cancer in childhood was a genetic (inherited) type, then there may be a risk of passing that type of cancer on to a child. You should check with your oncologist if you are not sure whether the type of cancer you had was genetic.

**What monitoring is recommended?**

Those who have had any of the cancer treatments that may affect ovarian function should have a yearly check-up that includes careful evaluation of progression through puberty, menstrual and pregnancy history, and sexual function. Blood may be tested for hormone levels (FSH, LH, and estradiol) if a problem is suspected. If any problems are detected, a referral to an endocrinologist (hormone specialist) and/or other specialists may be recommended. For people with ovarian failure, a bone density test (special type of x-ray) to check for thinning of the bones (osteoporosis) may also be recommended.
Health Link
Healthy living after treatment of childhood, adolescent, and young adult cancer

Written by: Marcia S. Leonard, RN, CPNP, C.S. Mott Children’s Hospital, Ann Arbor, MI.
Reviewed by Katy Tomlinson, BSN, RN; Lillian R. Meacham, MD; Melissa Acquazzino, MD, MS; and Kayla L. Foster, MD, MPH.

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Finding and Paying for Healthcare

As a childhood cancer survivor, it is important for you to have regular medical check-ups, since some of the treatments that you received may increase your risk for health problems as you get older. Sometimes it is difficult to find and pay for the medical care that you need. There are several things you can do to make sure you are getting the best possible care for your needs. Here are some suggestions.

**If possible, find a long-term follow-up clinic.** Many childhood cancer programs have long-term follow-up clinics. A directory of long-term follow-up clinics affiliated with Children’s Oncology Group institutions can be found at this link: https://www.cogmembers.org/public/lateeffects/default.aspx. If you are still followed in a childhood cancer center, or if there is a childhood cancer center near where you live, contact that center to discuss your options for obtaining long-term follow-up care. Long-term follow-up clinics usually screen for late effects and educate survivors about ways to lower the risk of health problems after cancer. They are generally an excellent place to get a complete health evaluation, but are not usually designed to meet the everyday healthcare needs of survivors and may only see survivors until they reach adulthood. Even if you are attending a long-term follow-up care clinic, it is also important to find a primary healthcare provider who can take care of your general medical needs.

**Choose a primary healthcare provider in your community.** The best primary healthcare providers for adults are usually those who specialize in family practice or internal medicine. The chance of finding a primary healthcare provider who has experience taking care of childhood cancer survivors is low, due to the rarity of cancer in children. However, it is important to look for a healthcare provider who is thorough, well-trained, and a good listener. Ask friends and family members to help you identify healthcare providers with these qualities who are practicing in your area. Make an appointment for a general check-up and discuss your past medical history and health risks during this visit. It is best to do this introductory visit at a time when you are well, and not when you are being seen because of an illness.

**Tell your healthcare provider about the Childhood Cancer Survivor Long-Term Follow-Up Guidelines,** available on the Children’s Oncology Group website at www.survivorshipguidelines.org. This comprehensive set of healthcare screening and management guidelines is designed for use by healthcare professionals who are providing ongoing medical follow-up for childhood cancer survivors.

**Organize a medical team to provide your local care.** Get advice from your childhood cancer doctor and your primary healthcare provider about who should be on your medical team. Your team should always include a primary healthcare provider and a dentist. Depending on your situation, you may also need to include other professionals that are important for your continued health, such as a physical therapist or psychologist. Your primary healthcare provider can help you select these individuals and provide referrals for their services.

**Share your medical records with all the members of your medical team.** If possible, ask the oncologist who treated your childhood cancer to provide you with a survivorship care plan that includes a summary of your diagnosis and treatment, future health risks, and recommended screening. Ask your oncologist to share a copy of your treatment summary with all your healthcare providers. Keep a copy of the care plan and important sections of your pediatric medical records in a personal medical file. Be sure that every new healthcare provider you see is aware of your medical history and any special health risks you may have because of your cancer treatment. If you need help in obtaining your medical records, call the hospital, clinic, or medical center where you received your treatment.
Be a partner in the healthcare that you receive. To find out if you are getting adequate care, ask yourself the following questions:

- Do I know my cancer diagnosis and specific treatment I received?
- Do I know about the health problems that can occur after this treatment?
- Have I shared this information with my healthcare providers?
- Does my healthcare provider check periodically for health problems specifically related to my childhood cancer?
- Does my healthcare provider advise me about things I should or should not do to keep healthy after my treatment for childhood cancer?

Explore all resources for paying for healthcare. Healthcare is expensive and people who have had a serious illness often face many hurdles when trying to obtain adequate follow-up care. In the United States, insurance companies are now required to provide coverage for childhood cancer survivors, regardless of pre-existing medical conditions. The law also now provides the option of coverage under a parent's health insurance policy for young adults under age 26. More information about your rights and protections under the health care law (commonly known as the “Affordable Care Act”), is available at this link: https://www.healthcare.gov/health-care-law-protections/. If you aren’t insured, you should seek assistance from a local social service organization or your hospital social worker to identify your coverage options.

As a survivor of childhood cancer, you have already overcome many obstacles. The process of obtaining and paying for healthcare can sometimes seem discouraging, but it is worth the effort.

Survivorship Healthcare Coverage Checklist

Define your current healthcare needs. Ask yourself:

- Do I mainly need a healthcare provider for general check-ups?
- Do I have chronic health problems that require frequent medical visits?
- Do I have problems that need periodic monitoring by specialists?
- Am I on expensive prescription medications?
- Do I require prosthetic or rehabilitation services?

Explore all resources for healthcare coverage:

- Coverage through a parent's or spouse's policy
- Health insurance coverage offered by your college or employer
- State or federal public assistance programs that may substantially lower the cost of coverage
- Discounted or free healthcare through health department clinics or church-based programs
- Low cost or free prescription programs provided by some pharmaceutical companies for people with low income

If you are insured, get the facts about your policy.

- What services are covered?
- Does your plan offer a discounted prescription program?
- Are referrals to specialists controlled through a primary care physician?
- Is coverage in effect only while the patient is a full-time student?
- Does coverage expire at certain age?
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Ask for help in understanding current resources and locating new ones.

- Ask family members, friends, hospital or clinic insurance managers, and insurance representatives to explain unclear details about insurance benefits.
- Call a clinic or hospital social worker to ask for help in finding state or community healthcare resources.
- Check out services offered by national nonprofit organizations (example, Lions Club for ocular prostheses).
- Be proactive in obtaining and maintaining health insurance coverage.
- Visit [www.healthcare.gov](http://www.healthcare.gov) to determine your options for insurance coverage and to determine whether you qualify for discounted or free coverage available to people with low income or disability.
- Avoid lapses in coverage. Plan for transitions in health insurance coverage that occur with college graduation, aging out of parental coverage, or job changes.

Be aware of the laws that help you keep insurance benefits. The following laws apply to survivors living in the United States:

- **ACA** (Affordable Care Act), the comprehensive health care reform law enacted in the United States on March 30, 2010, created a Health Insurance Marketplace and new rights and protections that make health insurance coverage fairer and easier to understand. More information is available at [www.healthcare.gov](http://www.healthcare.gov).
- **COBRA** (Consolidated Omnibus Budget Reconciliation Act) requires employers or larger businesses to make insurance available for a limited time to employees (and their dependents) who are fired or laid off.
- **HIPAA** (Health Insurance Portability and Accountability Act of 1996) allows people with pre-existing conditions to keep comprehensive insurance coverage when they are changing insurance plans or jobs. Under the new Health Care Law in the United States, HIPAA eligibility provides greater protections than are otherwise available under state law.

Be persistent when meeting obstacles. Try not to get overwhelmed.

- Complete and follow through with applications.
- Appeal denials with letters of support from your healthcare provider.
- Contact groups such as Candlelighters and the National Coalition of Cancer Survivors for more information about healthcare resources.

Recommended Resources

The National Coalition of Cancer Survivors is a patient-led advocacy organization for cancer survivors. Their website, [www.canceradvocacy.org](http://www.canceradvocacy.org), lists organizations and agencies that offer help regarding specific cancer-related issues, including finding affordable healthcare. Their phone number is (877) 622-7937.

Cancer Care, a nonprofit organization dedicated to providing emotional support, information, and practical help to people with cancer and their loved ones. Their site also has a searchable database to assist in finding local and national resources to help with financial and practical needs. 1-800-813- HOPE (4673) [www.cancercare.org](http://www.cancercare.org).

Written by: Melissa M. Hudson, MD, St. Jude Children’s Research Hospital, Memphis, TN; Sally Wiard, MSW, LCSW, Children’s Hospital of San Antonio, San Antonio, TX; and Allison Hester, RN, MSN, CPNP, Arkansas Children’s Hospital, Little Rock, AR. Adapted from the CCSS Newsletter, Spring 2003, used with permission.

Reviewed by Amelia DeRosa RN, BSN, CPON; Christine S. Yun, MSN, PNP, CPON; and Kayla L. Foster, MD, MPH.
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Additional health information for childhood cancer survivors is available at www.survivorshipguidelines.org

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Gastrointestinal Health after Cancer Treatment

Treatment for childhood cancer can sometimes cause scarring and chronic problems of the intestines (bowel) or other parts of the gastrointestinal (GI) system. It is important to know about the GI system so that you can recognize symptoms and keep your GI system healthy.

How does the gastrointestinal system work?

The GI system (also known as “the digestive system”) is a group of organs that break down (digest) the food that we eat. This allows the body to use food to build and nourish cells and provide energy.

What types of GI problems can arise after treatment?

The types of problems can vary depending on the treatment that was given. Generally, GI problems occurring after treatment for childhood cancer are related to surgery or radiation. The effects depend on the location of the surgery, the radiation treatment field, and the dose of radiation received.

Problems that can develop include:

- **Bowel obstruction** (blockage of the intestines)—the risk is higher for people who have had a combination of abdominal radiation and surgery.

- **Esophageal stricture** (scarring and narrowing of the tube that delivers food from the mouth to the stomach)—this is usually a result of radiation and can cause problems with swallowing.

- **Gallstones** (solid deposits of cholesterol or calcium salts that form in the gallbladder or bile ducts)—the risk is increased in people who had abdominal radiation.

- **Hepatic fibrosis** or cirrhosis (scarring of the liver)—the risk is increased for people who received radiation to the abdomen, or for those with a chronic liver infection (hepatitis).

- **Chronic enterocolitis** (inflammation of the intestines resulting in chronic diarrhea and abdominal pain)—the risk is increased after abdominal or pelvic radiation.

- **Colorectal cancer** (cancer of the large intestine)—the risk is increased for people who had abdominal or pelvic radiation (see related Health Link: Colorectal Cancer).

What treatments increase the risk for developing a gastrointestinal problem?

- **Surgery** involving the abdomen or pelvis

- **Radiation**:
  - Neck
  - Chest
  - Abdomen
  - Pelvis
  - Spine (cervical, thoracic, lumbar, sacral)

- **Other risk factors include**:
  - History of bowel adhesions (scarring)
What are the possible symptoms of a gastrointestinal problem?

- Chronic acid reflux (heartburn)
- Difficult or painful swallowing
- Chronic nausea or vomiting
- Abdominal pain
- Chronic diarrhea
- Chronic constipation
- Black tarry stools or blood in stool
- Weight loss
- Changes in appetite
- Abdominal distension/Feeling bloated
- Jaundice/Yellow eyes, yellow skin (see related Health Link: Liver Health)

If you develop any of these symptoms, see your healthcare provider. Symptoms that come on quickly or are severe (such as the sudden onset of abdominal pain and vomiting) may indicate a more urgent problem (such as a bowel obstruction) requiring immediate medical evaluation.

What medical tests are used to screen for a gastrointestinal problem?

Screening for problems affecting the GI system involves an annual physical examination by a qualified health care professional. X-rays, blood tests, and testing for small amounts of blood in the stool (called the guaiac test) are sometimes needed. An ultrasound may be needed if gallstones or gallbladder problems are suspected. Additionally, certain tests that examine the inside of the colon (colonoscopy) or esophagus (endoscopy) with special instruments are sometimes needed.

What can be done to prevent gastrointestinal problems?

- Develop a healthy nutrition plan. Suggestions for a healthy diet include:
  - Choose a variety of foods from all the food groups. Visit www.choosemyplate.gov for help developing a well-balanced meal plan.
  - Eat 5 or more servings a day of fruits and vegetables, including citrus fruits and dark-green and deep-yellow vegetables.
  - When drinking juice, choose 100% fruit or vegetable juice, and limit to about 4 ounces a day.
  - Eat plenty of high fiber foods, such as whole grain breads, rice, pasta and cereals. Avoid foods high in sugars (such as candy, sweetened cereals, and sodas).
  - Buy a new fruit, vegetable, low-fat food, or whole grain product each time you shop for groceries.
  - Decrease the amount of fat in your meals by baking, broiling or boiling foods and not eating fried foods.
  - Limit intake of red meat by substituting fish, chicken, turkey or beans. When you eat meat, select leaner cuts.
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and smaller portions.
- Limit fried and high-fat foods, such as fries, snack chips, cheeseburgers, and pizza.
- Choose low-fat milk and dairy products.
- Avoid salt cured, smoked, charbroiled and pickled foods.
- Be sure that you eat foods rich in calcium, such as milk, yogurt and dark green vegetables.

- Avoid cancer-promoting habits.
  - Do not smoke or use tobacco products.
  - Avoid second-hand smoke when at all possible.

- If you drink alcohol, use moderation.
  - Heavy drinkers (people who drink two or more hard drinks per day), especially those who use tobacco, have a higher risk of GI cancer and other gastrointestinal problems.
  - Limiting the use of alcohol can reduce these risks.

Written by: Sharon M. Castellino, MD, MSc, Children’s Healthcare of Atlanta - Egleston, Atlanta, GA; and Sheila Shope, RN, FNP, St. Jude Children’s Research Hospital, Memphis, TN.
Reviewed by Daniel Smith, DNP, FNP; Kayla L. Foster, MD, MPH; and Melissa Acquazzino, MD, MS.

Additional health information for childhood cancer survivors is available at www.survivorshipguidelines.org

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Growth Hormone Deficiency after Cancer Treatment

Some people who were treated for cancer during childhood may develop endocrine (hormone) problems as a result of changes in the function of a complex system of glands known as the endocrine system.

What is the endocrine system?

The endocrine system is a group of glands that regulates many body functions including growth, puberty, energy level, urine production, and stress response. Glands of the endocrine system include the pituitary, hypothalamus, thyroid, pancreas, adrenals, ovaries, and testes. The hypothalamus and pituitary are sometimes called the “master glands” because they control many of the other glands in the endocrine system. Unfortunately, some treatments given for childhood cancer can damage the endocrine system, resulting in a variety of problems.

What are hormones?

Hormones are chemical messengers that carry information from the endocrine glands through the bloodstream to the body’s cells. The endocrine system makes many hormones (such as growth hormone, sex hormones, adrenal and thyroid hormones) that work together to maintain specific bodily functions.

What is growth hormone deficiency?

Growth hormone (GH) is made by the pituitary gland. In order for children to grow to their full height potential, they need adequate amounts of GH. GH works with thyroid hormone, exercise, proper nutrition, and rest to help children and teenagers grow. GH also helps maintain normal blood sugar levels and is needed for the normal development of teeth. In addition to helping with bone growth, GH affects how well the heart and blood vessels work, how the body uses fat, makes muscle, and strengthens bones, and generally influences overall health throughout life. In healthy people, GH production continues into adulthood. Adults need small amounts of GH to maintain proper amounts of fat, muscle and bone. GH may also play a role in regulating mood and emotion.

Cancer treatments, such as radiation or surgery to structures in the head or brain, may cause malfunction of the glands that control growth. As a result, the pituitary gland may not make enough GH, resulting in GH deficiency. GH deficiency can also occur in people who have never had cancer treatment.

What are the signs and symptoms of growth hormone deficiency?

Slowing of growth (height) is one of the most obvious signs of GH deficiency in children. A GH deficient child usually grows less than 2 inches per year. Children with GH deficiency are smaller and tend to look younger than children their same age, but they usually have normal body proportions.

Adults who have GH deficiency may have a variety of different physical symptoms, such as thinning of the bones, decreased muscle strength, increased body fat, or high blood cholesterol levels. Adults may also have symptoms such as feeling tired, anxious, irritable, gloomy, unmotivated, or having a decreased interest in sex.
What are the risk factors for growth hormone deficiency?

Risk factors related to treatment for cancer during childhood include:

- Cancer treatment before reaching adult height, especially in very young patients
- Radiation to:
  - Head/brain
  - Total body irradiation (TBI)
- Surgery to the brain, especially the central region of the brain where the pituitary gland is located (suprasellar region)

What screening is recommended?

All childhood cancer survivors should have a yearly comprehensive health check-up including measurement of height and weight, assessment of pubertal status, nutritional status, and overall well-being. For patients with the risk factors listed above, this screening should be done every 6 months until growth is completed. If there are signs of poor growth, an x-ray of the wrist (bone age x-ray) should be done. Other possible causes of growth problems, such as low thyroid function, should also be checked.

If GH deficiency is suspected, your healthcare provider should refer you to an endocrinologist (hormone specialist) for further evaluation and treatment.

How is growth hormone deficiency treated?

Endocrinologists may suggest treatment options that involve supplementing or replacing GH that your pituitary gland is not making on its own with synthetic GH given by injection. GH is usually given for several years, until the person reaches an acceptable adult height or the greatest possible height. Your endocrinologist can give you information about how much growth is possible on GH therapy. Treatment options for GH deficiency that persists into adulthood should be discussed on an individual basis with your endocrinologist.

Written by: Debra A. Kent, RN, MSN, CPNP, Cincinnati Children’s Hospital Medical Center, Cincinnati, OH.

Reviewed by Lillian R. Meacham, MD; Angela Yarbrough DNP, APRN, FNP-BC, CPON; Christine Yun MSN, PNP, CPON; and Kayla L. Foster, MD, MPH.

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Hearing Loss after Cancer Treatment

Some chemotherapy drugs, other medications, or radiation needed for treatment of childhood cancer can damage hearing. Hearing loss interferes with daily living. If you received these treatments, it is important to have your hearing checked and to obtain treatment if hearing loss is found.

How do the ears work?

It's easier to understand hearing loss if you understand how the ears work. The ear is made up of three main parts, known as the outer, middle, and inner ear.

Outer ear

Sound waves travel through the air and first enter the body through the outer ear. The part of the ear that can be seen outside the body is called the pinna. The pinna collects and funnels sound into the auditory (ear) canal. The auditory canal is like a tunnel. It makes the sound louder and directs it toward the middle ear.

Middle Ear

The eardrum separates the outer ear from the middle ear, a chamber that is normally filled with air. Inside the middle ear are three tiny bones (ossicles) that form a chain connecting the eardrum to the opening of the inner ear. Sound waves cause the eardrum to vibrate. These vibrations cause the three tiny bones in the middle ear to move, transmitting the sound to the inner ear.

Inner Ear

The inner ear is known as the cochlea, and it is filled with fluid. The cochlea contains thousands of tiny nerve endings, known as sensory hair cells. Sounds travel in waves through the fluid of the inner ear. The sensory hair cells change the sound waves into nerve impulses that are sent to the brain by way of the auditory nerve (also known as the eighth cranial nerve). In the cochlea, the sensory hair cells are arranged in order of pitch, from low-pitched sounds (such as a man’s voice) to very high-pitched sounds (such as a bird’s chirping). Each hair cell is sensitive to a specific range of pitches.

What are the types of hearing loss?

Hearing loss that occurs in the outer or middle ear is called **conductive hearing loss**. This means that the hearing loss is due to a problem in transmission of sound from the air to the inner ear. An example of this would be changes in hearing because of fluid collection in the middle ear. Sometimes this happens when people have ear infections. The fluid “muffles” the sound when it is traveling through the middle ear.

Hearing loss that results from damage to the inner ear or auditory nerve is called **sensorineural hearing loss**. An example of this would be damage to the sensory hair cells in the inner ear from chemotherapy. Even though sound waves still move through the inner ear fluid, they can no longer be changed into nerve impulses, so the sound does not reach the brain. Sensory hair cells that process high-pitched sounds are usually damaged first, followed by damage to the sensory hair cells that process lower-pitched sounds.

Hearing loss with both conductive and sensorineural components is called **mixed hearing loss**.
What types of cancer therapy increase the risk of hearing loss?

The following cancer treatments can potentially cause hearing loss:

- Cisplatin chemotherapy
- Carboplatin chemotherapy if given in high doses for hematopoietic cell transplant (HCT) conditioning
- High doses of radiation (30 Gy or 3000 cGy/rads or higher) to the head or brain
- Surgery involving the brain, ear or auditory (eighth cranial) nerve
- Certain antibiotics (medicines used to treat infections) and diuretics (medicines that help the body get rid of excess water)

What are the effects of childhood cancer treatment on hearing?

High doses of radiation to the ear or brain can cause inflammation or ear wax buildup in the outer ear, problems with fluid buildup in the middle ear, or stiffness of the eardrum or middle ear bones. Any of these problems can result in conductive hearing loss. Radiation can also damage the sensory hair cells in the inner ear, causing sensorineural hearing loss. Damage from radiation may affect one or both ears, depending on the area of radiation treatment. Conductive hearing loss may improve over time, but sensorineural hearing loss is usually permanent.

Platinum chemotherapy (cisplatin and/or carboplatin) can cause damage to sensory hair cells in the inner ear, resulting in sensorineural hearing loss. Most often, the effect is similar in both ears and is permanent.

What are the symptoms of hearing loss?

Symptoms of hearing loss may include:

- Ringing or tinkling sounds in the ear
- Difficulty hearing in the presence of background noises
- Not paying attention to sounds (such as voices, environmental noises)
- School problems (see related Health Link: School after Cancer Treatment)
- Some people may have no symptoms at all

What monitoring is recommended?

People who are age 6 or older should be screened with a pure tone audiogram (hearing screening test). Children younger than age 6 or those who have abnormal results on their screening test should be evaluated by an experienced audiologist (a professional trained in hearing disorders).

- Hearing is usually evaluated by a series of tests. During an audiogram, the person wears earphones and listens for sounds of different pitches and different degrees of loudness. Speech audiometry tests the person's ability hear single words and sentences. Tympanometry tests the status of the middle ear and the movement of the eardrum in response to a puff of air.
- People who are not able to have an audiogram (such as those who are too young or who cannot understand the test instructions) can have their hearing tested using Auditory Brainstem Response (ABR). The person having this test is usually given medicine so that they go to sleep, and then their brainwave responses to various sounds are recorded.
How often should hearing be tested?

Everyone who had cancer treatment that can affect the ears (such as cisplatin and high doses of carboplatin, high doses of radiation to the brain) should have their hearing tested yearly until they are 6 years old, then every 2 years until they are 12 years old and then every 5 years. If hearing loss is found, testing should be repeated yearly or as advised by an audiologist. In addition, hearing should be tested anytime a hearing problem is suspected.

What can be done if hearing loss is detected?

If hearing loss is detected, it is important to be under the care of an audiologist or otologist (doctor who specializes in hearing disorders). Hearing loss can cause problems with a person’s ability to communicate and carry out daily activities. Younger children are at higher risk for school, learning, and social difficulties, and problems with language development. It is therefore very important for a person with hearing loss to find the services that will best help to make the most of their ability to communicate well. There are many options available, and these can be used in various combinations, depending on the hearing problem.

- **Hearing aids** make sounds louder. Several types are available, depending on the age and size of the person and the extent of hearing loss. Most children under 12 years of age wear a behind-the-ear model to allow for adjustments as the child grows. These are available in a variety of colors—allowing for personalization and assisting with the child’s acceptance of the hearing aid. Teenagers and adults may benefit from a smaller, in-the-ear or in-the-canal model. It is very important that the hearing aid batteries are fresh and that the hearing aid is turned to the “on” position when in use.

- **Auditory trainers** (also known as “FM trainers”) are devices that are particularly useful in the school setting. The person who is speaking (usually the teacher) wears a microphone that transmits sound over FM radio waves. The person with hearing loss wears a receiver that picks up the sound. This device can be worn alone or attached to the hearing aid and allows the person with hearing loss to hear the speaker clearly, even in a noisy environment.

- **Other assistive devices** are also available for people with hearing loss. These include telephone amplifiers and teletypewriters (TTYs—sometimes also referred to as Telephone Devices for the Deaf or TDDs). Specialized appliances designed for people with hearing loss include alarm clocks that vibrate and smoke detectors with flashing lights. Closed captioning for television is widely available. The Internet is also a helpful communication tool for people with hearing loss, providing options such as e-mail, online discussions, and access to information via websites. Additionally, cell phones offer text messaging, instant messaging, Internet access, and photo transmission.

- **Telecommunication relay services** are available in video and voice/text formats. The video relay service is internet-based and allows a person using signed language to communicate via a video interpreter, who translates the signed language into voice or text. The voice/text relay service allows a person using a teletypewriter to communicate through an operator, who then relays the message to the hearing person in spoken form.

- **Cochlear implants** may be an option for people with profound hearing loss who are unable to benefit from hearing aids. These electronic devices are surgically placed behind the ear and electrodes are threaded into the inner ear. A microphone and speech processor are then used to transmit sound to the electrodes, stimulating the auditory nerve and allowing sound perception by the brain. After the cochlear implant is installed, auditory training is given for a period of time to teach the individual to recognize and interpret sounds.
• **Alternate or supplementary communication methods**, including speechreading, signed language and cued speech, are available for people with significant hearing loss. Spoken language may also be an option, but usually requires an intensive educational approach with speech therapy. In the United States, healthcare organizations that receive federal funding are required to provide sign language interpreters when requested by a patient.

• **Community and educational resources** in the United States include services through local public school districts or referral agencies (available under the IDEA legislation, PL 105-17), such as intensive speech therapy and auditory trainers for classroom use. Sometimes special accommodations, such as seating in the front of the classroom are all that is needed, but this usually requires that the parent request an Individualized Education Plan (IEP) for the child through the school district (see related Health Link: *School after Cancer Treatment*). Many hospitals have a teacher or school liaison that can assist with arranging for the IEP and other specialized services that may be needed. The Americans with Disabilities Act (ADA, PL 101-336) guarantees people with hearing loss equal access to public events, spaces and opportunities, including text telephones and telephone amplifiers in public places, and assistive listening devices in theaters. Some theaters also offer special showings of newly released movies with captioning.

**What can I do to protect my hearing?**

If you have experienced hearing loss, or have received therapy that has the potential to damage your hearing, you should discuss this with your healthcare provider. Be sure to obtain prompt evaluation and treatment for ear infections, swimmer’s ear, and earwax impaction. Whenever possible, ask your healthcare provider to consider alternatives to medications that have the potential to cause further hearing loss, including certain antibiotics (aminoglycosides such as gentamicin), certain diuretics (“loop diuretics, such as furosemide), salicylates (such as aspirin) and medications for high iron levels. You should also take care to protect your ears from loud noises. In fact, loud noises can cause significant damage to your ears. Examples of items and activities that can be hazardous to your hearing include:

<table>
<thead>
<tr>
<th>Appliances</th>
<th>Occupations</th>
<th>Recreation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Power saws</td>
<td>Firefighters</td>
<td>Hunting</td>
</tr>
<tr>
<td>Vacuum cleaners</td>
<td>Construction workers</td>
<td>Boating or water skiing</td>
</tr>
<tr>
<td>Lawn mowers</td>
<td>Farmers</td>
<td>Motorcycling or four-wheeling</td>
</tr>
<tr>
<td>Yard trimmers or leaf blowers</td>
<td>Airport workers</td>
<td>Stereo headphones</td>
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<tr>
<td></td>
<td>Cab, truck, and bus drivers</td>
<td>Amplifiers</td>
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<tr>
<td></td>
<td>Hair stylists: constant exposure to loud hair dryers</td>
<td></td>
</tr>
</tbody>
</table>

If you cannot avoid exposure to noise, you should:

- Wear hearing protectors such as ear plugs or ear muffs
- Limit periods of exposure to noise (for example, if you are at a loud concert go to a quieter area for a while to give your ears a break)
- Be aware of the noise in your environment and take control of it when you can

Written by Wendy Landier, PhD, CPNP, Children’s Hospital of Alabama, Birmingham, AL. Portions adapted from “Noise and Hearing Loss, Do You Know…An Educational Series for Patients and Their Families,” St. Jude Children’s Research Hospital, Memphis, TN (used with permission).

Reviewed by L. Foster, MD, MPH; Beth Fisher, DNP, APRN, CPNP; and Melissa Acquazzino, MD, MS.
Health Link
Healthy living after treatment of childhood, adolescent, and young adult cancer

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Keeping Your Heart Healthy

Most childhood cancer survivors do not develop heart problems; however, certain types of cancer treatment given during childhood can result in damage to the heart. Because heart problems may occur many years after cancer treatment, it is important for childhood cancer survivors to be aware of any treatments they may have received that can affect the heart. With this knowledge, steps can be taken to keep their heart healthy, including regular medical check-ups and tests to monitor heart function. And if a problem develops, it can be detected and treated early.

How does the heart work?

The heart is a muscular organ that is at the center of the body's circulatory system. The heart is responsible for pumping blood with oxygen and nutrients to body tissues. There are four chambers (two atria and two ventricles) within the heart that work together to pump blood. Valves direct the flow of blood through the heart chambers and into the blood vessels. The rhythm of heart contraction and rate of the heartbeat are coordinated by nerves that send electrical impulses to different parts of the heart. A thin membrane (pericardium) surrounds and protects the heart and anchors it within the chest.

What types of cancer treatments can cause heart problems?

Some types of chemotherapy and radiation involving the heart can cause problems.

**Anthracycline chemotherapy**

The anthracyclines are a type of chemotherapy used to treat many childhood cancers. This type of chemotherapy can sometimes affect the heart. Commonly used anthracyclines include:

- Doxorubicin (Adriamycin®)
- Daunorubicin/Daunomycin (Cerubidine®)
- Idarubicin (Idamycin®)
- Mitoxantrone (Novantrone®)
- Epirubicin

**Radiation therapy**

Heart problems may also result from radiation therapy to the heart or surrounding tissues. This includes radiation to the following areas:

- Chest
- Spine (chest or “thoracic” portion)
- Abdomen
- Total body irradiation (TBI)
What heart problems can occur after treatment for childhood cancer?

There are several types of heart problems that may result from cancer treatments:

- The muscle cells of the heart may be damaged so that the heart doesn’t contract and relax normally (left ventricular dysfunction, cardiomyopathy).
- The electrical pathways that conduct impulses to control heart rhythm may be scarred or damaged, resulting in abnormally fast, slow, or irregular heartbeats (arrhythmias).
- The valves and blood vessels of the heart may be damaged, resulting in stiff or leaky valves (valvular stenosis or insufficiency).
- The protective covering of the heart may become inflamed (pericarditis) or scarred (pericardial fibrosis).
- The blood vessels of the heart may become scarred or blocked (coronary artery disease), preventing delivery of oxygen and nutrients to the heart and other tissues.

In severe cases, these problems may result in the death of heart tissue (heart attack or myocardial infarction), a dangerous heart rhythm (arrhythmia), or an inability of the heart to pump blood properly (congestive heart failure).

Which types of cancer treatment are associated with which heart problems?

- Anthracyclines: can cause problems with heart muscle function (left ventricular dysfunction, cardiomyopathy) and abnormal heart rhythms (arrhythmias).
- Radiation therapy: can cause scarring and stiffening of heart tissues which can result in an abnormal heart rhythm (arrhythmia) and/or problems with the heart muscle (cardiomyopathy), heart valves (valvular stenosis or insufficiency), blood vessels (coronary artery disease), or membrane surrounding the heart (pericarditis or pericardial fibrosis).

Are there other risk factors for heart problems?

Some other medical conditions may also increase the risk of heart problems from chemotherapy or radiation therapy. These include obesity, high blood pressure, high cholesterol or triglyceride levels in the blood, and diabetes. You may have a higher risk of having heart problems if these conditions run in your family. Heart disease is also more common in people who have gone through menopause, so survivors who go through an early menopause may be at higher risk. Many health behaviors can add to the risk of heart disease including smoking, having an inactive (sedentary) lifestyle, and eating a diet high in fat.

Who is at risk for developing heart problems?

The risk of developing a heart problem after childhood cancer treatment is related to several factors:

- The total dose of anthracycline chemotherapy
- The total dose of chest radiation
- The amount of the heart tissue included in the radiation treatment field
- Treatment with other medications that affect heart function
- The presence of other conditions that affect heart function

Most childhood cancer survivors who were treated with anthracyclines or chest radiation have no heart damage at all. Some survivors have very mild changes in heart size or function that have not gotten worse over time. Only a small number of survivors have developed severe heart problems leading to heart failure or dangerous heart rhythms.

Overall, the risk of developing heart problems after childhood cancer therapy is highest in survivors treated with higher doses of anthracyclines or chest radiation, especially those who received both treatments at a young age.
Because we do not understand why some survivors develop heart problems after treatment for childhood cancer and others do not (even when they have gotten the same treatment), it is important for each childhood cancer survivor treated with anthracyclines or chest radiation to continue to have regular medical check-ups so that if a problem with the heart develops, it can be detected and treated early.

**What are the symptoms of heart problems?**

- No symptoms may be noted with mild to moderate heart problems. Identification of problems may only be detected by cardiac tests such as ECHO, EKG, or MUGA.
- Shortness of breath
- Dizziness
- Lightheadedness, fainting or near-fainting
- Severe fatigue preventing exercise or normal play
- Chest pain that feels like a heavy pressure or fullness and travels to the arm, chin, or face
- Sweating, nausea, or shortness of breath with chest pain
- Sharp piercing pain in the center or the left side of the chest (often worsens with taking a deep breath)
- Very swollen feet or ankles (so swollen that if a finger is pressed firmly on the area for a few seconds it leaves an indentation)
- Cough and wheezing that doesn’t go away
- Periods of feeling your heart racing while at rest or skipping beats
- Abdominal symptoms (nausea or emesis)

**How does exercise affect the heart?**

Aerobic exercise (brisk walking, running) is generally safe and healthy for the heart. However, some types of intensive exercise are particularly stressful to the heart.

Survivors treated with high doses of anthracyclines (250 mg/m² or higher), or chest radiation therapy (30 Gy or 3000 cGy/rads or higher), or with a combination of anthracyclines (any dose) and chest radiation (≥15 Gy) should check with their healthcare provider before beginning any intensive exercise program. Those who plan to engage in strenuous or varsity team sports may benefit from evaluation by a heart specialist (cardiologist).

**What other conditions or activities can make heart problems worsen?**

A heart exposed to anthracyclines and/or chest radiation may not adapt well to situations that increase the workload of the heart. This includes:

- Pregnancy
- Use of stimulant medications or drugs (amphetamines, cocaine, diet pills, ephedra, mahuang, or performance enhancing drugs)

Illicit drugs should always be avoided. If you are at risk of heart problems from childhood cancer therapy and planning to use stimulant medications or become pregnant, it is important to discuss this with your healthcare provider. It may be recommended that you undergo heart testing such as an echocardiogram before becoming pregnant or taking certain types of medications that may cause excess stress to the heart.
Are there any other special precautions?

Survivors with prosthetic heart valves and those with currently active chronic graft-versus-host disease (cGVHD) following hematopoietic cell transplant (HCT) may need to take an antibiotic prior to dental work or other invasive medical procedures (such as those involving the respiratory, gastrointestinal, or urinary tracts) to prevent an infection called endocarditis. If you have a prosthetic heart valve or if you have active cGVHD, ask your doctor, heart specialist, and/or dentist if you should take antibiotics to prevent endocarditis before dental or other medical procedures.

What monitoring is required for potential heart problems?

Anyone treated with anthracycline chemotherapy or chest radiation for childhood cancer should have a yearly check-up with special attention to any symptoms relating to the heart. In addition, an electrocardiogram (ECG, EKG) should be done at the time the survivor enters long-term follow-up (usually about 2 years from completion of therapy). An echocardiogram or comparable imaging is also recommended at the first long-term follow-up visit, then according to the following schedule (or as recommended by your healthcare provider):

**Cardiac Imaging Schedule Recommendations**

<table>
<thead>
<tr>
<th>Anthracycline Dose*</th>
<th>Radiation Dose**</th>
<th>Recommended Frequency of ECHO</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;100 mg/m²</td>
<td>&lt; 15 Gy or none</td>
<td>No screening</td>
</tr>
<tr>
<td>&lt;100 mg/m²</td>
<td>15 to &lt; 30 Gy</td>
<td>Every 5 years</td>
</tr>
<tr>
<td>≥100 to &lt; 250 mg/m²</td>
<td>&lt; 15 Gy</td>
<td>Every 2 years</td>
</tr>
<tr>
<td>≥100 to &lt; 250 mg/m²</td>
<td>≥15 Gy</td>
<td></td>
</tr>
<tr>
<td>Any</td>
<td>≥30 Gy</td>
<td></td>
</tr>
<tr>
<td>≥250 mg/m²</td>
<td>Any</td>
<td></td>
</tr>
</tbody>
</table>

*Based on doxorubicin isotoxic equivalent dose  
**Based on radiation dose with potential impact to heart (radiation to chest, abdomen, spine [thoracic, whole], total body [TBI])

Survivors who received radiation at a dose of 30 Gy (3000 cGy) or higher to the heart or surrounding tissues or radiation at a dose of 15 Gy (1500 cGy) or higher plus anthracycline chemotherapy may be advised to undergo evaluation by a cardiologist for stress testing 5 to 10 years following radiation, with repeat testing as recommended by the cardiologist.

Survivors who received radiation to the heart or surrounding tissues should also have periodic blood tests to check for other cardiac risk factors (lipid profile and fasting glucose or hemoglobin A1C).

Additional evaluation by a cardiologist is recommended for survivors who are pregnant or planning pregnancy and received any of the following therapy:

- Anthracycline chemotherapy at a dose of 250 mg/m² or more
- Radiation at a dose of 30 Gy (3000 cGy) or higher to the heart or surrounding tissues
- Radiation to the heart (15 Gy) or higher in combination with anthracycline chemotherapy (at any dose)

Heart monitoring may be necessary due to the extra strain on the heart during the later stages of pregnancy and during labor and delivery. Suggested monitoring includes an echocardiogram before and periodically during pregnancy, especially during the third trimester, and cardiac monitoring during labor and delivery.
How are the heart tests done?

An electrocardiogram (ECG, EKG) is a test used to evaluate heart rate and rhythm. Electrodes (small sticky patches) are placed on the chest, arms, and legs. Wires are attached to the electrodes and the electrical impulses of the heart are then recorded.

An echocardiogram (ECHO; heart ultrasound) is used to test the muscle function of the heart and how well the heart pumps. The person lies on a table and has conductive jelly applied to the chest. Then a transducer (device that emits the ultrasound waves) is placed on the chest to obtain different views of the heart. Slight pressure is applied on the transducer and can sometimes cause discomfort. The test results are displayed on a monitor for the doctor to study later. Many measurements are done during this test to help find out if the heart muscle is pumping blood well. The ultrasound test also looks at the valves of the heart to see that they open and close normally. Electrodes are usually placed on the chest to monitor the heart’s electrical impulses during the test.

Cardiac magnetic resonance imaging (MRI) uses a large magnet, radio waves, and a computer to create detailed images of the heart. Radiation is not used during the MRI. The person lies on the scanning table, which slides into the circular opening of the MRI machine. Jewelry, eyeglasses, hearing aids, or other objects that may interfere with the MRI must be removed prior to the test. If contrast is needed, it will be injected into a vein. The scanner can be noisy, so you will be given earplugs to wear or music to listen to during the test to help block out the noise. Because of the strong magnet, people who have metal devices (such as a pacemaker, implanted infusion pump, or iron-based metal implant) cannot have MRIs.

A cardiac stress test measures heart function during periods when the heart is working hard. During this test, the heart and blood pressure are usually monitored while the person walks on a treadmill.

What happens if a problem with the heart is detected?

Your healthcare provider will advise you about the follow-up care you need. Sometimes, a referral to a cardiologist is needed for additional evaluation and/or treatment with medications.

What can be done to prevent heart problems?

With increasing age, the risk of certain types of heart disease (such as heart attacks and hardening of the arteries) also increases. Lifestyle factors that may increase the risk of heart problems include smoking, being overweight, eating a high fat diet, and not exercising. Medical conditions that increase the risk include diabetes, high blood pressure, and high blood cholesterol. You can reduce your risk of heart problems by:

- Avoid smoking and excessive alcohol intake.
- Maintaining a healthy body weight.
- Limiting the fat in your diet to no more than 30% of calories.
- Exercising regularly for at least 30 minutes on most days of the week.

Medical conditions that increase the risk of heart problems include obesity, high blood pressure, high cholesterol or triglyceride levels in the blood, and diabetes. If you have any of these conditions it is important to take medications or adjust your lifestyle as recommended by your healthcare provider.
Health Links

Healthy living after treatment of childhood, adolescent, and young adult cancer

Written by Debra L. Friedman, MD, Vanderbilt University/Ingram Cancer Center, Nashville, TN; Melissa M. Hudson, MD, St. Jude Children’s Research Hospital, Memphis, TN; and Wendy Landier, PhD, CPNP, Children’s Hospital of Alabama, Birmingham, AL.

Reviewed by Linda Rivard, RN, BSN; Kayla L. Foster, MD, MPH; and Melissa Acquazzino, MD, MS.

Additional health information for childhood cancer survivors is available at www.survivorshipguidelines.org

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Hepatitis after Cancer Treatment

Treatment for childhood cancer often requires transfusions of blood and blood products. Unfortunately, some of these life-saving blood products may have contained viruses that can cause hepatitis (infection of the liver). There are two main types of hepatitis that can be transmitted through blood products (hepatitis B and hepatitis C). Before the blood supply was routinely screened for these infections, people who received blood products may have been infected with these viruses. In the United States, routine screening of blood donors for hepatitis B began in 1971. The most accurate screening test for hepatitis C has been in use since 1992. Survivors who received blood products prior to these dates may have been infected with these viruses. (Note: The dates that blood donor screening for hepatitis began in countries outside of the United States may be different.)

Hepatitis B and C can also be spread through other types of blood contact (such as needle-sharing among drug users, tattoos, body piercing, kidney dialysis and organ transplantation). These infections can also be spread through sexual contact, or passed from mother to newborn baby during the birth process, but this is more likely to occur with hepatitis B than with hepatitis C.

What is the liver?

The liver is a triangular-shaped organ tucked under the rib cage on the right side of the body. In an average adult, the liver is about the size of a football and weighs about three pounds. It is responsible for filtering out toxins from the blood, aiding with digestion and metabolism, and producing many important substances including blood-clotting proteins.

What are the signs and symptoms of hepatitis?

Many people do not have symptoms of hepatitis when first infected. Some people have symptoms similar to the flu, such as fatigue, loss of appetite, nausea, vomiting, or low-grade fever. Some people may have symptoms indicating that the liver is not working well, such as yellow eyes and skin (jaundice), dark urine, severe itching, or pale (clay-colored) stools. In rare cases, people may become seriously ill and develop liver failure. Hepatitis may completely resolve and cause no further health problems. Unfortunately, some people who become infected with hepatitis B or C during childhood become “chronically” infected. Chronic infection is more common with hepatitis C. People with chronic hepatitis may have no symptoms and feel well, but they are at risk for scarring (cirrhosis) of the liver and other complications. In rare cases, liver cancer can develop. People with chronic hepatitis infections are also at risk for spreading the infection to others.

What are the signs of liver damage?

Most people with chronic hepatitis have no signs or symptoms. Chronic infection over a long time may cause progressive liver damage. Signs of liver damage include enlargement of the liver and spleen, swelling or collection of fluid in the abdomen, yellow color of the eyes and skin (jaundice), and problems with blood clotting.

What tests are done to check for hepatitis?

A blood test can be done to check for viral hepatitis. A positive antibody test for hepatitis B or C means that the person has been exposed to the virus. Additional testing may then be done to determine if there is an active infection.
Who is at risk for hepatitis B and C?
Anyone who received the following blood or serum products are at risk for hepatitis B (if transfused before 1972) and hepatitis C (if transfused before 1993):

- Packed red blood cells
- Whole blood
- White blood cells (granulocytes)
- Platelets
- Fresh frozen plasma
- Cryoprecipitate
- Immunoglobulin preparations (IVIG, VZIG)
- Bone marrow or stem cells from an allogeneic donor (someone other than yourself)

Other risk factors include:

- Blood clotting factors (such as Factor VIII or Factor IX) made before 1987
- Solid organ transplants (such as kidney, liver, or heart) before 1993
- Long-term kidney dialysis (lasting for at least several months)
- Illicit drug use
- Body piercing, tattoos
- Sharing razors, nail clippers, or toothbrushes with people who have hepatitis
- Occupational exposure to blood and body fluids
- High-risk sexual behavior (such as having multiple sexual partners, not using a condom, or having anal sex)

What follow up is needed for those at risk?

- Anyone who is at risk for hepatitis B or C should have blood tests done to see if they are infected.

If you have chronic hepatitis, you should also:

- See a liver specialist for evaluation and possible treatment.
- Tell your healthcare providers about all over-the-counter medications and supplements that you are taking.
- Do not drink alcohol, which can cause further liver damage.
- Avoid over-the-counter pain or fever-reducing medications containing acetaminophen (such as Tylenol® or “aspirin-free” products).
- Have a blood test to see if you have immunity to hepatitis A and B. If you do not have immunity, get immunized against these common infections to protect your liver (there is currently no vaccine to protect against hepatitis C).
- Discuss your hepatitis status with your healthcare providers. (If you are pregnant, discuss this with both your obstetrician and the baby’s pediatrician.)

How can the spread of chronic hepatitis be prevented?
Hepatitis B and C are not spread by casual contact, such as hugging or shaking hands. However, if you have hepatitis B or C, to prevent spreading the infection to others you should:

- Avoid direct contact of your blood and body fluids with others.
- Clean any spilled blood or body fluids with bleach.
Cover cuts or other open sores.

Avoid sharing sharp personal objects, such as razors, toothbrushes, nail clippers, ear or body rings, or any object that may come in contact with blood.

Be sure that new sterile needles are used for body piercing, injections, tattoos, or acupuncture. Never share needles.

Make sure all close household members and sexual partners are screened for hepatitis B. If they do not have immunity, they should be given the hepatitis B vaccine.

If you are sexually active, use barrier precautions (such as latex condoms) during intimate sexual contact.

Talk with your healthcare provider about whether your sexual partner should be tested for hepatitis C.

What else can I do to keep my liver healthy?

- Drink plenty of water.
- Eat a well-balanced, high-fiber diet.
- Cut down on fatty, salty, smoked and cured foods.
- Do not take more than the recommended doses of medications.
- Avoid taking unnecessary medications.
- Do not mix drugs and alcohol.
- Do not use illicit drugs.
- Be careful about using herbs and natural supplements, especially when combined with medications.
- Avoid exposure to chemicals (solvents, aerosol cleaners, insecticides, paint thinners, and other toxins) that can be harmful to the liver. If you must use these substances, wear a mask and gloves and work in a well-ventilated area.

Written by Wendy Landier, PhD, CPNP, Children’s Hospital of Alabama, Birmingham, AL.

Reviewed by Daniel Smith, DNP, FNP; Kayla L. Foster, MD, MPH; and Melissa Acqazzino, MD, MS.

Additional health information for childhood cancer survivors is available at www.survivorshipguidelines.org

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Hyperprolactinemia after Cancer Treatment

Hyperprolactinemia occurs when there is too much of the hormone known as prolactin in the body. Prolactin is a hormone made by the pituitary gland. Prolactin is important in breast development during pregnancy and milk production after childbirth. Too much prolactin can cause problems with functioning of the ovaries or testes. High levels of prolactin can cause galactorrhea (breast milk production by a person who is not breastfeeding), irregular or absent menstrual periods, or decreased testosterone levels that may result in a diminished sex drive (libido). In preteens and teens, high prolactin levels may interfere with normal pubertal development.

What are risk factors for hyperprolactinemia?
- Radiation to the pituitary gland in very high doses
- Development of a second tumor (usually non-cancerous) in the pituitary region
- Pregnancy
- Taking certain medications and drugs (such as marijuana and alcohol)
- Thyroid failure (a condition in which the thyroid gland fails to secrete enough thyroid hormone)

What screening is recommended?
All childhood cancer survivors should have a yearly comprehensive health check-up. If hyperprolactinemia is suspected, your healthcare provider may order a prolactin blood test, additional imaging (such as a CT scan or MRI of the brain), and should refer you to an endocrinologist (hormone specialist) for further evaluation and treatment.
How is hyperprolactinemia treated?

Correcting the thyroid problem may correct the high prolactin level. Endocrinologists may use medications to suppress prolactin production. If a tumor is detected, surgery or radiation is sometimes needed. The length and type of treatment varies for each patient and should be discussed with your doctor.

Written by Debra A. Kent, RN, MSN, CPNP, Cincinnati Children’s Hospital Medical Center, Cincinnati, OH

Reviewed by Lillian R. Meacham, MD; Daniel Smith, DNP, FNP; Christine Yun MSN, PNP, CPON®; and Kayla L. Foster, MD, MPH.

Additional health information for childhood cancer survivors is available at www.survivorshipguidelines.org

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Hypopituitarism after Cancer Treatment

Some people who were treated for cancer during childhood may develop endocrine (hormone) problems as a result of changes in the function of a complex system of glands known as the endocrine system.

What is the endocrine system?
The endocrine system is a group of glands that regulate many body functions including growth, puberty, energy level, urine production, and stress response. Glands of the endocrine system include the pituitary, hypothalamus, thyroid, pancreas, adrenals, ovaries, and testes. The hypothalamus and pituitary are sometimes called the “master glands” because they control many of the other glands in the endocrine system. Unfortunately, some treatments given for childhood cancer can damage the endocrine system, resulting in a variety of problems.

What are hormones?
Hormones are chemical messengers that carry information from the endocrine glands through the bloodstream to the body’s cells. The endocrine system makes many hormones (such as growth hormone, sex hormones, adrenal and thyroid hormones) that work together to maintain specific bodily functions.

What is hypopituitarism?
Hypopituitarism is the decrease or lack of one or more of the pituitary hormones. The lack of three or more of the pituitary hormones is referred to as panhypopituitarism.

Pituitary hormones include:
- **Growth hormone (GH)**—stimulates the growth of bone and other body tissues, and also affects how the body uses fat, makes muscle, strengthens bones, and generally influences overall health throughout life
- **Adrenocorticotropic hormone (ACTH)**—stimulates the adrenal gland to produce cortisol
- **Thyroid stimulating hormone (TSH)**—stimulates the thyroid gland to produce thyroid hormones
- **Reproductive hormones (gonadotropins)**, including luteinizing hormone (LH) and follicle stimulating hormone (FSH)—stimulate the testes and ovaries to make sex hormones
- **Antidiuretic hormone (ADH)**—helps to control the balance of water in the body by controlling urine output
- **Prolactin**—controls milk production during breastfeeding

What are risk factors for hypopituitarism?
Risk factors related to childhood cancer treatment include:
- Radiation to the brain, especially in doses of 30 Gy (3000 cGy/rads) or higher
- Surgical removal of the pituitary gland
- Damage to the hypothalamus or pituitary gland, which can occur during brain surgery, or can be caused by a tumor in or near the pituitary or hypothalamus
- Infections
What are the symptoms of hypopituitarism?

The symptoms depend on the specific hormones that are lacking. One or more of the following hormones may be affected:

- **Growth hormone (GH) deficiency** - GH affects the growth of body tissues and bone as well as fat, muscle, and sugar metabolism. For more information about growth hormone problems, see the related Health Link: Growth Hormone Deficiency after Cancer Treatment

- **Adrenocorticotropic hormone (ACTH) deficiency** - The adrenal glands (located on top of the kidneys) are stimulated by ACTH to produce cortisol. If the pituitary gland doesn’t make enough ACTH, then cortisol will not be made. Cortisol helps keep the body’s blood sugar at a normal level and helps the body deal with physical stress, such as fever or injury. For more information about ACTH deficiency, see the related Health Link: Central Adrenal Insufficiency after Cancer Treatment

- **Thyroid Stimulating Hormone (TSH) deficiency** - TSH stimulates the thyroid gland to release thyroxine, which is important for brain development, growth, and metabolism. People with too little thyroxine may develop the following symptoms: tiredness, sleeping too much, weight gain, slow growth, poor appetite, cold intolerance, dry skin, constipation, or hair that is dry, coarse, and thin. For more information about thyroid problems, see the related Health Link: Thyroid Disease after Cancer Treatment

- **Gonadotropin (FSH, LH) deficiency** - LH and FSH control the production of sex hormones. LH and FSH stimulate the testicles to make testosterone, and the ovaries to make estrogen and progesterone, resulting in development of sexual characteristics during puberty. If the body doesn’t have enough LH and FSH during puberty, there can be problems with pubertal development. For more information, see the related Health Links: Testicular and Reproductive Health after Cancer Treatment and Ovarian and Reproductive Health after Cancer Treatment

- **Antidiuretic Hormone (ADH) deficiency** - ADH (also known as “vasopressin”) is a hormone produced in the hypothalamus and stored in the pituitary gland. When the amount of water in the body is low, the pituitary gland releases ADH, sending a message to the kidneys to conserve water. This slows down the production of urine. When there is not enough ADH, too much urine will be produced, resulting in a condition known as diabetes insipidus. Symptoms of diabetes insipidus include excessive thirst and frequent urination.

What screening is recommended?

All cancer survivors should have a yearly comprehensive health check-up including measurement of height and weight, assessment of their progression through puberty, and assessment of overall well-being. If hypopituitarism is suspected, your healthcare provider should refer you to an endocrinologist (hormone specialist) for further evaluation and treatment.
Written by: Debra A. Kent, RN, MSN, CPNP, Cincinnati Children's Hospital Medical Center, Cincinnati, OH.
Reviewed by Lillian R. Meacham, MD; Shekinah Andrews, FNP; Christine Yun MSN, PNP, CPON®; and Kayla L. Foster, MD, MPH.

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Introduction to Long-Term Follow-Up after Cancer Treatment

**Congratulations!** You are transitioning to long-term follow-up after completing treatment. In long-term follow-up, the goal is to support your physical and emotional health, provide education about your diagnosis and treatment, and facilitate your success at home, school and work.

Even though you may not have seen a primary care provider during treatment, it is important to reestablish your relationship with a primary care provider for regular medical care. In some cases, your long-term follow-up care may continue at the same hospital or clinic where you received your treatment, but you may be seen by different doctors and nurses in a special long-term follow-up or survivorship program. In other cases, you may receive cancer follow up care from a healthcare provider who is closer to your home. No matter where you receive your care, it is important that you learn about your treatment, its impact on your long-term health and the follow up care you need so that you can stay in the very best health possible.

**Your cancer treatment summary**

When you transition to long-term follow-up care, it is important that you get a record of the cancer treatment that you received. This record, known as a *Summary of Cancer Treatment*, should contain the following information:

- **Name of the disease** that you had, the date when you were diagnosed, and the site/stage of the disease
  - Date(s) and description(s) of any relapses
  - Name, address, and phone number of hospital(s) or clinic(s) where you received your care
  - Name, address, and phone numbers of your cancer doctor (oncologist) and other health team members responsible for your care
  - Date that your cancer treatment was completed

- **Names of all the chemotherapy medicines** that you received and specific information about certain chemotherapy drugs as follows:
  - Total doses of anthracycline chemotherapy (such as doxorubicin, daunorubicin, idarubicin, epirubicin, and mitoxantrone)
  - Total doses of alkylating chemotherapies (such as cyclophosphamide, procarbazine, BCNU, melphalan, nitrogen mustard, ifosfamide, chlorambucil, CCNU, Thiotepa, and busulfan)
  - For cytarabine and methotrexate: How they were given (such as by mouth or into the vein), and if into the vein, whether you received “high dose” (1000 mg/m² or more in any single dose) or “standard dose” therapy
  - For carboplatin: Whether or not the dose was myeloablative (given during preparation for a bone marrow, cord blood, or stem cell transplant)
  - Total doses of other chemotherapy agents and how they were given should be included, if available

- **Radiation** therapy summary, including:
  - Part(s) of body that received radiation (radiation site or field)
  - Total radiation dose (including any boost doses) to each field

- **Name and dates of any treatment-related surgeries** that you had

- **Whether or not you received a hematopoietic cell transplant** (bone marrow, cord blood, or stem cell transplant), and if so, whether or not you developed chronic graft-versus-host disease
• Names of any other cancer treatment(s) that you received (such as radioiodine therapy or bioimmunotherapy)
• Names and dates of any significant complication(s), and treatments received for the complication(s)

Keep a copy of your cancer treatment summary in a safe place, and give a copy to each of your healthcare providers.

Your follow-up schedule
Most cancer survivors need long-term follow-up visits about once a year. During these visits, it is important to talk about your progress and check for problems that can happen after treatment for cancer. Talk with your healthcare provider about your individual situation and determine a schedule for follow-up care that best meets your needs.

Between visits
Once you transition to long-term follow-up care, you will usually need to identify a local healthcare provider that you can visit or call if you are injured or sick. Make an appointment for a check-up with this healthcare provider so that they can get to know you before an illness arises. If a problem comes up that may be related to your cancer treatment, your local healthcare provider can discuss this with your long-term follow-up team.

Late effects after treatment for childhood, adolescent, or young adult cancer
Problems that happen after treatment for cancer are known as “late effects.” Fortunately, most long-term survivors don’t have serious late effects, but it is important to catch any problems early. You may have already learned about some of the possible late effects that can happen after treatment for cancer. Some of the more common ones are reviewed here.

Growth
Treatment for cancer during childhood, especially radiation to the brain or spine, can sometimes slow or stunt growth. Yearly measurements help to predict whether you will reach a normal height. If you are “at risk” for being short as an adult, your healthcare provider may also recommend other specialized tests and treatments.

Heart
A small percentage of survivors treated with chest radiation or certain chemotherapy drugs known as “anthracyclines” (such as doxorubicin or daunomycin) have problems with the heart. This is most likely to happen in people who received higher doses of anthracycline chemotherapy or chemotherapy combined with radiation affecting the heart. Your healthcare provider may recommend tests to check your heart function, and may arrange for a cardiologist (heart specialist) to see you if the tests show any sign of problems.

Fertility
Radiation to the reproductive organs or brain and certain chemotherapy drugs can affect sexual development and reproduction. Some survivors may be at risk for delayed puberty, infertility (inability to have children), or premature ovarian insufficiency (early menopause). Check-ups and certain blood tests can help determine if you have any of these problems. These issues are important, and if you have any concerns, you should be sure to discuss them with your healthcare provider. If there is a problem, arrangements may be made for you to see a specialist.

Thyroid
Head or neck radiation can sometimes cause the thyroid gland to stop working properly. This gland helps regulate
growth, weight, and the balance of body chemicals. Blood tests can be done to check thyroid hormone levels. Low thyroid levels are easily treated with oral medication.

**Subsequent Cancers**
Some chemotherapy drugs and radiation can increase the risk of a subsequent (different) cancer. Some survivors may have genetic changes that put them at risk for second cancers. Tobacco, excessive sun exposure, and other chemicals and behaviors can also increase this risk. Talk with your healthcare provider about ways to lower your risk and to detect common cancers at an early stage.

**School and work**
Problems with schoolwork or job performance can occur as a result of some types of cancer treatment. Psychologists can work with your local school system to make sure that any special needs are met. Also, financial assistance for education and job training may be available through government programs. Social workers can help to explain these programs.

**Moving toward the future**
Thinking about developing late effects after surviving cancer can be anxiety provoking. Your long-term follow-up program is here to help you navigate the emotional and physical challenges of cancer survivorship. Regular health checks and recommended screening and surveillance testing are meant to put you in control of your health and provide the best chance of early detection of problems, if they occur, before they become severe. Work with your health care team to develop a follow up plan that works best for you.

Make healthy choices. Keep your follow-up appointments. And always remember that you are the most important member of your healthcare team!

Written by Wendy Landier, PhD, CPNP, Children’s Hospital of Alabama, Birmingham, AL. Portions adapted from “Introduction to the After Completion of Therapy Clinic,” St. Jude Children’s Hospital, Memphis, TN, used with permission.

Reviewed by Beth Fisher, DNP, APRN, CPNP, CPON, CHPPN; Christine S. Yun, MSN, PNP, CPON; and Kayla L. Foster, MD, MPH.

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Introduction to Long Term Follow Up

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Kidney Health after Cancer Treatment

The kidneys are vital organs responsible for filtering out waste products from the blood, controlling blood pressure, and stimulating red blood cell production. Treatment for childhood cancer can sometimes damage the kidneys. It is important to understand how the kidneys function so that you can keep your kidneys as healthy as possible.

How do the kidneys work?

The kidneys are two bean-shaped organs, each approximately the size of an adult fist, located below the rib cage near the middle of the back. The kidneys filter about 200 quarts of blood each day, removing harmful waste products and excess water, and returning important elements (such as calcium, sodium and potassium) to the blood. Filtering occurs in tiny units inside the kidneys, known as nephrons. Each kidney has approximately one million nephrons. After the blood is filtered by the nephrons, the excess water and waste products become urine. The urine flows from the kidneys to the bladder through tubes called ureters. The bladder then stores the urine until it is full, at which time the waste is emptied from the body through the urethra.

How is kidney function measured?

Kidney function is measured by calculating a glomerular filtration rate, or GFR. The GFR is a measure of how much blood your kidneys can filter each minute. The GFR is calculated using blood test results and information like your age, sex and height. A GFR of greater than 90 mL/min/1.73 m2 is considered normal. If your GFR is below 90 mL/min/1.73 m2, your provider may order additional tests such as a urinalysis to see if there is protein or blood in your urine.

What treatments for childhood cancer can cause kidney problems?

Certain treatments used for childhood cancer can sometimes cause kidney problems. There may also be other risk factors present that can increase the chance of kidney problems. If you have any of the following risk factors, you should take extra care to keep your kidneys healthy:

Radiation involving the kidneys, including:
- Kidney (renal or flank) radiation
- Abdominal radiation
- Total body irradiation (TBI)

Certain medications that can cause kidney damage, including:
- Cisplatin
- Carboplatin
- Ifosfamide
- Certain antibiotics used to treat bacterial and fungal infections, such as tobramycin, gentamicin, and amphotericin
- Certain medications used to treat graft-versus-host disease, such as cyclosporine and FK-506 (tacrolimus)

Other risk factors that may increase the chance of kidney problems include:
- Nephrectomy (surgical removal of a kidney)—see the related Health Link: Single Kidney Health
- Hematopoietic cell transplant (HCT)
Kidney Health

Medical conditions that may affect the kidney, such as high blood pressure, diabetes, or a tumor involving the kidney

History of urinary tract problems, such as frequent urinary tract infections, back-flow of urine into the kidney (reflux), or other urinary tract abnormalities

Cystectomy (removal of the bladder)—this increases the risk of chronic urinary tract infections and other kidney problems

What are the signs and symptoms of a kidney problem?

- Swelling, especially of the feet and ankles (edema)
- Low red blood count (anemia)
- High blood pressure (hypertension)
- People who have signs of serious kidney problems, such as edema, low red blood count, and hypertension, may also have other symptoms, including fatigue, nausea and vomiting, drowsiness, itchy skin, or headaches

What follow up is recommended?

- Have a medical check-up at least yearly. This should include a blood pressure check.
- Have blood test for kidney function (BUN and creatinine) and electrolytes (blood salts and minerals) at your first long-term follow up visit (at least 2 years after completing cancer treatment). Depending on the treatment you received and the results of this lab work, your provider may recommend labs to assess your kidney function at regular intervals.
- If you had a cystectomy (bladder removal), you should also have an evaluation by an urologist (urinary tract specialist) at least once a year.

What can I do to keep my kidneys healthy?

- Drink plenty of water, especially when playing sports, while out in the sun, and during hot weather.
- Call your healthcare provider immediately if you have symptoms of a urinary tract infection (burning when you urinate, urinating more frequently than usual, and/or feeling an urgent sensation to urinate).
- Use non-steroidal anti-inflammatory drugs with caution. These include pain or fever medicines (over-the-counter and by prescription) that contain aspirin, ibuprofen, or naproxen. These medications have been known to cause kidney damage (analgesic nephropathy), especially when taken in high doses or over long periods of time (more than 10 days). If you require long-term medications for management of pain, be sure to discuss options with your healthcare provider, and to choose medications that are safe for your kidneys.

Written by Anne Mauck, RN, MSN, CPNP, Virginia Commonwealth University/Massey Cancer Center, Richmond, VA.
Reviewed by Kayla L. Foster, MD, MPH; and Melissa Acquazzino, MD, MS.

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Late Effects after Limb Sparing Procedures

What is a “limb sparing procedure”?
A limb sparing procedure is a surgical operation that replaces a diseased bone and reconstructs a functional limb by using a metal implant, a bone graft from another person (allograft), or a combination bone graft and metal implant (allo-prosthetic composite).

What are the potential late effects after a limb sparing procedure?
- **Nonunion**—For people who had reconstruction with a bone graft, nonunion (non-healing) of the bones is a possible late complication. In the allograft procedure, the portion of bone removed due to tumor is replaced with donated bone. Nonunion occurs when one or both ends of the replaced bone do not heal, making fracture more likely, especially if the area is stressed. Surgery for additional bone grafting may be necessary.
- **Limb-length discrepancy**—Bones are constantly growing during childhood and adolescence, until adult height is reached. Each bone has a growth plate (area where growth activity occurs). Often, bone cancers are located near the growth plate, requiring removal of this area during the limb sparing procedure. Since the reconstructed section of bone cannot grow, a difference (discrepancy) in limb-length may occur over time. Surgeries or other procedures may be necessary to allow for growth.
- **Prosthetic loosening**—Sometimes the implanted joint can loosen or wear out, especially in people who are active. These complications may require further surgery to tighten or replace part or all of the implant. Any loosening of the implant should be reported to your orthopedic surgeon.
- **Contractures**—After a limb sparing procedure, muscles, tendons and ligaments sometimes stiffen or shrink, forming contractures (permanent tightening of the joint). This is more likely to occur in people who are not physically active. Periodic follow-up with a physical and/or occupational therapist helps prevent contractures from forming.
- **Difficulty engaging in physical activities to maintain a healthy weight.**
- **Chronic pain and/or infection**—Some people may develop persistent problems with pain and/or infection.

What is the recommended follow-up care after a limb sparing procedure?
- Follow-up visits are usually done by the orthopedic surgeon (bone specialist) every 6 months until the person is fully grown, then every year. These visits may include x-rays of the limb and follow-up intervals may lengthen as time progresses.
- Life-long follow-up by an orthopedic surgeon (ideally by an orthopedic oncologist) is recommended.
- Limitation of certain physical activities is sometimes necessary.

What can you do to promote health after limb sparing surgery?
- Physical and occupational therapy are important for successful rehabilitation after limb sparing surgery. Both passive and active range-of-motion exercises help maintain the best limb function.
- If there is pain, swelling, redness or any other signs of infection at the surgical site, or if you develop fever, contact your healthcare provider promptly.
- If your limb sparing surgery was complicated, your orthopedic surgeon may recommend antibiotics prior to dental procedures (including teeth cleaning), and for other invasive medical procedures such as those involving the respiratory, gastrointestinal, or urinary tracts. Infection can result if bacteria enter the bloodstream during these procedures and become attached to the internal metal components (screws, plates, rods, joints) of the endoprosthesis. The potential need for antibiotics should be discussed with your orthopedic surgeon and your dentist.
- Some metal implants may pose a problem when going through security screening, such as at the airport. It is good idea to carry a medical letter indicating that you received treatment for bone cancer and have a metal implant.
Written by Asako Komiya, RN, MSN, PNP, City of Hope Comprehensive Cancer Center, Duarte, CA.
Reviewed by Leeann Carmichael DNP, APN, FNP-BC; Kayla L. Foster, MD, MPH; and Melissa Acquazzino MD, MS.

Additional health information for childhood cancer survivors is available at www.survivorshipguidelines.org

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Liver Health after Cancer Treatment

Treatment for childhood cancer can sometimes damage the liver. It is important to know about how the liver functions so that you can keep your liver as healthy as possible.

What is the liver?
The liver is a triangular-shaped organ tucked under the rib cage on the right side of the body. In an average adult, the liver is about the size of a football and weighs about three pounds. The liver is responsible for filtering out toxins from the blood, aiding with digestion and metabolism, and producing many important substances, including blood-clotting proteins.

What are the signs and symptoms of liver damage?
Many people with liver damage have no symptoms at all. Some people may develop jaundice (yellowish eyes and skin), dark urine, pale (clay-colored) stools, severe itching, easy bruising or bleeding, chronic fatigue, nausea, loss of appetite, or other symptoms. The liver sometimes enlarges (hepatomegaly), and as liver damage increases, the liver may become hard (fibrosis) and scarred (cirrhosis). Eventually, there can be accumulation of fluid in the abdomen (ascites), swelling of the spleen (splenomegaly), or bleeding into the esophagus or stomach. Very rarely, liver cancer may develop.

Who is at risk?
People who had radiation to the abdomen or received certain chemotherapy medicines (methotrexate, mercaptopurine, and/or thioguanine) may be at risk for liver problems. Liver problems related to medications typically occur during cancer therapy and are unlikely to occur long after the end of treatment.

Other risk factors include:
- Medical conditions that involve the liver, such as a liver tumor or surgical removal of a large portion of the liver
- Development of sinusoidal obstruction syndrome (SOS, previously known as veno-occlusive disease [VOD]) during treatment
- Pre-existing liver problems
- Excessive alcohol use
- Chronic liver infection (hepatitis)—see related Health Link: Hepatitis after Childhood Cancer
- History of multiple transfusions
- Chronic graft-versus-host disease (as a result of bone marrow, cord blood, or stem cell transplant)

What tests are done to monitor the liver?
The following blood tests are used to monitor the liver.

- **Liver enzyme tests** monitor levels of specialized proteins that are normally present inside liver cells. If liver cells are damaged, these proteins can leak out, causing high blood levels of liver enzymes. The most common liver enzyme tests are:
  - Alanine aminotransferase (ALT), sometimes also called SGPT
  - Aspartate aminotransferase (AST), sometimes also called SGOT
- **Liver function tests** are indicators of how well the liver is working. Common liver function tests include:
  - Bilirubin (a waste product formed during the breakdown of red blood cells)
  - Albumin (a major blood protein that is produced by the liver)
  - Prothrombin Time (PT), a measure of blood clotting
Tests for liver infection, including specific tests for viral hepatitis A, B, and C
Test to check for iron overload (ferritin) related to multiple transfusions

What follow up is needed for those at risk?
A blood test to evaluate the liver (including ALT, AST, and bilirubin) should be done when the survivor enters into long-term follow-up. Those who have undergone a bone marrow, cord blood, or stem cell transplant should also have a blood test to check for iron overload (ferritin). The liver should also be checked for enlargement by a healthcare professional during yearly physical examinations. If problems are identified, additional tests and a referral to a liver specialist may be recommended. People at risk for hepatitis may need further testing (see related Health Link: Hepatitis after Cancer Treatment).

What can I do to keep my liver healthy?
• If you do not have immunity to hepatitis A and B, get immunized against these common infections in order to protect your liver (there is currently no vaccine to protect against hepatitis C). You can find out if you have immunity to hepatitis A and B by having a blood test (Hepatitis A IgG antibody and Hepatitis B surface antibody).
• If you drink alcohol, do so in moderation.
• Drink plenty of water.
• Eat a well-balanced, high-fiber diet. Cut down on fatty, salty, smoked and cured foods.
• Do not take more than the recommended doses of medications.
• Avoid taking unnecessary medications.
• Do not mix drugs and alcohol.
• Do not use illicit drugs.
• Check with your healthcare provider before starting any new over-the-counter medications or herbs and supplements to be sure that they do not have harmful effects on the liver.
• If you are sexually active, use barrier protection (such as latex condoms) during intimate sexual contact to prevent infection by viruses that can damage the liver.
• Avoid exposure to chemicals (solvents, aerosol cleaners, insecticides, paint thinners, and other toxins) that can be harmful to the liver. If you must use these substances, wear a mask and gloves and work in a well-ventilated area.

Written by Wendy Landier, PhD, CPNP, Children’s Hospital of Alabama, Birmingham, AL.
Reviewed by Daniel Smith, DNP, FNP; Kayla L. Foster, MD, MPH; and Melissa Acquazzino, MD, MS.

Additional health information for childhood cancer survivors is available at www.survivorshipguidelines.org

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Mental Health after Cancer Treatment

The Cancer Experience

**Diagnosis and Treatment**

Diagnosis and treatment are difficult times for people with cancer and their families. During diagnosis, children or teens have tests and procedures that are new, sometimes painful and often scary. For parents, the anxiety of waiting for the results of these tests and procedures can be the worst part of this time. Learning the diagnosis can be a relief, especially when effective treatments are available. These treatments, though, can be unpleasant for children to have and upsetting for families to watch or give. Tests and procedures are repeated during treatment to find out if the treatment plan is working or should change. Children and teens with cancer and their parents are frequently at the hospital, sometimes away from other family, friends, home, work, or school for long periods of time. Parents worry about whether their child’s cancer will be cured, how to minimize their suffering, and how to make the most of life. Brothers and sisters also worry about, and are sometimes jealous of the sibling with cancer. Childhood cancer survivors and their siblings can be concerned about their parents, and keep worries and feelings to themselves to try to protect their parents. As a result, people diagnosed with cancer, their parents, and their siblings can feel angry, lonely, sad, and afraid during treatment. Periods of anxiety and depression can occur.

**After Treatment Ends**

For survivors and their families, the end of treatment can bring new feelings as they come to know the good (and sometimes not so good) outcomes of successful treatment. During treatment, people tend to be concerned with getting through the day-to-day. It is after treatment that people can begin to think about and come to terms with their experience. People can have a range of feelings after treatment ends, and the blend of feelings can be as unique as each person. Survivors and their families often fear that the original cancer will return. Regular testing for recurrent cancer or late effects, and even just talking about possible late effects can cause stress. The diagnosis of a late effect related to cancer treatment or a new health problem unrelated to childhood cancer can also be sources of distress. Anniversaries of cancer events, such as the date of diagnosis or end of treatment, and life changes such as school entry or the normalization of peer relationships can bring on feelings that include relief and happiness, sadness about the loss of a regular childhood, and guilt over having survived when others did not. Some survivors may feel vulnerable because of their cancer experience and can be concerned about their health and act with caution. Parents of childhood cancer survivors very much want to protect all their children from harm. These protective feelings can increase usual tensions between parents and teenagers over issues related to growing independence, especially in matters that can affect health. Other individuals who have had cancer believe that having survived cancer, they can do anything—and this makes them feel invincible. These feelings can lead some survivors to undertake difficult studies, work, or hobbies. The same feelings can lead other survivors to take part in unhealthy or risky behaviors.

**Some Reactions to the Stresses of Survivorship**

For the most part, childhood cancer survivors and their family members respond well to the stresses of survivorship. Sometimes though, physical problems or other stresses related to childhood cancer and everyday life can lead to intensely distressing emotions that need medical attention. Some survivors, and their family members, can experience periods of high anxiety that may or may not be triggered by reminders of the upsetting aspects of treatment. They may develop three types of symptoms typically seen in people with posttraumatic stress disorder (PTSD), including (1) unwanted recall of unpleasant memories of cancer, (2) physical or emotional overreactions, and (3) going out of the way to avoid reminders of cancer. For the most part, childhood cancer survivors and their family members do not develop all...
three types of symptoms and PTSD. Yet one or two of these symptoms can nonetheless get in the way of relationships, school, work, and other key areas of daily life after cancer.

Personal growth can be another reaction to the stresses of life after cancer. After years of living with childhood cancer, some survivors and their family members may find that they have undergone meaningful and beneficial changes in themselves, their relationships with other people, and their values as a result of their experiences. Furthermore, they may have been able to find some positive changes in their lives as a result of surviving the cancer experience. Experiencing these positive changes is sometimes referred to as posttraumatic growth.

**Risk Factors**

Several factors can affect the development of depression and anxiety with symptoms of posttraumatic stress after diagnosis and treatment of childhood cancer, including:

- Female gender
- Adolescent or young adult age
- Prior trauma
- Mental health or learning difficulties before childhood cancer
- Developing health problems or physical limitations due to cancer treatment
- Low levels of social support
- Parental history of depression, anxiety, or PTSD
- Central nervous system (CNS) cancers (brain or spine) or treatment (radiation to the head/spine or intrathecal chemotherapy)
- Treatment with hematopoietic cell transplant (bone marrow or stem cell transplant)

**When to Seek Help**

People with distress that (1) lasts two weeks or more, and/or (2) interferes with their ability to do daily home, school or work tasks, should call their healthcare provider to discuss the need for a referral to a mental health professional. Because physical health problems can cause these same symptoms, a thorough check-up by your primary healthcare professional is recommended if they occur. Some possible signs that help is needed can include:

- Changes in appetite and weight
- Crying easily or being unable to cry
- Constant tiredness and low energy level
- Sleeping more than usual or being unable to sleep
- Feeling hopeless
- Thoughts of hurting yourself or others
- Engaging in self-harm behaviors (ie. cutting)
- Alcohol or drug use to avoid unpleasant feelings
- Increased irritability
- Decreased interest in activities that had been pleasurable in the past
- Unwanted recall of painful aspects of cancer
- Feeling extremely fearful, upset, or angry when thinking about cancer
- Physical reactions (rapid heart rate, shortness of breath, nausea) when thinking about cancer
- Avoiding health care visits
- Refusing to talk about cancer
Share Your Concerns with Your Healthcare Provider

If you experience distress, discuss it with your primary health care provider or childhood cancer specialist. Your distress may be related to your cancer experience, worries about late effects, or other events in your life. In any case, there is treatment. Talking with others about your fears and worries is a first step in gaining control over them. In addition to receiving help from a health care provider, some people also find support through support groups, participation in activities at their place of worship, or their faith.

Treatment Options

Treatments for depression, anxiety and posttraumatic stress symptoms include counseling in group or individual sessions and, sometimes, medication. Medication usually works in combination with some form of counseling. Mental health professionals (including mental health nurse practitioners, psychiatrists, psychologists, and social workers) provide treatment for depression and anxiety in a variety of community settings. Your primary healthcare provider can help you find a suitable mental health professional in your community.

Resources

Support is available to childhood cancer survivors and their families who have anxiety and depression after treatment. These are just a few of the many resources available:

**American Cancer Society** [www.cancer.org](http://www.cancer.org)
This site provides web-based support network, other programs and services, and stories of hope for cancer survivors and their families.

**American Psychiatric Association** [www.psychiatry.org](http://www.psychiatry.org)
This site provides guidelines for choosing a psychiatrist.

**The Anxiety and Depression Association of America** [www.adaa.org](http://www.adaa.org)
This site provides information that can help people with anxiety disorders and depression find treatment and develop self-help skills.

**American Childhood Cancer Organization** [www.acco.org](http://www.acco.org)
This site offers education, support, service, and advocacy for childhood cancer survivors, their families and the professionals who care for them.

**Childhood Cancer Guides** [www.childhoodcancerguides.org](http://www.childhoodcancerguides.org)
This site provides articles related to psychosocial aspects of survivorship.

**Children’s Oncology Group** [www.childrensoncologygroup.org](http://www.childrensoncologygroup.org)
This site provides parents and families with information related to specific cancer type, treatment stage and age group as well as tips on navigating the health care system, getting and giving support, and maintaining a healthy lifestyle.

**National Institute of Mental Health** [www.nimh.nih.gov](http://www.nimh.nih.gov)
This site provides general information about anxiety or depression, available treatments, finding a mental health provider, and access to research reports and other relevant information. See these specific areas of the web site:

- [www.nimh.nih.gov/health/topics/depression](http://www.nimh.nih.gov/health/topics/depression)
Revised by Sheila J. Santacroce, PhD, APRN, CPNP, UNC Lineberger Comprehensive Cancer Center, Chapel Hill, NC. Originally adapted by Debra A. Kent, RN, MSN, CPNP, Cincinnati Children’s Hospital Medical Center, Cincinnati, OH, from “Dealing with Emotions after Childhood Illness” by Melissa Hudson, MD, After Completion of therapy (ACT) Clinic, St. Jude Children’s Research Hospital, Memphis, TN.

Reviewed by by Leeann Carmichael, DNP, APN, FNP-BC; Christine S. Yun, MSN, PNP, CPON; and Kayla L. Foster, MD, MPH.

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Testicular and Reproductive Health after Cancer Treatment

The effects of childhood cancer therapy on reproductive function depend on many factors, including the specific type and location of the cancer, and the treatment that was given. It is important to understand how the testes function and how they may be affected by cancer treatment.

The reproductive system

The reproductive system contains many structures and is controlled by the pituitary gland in the brain. The testes are located in the scrotum (the loose pouch of skin behind the penis). The testes are made up of leydig cells (cells that produce the hormone—testosterone) and sertoli cells (cells that support the sperm production). At the time of puberty, the pituitary gland in the brain releases two hormones (FSH and LH) that signal the testes to begin producing sperm and testosterone. As puberty progresses, testosterone causes deepening of the voice, enlargement of the penis and testes, growth of facial and body hair, and muscular development of the body.

How does cancer therapy affect the testes?

Cancer therapy can cause infertility (the inability to initiate a pregnancy). Infertility can occur following treatment with certain types of chemotherapy, radiation to the brain or testes, or surgery involving the reproductive system.

Another possible effect of cancer therapy is testosterone deficiency, also known as “hypogonadism”. When this occurs, the testes are unable to produce enough testosterone hormone. If this happens before the age of puberty, puberty may not start without hormone medication prescribed by a doctor. If it develops after puberty, testosterone therapy may be needed to maintain muscular development, bone and muscle strength, proper distribution of body fat, sex drive, and the ability to have erections.

What are the causes of male reproductive problems after childhood cancer treatment?

Chemotherapy of the “alkylator” type (such as cyclophosphamide, thiotepa, melphalan and busulfan) and heavy metals (such as cisplatin and carboplatin) may cause testicular damage. The total dose of chemotherapy used during cancer treatment is important in determining the likelihood of damage. The higher the total dose, the more potential for developing problems such as infertility or testosterone deficiency. If alkylating or heavy metal chemotherapy was used in combination with radiation, the risk for testicular damage is increased.

Radiation therapy can affect testicular function in two ways:

- **Radiation aimed directly at or near the testes.** The sperm-producing cells are very sensitive to the effects of radiation therapy. Most individuals who receive radiation to the testes at doses of 6 Gy (600 cGy/rads) or higher will be infertile. The testosterone producing cells are more resistant to the effects of radiation and chemotherapy, but if testicular radiation was given in doses of 12 Gy (1200 cGy/rads) or higher, the leydig cells may be damaged, resulting in testosterone deficiency (in addition to infertility).

- **Radiation to the hypothalamic and pituitary gland regions in the brain.** The hypothalamus and pituitary gland regulate the production of two hormones (LH and FSH) needed to signal the testes to make testosterone and sperm. People with low levels of these hormones will need to take testosterone hormone replacement. For some
survivors, it is possible to regain fertility with the use of specialized hormone treatments. Individuals who have infertility as a result of brain radiation and wish to achieve fertility should see a fertility specialist.

**Surgery** that involves removal of both testicles (bilateral orchiectomy) will result in infertility and testosterone deficiency. Pelvic surgery, such as retroperitoneal lymph node dissection (RPLD), or spinal surgery sometimes results in nerve damage that may prevent the ejaculation of sperm. Removal of the prostate or bladder may result in difficulties achieving an erection and/or ejaculation. In these situations, sperm production may be unaffected and fertility may still be possible by using specialized techniques, such as sperm harvesting and artificial insemination. If fertility is desired, consultation with a fertility specialist is recommended.

What types of cancer therapy increase the risk of problems with testicular function?

- **Chemotherapy** - the class of drugs called “alkylators” can cause infertility when given in high doses. Very high doses may occasionally cause testosterone deficiency. Heavy metal chemotherapy can also affect testicular function. Examples of these drugs are:
  - Alkylating agents:
    - Busulfan
    - Carmustine (BCNU)
    - Chlorambucil
    - Cyclophosphamide (Cytoxan®)
    - Ifosfamide
    - Lomustine (CCNU)
    - Mechlorethamine (nitrogen mustard)
    - Melphalan
    - Procarbazine
    - Thiotepa
  - Heavy metals:
    - Carboplatin
    - Cisplatin
  - Non-classical alkylators:
    - Dacarbazine (DTIC)
    - Temozolomide

- **Radiation therapy** to any of the following areas may cause infertility:
  - Testes
  - Total body irradiation (TBI)
  - Head/brain especially if dose was 30 Gy (3000 cGy/rads) or higher

  In addition to causing infertility, high doses of radiation to the testes (usually 12 Gy or higher) or brain (usually 30 Gy or higher) may also cause testosterone deficiency.

- **Surgery**es that may cause infertility or disrupt normal sexual functioning include:
  - Removal of both testicles (this surgery will always result in infertility)
  - Removal of one testicle or a portion of one testicle
  - Retroperitoneal lymph node dissection (RPLD)
  - Removal of tumor in the retroper!itoneal area
  - Pelvic surgery
  - Cystectomy (removal of the bladder)
  - Prostatectomy (removal of the prostate)
Spinal surgery
- Removal of tumor near the spinal cord

In addition, removal of both testicles will result in testosterone deficiency, and removal of one testicle or a portion of one testicle may result in low testosterone levels.

What monitoring is recommended?

Individuals whose treatment places them at risk for problems with the reproductive system should have a yearly check-up that includes careful evaluation of their sexual development. Blood may be tested for hormone levels (AM testosterone, LH, FSH, and inhibin). If any problems are detected, a referral to an endocrinologist (hormone specialist), urologist (specialist in the reproductive system) and/or fertility specialist may be recommended. Individuals who have had both testes removed should begin seeing an endocrinologist starting at about age 11 for hormone replacement.

People who have had fertility preservation procedures (saving sperm outside of the body or “cryopreserved”), should review previous fertility counseling and current options for family building with a fertility specialist.

What can be done for testosterone deficiency?

Individuals with low testosterone levels should receive testosterone replacement therapy. Testosterone is available in several forms, including skin patches, injections, and topical gel. Your endocrinologist will determine which form of therapy is best for you.

How will I know if I am infertile?

Infertility, the inability to initiate a pregnancy after a year of unprotected intercourse, can occur after cancer treatment. Recovery of the ability to make sperm may occur in some survivors. When recovery occurs, it usually happens in the first few years after completion of cancer treatment. The best way to assess the ability to make sperm is a semen analysis which evaluates the number of sperm produced, the motility (movement of the sperm) and morphology (what the sperm look like). The specimen is produced after several days of abstinence. If the patient is unable to produce a semen specimen or prefers not to, an FSH and inhibin level may provide some insight into the ability to make sperm. A high FSH or low inhibin suggest impaired ability to make sperm.

A semen analysis that shows azoospermia (no sperm in the semen sample) on more than one sample is an indicator of infertility. Patients with oligospermia (low sperm count) may still be able to have children with the help of fertility specialists.

In general, contraception should be used unless pregnancy is desired.

What if only one testicle or a portion of one testicle was surgically removed?

Although fertility and testosterone production are not usually affected if only one testicle or a portion of one testicle was surgically removed, you should take precautions to protect the remaining testicle from injury by always wearing an athletic supporter with a protective cup when participating in any activities that may potentially cause injury to the groin area (such as contact sports, baseball, etc.).

What are the risks if pregnancy occurs after childhood cancer treatment?

Fortunately, in most cases, there is no increased risk of cancer or birth defects in children born to childhood cancer survivors. In rare cases, if the type of cancer in childhood was a genetic (inherited) type, then there may be a risk of passing that type of cancer on to a child. You should check with your oncologist if you are not sure whether the type of cancer you had is associated with a genetic risk that can be passed on.
Written by Marcia S. Leonard, RN, CPNP, C.S. Mott Children’s Hospital, Ann Arbor, MI.
Reviewed by Katy Tomlinson, RN, BSN; Lillian R. Meacham, MD; Melissa Acquazzino, MD, MS; and Kayla L. Foster, MD, MPH.

Additional health information for childhood cancer survivors is available at www.survivorshipguidelines.org

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Neurogenic Bladder after Cancer Treatment

Certain types of cancer and certain cancer treatments can cause damage to the urinary bladder. The information in this Health Link will help you to recognize the signs and symptoms of a neurogenic bladder.

What is the urinary bladder?
The urinary bladder is a hollow organ that stores urine. It is located behind the pubic bone. The kidneys filter the blood and make urine, which enters the bladder through two tubes called “ureters.” Urine leaves the bladder through another tube, the urethra.

What are the risk factors for neurogenic bladder?
- Tumors involving the bladder, prostate, pelvis, or spine
- Radiation therapy to these areas
- Surgery to these areas

What is a neurogenic bladder?
A neurogenic bladder is abnormal function of the bladder caused by damage to the nerves that control the bladder’s ability to fill, store and empty urine. Abnormal bladder function can cause the bladder to be underactive (not emptying completely) or overactive (emptying too frequently or quickly). People with neurogenic bladders also have a higher risk of urinary tract infections (UTIs) and kidney damage.

What are the symptoms of a neurogenic bladder?
There may be a sudden urge to urinate or the need to urinate frequently. There may also be dribbling during urination, straining to urinate, or the inability to urinate.

Who is at risk of a neurogenic bladder?
People who have had tumors involving the bladder, prostate, pelvis, or spine are at risk of developing neurogenic bladder. Also, people who had surgery or radiation in these areas may be at risk.

How is a neurogenic bladder diagnosed?
If a neurogenic bladder is suspected, an evaluation should be done by a urologist. A urologist is a physician who specializes in disorders of the urinary tract. The urologist will order tests to determine how well the bladder is able to store and empty urine, such as a voiding cystourethrogram (VCUG) or bladder cystometry.

What can I do if I have a neurogenic bladder?
Treatment of neurogenic bladder is based on your individual needs. Medications may be useful for an overactive bladder or for a bladder that fails to store urine properly. Surgery to enlarge the size of the bladder may be needed if the medications are not successful.

Removal of urine by insertion of a small, clean tube in the urethra several times a day (intermittent catheterization) may be necessary if you cannot completely empty your bladder. This helps prevent high pressure in the bladder that interferes with flow of urine from the ureters and kidneys.
Health Link

Healthy living after treatment of childhood, adolescent, and young adult cancer

When should I call my healthcare provider?

Call your healthcare provider if you are awakened more than usual during the night to urinate, if leakage of urine occurs, any time fever or pain is present, or if blood is seen in the urine.

Written by Patricia Shearer, MD, MS, Emory Healthcare, Johns Creek, GA; Michael L. Ritchey, MD, Phoenix Childrens Hospital, Phoenix, AZ; Fernando A. Ferrer, MD, Children’s Hospital and Medical Center of Omaha, Omaha, NE; and Sheri L. Spunt, MD, Lucile Packard Children’s Hospital Stanford University, Palo Alto, CA.

Reviewed by Linda Rivard, RN, BSN, CPON; Kayla L. Foster, MD, MPH; and Christine Yun, MSN, PNP, CPON.

Additional health information for childhood cancer survivors is available at www.survivorshipguidelines.org

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Osteonecrosis after Cancer Treatment

What is osteonecrosis?

Osteonecrosis is a disorder resulting from a temporary or permanent loss of blood supply to the bone. Blood carries essential nutrients and oxygen to the bones. When the blood supply is disrupted, the bone tissues (osteo) begin to break down (necrosis). This can weaken the bone and eventually result in its collapse. If this occurs near a joint, it can lead to the collapse of the joint surface, resulting in pain and inflammation (arthritis). Osteonecrosis is also referred to as avascular necrosis or “AVN,” “aseptic necrosis,” and “ischemic bone necrosis.”

Osteonecrosis can occur in any bone, but most commonly affects the ends (epiphysis) of long bones such as the thigh bone (femur), causing hip and knee problems. Other common sites include the bones of the upper arms, shoulders, and ankles. Osteonecrosis can occur in a single bone, but more commonly occurs in several bones at one time (multifocal osteonecrosis).

Osteonecrosis can sometimes be disabling, depending on what part of the bone is affected, how large an area is involved, and how well the bone rebuilds itself. Normal bone continuously breaks down and rebuilds itself. This process keeps the bones strong. Osteonecrosis is the result of bone tissues breaking down faster than the body can repair them. If the disorder progresses, it can lead to pain and arthritis.

What causes osteonecrosis?

Osteonecrosis is caused by interruption of the blood supply to the bone. If blood vessels are blocked with fat, become too thick or too small, or get too weak, they may not be able to provide the amount of blood necessary for the bone tissue to survive.

What are the risk factors for osteonecrosis?

Corticosteroids (such as prednisone and dexamethasone) given during cancer treatment can affect the bone and blood vessels, resulting in osteonecrosis. People who have undergone hematopoietic cell transplant (bone marrow, cord blood, or stem cell transplant) are also at risk for developing osteonecrosis. Other factors that increase the risk of osteonecrosis in people who received corticosteroid therapy or hematopoietic cell transplant (HCT) include treatment with high doses of radiation to weight bearing bones, treatment with older radiation approaches (before 1970), being pubertal or post-pubertal at the time of treatment, having sickle cell disease, receiving total body irradiation (TBI), undergoing an allogeneic transplant (from a donor) and having prolonged treatment with corticosteroids for chronic graft-versus-host disease following HCT. Osteonecrosis is most likely to occur during the time that cancer is being treated, but it can also sometimes happen after completion of cancer therapy.

Steroids and osteonecrosis

Corticosteroids (such as prednisone and dexamethasone) are commonly used for treatment of many cancers, such as leukemia and lymphoma. Dexamethasone is also sometimes used for treatment of nausea and vomiting associated with chemotherapy and to control brain swelling. There is no clear explanation as to how corticosteroids cause osteonecrosis, but it is believed that they may interfere with the body’s ability to break down fatty substances. These substances can clog the blood vessels, causing them to narrow. This reduces the amount of blood that gets into the bone.
What are the symptoms of osteonecrosis?

People in the early stages of osteonecrosis may not have any symptoms. For some individuals, the first symptoms may be mild joint pain either with movement or at rest and, when caught early, may heal with conservative treatment. More severe osteonecrosis can result in significant pain and impaired mobility.

How is osteonecrosis diagnosed?

If you or your child develops joint pain concerning for osteonecrosis, your provider may recommend images of the joint. This can include an X-Ray, MRI, CT or bone scan.

How is osteonecrosis treated?

The goals of treatment for osteonecrosis are pain control, maintaining joint function and preventing further damage. Treatment can be conservative or surgical. To decide the best treatment, the following factors are considered:

- The person’s age
- The stage of the disorder (early or late)
- The location and the amount of bone affected (small or large)
- The status of cancer and cancer treatment

Conservative treatment

- **Medication**—to reduce pain
- **Reduced weight bearing**—to slow the damage and promote natural healing. Crutches may be recommended to limit weight or pressure on the affected joint
- **Range of motion exercises**—to keep the joints flexible. This is also important to maintain movement and increase circulation in the joints. This can promote healing and may relieve pain. Physical therapists can teach the correct exercises
- **Electrical stimulation**—to induce bone growth

Conservative treatments may be used alone or in combination, but they may not provide lasting improvement. Some people may require surgery to permanently repair or replace the joint.

Surgical Treatment

- **Core decompression**—is a surgery that removes the inner layer of bone. This may reduce pressure within the bone and create an open area for new blood vessels to grow. Sometimes a piece of healthy bone with good blood vessels (bone graft) is put in this area to speed up the process. This procedure works best in the early stages of osteonecrosis and should help relieve pain and promote healing.
- **Osteotomy**—is a surgery that involves taking out a piece of bone, usually a wedge, to reposition the bone so that the tissue lacking blood supply (avascular area) bears less weight than nearby healthy bone.
- **Arthroplasty**—is also referred to as joint replacement. The affected bone is removed and replaced with an artificial joint. This treatment may be needed in the late stages of osteonecrosis and when a joint is destroyed.

Health Promoting Behaviors/Interventions

- Avoid activities that put a lot of stress on your joints. Activities that stress the joints include running, jumping, football, soccer, volleyball, basketball, and similar sports. Low impact activities, such as swimming and bicycling, can be good for joint health.
- Be consistent with recommended exercises.
Rest joints when they hurt.

- Let your healthcare provider or physical therapist know if there are any changes in your symptoms.
- Take pain or anti-inflammatory medications as prescribed.
- Mind-body therapies such as massage, acupuncture, biofeedback, and relaxation techniques may improve pain control, increase blood flow and reduce stress.

Resources

- National Institute of Arthritis and Musculoskeletal and Skin Diseases
  National Institutes of Health, 1 AMS Circle, Bethesda, MD 20892-3675
  Phone: 301-495-4484 or 877-226-4267 (toll free), TTY: 301-565-2966
  Fax: 301-718-6366. Web: https://www.niams.nih.gov/health-topics/osteonecrosis

- American Academy of Orthopaedic Surgeons
  9400 West Higgins Road, Rosemont, IL 60018
  Phone: 847-823-7186 (toll free). Web: www.aaos.org

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Osteoradionecrosis after Cancer Treatment

What is osteoradionecrosis?

Osteoradionecrosis (ORN) is a problem with bone healing that can occur in people who received high doses of radiation, particularly to the jaw. This complication can occur after dental surgery or extraction of teeth. High doses of radiation can decrease the bone’s blood supply. If this happens, the bone gets less oxygen than it needs, resulting in the death (necrosis) of bone tissue. The most commonly affected bone is the jawbone (mandible).

Who is at risk for osteoradionecrosis?

Survivors who received high doses of radiation to the jaw area (40 Gy or 4000 cGy/rads or higher) are at risk for this complication. Radiation fields that often include the jawbone are as follows:

- Head/brain
- Neck
- Spine (“cervical” portion)

It is important to obtain your medical records so that you know exactly how much radiation you received and where the radiation was directed. For example, survivors exposed to radiation doses of 50 Gy or higher to the jawbone have the highest risk for the development of ORN.

When does osteoradionecrosis occur?

Although it is uncommon, ORN most often occurs when a survivor undergoes a dental procedure (such as pulling of tooth) or other surgery involving the jawbone.

What are the symptoms of osteoradionecrosis?

Symptoms of ORN may occur months to years after radiation. Common symptoms include mouth pain, jaw swelling and difficulty opening the mouth fully (trismus).

How is osteoradionecrosis diagnosed?

ORN can be diagnosed by physical examination and imaging studies (x-ray, CT scan and/or MRI). Sometimes, a surgeon may need to take a sample (biopsy) of the problem area to make a definite diagnosis. Radiation therapy records should be reviewed to determine the location and dose of radiation that was given.

How is osteoradionecrosis treated?

Treatment of ORN is mainly through control of uncomfortable symptoms. Salt-water rinses and light scrubbing of affected tissues may be helpful. Antibiotics may help if a wound becomes infected. Hyperbaric oxygen therapy (oxygen delivered in a pressurized chamber) is sometimes used to increase the amount of oxygen given to the affected tissues and improve the chance of healing.

Is there anything I can do to prevent osteoradionecrosis?

People who received radiotherapy involving the jaw should:

- Tell their dentist that they received radiation. The dentist will then be able to get details about the radiation treatment before doing any tooth extractions that could lead to ORN.
• Have regular dental care and take good care of their teeth and gums, since the risk for cavities is higher in people who received large doses of radiation. The dentist may order daily fluoride treatments to reduce the risk of cavities and the need for extracting teeth in the future. (See related Health Link: Dental Health)

Resources

The Oral Cancer Foundation
3419 Via Lido #205, Newport Beach, CA 92663
Phone 949-723-4400
Web: https://oralcancerfoundation.org/complications/osteoradionecrosis/

Written by Arnold Paulino, MD, MD Anderson Cancer Center, Houston, TX.
Reviewed by Kayla L. Foster, MD, MPH; Sarah Ford, MS, PA-C; and Melissa Acquazzino, MD, MS.

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Peripheral Neuropathy after Cancer Treatment

What is peripheral neuropathy?
Peripheral neuropathy, or damage to the peripheral nerves (nerves outside the brain or spinal cord), is a potential side effect of chemotherapy drugs and may cause the hands or feet to hurt, tingle, and feel numb or weak. Though the discomfort is felt in a muscle or joint, the real damage is to the nerves that control the muscles. Nerves are made up of special cells that carry messages to and from the brain and spinal cord. Damage to the nerve is often caused by a breakdown of the myelin sheath, the coating around nerve fibers that acts as an electrical insulator. There may also be direct damage to the nerve cells from pressure or trauma (for example from a tumor or surgery). Symptoms usually start during treatment and persist and are not late in onset. Symptoms often improve once treatment has stopped, but for some survivors, symptoms may persist for months or years.

Symptoms
- Burning, tingling, or prickling sensation usually in the hands or feet
- Numbness or sensitivity to pain or temperature
- Extreme sensitivity to touch
- Sharp shooting pain
- Poor balance or coordination
- Loss of reflexes
- Muscle weakness
- Noticeable changes in the way you walk

Muscle weakness may begin around the arch of the foot and in the palm of the hand. It may be difficult to grip things or to perform certain tasks or activities such as writing, buttoning clothes, or tying shoes. The muscles that pull the foot up may weaken and the reflexes may be lost, causing the front part of the foot to fall flat to the floor. This may result in poor balance or coordination, especially when tired. There may be a tendency to drag the feet or lift them high to prevent the feet from dragging.

Who is at risk?
People who have received any of the following chemotherapy drugs may be at risk:
- Vincristine
- Vinblastine
- Cisplatin
- Carboplatin

People at highest risk for peripheral neuropathy are those who have received higher doses of these drugs or combinations of these drugs. Other risk factors include surgery, severe weight loss, and diabetes or a pre-existing nerve disease. Prolonged pressure on nerves from artificial limbs, wheelchairs, or crutches can also contribute to nerve damage.
Treatment

Rehabilitation services

Because there is no treatment that can cure or reverse nerve damage, treatment is directed toward symptom management. Physical therapy is often helpful in providing exercises to improve strength, balance, and coordination. Occupational therapy can provide help to improve hand/eye coordination and other skills needed for daily life.

Orthotic devices

Support for feet or ankles can be improved with orthotic devices. Arch supports or splints help prevent the arch from flattening and help improve walking. Splints called ankle-foot-orthoses (AFOs) may be recommended to prevent the ankle from moving too much from side to side and to support the foot when walking.

Pain management

Your healthcare provider may prescribe medication to control the pain, tingling, and burning sensation. The type of medication depends on the frequency and severity of pain. It is also important to know that some medications will have side effects of their own. Elastic stockings, warm packs, or exercise may also help with the discomfort. These measures will not replace medication but may decrease the need for them. They may also assist in improving mobility and independence.

Additional recommendations

- Avoid shoes that are too tight or too loose—Just as shoes that are too tight can cause throbbing, rubbing, and cramping, shoes that are too loose can worsen pain and may not provide enough support for already wobbly feet. Well-fitting sneakers or shoes that provide support but are also flexible are best.
- Be sensitive to temperature—Many people report that neuropathy feels worse in hot weather or when feet are heavily covered, which may prevent adequate air circulation.
- Keep feet uncovered in bed—Bed sheets resting on toes can cause discomfort due to friction between the sheet and toes.
- Massage—Massaging your hands or feet or having someone else massage them can be extremely soothing and relaxing and can increase circulation and boost endorphins (chemicals produced in the body that help control pain).
- Cool soaks—Cool water soaks to painful hands or feet can sometimes dull pain enough to fall asleep or until pain medication has time to work.

For additional information, contact:

The Foundation for Peripheral Neuropathy
485 Half Day Road, Suite 350, Buffalo Grove, IL 60089
Phone: 877-883-9942
Website: www.foundationforpn.org
Health Link
Healthy living after treatment of childhood, adolescent, and young adult cancer

Written by Susan V. Shannon, RN, MSN, CPNP, CPON®, Miller Children’s and Women’s Hospital Long Beach, Long Beach, CA.
Reviewed by Kayla L. Foster, MD, MPH; Beth Fisher, DNP, APRN, CPNP; and Melissa Acquazzino, MD, MS.

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Precocious Puberty after Cancer Treatment

Some people who were treated for cancer during childhood may develop endocrine (hormone) problems as a result of changes in the function of a complex system of glands known as the endocrine system.

What is the endocrine system?
The endocrine system is a group of glands that regulate body functions including growth, puberty, energy level, urine production, and stress response. Glands of the endocrine system include the pituitary, hypothalamus, thyroid, pancreas, adrenal, ovaries, and testes. The hypothalamus and pituitary are sometimes called the “master glands” because they control many of the other glands in the endocrine system. Unfortunately, some treatments given for childhood cancer can damage the endocrine system, resulting in a variety of problems.

What are hormones?
Hormones are chemical messengers that carry information from the endocrine glands through the bloodstream to the body’s cells. The endocrine system makes many hormones (such as growth hormone, sex hormones, adrenal and thyroid hormones) that work together to maintain specific bodily functions.

What is the normal age for puberty to begin?
Puberty normally begins between the ages of 8 and 13 in children born with ovaries, and 9 and 14 in children born with testes. The timing of puberty is influenced by a person’s genetic background, and the onset of puberty at a young age may run in families. Most children born with ovaries begin to develop breasts and then pubic hair at around age 10 or 11. Menstrual periods usually start at around 12 to 13 years of age but may occur earlier or later and still be normal. Children born with testes usually begin to develop enlargement of the testicles and then pubic hair between 11 and 12 years of age.

What is precocious puberty?
Precocious puberty means having signs of puberty (such as pubic hair or breast growth) at an age younger than is normally expected. Most healthcare providers agree that a child born with ovaries has precocious puberty if sexual traits develop earlier than age 8, and a child born with testes has precocious puberty if sexual traits develop prior to age 9.

The early release of hormones that cause precocious puberty also causes a growth spurt, with rapid bone growth. Early bone maturation results in less time for growth, so the child with precocious puberty will have a final adult height that is actually much shorter than expected.

What are the risk factors for developing precocious puberty?
- Radiation to the head or brain, especially doses of 18 Gy (1800 cGy/rads) or higher
- Children with ovaries
- Younger age at the time of cancer treatment
- Being overweight or obese
Why does precocious puberty happen?

The hypothalamus and pituitary gland in the brain may be damaged after radiation treatments. The damage causes them to signal the ovaries or testicles to make sex hormones at an earlier time. In other cases, signs of puberty occur early because of abnormalities in the ovaries, testes or adrenal glands. Tests are done to learn if the cause of precocious puberty is in the brain or in another part of the body.

What screening is recommended?

All childhood cancer survivors should have a yearly comprehensive health check-up including measurement of height and weight, and evaluation of pubertal progress. If there are signs of accelerated growth or precocious puberty, your healthcare provider may order a blood test to check sex hormones produced in the brain (FSH—follicle stimulating hormone; LH—luteinizing hormone), testes (testosterone) or ovaries (estradiol) as well as possibly order an x-ray that measures the developmental age or maturation of bone (bone age). Your healthcare provider should refer you to an endocrinologist (hormone specialist) for further evaluation and treatment.

How is precocious puberty treated?

Endocrinologists may use medications to temporarily stop puberty and to decrease the rate of bone maturation. It is also important to evaluate and manage the psychological effects of beginning puberty too early. Although children with precocious puberty may have a mature physical appearance, their thoughts, emotions, and behaviors may still be that of their actual (chronological) age.

Written by Debra A. Kent, RN, MSN, CPNP, Cincinnati Children's Hospital Medical Center, Cincinnati, OH.
Reviewed by Lillian R. Meacham, Daniel Smith, DNP, FNP; Christine Yun MSN, PNP, CPON®; and Kayla L. Foster, MD, MPH.

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Pulmonary Health after Cancer Treatment

The lungs are very important organs that supply oxygen to the body. Sometimes, treatments given for childhood cancer can cause lung damage. If you received any treatments that may cause lung problems, it is important to learn about the lungs, and what you can do to keep them as healthy as possible.

How the lungs function

The lungs transfer oxygen from the air to the blood, where it is circulated to the body tissues. The lungs also remove carbon dioxide, a waste product made by the body's cells. For oxygen to reach the blood, it must move through tiny air sacs (alveoli) in the lungs and into tiny blood vessels (capillaries) that surround each air sac. When the air sacs become damaged or scarred, there is less area for oxygen to enter the bloodstream, and less oxygen reaches the blood. The person may then need to breathe faster in order to get enough oxygen. This can make the person feel short of breath. Other lung problems can be caused by inflammation (swelling) of the air passages in the lungs or increased mucous production as a result of irritation or infection. Symptoms can include cough, wheezing, chest pain, and shortness of breath.

Am I at risk for lung problems?

If you received any of the following treatments during your cancer therapy, you may be at risk for developing lung problems:

- Bleomycin (See the “Bleomycin Alert” Health Link for more information)
- Carmustine (also known as BCNU)
- Lomustine (also known as CCNU)
- Busulfan
- Radiation to the chest or axilla (underarm area)
- Total body irradiation (TBI)
- Surgery involving the chest or lung (this does NOT include surgery for placement of a central line, such as a Hickman, Broviac, Port-a-Cath or Mediport)
- Chronic graft-versus-host disease (cGVHD) following bone marrow transplant or stem cell transplant from a donor other than yourself (allogeneic transplant)
- Certain chemotherapy drugs known as anthracyclines, such as daunorubicin (Daunomycin®), doxorubicin (Adriamycin®), Mitoxantrone (Novantrone®), idarubicin (Idamycin®) and epirubicin can damage the heart and may contribute to lung problems, especially if given in combination with bleomycin, BCNU, CCNU, and radiation treatment.

Other factors that may increase your risk are:

- Younger age at the time of cancer treatment
- A history of lung infections, asthma or other lung problems
- Tobacco use or exposure to secondhand smoke
- Inhaled drugs, such as smoking marijuana, vaping, or cocaine

What problems can develop?

Problems can include scarring of the lungs (pulmonary fibrosis), repeated lung infections (such as chronic bronchitis, bronchiectasis, or recurrent pneumonia), inflammation of the lung tissues and small airways within the lungs.
(bronchiolitis obliterans), and rupture of the tiny air sacs in the lungs or thickening and blockage of air passages within the lungs (restrictive/obstructive lung disease).

What are the symptoms of lung damage?
Symptoms may include shortness of breath, frequent coughing and/or wheezing, chest pain, and frequent lung infections, such as bronchitis or pneumonia. Becoming easily fatigued or short of breath during mild exercise (exercise intolerance) is sometimes an early symptom of lung damage. If you begin to experience these symptoms, discuss them with your healthcare provider. A consultation with a lung specialist (pulmonologist) may be recommended.

What monitoring is recommended if I have no symptoms?
- A yearly medical check-up is recommended.
- Pulmonary function tests (including DLCO and spirometry) may show lung problems that are not apparent during a check-up. For this reason, it is helpful to have these tests done at least once (at least two years after completing cancer treatment) to find out if there are any problems. Your healthcare provider can decide if further testing is needed based on these results.

Are there any special precautions I should take?
If you have had any of the treatments listed above you should:
- Get the pneumococcal (pneumonia) vaccine.
- Get yearly influenza (flu) vaccines.
- Avoid SCUBA diving, unless you have had a complete check-up and have been advised by a pulmonologist (lung specialist) that diving is safe.

What can I do to prevent lung problems?
- Avoid or quit smoking.
- Avoid second-hand smoke.
- Get regular physical exercise.
- Avoid inhaled drugs, such as marijuana, vaping, or cocaine.
- Avoid breathing toxic fumes from chemicals, solvents, and paints.
- Follow all safety rules in your workplace, such as the use of protective ventilators in some work environments. Report any unsafe working conditions to the Occupational Safety and Health Administration (OSHA).

Where can a smoker find help in order to quit?
Your most important resources for quitting smoking are your family, friends and your healthcare provider. Listed below are some additional sources of education and support:

Telephone Resources
If you don’t have access to the Internet, you can call the following organizations to request educational materials (usually free) about how to quit smoking:
American Cancer Society: 1-800-ACS-2345
American Heart Association: 1-800-AHA-USA1
American Lung Association: 1-800-LUNG-USA
National Cancer Institute: 1-800-QUIT-NOW
On-Line Resources

If you have access to the Internet, you may find the following websites helpful:

Information from the National Institutes of Health to help you quit smoking is available at: www.smokefree.gov

The Center for Disease Control's Tobacco Information and Prevention Source (TIPS) includes guides for quitting the tobacco habit and is available online at: www.cdc.gov/tobacco/campaign/tips

The American Lung Association's free online "Stop Smoking" program is available online: www.lung.org/stop-smoking/

Where can I find more information about how to keep my lungs healthy?

More information about the lungs, and how to keep them healthy, is available at:

The National Heart, Lung and Blood Institute's web site with general information for: www.nhlbi.nih.gov/health-topics/

The National Lung Health Education Program has information about how to keep lungs healthy: www.nlhep.org

Written by Charlene Maxen, RN, CNP, CPON®, Childrens Hospital Medical Center of Akron, Akron, OH; and Sarah E. Friebert, MD, Childrens Hospital Medical Center of Akron, Akron, OH.

Reviewed by Leann Carmichael, DNP, APN, FNP-BC; Melissa Acquazzino, MD, MS; and Kayla L. Foster, MD, MPH.

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Raynaud’s Phenomenon after Cancer Treatment

What is Raynaud’s Phenomenon?

Raynaud’s is a condition that may cause some areas of your body to feel numb and cool in response to cold temperatures or stress. Raynaud’s causes occasional narrowing of blood vessels, limiting blood flow for brief periods of time. This is called a vasospasm. During periods of vasospasm, the skin is deprived of oxygen and may become pale and then turn a bluish color. As the blood vessels relax and blood flow resumes, the skin may become red. The hands and feet are most affected, but Raynaud’s may also involve the nose, lips, cheeks, and earlobes.

Symptoms

- Changes in skin color (often from white to blue to red)
- Changes in skin temperature (affected areas feel cooler)
- Numbness or prickly feeling in the fingers (not thumbs) and toes
- Occasional episodes of pain (described as throbbing) and swelling

What happens during an attack?

For most people, cold temperature or stress triggers an attack. Typically, when the body is exposed to cold, the hands and feet lose heat rapidly. To conserve heat, the body reduces blood flow near the skin surface and moves it deeper in the body. For people with Raynaud’s, this normal response is exaggerated by sudden spasms of the small blood vessels that supply blood to the fingers and toes. This greatly reduces the blood supply to the hands and feet, causing changes in the skin color and temperature. The first sign is often pallor (or whiteness), in response to the spasm. The skin may then appear blue (cyanotic) and feel numb or cold, because of a lack of oxygen-rich blood. Finally, the skin may turn red and become swollen, as the small blood vessels relax and dilate, and blood flow returns. Commonly, throbbing and tingling may occur in the fingers and toes as the attack ends. Raynaud’s attacks can last from seconds to hours.

Who is at risk?

Childhood cancer survivors who received treatment with vinblastine or vincristine sometimes develop Raynaud's.

Prevention

Raynaud’s is usually a chronic condition that you may need to manage for life. Some people may see improvement slowly over several years. Prevention of attacks is key:

- **Dress warmly when outdoors.**
- **Take precautions indoors.** Wear socks. Avoid drafts (i.e. refrigerator or freezer). Wear mittens when handling cold items. Use the air conditioner sparingly. Use insulated drinking glasses.
- **Avoid putting unprotected hands in cold water.**
- **Do not use tobacco or drugs such as cocaine.** Nicotine and cocaine constrict blood vessels and causes the skin temperature to drop, which may lead to an attack.
- **Exercise.** Regular exercise can enhance circulation and help control stress.
- **Manage stress.** Since stress is often a trigger for Raynaud’s attacks, managing stress may help make the attacks shorter and less frequent.
Treatment

Treatment is directed at reducing the number and severity of attacks to prevent tissue damage. People with Raynaud’s phenomenon may try to control their stress and body temperature by using relaxation techniques such as guided imagery and deep breathing exercises. A psychologist may be helpful in designing a biofeedback program that meets your needs.

Medications

Medications that help to dilate blood vessels and promote circulation are sometimes prescribed for management of severe symptoms. Certain prescription medications can sometimes make symptoms worse. These include birth control pills and some heart and blood pressure medicines. If you are taking any of these medications and are having symptoms of Raynaud’s phenomenon, consult with your healthcare provider regarding possible alternatives.

Certain over-the-counter cold or diet pills can make symptoms worse and should be avoided. These include drugs that contain pseudoephedrine (such as Actifed® and Sudafed®).

Biofeedback

Using your mind to control stress and body temperature may help to decrease the severity and frequency of attacks. This may include guided imagery and/or deep breathing exercises. A psychologist may be helpful in designing a biofeedback program that meets your needs.

Written by Susan V. Shannon, RN, MSN, CPNP, CPON®, Miller Children’s and Women’s Hospital Long Beach, Long Beach, CA.
Reviewed by Kayla L. Foster, MD, MPH; Beth Fisher, DNP, APRN, CPNP; and Melissa Acquazzino, MD, MS

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Reducing the Risk of Subsequent Cancers

The risk of cancer increases for everyone as they age. Several studies have shown that as childhood cancer survivors become older, they have a slightly higher risk of developing (a subsequent) cancer compared to people their same age in the general population. Things that can contribute to this risk are the person’s age during cancer therapy, their specific treatment, and their genetic and family history.

Who is at risk for a subsequent cancer?

- **People who received certain chemotherapy drugs.** Some treatments for childhood cancer increase the risk of developing subsequent cancer as survivors age. The risk of developing a leukemia from treatment is increased for people who were treated with high doses of alkylating agents (such as cyclophosphamide or nitrogen mustard), heavy metals (such as cisplatin or carboplatin, epipodophyllotoxins (such as etoposide or teniposide), and anthracycline chemotherapy drugs (such as doxorubicin or daunorubicin), and for those who received an autologous hematopoietic cell transplant. While leukemias from treatment are rare, the risk is highest within the first 10 years after completing cancer treatment and then decreases over time.

- **People who received radiation therapy, especially at a young age.** Radiation therapy given for childhood cancer increases the risk of developing a secondary solid tumor as a person ages. The most common sites include the skin, breast, central nervous system (the brain and spine), thyroid gland, lungs and bones. In contrast to secondary leukemias, secondary solid tumors most commonly occur 10 or more years after treatment. The risk of developing a secondary solid tumor is increased when radiation is delivered at high doses and over large fields to children at a young age.

- **People who have a history of cancer in their family.** Some cancer patients have inherited gene changes (mutations) that increase the chances of getting a second cancer. But overall, these inherited changes are relatively uncommon and account for less than 10 percent of patients with cancer. Doctors suspect the presence of a cancer gene when a family history shows multiple cancers among young people in every generation, or when cancer occurs in both sides of paired organs (such as the eyes, breasts, kidneys, etc.) If you have any questions or think that cancer may “run in your family” you should talk to your healthcare provider. A review of your family medical history will tell whether genetic counseling or testing is needed.

What should you do to decrease your risk and detect a subsequent cancer early?

Reviewing your cancer treatment and family history with your healthcare provider or cancer specialist is important to understand your risk for developing a subsequent cancer. Depending on your treatment and what cancer you may at risk of developing, early or more frequent screening for adult cancers such as color and breast may be recommended to promote early detection and treatment of subsequent cancers, when they are most likely to be cured. Be sure to get all screening tests that are recommended for you.

What monitoring is recommended?

By practicing health maintenance behaviors, you can improve your awareness of changes in your body and increase the likelihood that problems will be detected at earlier stages. **All childhood cancer survivors should have a yearly comprehensive health check-up.** You should also have any cancer screening evaluations appropriate for you based on your age, sex, and treatment history. **Knowing the details of your previous medical history, including exposures to chemotherapy, radiation, and surgery, is vital to your future health.** This information should be available to you or your healthcare provider from the hospital or clinic where you received your cancer therapy. Developing a relationship with a primary care provider who knows your cancer treatment history, risks of late complications, and recommended screening evaluations will improve the chances of catching problems at earlier, more treatable stages.
What symptoms should I be alert for?
Be sure to report any new or persistent symptoms to your healthcare provider promptly.

Symptoms that you should report include:

- Easy bruising or bleeding
- Excessive fatigue
- Changes in moles
- Lumps
- Changes in bowel habits
- Blood in the stools
- Persistent cough or hoarseness
- Bloody sputum
- Discolored areas or sores in the mouth that do not heal
- Persistent headaches
- Paleness of the skin
- Bone pain
- Sores that do not heal
- Difficulty swallowing
- Persistent abdominal pain
- Painful urination or defecation
- Shortness of breath
- Vision changes
- Persistent early morning vomiting

What can I do to lower the risk of getting a second cancer?

Avoid cancer-promoting habits. Survivors should not smoke, vape, or chew tobacco and should avoid exposure to secondhand smoke when at all possible. Because skin cancers are one of the most common second cancers after childhood cancer, especially for those treated with radiation therapy, you should take extra care to protect your skin from sun exposure. This includes regularly using sunscreen with sun protection factor (SPF) of 15 or more, wearing protective clothing, avoiding outdoor activities from 10 am to 2 pm when the sun’s rays are most intense, and not tanning.

Drink alcohol only in moderation. Heavy drinkers, especially those who use tobacco, have a high risk of cancer of the mouth, throat, and esophagus. The risk of breast cancer may be increased in women who drink alcohol. Limiting the use of alcohol can reduce these cancer risks and decrease the chances of other alcohol-related problems, such as liver disease.

Eat healthy. A high intake of dietary fat has been linked to the risk of several common adult cancers. People who eat high-fat diets have a greater risk of getting colon cancer; this may also be true for breast and prostate cancers. High-fat diets are also associated with obesity, heart disease, and other health problems. To reduce all of these risks, daily fat intake should be limited to 30% or less of your total calories.

Dietary fiber is found in whole grains, several types of vegetables, and certain fruits. Fiber reduces the time it takes for waste to pass through the intestinal tract. High-fiber foods also tend to be low in fat.

Eating cruciferous vegetables also helps reduce cancer risk. Cruciferous vegetables include cabbage, Brussel sprouts, broccoli, and cauliflower. Eating these vegetables is thought to protect against cancer by blocking the effects of cancer-causing chemicals in other foods. Cruciferous vegetables are also high in fiber and low in fat. These foods should be included frequently in the diet.

Some chemicals used to preserve foods are cancer-promoting (carcinogenic) in large quantities. Diets high in salt-cured and pickled foods and lunchmeats that contain preservatives like nitrites can increase the risk of cancer in the stomach and esophagus. Some of these foods, especially lunchmeats, are also high in fat. Foods of this kind should be eaten rarely and in small portions.

Diets rich in vitamins C and A have been shown to reduce cancer risk in animal studies. People whose diets are rich in vitamin C appear less likely to get cancer, especially cancer of the stomach and esophagus. The best way to get these
Healthy living after treatment of childhood, adolescent, and young adult cancer

Health Link

nutrients is to eat lots of fresh fruits and vegetables. Citrus fruits, melons, cruciferous vegetables, and greens are high in vitamin C. Good sources of vitamin A are dark green and deep yellow vegetables and certain fruits. If your diet is low in vitamins, a vitamin supplement may help, but avoid extra high doses, since these can cause serious side effects.

Get vaccinated. Certain cancers are associated with preventable infections. Two of the most common are hepatitis B and human papillomavirus virus (HPV). Vaccines are now available to protect against these cancer-causing viruses. Check with your health care provider to determine if either of these vaccines is recommended for you.

Start today by taking time to review your health habits, and practice healthy behaviors that will help keep your risk of second cancers to a minimum.

Written by Melissa M. Hudson, MD, St. Jude Children's Research Hospital, Memphis, TN; and Allison Hester, RN, MSN, CPNP, Arkansas Children's Hospital, Little Rock, AR. Portions adapted from CCSS Newsletter, Fall 1999 and Winter 2001, used with permission.

Reviewed by Smita Bhatia, MD, MPH; Debra L. Friedman, MD; Fran Wiley, RN, MN; and Jill Meredith RN, BSN, OCN®.

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Scoliosis and Kyphosis after Cancer Treatment

The spine, or “backbone” is a group of bones stacked in a straight line down the middle of the back, held together with muscles and ligaments. Treatment for childhood cancer can sometimes result in abnormal curvatures of the spine, known as scoliosis and kyphosis.

What is scoliosis?

Scoliosis is a sideways rotation of the spine. Instead of appearing as a straight line when viewed from the back, the spine appears curved, like the letter “S” or the letter “C.”

Signs of scoliosis may include:
- Uneven shoulder blades
- Uneven hips
- Uneven waist
- “Leaning” of the back to one side
- Head not centered above pelvis
- One leg longer than the other

What is kyphosis?

Kyphosis is an abnormal rounding of the upper part of the back. When viewed from the side, it may appear as if the person is slouching or has a “hump” on the back.

What causes scoliosis?

Scoliosis occurs in many young people, especially teenagers, and is most often “idiopathic,” meaning that the cause is not known. However, people who underwent surgery involving the spine or chest, or those who received radiation to the chest, abdomen, or spine, especially when combined with surgery, are at increased risk for uneven development of the muscles, bones, and soft tissues of the back, resulting in scoliosis.

What causes kyphosis?

Kyphosis sometimes develops from stretching of the spinal ligaments, causing the natural curve of the spine to increase. Kyphosis can also be caused by uneven development of the back muscles and ligaments as a result of radiation.

What are the risk factors for scoliosis after treatment for childhood cancer?

Cancer treatment-related risks include:
- Surgery involving the spine or chest (not including placement of a central line)
- Radiation to the trunk (including any area from the shoulders down to the pelvis), especially if:
  - The dose was 20 Gy (2000 cGy/rads) or higher.
  - Younger age at the time of radiation treatment.
  - The radiation treatment area was to one half of the chest or abdomen.
  - There was also surgery to the chest, abdomen, or spine.
- A tumor in or near the spine
- Individuals with neurofibromatosis are also at increased risk.
How is the diagnosis made?

Signs of scoliosis or kyphosis may be detected on physical examination. X-rays of the spine confirm the diagnosis. Scoliosis is diagnosed when there is at least a 10-degree lateral (side-to-side) curve on the x-ray. Kyphosis is diagnosed when there is at least a 50-degree curve on the x-ray.

What treatment is needed?

Treatment for kyphosis and scoliosis is usually done in stages. The first stage is usually “observation.” During this stage, the curve is closely monitored, especially during periods of rapid growth, such as during puberty. If the curve does not get worse, observation may be all that is necessary.

If the curve progresses, the next step is usually bracing (a plastic body brace worn under the clothing). The goal of bracing is to halt progression or help correct the abnormal spinal curvature.

The final treatment step is surgery. This is done in cases of serious curves that are not manageable with observation or bracing alone.

What monitoring is required?

If scoliosis or kyphosis is suspected, an x-ray of the spine should be obtained. If the curve is more than 10 degrees for scoliosis or more than 50 degrees for kyphosis, a referral is usually made to an orthopedic (bone) specialist.

Written by Wendy Landier, PhD, CPNP, Children’s Hospital of Alabama, Birmingham, AL.
Reviewed by Leeann Carmichael, DNP, APN, FNP-BC; Kayla L. Foster, MD, MPH; and Melissa Acquazzino, MD, MS.
Keeping Your Single Kidney Healthy

The kidneys are vital organs responsible for filtering out waste products from the blood, controlling blood pressure, and stimulating red blood cell production. Treatment for childhood cancer sometimes requires removal of one kidney (nephrectomy). Although you can live a healthy life with only one kidney, it is important that you take steps to protect your remaining kidney to keep it as healthy as possible.

What follow up is recommended?

• **Have a medical check-up at least yearly.** This should include a blood pressure check and urine test.

• **Have a blood test for kidney function (BUN, creatinine) and electrolytes (blood salts and minerals) at your first long-term follow-up visit** (at least 2 years after completing cancer treatment), and then yearly testing to monitor kidney function.

• If you have high blood pressure, protein in the urine, or other signs of worsening kidney problems, you should have an **evaluation by a nephrologist** (kidney specialist).

What can I do to keep my kidney healthy?

• **Drink plenty of water,** especially when playing sports, while out in the sun, and during hot weather.

• **Call your healthcare provider immediately if you have symptoms of a urinary tract infection** (burning when you urinate, urinating more frequently than usual, and/or feeling an urgent sensation to urinate).

• **Check with your healthcare provider or pharmacist before taking any new medicines** (prescription, over-the-counter, or herbal). Be sure that your healthcare provider or pharmacist is aware that you have a single kidney.

• **Use non-steroidal anti-inflammatory drugs with caution.** These include pain or fever medicines (over-the-counter and by prescription) that contain aspirin, ibuprofen, or naproxen. These medications have been known to cause kidney damage (analgesic nephropathy), especially when taken in high doses or over long periods of time (more than 10 days). If you require long-term medications for management of pain, be sure to discuss the alternatives with your healthcare provider, and to choose medications that are safe for your kidneys.

• **Physical activity, including sports, is good for your health.** Kidney injuries from sports are uncommon, and those that do occur rarely cause permanent damage or kidney loss. Overall, most physical activity poses little or no risk to the kidney and is strongly encouraged to maintain good general health. Talk with your health care provider about your kidney health to help you decide whether to participate in certain sports.

• **Serious kidney injuries are rare.** When they do occur, they are most commonly caused by car accidents, all-terrain vehicles, and falls. To protect your single kidney, always wear your seatbelt properly when riding in a vehicle. Lap belts should be worn across the hips, not around the waist. If you are involved in an accident and a kidney injury is suspected, seek medical attention right away.

Are there any other risk factors for kidney problems?

Certain treatments for childhood cancer can sometimes cause kidney problems. These include radiation to the kidney, chemotherapy that can affect the kidney (cisplatin, carboplatin, and/or ifosfamide), other medications that can affect the kidney (certain antibiotics or medications used for treatment of graft versus host disease) or hematopoietic cell transplant (HCT). In addition, other risk factors that may increase the chance of kidney problems include medical
conditions, such as high blood pressure or diabetes, urinary tract problems such as frequent urinary infections or back-flow of urine into the kidney (reflux), or bladder removal (cystectomy). If you have any of these risk factors, please read the related Health Link: Kidney Health.

Written by Wendy Landier, PhD, CPNP, Children’s Hospital of Alabama, Birmingham, AL.
Revised by Maki Okada, CPNP, FNP-BC, CPON®, Miller Children’s and Women’s Hospital Long Beach, Long Beach, CA.
Reviewed by Kayla L. Foster, MD, MPH; and Melissa Acquazzino, MD, MS.

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Skin Health after Cancer Treatment

The skin is the largest organ in the body and it is the body’s first line of defense against outside invaders. It also keeps the body temperature normal and stores water, fat, and vitamin D. This important organ requires care and monitoring. Treatment for childhood cancer sometimes causes damage to the skin.

Who is at risk?

- Survivors who received radiation to any part of the body, including total body irradiation (TBI).
- Survivors with chronic graft-versus-host disease (GVHD) following bone marrow or stem cell transplant.

What problems can occur?

The following are possible long-term skin effects that may be seen after cancer therapy.

Telangiectasias

These small blood vessels on the surface of the skin are commonly referred to as “spider veins,” and in the cancer survivor they can occur in the field of radiation. Telangiectasias are caused by changes to the lining of blood vessels resulting from radiation. These do not typically cause any health problems and require no specific care.

Fibrosis

Fibrosis is caused by scarring of the lining of blood vessels, resulting in a “woody” skin texture. The skin may not be as flexible in the fibrotic area and may be more easily injured. Care of fibrotic skin should include routine moisturizing and avoidance of trauma. Because the blood supply is not as good in fibrotic skin, healing may be slow after cuts and scrapes, so avoiding these when at all possible is important.

Scleroderma

People who have chronic GVHD following bone marrow or stem cell transplant sometimes develop scleroderma. In this condition, the donor white blood cells do not recognize the patient's skin cells as their own, and begin to attack them. This causes the skin to become stiff and inflexible. This may happen anywhere on the body, but if it happens to the skin around joints, it can make the joints less mobile. The therapy for scleroderma is treatment of the underlying GVHD. It is also important to avoid injury to this skin, since healing time will be prolonged.

Vitiligo

Vitiligo is loss of pigment on patches of the skin. This can occur after bone marrow or stem cell transplant from a person other than yourself (allogeneic transplant) and may be due to GVHD or other autoimmune reactions seen after transplant. In this situation, the white blood cells do not recognize certain normal skin cells (melanocytes) and so they attack and destroy them. Melanocytes are the cells in the body that control skin color. Without melanocytes, the skin has a milky white appearance. Vitiligo usually occurs only in patches. The therapy for vitiligo is treatment of the underlying GVHD or autoimmune process. Even the skin because the damage to the melanocytes may be permanent. While all skin should be protected from sun, skin that has lost its pigment is very vulnerable, and sunscreen should always be applied to these areas before going outdoors.

Hyperpigmentation

Hyperpigmentation is a darkening of the skin that may occur after radiation or some types of chemotherapy. The chemotherapy agents most commonly associated with hyperpigmentation include bleomycin, busulfan,
cyclophosphamide, daunorubicin, 5-flourouracil, hydroxyurea and methotrexate. The dark discoloration can occur on the skin or nails. There is no specific treatment for hyperpigmentation associated with cancer therapy, but it usually continues to fade over time without any treatment.

**Skin Cancers**

People who have received radiation are at risk for developing skin cancers, usually in the radiation field. Other risk factors include light skin color, chronic sun exposure, severe sunburn, atypical moles or a large number of moles on the body, and a family history of skin cancer. The good news about skin cancer is that if it is diagnosed early, it is usually very treatable. There are three major forms of skin cancer:

- **Basal cell carcinoma** (BCC) is the most frequent form of skin cancer. BCC usually appears as a rough, raised, area of skin. As the BCC progresses, it may become an ulcer or sore that does not heal. BCC can occur anywhere on the skin, but is seen most frequently in areas of sun and/or radiation exposure. Protecting your skin from the sun is the most important thing you can do to avoid developing BCC. Treatment for BCC is surgical removal of the affected skin. BCC can spread to surrounding tissues but does not usually spread throughout the body and is not usually life threatening.

- **Squamous cell carcinoma** (SCC) is another form of skin cancer that can develop from exposure to sun or radiation. Its appearance is similar to BCC, usually an ulcerated sore that does not heal. SCC can be more aggressive than BCC and can spread more readily to surrounding tissues and even to other parts of the body. With early surgical treatment SCC is usually curable, so it is important to report any suspicious sores to your healthcare provider right away.

- **Melanoma** is a much more serious form of skin cancer. Unlike BCC, left untreated it can spread to other organs and can be lethal. Melanoma often arises from moles. The key to successful treatment of melanoma is early diagnosis. Moles should be monitored for changes. Monitoring of moles can be remembered using the “ABCD” warning signs:
  
  A is for Asymmetry (one half of the mole looks different than the other half)
  B is for Border (moles that have an irregular, scalloped or poorly defined border)
  C is for Color (variations in color from one area of the mole to another, such as different shades of tan and brown or black, or colors such as white, red, or blue within a mole)
  D is for Diameter (moles larger than 6 millimeters – about the diameter of a pencil eraser – should be evaluated).

If you notice any of the “ABCD” warning signs, have your healthcare provider check the mole. Moles that have any of these warning signs usually need to be removed.

**What monitoring is needed?**

If you have any of the following risk factors, you should routinely check your skin for changes, and have a thorough skin examination by a healthcare provider at least once a year:

- You received radiation to any area, including total body irradiation (TBI)
- You underwent a hematopoietic cell transplant
- You have ever had skin cancer or melanoma, or you have a family history of skin cancer or melanoma
- You have “dysplastic” (atypical) moles
- You had a severe sunburn at a young age
What can I do to keep my skin healthy?

The most important thing to remember in caring for your skin is to protect it from the sun. Here are some things you can do:

- Wear protective clothing or sunscreen at all times when your skin is exposed to the sun, even on cloudy or hazy days. The American Cancer Society recommends a sunscreen with an SPF (sun protection factor) of 15 or higher.
- Sand, snow, concrete, water and high altitudes all increase the risk of sun damage—take extra caution to protect your skin in these environments.
- Do not attempt to tan your skin—avoid tanning booths.
- Avoid outdoor activities from 10 am to 2 pm when the sun’s rays are most intense (11 am to 3 pm during daylight savings time). Plan outdoor activities in the early morning or late afternoon hours.
- Reapply sunscreen frequently or use a water-resistant sunscreen when swimming or perspiring heavily. This will not only help to protect you from developing skin problems but will also help you to maintain a youthful appearance.

If you have any questions or concerns about your skin, contact your healthcare provider. Take good care of your skin and it will take care of you!

Written by Kathy J. Ruble, RN, MSN, CPNP, AOCN®, Johns Hopkins University/Sidney Kimmel Cancer Center, Baltimore, MD.
Reviewed by Amelia DeRosa RN, BSN, CPON®; Kayla L. Foster, MD, MPH; and Christine Yun MSN, PNP, CPON®.

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Precautions for People Without a Functioning Spleen

The spleen is an organ about the size of a person’s fist that is located in the upper left side of the abdomen under the rib cage. The spleen helps the body fight infection by filtering the blood. Individuals who lack a functioning spleen are at increased risk for developing serious infections by specific bacteria (Streptococcus pneumoniae, Haemophilus influenzae, and Neisseria meningitidis) and some parasites transmitted by insects (malaria and Babesia).

Who is at risk for a non-functioning spleen and infections?

- Individuals who had their spleen surgically removed (splenectomy)
- Individuals who received a high dose of radiation (at least 40 Gy/4000 cGy) to the abdomen
- Individuals with active chronic graft-versus-host disease following a bone marrow or stem cell transplant

What are the signs of infection and when should I seek treatment?

- Fever is an important sign of infection. A fever is a temperature at or above 101°F (38.3°C).
  - If you have a fever and a non-functional spleen (or have undergone splenectomy), you should seek urgent medical attention. Fever may be a sign of a serious bacterial infection and requires blood work and the administration of antibiotics to determine if a bacterial infection is present.
- Other symptoms of infection include unusual tiredness, muscle aches, chills, headache, vomiting, diarrhea, and abdominal pain. These symptoms can be warning signs of infection even without a fever. Take your temperature regularly any time you develop symptoms of infection or appear ill.
- If you are having symptoms that you are not sure are related to an infection, contact your healthcare provider for further recommendations.

Is there anything I can do to decrease the risk of infection?

- Vaccinations against haemophilus influenza (HiB), pneumococcus (PCV and PPSV), meningococcus (Men-ACWY, MenB), and influenza can decrease the risk of a serious infection.
- In some cases your health care provider may recommend antibiotics to prevent an infection. These antibiotics are called “prophylactic” antibiotics and are taken daily. Antibiotics can decrease the risk of infection in younger children or individuals who are at higher risk of infection.

What vaccines should an individual receive if they have a non-functioning spleen?

- In addition to the recommended vaccinations for all children and adolescents, individuals with a non-functioning spleen should receive the following immunizations:
  - Due to the increased risk of pneumococcal infections, individuals over 2 years of age should receive the PPSV23 vaccine at least 8 weeks after their last dose of routine pneumococcal vaccination and then revaccinate with PPSV23 vaccine 5 years after the first dose.
  - Vaccination to meningococcus is recommended for individuals without a functional spleen as early as 2 months of age. The number and timing of doses is dependent on the type of vaccine received and age at initiation. Vaccination for meningococcal serogroup B is also recommended above 10 years of age.
- Vaccines can be given by your primary care provider.
- Some primary care providers may not be familiar with your specific catch up or booster vaccine schedule. Make sure to give your primary care provider your cancer team’s contact information for questions.
Other precautions

Individuals with a non-functioning spleen are at increased risk for other infections:

- **Malaria:** If you travel to countries where malaria is common, take special precautions to avoid getting malaria. Ask your healthcare provider for anti-malarial medications before travel to infested areas. During travel, use insect repellants and other protective measures, such as netting and protective clothing.

- **Animal/Human Bites:** Animal and human bites can result in serious bacterial infections in individuals with a nonfunctioning spleen. If you receive a bite that breaks the skin, seek immediate medical attention for treatment with antibiotics.

- **Ticks:** People without a nonfunctioning spleen are at increased risk for an infection caused by Babesia, a parasite transmitted by deer ticks. Deer ticks are most commonly found in the northeastern United States. You should wear protective clothing and use insect repellants when going outdoors in tick-infested areas. If you receive a tick bite while in an area infested with Babesia, you should remove the tick and talk to your healthcare provider about what to do.

**How will my healthcare providers know about my non-functioning spleen?**

- Be sure to tell your doctors, dentists, and other healthcare providers that you do not have a functioning spleen.
- You should wear a medical alert emblem (bracelet or necklace) in case of a medical emergency.
- Consider carrying a wallet card, with guidelines for healthcare professionals regarding the management of fever in people without a functioning spleen.

Written by S. Ashley Speckhart, MD, MPH, Maine Children’s Cancer Program, Teresa Sweeney, RN, MSN, CPNP, St. Jude Children’s Research Hospital, Memphis, TN; and Wendy Landier, PhD, CPNP, Children’s Hospital of Alabama, Birmingham, AL.

Reviewed by Kayla L. Foster, MD, MPH and Melissa Acquazzino, MD, MS.

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MEDICAL ALERT: Asplenic Patient

This patient is asplenic and at risk for potentially fatal, overwhelming infections. Immediate medical attention is required for fever of $\geq 101^\circ F$ ($38.3^\circ C$) or other signs of serious illness. Suggested management includes:

1. Physical exam, CBC and blood culture.

2. Administration of a long-acting, broad-spectrum parenteral antibiotic (e.g., ceftriaxone) accompanied by close clinical monitoring while awaiting blood culture results.

3. Hospitalization and broadening of antimicrobial coverage (e.g., addition of vancomycin) may be necessary under certain circumstances, such as the presence of marked leukocytosis, neutropenia, or significant change from baseline CBC; toxic clinical appearance; fever $\geq 104^\circ F$; meningitis, pneumonia, or other serious focus of infection; signs of septic shock; or previous history of serious infection.
Thyroid Disease after Cancer Treatment

Some people who were treated for cancer during childhood may develop endocrine (hormone) problems as a result of changes in the function of a complex system of glands known as the endocrine system.

What is the endocrine system?
The endocrine system is a group of glands that regulate many body functions including growth, puberty, energy level, urine production, and stress response. Glands of the endocrine system include the pituitary, hypothalamus, thyroid, pancreas, adrenals, ovaries, and testes. The hypothalamus and pituitary are sometimes called the “master glands” because they control many of the other glands in the endocrine system. Unfortunately, some treatments given for childhood cancer can damage the endocrine system, resulting in a variety of problems.

What are hormones?
Hormones are chemical messengers that carry information from the endocrine glands through the bloodstream to the body’s cells. The endocrine system makes many hormones (such as growth hormone, sex hormones, adrenal and thyroid hormones) that work together to maintain specific bodily functions.

What is the thyroid gland?
The thyroid gland is located in the lower part of the neck in front of the throat. The gland makes two hormones, thyroxine (T4) and triiodothyronine (T3), that play an important role in growth and brain development and help to regulate the body’s metabolism. The thyroid gland is controlled by the pituitary, a gland in the brain that makes thyroid stimulating hormone (TSH). TSH is released from the pituitary in response to the levels of T4 and T3 in the blood. If the levels are low, the pituitary makes more TSH to signal the thyroid to increase the production of thyroid hormones. If T4 and T3 are high, the pituitary makes less TSH to signal the thyroid gland to slow down production.
What are the possible late effects?

Damage to the thyroid gland after childhood cancer can be caused by surgical removal of all or part of the thyroid gland, treatment with tyrosine kinase inhibitors, high doses of MIBG (sometimes used in the treatment of neuroblastoma), and/or treatment with radiation to the head, brain or neck. This damage is usually very easy to treat, although it may not show up for years after treatment. Regular check-ups may help find thyroid problems early so that the proper treatment can be started. Several different types of thyroid problems may develop including an underactive thyroid (hypothyroidism), overactive thyroid (hyperthyroidism), and growths on the thyroid that may be benign (nodules) or malignant (cancer).

What is hypothyroidism?

Hypothyroidism occurs when the thyroid gland is not active enough. This is the most common thyroid problem seen in childhood cancer survivors. This can occur if the brain doesn’t make TSH to properly signal the thyroid gland to work or if the thyroid gland is damaged or has been removed and cannot make enough thyroid hormone. When the thyroid gland is underactive, thyroid hormone levels are low and the body’s metabolism slows down.

Signs and symptoms of hypothyroidism may include:

- Slowing of normal growth
- Weight gain
- Dry skin
- Brittle hair/hair loss
- Constipation
- Weakness
- High cholesterol level
- Feeling tired and listless
- Hoarse voice
- Mood changes
- Feeling cold all of the time
- Difficulty concentrating
- Delayed puberty
- Irregular menstrual cycles
- Muscle and joint aches
- Poor exercise tolerance
- Puffiness around the eyes
- Low heart rate or blood pressure

What is hyperthyroidism?

Hyperthyroidism occurs when the thyroid gland is too active. In this condition thyroid hormone levels are high and the body’s metabolism speeds up.

Signs and symptoms of hyperthyroidism may include:

- Jitteriness
- Anxiety
- Problems concentrating
- Feeling tired
- Muscle weakness
- Tremors
- Fast or irregular heartbeat
- Increased sweating
- Feeling hot all of the time
- Diarrhea
- Weight loss
- Irregular menstrual periods
- Bulging or protruding eyes
- Neck tenderness and swelling
- Poor exercise tolerance
What are thyroid nodules and thyroid cancer?

**Thyroid nodules and thyroid cancer** are growths that usually begin as slow-growing, painless lumps in the neck. Most thyroid growths do not cause any symptoms. They may occur many years after cancer treatment.

Who is at risk for thyroid problems?

People who received radiation that may have affected the thyroid gland directly are at risk for primary hypothyroidism, compensated hypothyroidism, thyroid nodules, and/or thyroid cancer. People who received radiation to the thyroid gland in high doses, especially more than 30 Gy or 3000 cGy/rads, are also at risk for hyperthyroidism. The following radiation fields have the potential to affect the thyroid gland directly:

- Head/brain
- Neck
- Spine (cervical/neck portion)
- Total body irradiation (TBI)

In addition, people who received radioiodine therapy (I-131), high doses of MIBG, or tyrosine kinase inhibitors or had their thyroid gland partially or completely removed surgically (thyroidectomy) are also at risk for hypothyroidism.

People who received high doses of radiation (30 Gy or 3000 cGy/rads or higher) to the head/brain are at risk for hypothyroidism.

Other factors that have been shown to increase the risk of thyroid problems after childhood cancer include being:

- Treated with higher radiation doses
- Treated at a young age
- Born with ovaries

Thyroid problems may occur soon after radiation, but generally do not occur until several years later. If treated promptly, thyroid problems are easily managed.

What screening is recommended?

All childhood cancer survivors should have a yearly comprehensive health check-up including measurement of height and weight, examination of the thyroid gland, and blood tests to measure the levels of TSH and T4. During periods of rapid growth, healthcare providers may recommend more frequent monitoring of thyroid levels.

Survivors at risk for thyroid problems who are planning to become pregnant should have their thyroid levels checked before attempting pregnancy. It is important to do this before becoming pregnant, as there is a higher chance of having babies with developmental problems if untreated thyroid disease is present. It is also important to monitor thyroid levels periodically during pregnancy.

How are thyroid problems treated?

If problems with thyroid levels are identified, you may be referred to an endocrinologist (hormone specialist) for evaluation and to discuss treatment, such as medication, if needed. If a lump is detected on the thyroid, you may also be referred to a surgeon or other specialist for further evaluation and management.
Health Link

Written by Melissa M. Hudson, MD, St. Jude Children’s Research Hospital, Memphis, TN; and Wendy Landier, PhD, CPNP, Children’s Hospital of Alabama, Birmingham, AL.

Reviewed by Charles A. Sklar, MD; Debra L. Friedman, MD, Julie Blatt, MD; Joan Darling, PhD; and Susan F. Shaw, RN, MS, PNP.

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Vaccines after Treatment for Cancer Survivors Treated with Chemotherapy and/or Radiation (Non-HCT)

Vaccines are an important tool to protect against infections and prevent infection-related deaths. Vaccines help the immune system recognize and fight serious infections. Most vaccines are given during childhood and provide protection against infection into adulthood. After cancer treatment, survivors may need to catch up on recommended childhood vaccines that were missed during treatment or get booster vaccines to protect against vaccine-preventable infections.

Sometimes recommended vaccine doses are delayed during cancer treatment. After completing treatment for cancer, it is important to make a plan to catch up on missed vaccines, even if delayed by months or years.

For childhood cancer survivors who have not missed any vaccinations during treatment, an extra dose of a vaccine (a “booster” vaccine) may be recommended to strengthen the immune system against vaccine-preventable infections.

**Who should get booster vaccines?**
- All children and adolescents who have received chemotherapy and/or abdominal radiation should discuss vaccines with their cancer team and primary care provider.
- Your child’s provider may recommend boosters with or without checking antibody levels (also called titers) that confirms loss of immunity before vaccines are given.

**Why should childhood cancer survivors receive vaccines or booster doses?**
- Vaccines and booster shots after cancer treatment protect from infection and infection-related death.

**How do vaccines and booster doses work?**
- Vaccines protect you from infection by creating an immune response which makes antibodies and memory cells, your body’s tools to effectively fight off viruses and bacteria. These antibodies and cells remain in the body for many years and protect against infections into adulthood.
- A booster vaccine is an additional dose of a vaccine. Booster vaccines “boost” the number of antibodies and cells to fight an infection that you have been vaccinated for in the past and provides greater protection against infection.

**What are the risks of booster vaccines?**
- Booster vaccines are considered very safe.
- Common side effects include swelling and/or discomfort at the vaccination site and low-grade fever.
- Serious reactions are rare. If you have concerns about vaccine safety, more information can be found at the Centers for Disease Control website: [https://www.cdc.gov/vaccines/schedules/index.html](https://www.cdc.gov/vaccines/schedules/index.html)
Health Link
Healthy living after treatment of childhood, adolescent, and young adult cancer

Where should my child go to receive vaccines?

- Vaccines can be given by your primary care provider.
- Some primary care providers may not be familiar with your specific catch up or booster vaccine schedule. Make sure to give your primary care provider your cancer team’s contact information for questions.

When should my child get vaccines after cancer treatment?

- Most vaccines are delayed at least six months after cancer treatment ends.
- The timing of vaccination should be given to you by your cancer team. Certain treatments such as steroids, IVIG, and immune suppression drugs may affect your vaccine schedule.

Are there any vaccines that protect against cancer?

- Yes!
  - The Hepatitis B virus vaccine protects against liver cancer caused by the Hepatitis B virus.
  - The human papilloma virus (HPV) vaccine protects against a virus known to cause many different types of cancer (head and neck cancers, cervical cancer, vaginal cancer, anal cancer, penile cancer, and vulvar cancer).
  - Survivors of childhood cancer are at increased risk of HPV-related cancers and should receive a three-dose series of the vaccination, regardless of the age at which the first vaccine was given.

Written by S. Ashley Speckhart, MD, MPH, Maine Children’s Cancer Program, Scarborough, ME; and Kayla L. Foster, MD, MPH, Baylor College of Medicine/Texas Children’s Hospital, Houston, TX.

Reviewed by Melissa Acquazzino, MD, MS; Greg Guilcher, MD; Hesham Eissa, MD; Linda Rivard, RN, BSN, CPON®, Daniel Smith DNP, FNP; and Christine Yun MSN, PNP, CPON®.

Additional health information for childhood cancer survivors is available at [www.survivorshipguidelines.org](http://www.survivorshipguidelines.org)

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Vaccines after Treatment for Cancer Survivors Treated with Hematopoietic Cell Transplant (HCT)

Vaccines are an important tool to protect against infections and prevent infection-related deaths. Vaccines help the immune system recognize and fight serious infections. Most vaccines are given during childhood and provide protection against infection into adulthood. After cancer treatment, survivors may need to catch up on recommended childhood vaccines that were missed during treatment or get booster vaccines to protect against vaccine-preventable infections.

Who should be revaccinated?

- All individuals who received either an allogeneic HCT (transplant from a donor) or an autologous HCT (transplant with your own cells) should repeat the vaccination series for most vaccines.
- An individualized plan for you or your child should be discussed with your transplant team.

Why should individuals who received a hematopoietic transplant be revaccinated?

- Infection is one of the most common causes of illness and death following a transplant.
- Revaccination after a hematopoietic transplant can protect from infection and infection-related death.

How do vaccines work?

- Vaccines protect you from infection by creating an immune response which makes antibodies and memory cells, your body’s tools to effectively fight off viruses and bacteria. These antibodies and cells remain in the body for many years and protect against infections into adulthood.

What are the risks of revaccination?

- Vaccines and revaccination are considered very safe.
- Common side effects include swelling and/or discomfort at the vaccination site and low-grade fever.
- Serious reactions are rare. If you have concerns about vaccine safety, more information can be found at the Centers for Disease Control website: https://www.cdc.gov/vaccines/schedules/index.html

Where should my child go to receive vaccines?

- Your transplant team will provide you and your primary care provider a list of the recommended vaccinations.
- Vaccines can be given by your transplant team or your primary care provider.

When should my child get vaccines after treatment?

- The timing of vaccination should be given to you by your transplant team. Certain treatments such as steroids, IVIG, and immune suppression drugs or conditions such as graft vs. host disease may affect your vaccine schedule.
- Most vaccines are delayed for 6 months following the date of transplant. Some vaccines called live vaccines are delayed even longer (up to two years after transplant) and should only be started after confirming with the primary transplant team.
Health Link

Healthy living after treatment of childhood, adolescent, and young adult cancer

Are there any vaccines that protect against cancer?

- The Hepatitis B virus vaccine protects against liver cancer caused by the Hepatitis B virus.
- The human papilloma virus (HPV) vaccine protects against a virus known to cause many different types of cancer (head and neck cancers, cervical cancer, vaginal cancer, anal cancer, penile cancer, and vulvar cancer).
  * Survivors of childhood cancer are at increased risk of HPV-related cancers and should receive a three-dose series of the vaccination, regardless of the age at which the first vaccine was given.

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