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**Hematopoietic Cell Transplant**

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COG Long-Term Follow-Up Guidelines Content Outline

Long-Term Follow-Up Guidelines

- Abstract
- Disclaimer
- Contributors
  - Panel of Experts
  - Task Force Membership
  - Health Link Authors and Reviewers
  - Guideline Development Task Force—Initial Versions
  - Reviewers – Initial Versions

- Introductory Material
  - Introduction
  - Explanation of Scoring
  - Instructions for Use
  - New to this Version of the COG LTFU Guidelines
  - Long-Term Follow-Up Guidelines

Appendix I: Materials for Clinical Application of LTFU Guidelines

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  - Abbreviations
  - Chemotherapy Agents
  - Radiation Fields Defined

- Summary of Cancer Treatment
  - Summary of Cancer Treatment—Introduction
  - Template for Summary of Cancer Treatment (Abbreviated)
  - Template for Summary of Cancer Treatment (Comprehensive)
  - Key for Completing Summary of Cancer Treatment (Comprehensive Version)

- Tools for Guideline Application
  - Patient-Specific Guideline Identification Tool
  - Health Link Index by Guideline Section Number

Appendix II: Health Links (Patient Education Materials)

- Health Links Index by Title
- Health Links

Suggested Citations for COG Long-Term Follow-Up Guidelines

Guidelines

Guidelines Methodology

Health Links Background and Application
Abstract – Version 4.0

The Children’s Oncology Group Long-Term Follow-Up Guidelines for Survivors of Childhood, Adolescent, and Young Adult Cancers

Release date: October 2013

Status: Updated from Version 3.0 incorporating modifications based on recommendations from the Children’s Oncology Group’s Long-Term Follow-Up Guideline Core Committee and its ten 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 patients 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 4.0 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.
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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Long-Term Follow-Up Guidelines 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 4.0 of the Children’s Oncology Group Long-Term Follow-Up Guidelines for Survivors of Childhood, Adolescent, and Young Adult Cancers:

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

Wendy Landier, PhD, RN, CPNP, CPON®
Co-Chair—COG LTFU Guidelines Core Committee
Clinical Director, Center for Cancer Survivorship
City of Hope Comprehensive Cancer Center
Duarte, CA

Louis S. Constine, MD, FASTRO
Co-Chair—COG LTFU Guidelines Core Committee
Professor of Radiation Oncology and Pediatrics
Vice Chair, Department of Radiation Oncology
James P. Wilmot Cancer Center
University of Rochester Medical Center
Rochester, NY

Smita Bhatia, MD, MPH
Co-Chair—COG LTFU Guidelines Core Committee
Professor and Chair, Department of Population Sciences
City of Hope National Medical Center
Associate Director, Population Research
City of Hope Comprehensive Cancer Center
Duarte, CA

Saro Armenian, DO, MPH
Chair, COG Survivorship and Outcomes Committee
Assistant Professor, Department of Population Sciences
City of Hope Comprehensive Cancer Center
Duarte, CA

F. Daniel Armstrong, PhD
Professor and Associate Chair, Department of Pediatrics
Director, Mailman Center for Child Development
University of Miami School of Medicine
Miami, FL

K. Scott Baker, MD, MS
Professor of Pediatrics
Director, Pediatric Blood and Marrow Transplant Program
and Cancer Survivor Program
Seattle Children’s Hospital
Seattle, WA

Joan Darling, PhD
COG Patient Advocacy Committee Representative
Lincoln, NE

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

Nina Kadan-Lottick, MD, MSPH
Associate Professor
Department of Pediatrics
Yale University School of Medicine
New Haven, CT

Matthew J. Krasin, MD
Associate Member
Radiological Sciences
St. Jude Children’s Research Hospital
Memphis, TN

Marcia Leonard, RN, PNP
Coordinator, Late Effects Program
C. S. Mott Children’s Hospital
University of Michigan
Ann Arbor, MI

Anna T. Meadows, MD
Professor of Pediatrics
University of Pennsylvania School of Medicine
Director, Follow-Up Program
The Children’s Hospital of Philadelphia
Philadelphia, PA

Paul Nathan, MD, MSc, FRCP(C)
Director, Aftercare Program
Hematology/Oncology
The Hospital for Sick Children
Toronto, Ontario, Canada

Joseph P. Neglia, MD, MPH
Professor of Pediatrics
Division of Hematology, Oncology, Blood and Marrow Transplantation
Department Head, Pediatrics
University of Minnesota School of Medicine
Minneapolis, MN

Leslie L. Robison, PhD
Chair, Epidemiology and Cancer Control
St. Jude Children’s Research Hospital
Memphis, TN

Charles A. Sklar, MD
Director, Long-Term Follow-Up Program
Memorial Sloan Kettering Cancer Center
New York, NY

Julia Steinberger, MD, MS
Professor, Division of Cardiology
Department of Pediatrics
University of Minnesota School of Medicine
Minneapolis, MN
# Guidelines Task Force Membership 2009–2012

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<td>M. Jacob Adams, MD, MPH</td>
<td>University of Rochester</td>
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<td>Saro Armenian, DO, MPH, Chair</td>
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<td>Pediatric oncology</td>
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<td>Gregory Aune, MD, PhD</td>
<td>University of Texas Health Science Center, San Antonio</td>
<td>Pediatric oncology</td>
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<td>Brigham and Women’s Hospital</td>
<td>Medical oncology</td>
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<td>Robert Goldsby, MD</td>
<td>UCSF School of Medicine</td>
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<td>Hiroto Inaba, MD</td>
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<td>Charlene Maxen, RN, CNP, CPON</td>
<td>Children’s Hospital Medical Center of Akron</td>
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<td>Sadhna Shankar, MD, MPH, Chair</td>
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## Task Force Membership 2009–2012 (cont)

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<td>Ann &amp; Robert H. Lurie Children’s Hospital of Chicago</td>
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<td>Lisa Kenney, MD, <em>Silo Leader</em></td>
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<td>St. Jude Children’s Research Hospital</td>
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<td>Soraya Beiraghi, DDS</td>
<td>University of Minnesota</td>
<td>Pediatric dentistry</td>
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<td><strong>Hepatic</strong></td>
<td>Sharon Castellino, MD, MSH, <em>Chair</em></td>
<td>Wake Forest University Health Sciences</td>
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<td>Joan Darling, PhD</td>
<td>Children’s Oncology Group</td>
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<td>Cherry Estilo, DMD</td>
<td>Memorial Sloan-Kettering Cancer Center</td>
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<td>Kevin McMullen, MD</td>
<td>Riley Hospital for Children</td>
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<td>Cesar Migueiei, DDS, DS, MS, PhD</td>
<td>University of Tennessee Health Science Center</td>
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<td>Andrew Muir, MD, MSH</td>
<td>Duke University Medical Center</td>
<td>Pediatric Gastroenterology</td>
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<td>Man Wai Ng, DDS, MPH</td>
<td>Children’s Hospital Boston</td>
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<td>Melissa Rayburg Jefferson, MD</td>
<td>Children’s Mercy Hospitals and Clinics</td>
<td>Pediatric oncology, Epidemiology</td>
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<td>Kathy Rube, PhD, RN, CPNP</td>
<td>Johns Hopkins University</td>
<td>Pediatric oncology, Epidemiology</td>
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<td>Marie-Ellen Sarvida, MD</td>
<td>Loyola University Medical Center</td>
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<td>Sheila Shope, RN, FNP</td>
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# Task Force Membership 2009–2012 (cont)

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<td>Rajaram Nagarajan, MD, MPH</td>
<td>Cincinnati Children’s Hospital Medical Center</td>
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<td>St. Jude Children’s Research Hospital</td>
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<td>Children’s Hospitals and Clinics of Minnesota</td>
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<td>Children’s Healthcare of Atlanta/Emory University</td>
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<td>Kimberley Dilley, MD, MPH</td>
<td>Ann &amp; Robert H. Lurie Children's Hospital of Chicago</td>
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<td>Laura Greve, PsyD</td>
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<td>Tracy Howk, MSW</td>
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<td>Chad Jacobsen, MD</td>
<td>Carolinas Medical Center/Levine Cancer Institute</td>
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<td>Nina-Kadan Lottick, MD, Chair</td>
<td>Yale University</td>
<td>Pediatric oncology</td>
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<td>James Klosky, PhD, Chair, Silo Leader</td>
<td>St. Jude Children's Research Hospital</td>
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<td>Kevin Krull, PhD, Chair, Silo Leader</td>
<td>St. Jude Children's Research Hospital</td>
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<td>Alicia Kunin-Batson, PhD, Silo Leader</td>
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<td>Jennifer Levine, MD</td>
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<td>Children's Healthcare of Atlanta/Emory University</td>
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<td>Sunila Patel, PhD</td>
<td>City of Hope</td>
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<td>Sheila Judge Santacroce, PhD, APRN, CPNP</td>
<td>Yale University</td>
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<td>Sally Wiard, MSW</td>
<td>University of Texas Health Science Center, San Antonio</td>
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<td>Joann Ater, MD</td>
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<td>Jean Belasco, MD</td>
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<td>Gregory Wheeler, MD</td>
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<td>Kristin Knight, MS, CCC-A</td>
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<td>Teresa Sweeney, RN, MSN, CPNP</td>
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</tr>
</tbody>
</table>
Long-Term Follow-Up Guidelines Health Link Authors

The following individuals participated in writing the patient education materials (Health Links) for the *Children's Oncology Group Long-Term Follow-Up Guidelines for Survivors of Childhood, Adolescent, and Young Adult Cancers*:

Thomas R. Baker, CP  
CFI Prosthetics and Orthotics  
Memphis, TN

Julie Blatt, MD  
Division of Pediatric Hematology-Oncology  
University of North Carolina  
Chapel Hill, NC

Sharon M. Castellino, MD  
Department of Pediatrics, Hematology/Oncology  
Wake Forest University Health Sciences  
Winston-Salem, NC

Eric J. Chow, MD, MPH  
Hematology/Oncology  
Seattle Children's Hospital  
Seattle, WA

Kimberley Dilley, MD, MPH  
Hematology/Oncology/Transplant  
Ann & Robert H. Lurie Children's Hospital  
Chicago, IL

Debra Eshelman Kent, RN, MSN, CPNP  
Cincinnati Children's Hospital Medical Center  
Cincinnati, OH

Fernando A. Ferrer, MD  
Department of Surgery  
Connecticut Children's Medical Center  
Hartford, CT

Sarah Friebert, MD  
Division of Hematology/Oncology  
Children's Hospital Medical Center of Akron  
Akron, OH

Debra L. Friedman, MD, MS  
Pediatric Hematology-Oncology  
Vanderbilt University/Ingram Cancer Center  
Nashville, TN

Sharon Friedlich, RN, MS, CPNP  
Pediatric Hematology/Oncology  
University of Wisconsin Children's Hospital  
Madison, WI

Allison Hester, RN, MSN, CPNP  
Arkansas Children's Hospital  
Little Rock, AR

Melissa M. Hudson, MD  
After Completion of Therapy Clinic  
St. Jude Children's Research Hospital  
Memphis, TN

Asako Komiya, RN, RSN, PNP  
Department of Epidemiology and Outcomes Research  
City of Hope Comprehensive Cancer Center  
Duarte, CA

Deborah Lafond, MS, RNCS, PNP, CPON®  
Hematology/Oncology  
Children's National Medical Center  
Washington, DC

Wendy Landier, PhD, RN, CPNP, CPON®  
Department of Pediatric Hematology/Oncology  
City of Hope Comprehensive Cancer Center  
Duarte, CA

Marcia Leonard, RN, CPNP  
Pediatric Hematology/Oncology and Long-Term Follow-Up Clinic  
C.S. Mott Children's Hospital  
Ann Arbor, MI

Tori Marchese, PhD, PT  
Penn State Hershey Medical Center  
Hershey, PA

Anne Mauck, RN, MSN, CPNP  
Pediatric Hematology/Oncology  
Virginia Commonwealth University Health System  
Richmond, VA

Charlene Maxen, RN, CNP, CPON®  
Division of Hematology/Oncology  
Children's Hospital Medical Center of Akron  
Akron, OH

Lillian R. Meacham, MD  
Division of Pediatric Endocrinology  
Emory University/Children's Healthcare of Atlanta  
Atlanta, GA

Katherine Myint-Hpu, MSN, MPH, PNP  
Leukemia/Lymphoma Clinic  
Georgetown University Hospital  
Washington, DC

Rajaram Nagarajan, MD, MPH  
University of Minnesota Cancer Center  
Pediatric Hematology/Oncology/BMT  
Minneapolis, MN

Kevin Oeffinger MD  
Division of Pediatrics  
Memorial Sloan-Kettering Cancer Center  
New York, NY

Arnold Paulino, MD  
Division of Radiation Oncology  
Methodist Hospital  
Houston, TX

Sunita Patel, PhD  
Department of Pediatric Hematology/Oncology  
City of Hope Comprehensive Cancer Center  
Duarte, CA

Michael Ritchey, MD  
Pediatric Urology Associates  
Phoenix, AZ

Kathy Ruble, RN, CPNP, AOCN®  
Long Term Follow-Up Program  
Johns Hopkins University  
Baltimore, MD

Sheila Judge Santacroce, PhD, APRN, CPNP  
School of Nursing  
Yale University  
New Haven, CT

Margery Schaffer, RN, MSN, CPNP  
Department of Hematology/Oncology  
Children's Medical Center  
Dayton, OH

Susan Shannon, RN, MSN, CPNP, CPON®  
“STAR” Late Effects Program  
Miller Children's Hospital  
Long Beach, CA

Patricia Shearer, MD, MS  
University of Maryland Medical Center  
Baltimore, MD

Sheila Shope, RN, FNP  
After Completion of Therapy Clinic  
St. Jude Children's Hospital  
Memphis, TN
Health Link Authors (cont)

Sheri L. Spunt, MD
Hematology/Oncology
Lucile Packard Children's Hospital
Stanford University
Palo Alto, CA

Teresa Sweeney, RN, MSN, CPNP
After Completion of Therapy Clinic
St. Jude Children's Research Hospital
Memphis, TN

Sally Wiard, MSW, LCSW
University of Texas Health Science Center
San Antonio, TX

Health Link Graphic Artist
Devika Bhatia
Westridge School
Pasadena, CA
The following individuals participated in reviewing the patient education materials (Health Links) for the Children’s Oncology Group Long-Term Follow-Up Guidelines for Survivors of Childhood, Adolescent, and Young Adult Cancers:

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<tr>
<td>Daniel Armstrong, PhD</td>
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<tr>
<td>Lisa Bashore, PhD, RN, CPNP, CPON®</td>
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<td>Jill Meredith, RN, BSN, OCN®</td>
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<td>Revonda Mosher, RN, MSN, CPNP, CPON®</td>
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<td>Kevin Oeffinger, MD</td>
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<td>Josee Pacifico, RN, BSc (N)</td>
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<td>Rebecca D. Pentz, PhD</td>
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<td>Priscilla Rieves, MS, RN, CPNP</td>
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<td>Kathleen Ruccione, RN, MPH, FAAN, CPON®</td>
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<td>E. Clifton Russell, MD</td>
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<td>Susan Shaw, RN, MS, PNP</td>
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<td>Charles A. Sklar, MD</td>
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<td>Johanne Soucy, RN, B.SC.N</td>
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<td>Karen Stormer, RN, CNS, CPON®</td>
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<td>Joetta Deswarte-Wallace, RN, MSN</td>
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<td>Edward Walz, MD</td>
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<td>Fran Wiley, RN, MN</td>
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<td>Roberta G. Williams, MD</td>
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<td>Catherine L. Woodman, MD</td>
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<td>Lise Yasui</td>
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<td>Octavio Zavala</td>
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Long-Term Follow-Up Guidelines
Guideline Development Task Force – Initial Versions

The Children's Oncology Group Nursing Discipline and Late Effects Committee 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* collaboratively through the efforts of the following individuals:

Melissa M. Hudson, MD
Vice-Chair – COG Late Effects Committee
Member, Department of Oncology
Director, After Completion of Therapy Clinic
St. Jude Children's Research Hospital
Memphis, Tennessee

Wendy Landier, PhD, RN, MSN, CPNP, CPON®
Chair – COG Nursing Clinical Practice Subcommittee
Clinical Director – Survivorship Clinic
City of Hope Comprehensive Cancer Center
Duarte, California

Debra Eshelman Kent, RN, MSN, CPNP
Late Effects Section Leader – COG Nursing Clinical Practice Subcommittee
Pediatric Nurse Practitioner
Cincinnati Children's Hospital Medical Center
Cincinnati, OH

Joan Darling, PhD
COG Patient Advocate Committee Representative
Lincoln, Nebraska

Allison Hester, RN, MSN, CPNP
Pediatric Nurse Practitioner
Arkansas Children's Hospital
Memphis, Tennessee

Teresa Sweeney, RN, MSN, CPNP
Pediatric Nurse Practitioner
After Completion of Therapy Clinic
St. Jude Children's Research Hospital
Memphis, Tennessee

**Special Acknowledgment**

With sincere appreciation to

Louis S. “Sandy” Constine, MD
Vice Chair, Department of Radiation Oncology
James P. Wilmont Cancer Center
University of Rochester Medical Center

*for his in-depth expert review and extensive contributions to all radiation-related sections in all versions of the COG LTFU Guidelines*
The following individuals participated in the review process during development of 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*:

Arlina Ahluwalia, MD  
Department of General Internal Medicine  
Stanford University  
Palo Alto, CA

F. Daniel Armstrong, PhD  
Department of Pediatrics  
University of Miami School of Medicine  
Miami, FL

Lisa Bashore, RN, MS, CPNP  
Pediatric Hematology/Oncology  
Cook Children's Medical Center  
Fort Worth, TX

Smita Bhatia, MD, MPH  
Division of Population Sciences  
City of Hope Comprehensive Cancer Center  
Duarte, CA

Julie Blatt, MD  
Division of Pediatric Hematology-Oncology  
University of North Carolina  
Chapel Hill, NC

Susan Bock, BSN, RN  
Department of Pediatric Specialties  
Gundersen Lutheran Clinic  
LaCrosse, WI

Cathy Bourne, RN, BHSc(N)  
Pediatric Hematology/Oncology  
Cancer Care Manitoba  
Winnipeg, Manitoba, Canada

Julianne Byrne, PhD  
Department of Hematology-Oncology  
Children's National Medical Center  
Washington, DC

Hope Anne Castoria, BSN, RN, CPON®  
Tomorrow Children's Institute  
Hackensack University Medical Center  
Hackensack, NJ

Laurie Cohen, MD  
Division of Endocrinology  
Dana Farber Cancer Institute  
Boston, MA

Louis S. Constine, MD  
Department of Radiation Oncology  
University of Rochester Medical Center  
Rochester, NY

Lola Cremer, PT  
Division of Rehabilitation Services  
St. Jude Children's Research Hospital  
Memphis, TN

Sarah Donaldson, MD  
Radiation Oncology/Radiation Therapy  
Stanford University Medical Center  
Stanford, CA

Patty Feist  
Patient Advocate  
Boulder, CO

Paul Fisher, MD  
Neurology and Pediatrics  
Stanford University Medical Center  
Stanford, CA

Carolyn R. Freeman, MB, BS, FRCPC  
Department of Radiation Oncology  
McGill University Health Centre  
Montreal, Quebec, Canada

Debra L. Friedman, MD, MS  
Pediatric Hematology-Oncology  
Vanderbilt University/Ingram Cancer Center  
Nashville, TN

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

Mark Greenberg, MB, BCh  
Department of Haematology/Oncology  
Hospital for Sick Children  
Toronto, Ontario, Canada

Wendy Hobbie, MSN, RN, PNP  
Division of Oncology  
Children's Hospital of Philadelphia  
Philadelphia, PA

Nina Kadan-Lottick, MD, MSPH  
Department of Pediatrics  
Yale University School of Medicine  
New Haven, CT

Nancy Keene  
Patient Advocate  
Annandale, VA

Lisa B. Kenney, MD, MPH  
Perini Quality of Life Clinic  
Dana-Farber Cancer Institute  
Boston, MA

Winnie Kittilo, RN, MS  
COG Patient Advocacy Committee  
Douglasville, GA

Margaret Kulm, RN, MA  
COG Patient Advocacy Committee  
Port Ludlow, WA

Missy Layfield  
COG Patient Advocacy Committee  
Cedar Falls, IA

Marcia Leonard, RN, CPNP  
Department of Pediatric Hematology/Oncology  
C.S. Mott Children's Hospital  
Ann Arbor, MI

Mary Leonard, MD, MSCE  
Division of Nephrology  
Children's Hospital of Philadelphia  
Philadelphia, PA

Louis A. Leone, Esq.  
COG Patient Advocacy Committee  
Walnut Creek, CA

Neyssa Marina, MD  
Pediatric Hematology Oncology  
Stanford University Medical Center  
Stanford, CA

Leonard Mattano, MD  
Pediatric Hematology/Oncology  
Kalamazoo Center for Medical Studies  
Michigan State University  
Kalamazoo, MI

Anne Mauck, RN, MS, CPNP  
Pediatric Hematology/Oncology  
Virginia Commonwealth University Health System  
Richmond, VA
Reviewers – Initial Versions (cont)

Charlene Maxen, RN, CNP, CPON®
Hematology/Oncology
Childrens Hospital Medical Center - Akron
Akron, OH

Lillian Meacham, MD
Division of Pediatric Endocrinology
Children's Healthcare of Atlanta
Atlanta, GA

Anna T. Meadows, MD
Division of Oncology
Children's Hospital of Philadelphia
Philadelphia, PA

Grace Powers Monaco, JD
Childhood Cancer Ombudsman Program
Heathsville, VA

Raymond Mulhern, PhD
Division of Behavioral Medicine
St. Jude Children's Research Hospital
Memphis, TN

John R. Mussman
COG Patient Advocacy Committee
Chicago, IL

Michael Neel, MD
Division of Orthopedics
St. Jude Children's Research Hospital
Memphis, TN

Joseph P. Neglia, MD, MPH
Department of Pediatrics
Division of Hematology, Oncology, Blood and Marrow Transplantation
University of Minnesota School of Medicine
Minneapolis, MN

Mary Nelson, RN, MS, CPNP, CPON®
Childrens Center for Cancer and Blood Diseases
Childrens Hospital Los Angeles
Los Angeles, CA

Kevin Oeffinger, MD
Department of Pediatrics
Memorial Sloan-Kettering Cancer Center
New York, NY

Roger Packer, MD
Department of Neurology
Children's National Medical Center
Washington, DC

Arnold Paulino, MD
Department of Radiation Oncology
Children's Healthcare of Atlanta – Emory Clinic
Atlanta, GA

Rebecca D. Pentz, PhD
COG Patient Advocacy Committee
Atlanta, GA

Leslie L. Robison, PhD
Department of Epidemiology and Cancer Control
St. Jude Children's Research Hospital
Memphis, TN

David Rosenthal, MD
Department of Pediatrics/Cardiology
Lucile Packard Children's Hospital at Stanford
Palo Alto, CA

Kathy Ruble, RN, MSN, CPNP, AOCN®
Pediatric Oncology
Johns Hopkins Hospital
Baltimore, MD

Kathleen Ruccione, RN, MPH, FAAN, CPON®
Childrens Center for Cancer and Blood Diseases
Childrens Hospital Los Angeles
Los Angeles, CA

Jean Sanders, MD
Pediatric Marrow Transplantation
Children's Hospital Regional Medical Center
Seattle, WA

Cindy Schwartz, MD
Pediatric Hematology/Oncology
Rhode Island Hospital
Providence, RI

Susan Shaw, RN, MS, PNP
Center for Children’s Cancer and Blood Disorders
State University of New York at Syracuse
Syracuse, NY

Charles A. Sklar, MD
Department of Pediatrics/Endocrinology
Memorial Sloan-Kettering Cancer Center
New York, NY

Jacque Toia, RN, ND, CPNP
Hematology/Oncology
Children's Memorial Medical Center
Chicago, IL

Deborah Weber, PhD
Department of Psychiatry
Boston Children’s Hospital
Boston, MA

Susan L. Weiner, PhD
The Children’s Cause, Inc.
Silver Spring, MD

Fran Wiley, RN, MN
COG Patient Advocacy Committee
Los Angeles, CA

Suzanne L. Wolden, MD
Department of Radiation Oncology
Memorial Sloan-Kettering Cancer Center
New York, NY

Catherine L. Woodman, MD
COG Patient Advocacy Committee
Iowa City, IA

Lise Yasui
COG Patient Advocacy Committee
Philadelphia, PA

Joseph Zins, PhD
COG Patient Advocacy Committee
Cincinnati, OH

Octavio Zavala
COG Patient Advocacy Committee
Los Angeles, CA
Introductory Material

CHILDREN'S ONCOLOGY GROUP

The world's childhood cancer experts
Introduction – Version 4.0
The Children’s Oncology Group Long-Term Follow-Up Guidelines for Survivors of Childhood, Adolescent, and Young Adult Cancers

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. 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 this regard, 101 (74%) of the screening recommendations outlined for the 156 therapeutic exposures in the COG-LTFU Guidelines comprise assessments derived primarily from the H&P, with 80 (51%) relying solely on the H&P and 31 (20%) relying on the H&P plus a baseline diagnostic study (e.g., lab, imaging), whereas 41 (26%) include periodic laboratory, diagnostic imaging, or other testing, and 4 (3%) 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 43 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, and a tool to assist in identifying guideline applicability for individual patients based on therapeutic exposures.

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 (a) promotes healthy lifestyles, (b) provides for ongoing monitoring of health status, (c) facilitates early identification of late effects, and (d) provides timely intervention for late effects.

Target Population
The recommendations for periodic screening evaluations provided in the Children’s Oncology Group Long-Term Follow-Up Guidelines for Survivors of Childhood, Adolescent, and Young Adult Cancers 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.

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.
## 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 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 patients 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 Nursing Discipline and Late Effects Committee and are maintained and updated by the Children’s Oncology Group’s Long-Term Follow-Up Guidelines Core Committee and its associated Task Forces. 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.

## Funding Source

This work was supported by the Children’s Oncology Group Chair’s Grant U10 CA098543 from the National Cancer Institute.

## Evidence Collection

Pertinent information from the published medical literature over the past 20 years (updated as of October 2013) 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.
Introduction (cont)

**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).

**Grading Criteria**

The guidelines were scored by the multidisciplinary panel of experts using a modified version of the National Comprehensive Cancer Network “Categories of Consensus” system. Each score reflects the expert panel’s assessment of 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 the expert panel’s collective clinical experience. “High-level evidence” (category 1) was defined as evidence derived from high quality case control or cohort studies. “Lower-level evidence” (category 2A and 2B) was defined as evidence derived from non-analytic studies, case reports, case series and clinical experience. 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.

**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 18 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 Late Effects 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. In 2009, related task forces were merged, reducing the number of task forces to 10. Task force members are assigned according to their respective areas of expertise and clinical interest and membership is updated every 2 years. A list of these task forces and their membership is included in the “Contributors” section of this document, reflecting contributions and recommendations since the previous release of these guidelines. (Version 3.0 – October 2008).

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 this document). 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 10 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.survivorguidelines.org](http://www.survivorguidelines.org).

Definitions

“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. “Consensus” is defined as general agreement among the panel of experts.

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.
Introduction (cont)

| 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 patients, 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 patients 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 Marc E. Horowitz, MD, (mehorowi@txch.org) or Susan Krause (skrause@txch.org). |
**Explanation of Scoring for the Long-Term Follow-Up Guidelines**

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:

<table>
<thead>
<tr>
<th>Category</th>
<th>Statement of Consensus</th>
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<tr>
<td>1</td>
<td>There is uniform consensus of the panel that: (1) there is high-level evidence linking the late effect with the therapeutic exposure and (2) the screening recommendation is appropriate based on the collective clinical experience of panel members.</td>
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<tr>
<td>2A</td>
<td>There is uniform consensus of the panel that: (1) there is lower-level evidence linking the late effect with the therapeutic exposure and (2) the screening recommendation is appropriate based on the collective clinical experience of panel members.</td>
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<tr>
<td>2B</td>
<td>There is non-uniform consensus of the panel that: (1) there is lower-level evidence linking the late effect with the therapeutic exposure and (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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</tbody>
</table>

**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.
**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>Risk Factors</td>
<td>Host factors (e.g., age, sex, race, genetic predisposition), treatment factors (e.g., cumulative dose of therapeutic agent, mode of administration, combinations of agents), medical conditions (e.g., pre-morbid or co-morbid conditions), and health behaviors (e.g., diet, smoking, alcohol use) that may increase risk of developing the complication.</td>
</tr>
<tr>
<td>Highest Risk Factors</td>
<td>Conditions (host factors, treatment factors, medical conditions and/or health behaviors) associated with the highest risk for developing the complication.</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>
<tr>
<td>Health Counseling/ Further Considerations</td>
<td><strong>Health Links:</strong> 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 <a href="http://www.survivorshipguidelines.org">www.survivorshipguidelines.org</a>. <strong>Counseling:</strong> Suggested patient counseling regarding measures to prevent/reduce risk or promote early detection of the potential treatment complication. <strong>Resources:</strong> Books and websites that may provide the clinician with additional relevant information. <strong>Considerations for Further Testing and Intervention:</strong> Recommendations for further diagnostic evaluations beyond minimum screening for individuals with positive screening tests, recommendations for consultation and/or referral, and recommendations for management of exacerbating or predisposing conditions.</td>
</tr>
</tbody>
</table>
Instructions for Use (cont)

| 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. |
| Cancer Screening Recommendations | Sections 157–166 contain preventive screening recommendations for common adult-onset cancers, organized by column as follows: **Organ:** The organ at risk for developing malignancy. **Population Risk Factors:** Risk factors such as age, gender, genetic susceptibility, personal or family history, health-related behaviors or comorbidities generally associated with increased risk for the specified malignancy in general populations. **Highest Risk Factors:** Populations considered by the panel of experts or other evaluating bodies (such as the American Cancer Society) as being at significantly increased risk for the specified malignancy. Risk factors may include therapeutic exposures resulting from cancer treatment, as well as other factors listed above (e.g., genetic susceptibility). **Periodic Evaluations:** **Standard Risk:** Guidelines provided under the “Standard Risk” category are per the American Cancer Society recommendations for standard-risk populations and are included here for reference. In addition, clinicians are encouraged to consult recommendations from other organizations, such as the U.S. Preventive Services Task Force (www.ahrq.gov/clinic/serfiles.htm). **Highest Risk:** Recommendations for high-risk populations, when applicable, are specified and may differ from recommendations for the standard risk groups due to the significantly increased risk of the specified malignancy within the high-risk group. |

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.

The following documents are also included to further assist with application of these guidelines:

| Explanation of Scoring | Elucidation of the process used by the panel of experts to assign scores to each guideline section. |
| Patient-Specific Guideline Identification Tool | Due to significant overlap of toxicities between therapeutic agents, and in order to avoid an enormously lengthy document, duplicate entries have been avoided as much as possible. Therefore, use of the Patient-Specific Guideline Identification Tool is imperative in order to determine each potential late effect associated with each therapeutic agent within this document (see Appendix I). |

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 expo-
sure-based follow-up recommendations from these guidelines, the following information regarding the survivor’s diagnosis and treatment is required, at minimum:

- Date of diagnosis
- Survivor’s sex
- Survivor’s date of birth
- Names of all chemotherapy agents received. For list of chemotherapeutic agents addressed by these guidelines (Sections 10–43), see the “Chemotherapy” portion of the Patient-Specific Guideline Identification Tool in Appendix I. For list of 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), and age at first anthracycline dose (if unknown, age at first exposure is presumed to be age at diagnosis).
- For carboplatin: Whether patient received myeloablative dose (i.e., for hematopoietic cell transplant [HCT] conditioning).
- 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/m^2) versus “standard dose” (all single doses < 1000 mg/m^2)
- All radiation field(s) and total radiation dose (in Gy) to each field (for chest radiation, include age at first dose). For list of radiation fields addressed by these guidelines (Sections 44–102), see “Radiation” portion of the Patient-Specific Guideline Identification Tool in Appendix I. For clarification of anatomical areas included in common radiation fields, see Radiation Fields by Anatomic Region and Radiation Fields Defined in Appendix I. For clarification regarding radiation dose calculations for determining screening recommendations for individual patients, see Determining Applicability of Radiation Sections for Specific Patients Based on Exposure on page 56 of guidelines and in Appendix 1.
- Whether or not the survivor underwent a hematopoietic cell transplant (HCT), and if so, whether or not the survivor has a history of chronic graft-versus-host disease (cGVHD).
- Names of all relevant surgical procedures. For list of surgical procedures addressed by these guidelines (Sections 120–152), see “Surgery” portion of the Patient-Specific Guideline Identification Tool in Appendix I.
- Names of all other therapeutic modalities. For list of other therapeutic modalities addressed by these guidelines (Sections 153–156), see “Other Therapeutic Modalities” portion of the Patient-Specific Guideline Identification Tool in Appendix I.

2. Develop a list of guideline sections relevant to the survivor:

- Sections 1–6 (“Any Cancer Experience”) and 157 (“General Health Screening”) are relevant to all survivors.
- For survivors diagnosed prior to 1993, include relevant sections based on date of diagnosis:
  - If survivor was diagnosed prior to 1992, include Section 7
  - If survivor was diagnosed prior to 1993, include Section 8
  - If survivor was diagnosed between 1977 and 1985, include Section 9
- For survivors who received chemotherapy, include relevant sections:
Instructions for Use (cont)

- If survivor received any chemotherapy, include Section 10.
- Review “Chemotherapy” portion of the Patient-Specific Guideline Identification Tool in Appendix I and include Sections 11–43 as applicable based on survivor’s chemotherapy exposures (Note: Some alkylating agent sections are gender-specific)

- For survivors who received radiation therapy, include relevant sections:
  - If survivor received any radiation therapy, include Sections 44–47. Exception: If the survivor’s only radiation exposure was TBI, do NOT include Sections 46 or 47.
  - Review “Radiation” portion of the Patient-Specific Guideline Identification Tool in Appendix I and include Sections 48–102 as applicable based on survivor’s radiation exposures (Note: Some sections are gender-specific and some are relevant only for patients who received the minimum specified dose of radiation to the indicated field or anatomic area.

- For survivors who underwent hematopoietic cell transplant (HCT), include Sections 103–110. If the survivor has a history of chronic GVHD (cGVHD), also include Sections 111–119 (Note: Section 116 is applicable only to survivors with currently active cGVHD; Section 118 is applicable only to females; Copies of the radiation sections applicable to TBI are reproduced and grouped together for convenience at the end of the HCT section on page 129).

- For survivors who underwent surgery, review “Surgery” portion of the Patient-Specific Guideline Identification Tool in Appendix I and include Sections 120–152 as applicable based on survivor’s surgical history. (Note: Some sections are gender-specific).

- For survivors who received other therapeutic modalities, review “Other Therapeutic Modalities” portion of the Patient-Specific Guideline Identification Tool in Appendix I and include Sections 153–156 as applicable.

- Include cancer screening guidelines (Sections 157–166) as applicable based on survivor’s sex and current age. (Note: For survivors whose radiation exposure triggers Section 77, there is no need to include Section 157; for survivors whose radiation exposure triggers Section 90, there is no need to include Section 159).

3. 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
Instructions for Use (cont)

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 Pasport for Care® application is available to Children’s Oncology member institutions at no cost. For additional information, please contact Marc E. Horowitz, MD, (mehorowi@txch.org) or Susan Krause (skrause@txch.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:

Melissa M. Hudson, MD
St. Jude Children’s Research Hospital
Memphis, Tennessee
(901) 595-3445
melissa.hudson@stjude.org

Louis S. “Sandy” Constine, MD
University of Rochester Medical Center
Rochester, NY
585-275-5622
louis_constine@urmc.rochester.edu

Wendy Landier, PhD, RN, CPNP
City of Hope National Medical Center
Duarte, California
(626) 471-7320
wlandier@coh.org

Smita Bhatia, MD, MPH
City of Hope National Medical Center
Duarte, California
(626) 471-7321
sbhatia@coh.org
New to Version 4.0 of the COG Long-Term Follow-Up Guidelines

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.

- The following NEW sections have been added:
  - Impaired glucose metabolism/Diabetes mellitus related to abdominal radiation (Section 84)
  - Dyslipidemia related to TBI (Section 85)
  - Renal toxicity related to hematopoietic cell transplantation (Section 110)
  - Overweight/obesity related to neurosurgery affecting the hypothalamic-pituitary axis (Section 133)
  - Diabetes insipidus related to neurosurgery affecting the hypothalamic-pituitary axis (Section 134)
  - Scoliosis/kyphosis related to neurosurgery-spine (Section 139)
  - Scoliosis/kyphosis related to thoracic surgery (Section 151)

- The following existing sections from version 3.0 of the COG LTFU Guidelines have been divided into more than one section in version 4.0:
  - Psychosocial disorders; Mental health disorders; Risky behaviors; Psychosocial disability due to pain; Fatigue (Section 1, v3.0), now divided into: Adverse psycho-social/QoL effects (Section 1); Mental health disorders (Section 2); Risky behaviors (Section 3); Psychosocial disability due to pain (Section 4); Fatigue (Section 5); Limitations in healthcare and insurance access (Section 6)
  - Alkylating agents and gonadal dysfunction-testicular (Section 7 [male], v3.0), now divided into: Alkylating agents and reduced fertility (Section 11) and Alkylating agents and testosterone deficiency/insufficiency; delayed/arrested puberty (Section 12)
  - Ototoxicity related to radiation (Section 58, v3.0), now divided into: Tympanosclerosis; ototosclerosis, eustachian tube dysfunction; conductive hearing loss (Section 66) and Sensorineural hearing loss; tinnitus (Section 67)
  - Orchiectomy and gonadal dysfunction-testicular (Section 125, v3.0), now divided into: Unilateral orchiectomy; Reduced fertility, testosterone insufficiency (Section 143) and Bilateral orchiectomy; Infertility; testosterone deficiency (Section 144)
  - All sections previously divided into “Male” and “Female” sub-sections have been re-categorized as stand-alone male or female sections in version 4.0, as follows:
    - Alkylating agents and gonadal dysfunction (Section 7 [male and female], v3.0), now categorized as: Section 11 (male-reduced fertility), Section 12 (male-testosterone deficiency/insufficiency; delayed/arrested puberty) and Section 13 (female-delayed/arrested puberty; premature menopause; infertility)
    - Anthracyclines and cardiac toxicity (Section 28 [male and female], v3.0), now categorized as: Section 33 (male) and Section 34 (female)
    - Cranial radiation and precocious puberty (Section 51 [male and female], v3.0), now categorized as: Section 56 (male) and Section 57 (female)
    - Cranial radiation and hyperprolactinemia (Section 52 [male and female], v3.0), now categorized as: Section 58 (male) and Section 59 (female)
    - Cranial radiation and gonadotropin deficiency (Section 54 [male and female], v3.0), now categorized as: Section 61 (male) and Section 62 (female)
    - Chest radiation and cardiac toxicity (Section 71 [male and female], v3.0), now categorized as: Section 80 (male) and Section 81 (female)
    - Hematopoietic cell transplant and solid tumors (Section 93 [male and female], v3.0), now categorized as: Section 104 (male) and Section 105 (female)
• Nephrectomy (Section 114 [male-hydrocele/renal toxicity and female-renal toxicity], v3.0), now categorized as: Section 127 (male-hydrocele/renal toxicity) and Section 128 (female-renal toxicity)
• Neurosurgery-spinal cord and psychosexual dysfunction (Section 121 [male and female], v3.0), now categorized as: Section 137 (male) and Section 138 (female)
• Pelvic surgery or Cystectomy and sexual dysfunction (Section 128 [male and female], v3.0), now categorized as: Section 147 (male) and Section 148 (female)

• The following sections have been removed from version 4.0 of the COG LTFU Guidelines:
  – Dyslipidemia related to platinum chemotherapy (Section 17, v3.0)
  – Metabolic syndrome related to cranial radiation/TBI (Section 49, v3.0)
  – Kyphosis related to musculoskeletal radiation (Section 90, v 3.0): Kyphosis is now merged with Scoliosis in Section 101 of version 4.0 of the COG LTFU Guidelines
  – Hydrocele related to Pelvic Surgery or Cystectomy (Section 129 [male], v3.0)

• The following modifications have been made to therapeutic exposures:
  – Carboplatin at any dose added as a therapeutic exposure for ototoxicity in patients diagnosed at less than 1 year of age (Section 20; score = 1); Info Link added to provide rationale for this change
  – Radiation threshold for screening reduced from ≥ 40 Gy to ≥ 30 Gy for
    • Radiation to the neuroendocrine axis and gonadotropin deficiency: Section 61 (male; score = 1) and Section 62 (female; score = 1)
    • Radiation to the neuroendocrine axis and central adrenal insufficiency: Section 63 (score = 1)
  – Chest (thorax) and whole lung radiation removed as therapeutic exposures related to thyroid dysfunction, thyroid nodules, and thyroid cancer: Sections 71, 72, 73, 74 (score = 1 for each section)
  – Cranial and nasopharyngeal radiation removed as therapeutic exposures for hyperthyroidism: Section 74
  – “Autologous” specified as the sole type of hematopoietic cell transplant associated with the potential late effect of therapy-related acute myeloid leukemia/ myelodysplasia (Section 103; score = 1)
  – Pulmonary lobectomy, pulmonary metastasectomy, pulmonary wedge resection as therapeutic exposures for pulmonary dysfunction changed to: Thoracic surgery (includes thoracotomy, chest wall surgery, rib resection, pulmonary lobectomy, pulmonary metastasectomy, pulmonary wedge resection): Section 150 (score = 2A)

• The following modifications have been made to potential late effects:
  – “Psychosocial Disorders” re-categorized as “Adverse Psychosocial/QoL Effects” and additional potential late effects added: Dysfunctional marital relationships; Under-Unemployment; Dependent living (Section 1; score = 2A)
  – Additional potential late effect (suicidal ideation) added to: Mental health disorders (Section 2; score = 2A)
  – Additional potential late effect (microdontia) added to: Dental abnormalities (Section 10; score = 1)
  – Info Link added to explain that ifosfamide-related renal toxicity typically occurs during the acute treatment phase and improves or progresses over time (Section 19) (score = 1)
  – Additional potential late effect (hypertension) added to Renal toxicity related to Heavy metals (Section 22; score = 1)
  – Additional potential late effects (glomerular injury; hypertension) added to Renal toxicity related to Methotrexate/high-dose IV, IM, PO (Section 28; score = 2A)
– Additional potential late effect (deficits in fine motor dexterity) added to Neurocognitive deficits related to: Cytarabine/high-dose IV (Section 23; score = 2A), Methotrexate/high-dose IV, IT, IO (Section 30; score = 1), and cranial/ear-infratemporal radiation/TBI (Section 49; score = 1)
– Additional potential late effect (language deficits) added to: Neurocognitive deficits related to cranial/ear-infratemporal radiation/TBI (Section 49; score = 1)
– Additional potential late effect (cavernomas) added to: Cerebrovascular complications related to cranial radiation (Section 51; score = 1); Info link added to explain clinical implications of cavernomas
– Additional potential late effect (focal nodular hyperplasia [FNH]) added to: Hepatic fibrosis/cirrhosis related to liver radiation (Section 86; score = 1); Info link added to explain clinical implications of FNH
– Additional potential late effect (asymptomatic bacteriuria) added to: Cystectomy-related complications (Section 122; score = 1)
– Potential late effect related to neurosurgery-spinal cord changed from “sexual dysfunction” to “psychosexual dysfunction” (Sections 137, 138; score = 2A)

• The following modifications have been made to screening recommendations:
  – CBC with differential yearly x 10 years removed as screening for t-AML/MDS and added to Considerations for further testing and intervention (as clinically indicated), in the following sections:
    • Alkylating agents (Section 14)
    • Anthracyclines (Section 32)
    • Epipodophyllotoxins (Section 43)
    • Autologous hematopoietic cell transplant (Section 103)
  – Chest x-ray (baseline, repeat as clinically indicated) removed as screening for pulmonary fibrosis from
    • Busulfan, carmustine [BCNU], lomustine [CCNU] (Section 15)
    • Bleomycin (Section 35)
    • Radiation with potential impact to the lungs (Section 79)
    • Hematopoietic cell transplant with any history of chronic graft-versus-host disease (Section 114)
    • Thoracic surgery (Section 150)
  – Urinalysis (yearly) removed as screening for hemorrhagic cystitis and added to Considerations for further testing and intervention (for patients with a positive history) in the following sections:
    • Cyclophosphamide, ifosfamide (Section 17)
    • Radiation with potential impact to the bladder (Section 92)
  – Urinalysis (yearly) removed as screening for bladder cancer and added to Considerations for further testing and intervention (for patients with a positive history) in the following sections:
    • Cyclophosphamide (Section 18)
    • Radiation with potential impact to the bladder (Section 94)
– Serum testosterone (males at age 14 and as clinically indicated) modified to indicate that specimen is ideally obtained in the morning for
  • Alkylating agents and testosterone deficiency/insufficiency; delayed/arrested puberty (Section 12)
  • Radiation to the hypothalamic-pituitary axis and gonadotropin deficiency (Section 61)
  • Pelvic/testicular radiation and testosterone deficiency/insufficiency; delayed/arrested puberty (Section 99)
  • Unilateral orchiectomy and testosterone insufficiency (Section 143)
– FSH, LH (males at age 14 and as clinically indicated) removed as screening for
  • Alkylating agents and testosterone deficiency/insufficiency; delayed/arrested puberty (Section 12)
  • Pelvic/testicular radiation and testosterone deficiency/insufficiency; delayed/arrested puberty (Section 99)
– FSH (males at age 14 and as clinically indicated) retained/added as secondary screening for reduced fertility in sexually mature patients if unable to obtain semen analysis for:
  • Alkylating agents and gonadal dysfunction (testicular)—reduced fertility (Section 11)
  • Pelvic/testicular radiation and gonadal dysfunction (testicular)—reduced fertility (Section 98)
  • Unilateral orchiectomy and gonadal dysfunction (testicular)—reduced fertility (Section 143)
– Hemoglobin A1c (every 2 years) added as an option (in place of fasting blood glucose) for
  • Chest radiation and cardiac toxicity (Sections 80, 81)
– Endocrinology evaluation (yearly) replaces previous recommendation for “8:00 a.m. serum cortisol yearly × 15 years” for
  • Radiation to the hypothalamic-pituitary axis ≥30 Gy and central adrenal insufficiency (Section 63)
– Breast cancer screening (Sections 77 and 157):
  • Recommendation added for clinicians to discuss benefits and risks/harms of screening for patients who received TBI or 10–19 Gy radiation with potential impact to the breast
  • If decision is made to screen patients who received < 20 Gy radiation with potential impact to the breast, screening recommendations are identical to those for patients who received ≥ 20 Gy and include: Mammogram and breast MRI yearly beginning 8 years after radiation or at age 25, whichever occurs last; Clinical breast exam yearly from puberty until age 25, then every 6 months; and Breast self-examination monthly
– Examination of external genitalia (yearly) and gynecological consultation when age-appropriate added as screening for
  • Hematopoietic cell transplant with any history of chronic graft-versus-host disease and vaginal fibrosis/stenosis (Section 118)
– Evaluation by neurologist modified to “as clinically indicated” rather than “every six months” for
  • Neurosurgery–brain and seizures (Section 131)
– Endocrinology consultation (or gynecology–females) for initiation of hormonal replacement therapy modified from “At age 11” to “At age 11 or immediately for post-pubertal patients” for
  • Bilateral oophorectomy (Section 142)
  • Bilateral orchiectomy (Section 144)
– Cervical cancer screening recommendations (Section 158) updated to reflect current American Cancer Society recommendations (i.e., changes to PAP/HPV testing)
– Lung cancer screening recommendations (Section 161) updated to include the following statement for patients at highest risk: “Clinician should discuss the benefits and risks/harms of spiral CT scanning”

• The following modifications have been made to Health Counseling/Further Considerations:
  – Added recommendations for minimum intake of Vitamin D as per the American Academy of Pediatrics to the following sections:
    • Methotrexate and reduced bone mineral density (Section 27)
    • Corticosteroids and reduced bone mineral density (Section 37)
    • Hematopoietic cell transplant and reduced bone mineral density (Section 109)
  – Added Info Link regarding metabolic syndrome, and recommendations to consider evaluation for other co-morbid conditions, including dyslipidemia, hypertension, or impaired glucose metabolism for
    • Overweight/obesity related to cranial radiation (Section 54)
  – Updated recommendations regarding monitoring growth and indications for endocrinology referrals for
    • Cranial radiation and growth hormone deficiency (Section 55)
  – Added information regarding induction of spermatogenesis with gonadotropins for
    • Radiation to the neuroendocrine axis and gonadotropin deficiency (Section 61)
  – Added recommendations for counseling patients regarding risk of life-threatening infections and indication for medical alert bracelets for
    • Splenic radiation and functional asplenia (Section 82)
    • Hematopoietic cell transplant with currently active chronic graft-versus-host disease and functional asplenia (Section 116)
    • Splenectomy and anatomic asplenia (Section 149)
  – Added recommendation for consideration of periodic monitoring of serum testosterone levels in males with low normal testosterone, as they age or if they become symptomatic, for
    • Pelvic/testicular radiation and testosterone deficiency/insufficiency; delayed/ arrested puberty (Section 99)
  – Updated antibiotic prophylaxis recommendations to indicate lack of current consensus for patients with orthopedic implants for
    • Limb sparing procedures (Section 126)
  – Revised sports/physical activity recommendations for
    • Nephrectomy and renal toxicity (Sections 127, 128)
  – Updated to reflect recommendations for sperm retrieval in men with erectile/ejaculatory dysfunction who desire paternity for
    • Neurosurgery-spinal cord and erectile dysfunction; ejaculatory dysfunction (Section 137)
    • Pelvic surgery/cystectomy and retrograde ejaculation; anejaculation; erectile dysfunction (Section 147)
  – Added consideration for gynecologic consultation in patients with positive history for
    • Neurosurgery-spinal cord and psychosexual dysfunction (Section 138)
– Added importance of monitoring cardiovascular health in hypogonadal females for
  • Bilateral oophorectomy and hypogonadism/infertility (Section 142)
– Added importance of monitoring for surgical complications after prosthesis placement and cautioned that orchiectomy can be associated with psychological distress related to altered body image for
  • Unilateral orchiectomy (Section 143)
  • Bilateral orchiectomy (Section 144)
– The following modifications have been made to the Health Links:
  – Added new Health Link: “Cardiovascular Risk Factors” (relevant to Sections 19, 22, 28, 33, 34, 54, 80, 81, 84, 85, 91, 110, 128, 133)
  – Modified the following Health Links:
    • Bone Health: Added recommendations for minimum daily intake of Vitamin D as per the American Academy of Pediatrics
    • Central Adrenal Insufficiency: Revised to reflect lower radiation dose for screening (> 30 Gy) and revised screening recommendations (endocrinology evaluation rather than yearly blood test)
    • Dental Health: Removed statement that xerostomia generally occurs only with radiation doses > 40 Gy.
    • Diet and Physical Activity: Updated “My Pyramid” to “My Plate”
    • Finding and Paying for Healthcare: Updated with information regarding new insurance options in the United States under the Affordable Care Act
    • Hearing Loss: Updated to indicate risk of hearing loss in survivors who received conventional doses of carboplatin prior to one year of age
    • Hypopituitarism: Updated to include antidiuretic hormone deficiency and diabetes insipidus related to neurosurgery
    • Limb Sparing Procedures: Updated to reflect lack of consensus regarding antibiotic prophylaxis recommendations
    • Pulmonary Health: Updated to remove chest x-ray, and to recommend avoidance of inhaled drugs (such as marijuana)
    • Scoliosis and Kyphosis: Added information regarding surgical procedures (thoracic and spinal surgeries) that may increase risk of developing scoliosis and kyphosis (from new Sections 139 and 151)
    • Reducing the Risk of Second Cancers: Updated with information regarding the role of vaccination in preventing Hepatitis B and HPV-related cancers
    • Single Kidney Health: Updated to reflect revised sports/physical activity recommendations for mononephric survivors; removed reference to Single Kidney Health Link from renal toxicity sections (Sections 19, 22, 28, 91)
    • Splenic Precautions: Updated to reflect current vaccine recommendations
    • Additional minor modifications made throughout Health Links to reflect current content of version 4.0 of the COG LTFU Guidelines
– Anthracycline isotoxic dose equivalent formula for Daunorubicin has been updated (see Sections 33, 34)
– The Info Link regarding prophylactic antibiotic therapy and immunizations for functionally or anatomically asplenic patients has been updated to indicate that clinicians should refer to the current edition of the AAP Red Book for recommendations (Sections 82, 116, 149)
– Information regarding the role of the human papillomavirus (HPV) vaccine in prevention of post-transplant malignancies has been added (Sections 104, 105)
– Radiation fields by anatomic area have been updated (see pages 56–57 of guidelines)
• The text that introduces the hematopoietic cell transplant sections (103–119) now precedes Section 103, since it is relevant to all hematopoietic cell transplant sections
• “Risk Factors” and “Highest Risk Factors” have been updated, based on current literature as reviewed by the Task Forces
• Links for general health screening have been updated (Section 166)
• Updated references have been added and outdated reference removed throughout the guidelines

In addition, the following modifications have been made to Version 4.0 of these guidelines:
• Links to all sections relevant to TBI have been added before the HCT section of the guidelines (see page 129)
• The “Radiation Reference Guide” has been updated to reflect modifications to section numbers and other changes as described above (see Appendix 1)
• The “Patient-Specific Guideline Identification Tool” has been updated to modifications to section numbers and other changes as described above (see Appendix 1)
• French translations of some Health Links have been added
Guidelines

CHILDREN’S ONCOLOGY GROUP

The world’s childhood cancer experts
### ANY CANCER EXPERIENCE

<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling/ Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Any Cancer Experience</td>
<td>Adverse Psychosocial/QoL Effects: Social withdrawal, Educational problems, Dysfunctional marital relationships, Under-employment/Unemployment, Dependent living</td>
<td>Host Factors: Female sex, Family history of depression, anxiety, or mental illness, Younger age at diagnosis, Neurocognitive problems, Physical limitations. Social Factors: Lower household income, Lower educational achievement</td>
<td>Host Factors: CNS tumor, CNS-directed therapy, Hearing loss, Premorbid learning or emotional difficulties. Social Factors: Failure to graduate from high school</td>
<td>History: Psychosocial assessment with attention to: - Educational and/or vocational progress - Social withdrawal</td>
<td>Yearly: Health Counseling/ Further Considerations</td>
</tr>
</tbody>
</table>

#### Info Link
The Children’s Oncology Group Long-Term Follow-Up Guidelines apply to patients who have been off therapy for a minimum of 2 years.

### SECTION 1 REFERENCES


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**SYSTEM = Psychosocial**  
**SCORE = 2A**
<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling/ Further Considerations</th>
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**SECTION 1 REFERENCES – continued**


### ANY CANCER EXPERIENCE

<table>
<thead>
<tr>
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<td>2</td>
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<td>Mental health disorders</td>
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<td>Female sex</td>
<td>CNS tumor</td>
<td>Psychosocial assessment with attention</td>
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<td>Post-traumatic stress</td>
<td>Family history of depression,</td>
<td>CNS-directed therapy</td>
<td>to:</td>
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<td>Suicidal ideation</td>
<td>anxiety, or mental illness</td>
<td>Premorbid learning or</td>
<td>- Depression</td>
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<td>Lower educational achievement</td>
<td>health</td>
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<td>Hematopoietic Cell Transplant</td>
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<td>Medical Conditions</td>
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<td>Chronic pain</td>
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</table>

**Host Factors**
- Female sex
- Family history of depression, anxiety, or mental illness

**Social Factors**
- Lower household income
- Lower educational achievement

**Treatment Factors**
- Hematopoietic Cell Transplant

**Medical Conditions**
- Chronic pain

**SYSTEM = Psychosocial**

**SCORE = 2A**

### SECTION 2 REFERENCES


### ANY CANCER EXPERIENCE (CONT)

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<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling/ Further Considerations</th>
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<tr>
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<td>Any Cancer Experience</td>
<td>Risky behaviors</td>
<td>Social Factors</td>
<td>Host Factors</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>
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<td>Older age at diagnosis</td>
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<td>Social Factors</td>
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<td>Resources</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Lower educational achievement</td>
<td></td>
<td>'Childhood Cancer Survivors' by Nancy Keene, Wendy Hobbie &amp; Kathy Ruccione, Childhood Cancer Guides, 2012 See also: <a href="http://www.cancer.gov">www.cancer.gov</a> ('Facing Forward' series for survivors; smoking cessation information); <a href="http://www.cancer.org">www.cancer.org</a> (smoking cessation)</td>
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### SECTION 3 REFERENCES


### ANY CANCER EXPERIENCE

<table>
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<th>Therapeutic Agent(s)</th>
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<tr>
<td>4</td>
<td>Any Cancer Experience</td>
<td>Psychosocial disability due to pain</td>
<td>Treatment Factors: Amputation, Radiation to bone/joint, Limb-sparing surgery, Vincristine exposure</td>
<td>Host Factors: CNS tumor, Hodgkin lymphoma</td>
<td>HISTORY: Psychosocial assessment Yearly</td>
<td>System = Psychosocial Score = 2A</td>
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#### SECTION 4 REFERENCES


### ANY CANCER EXPERIENCE

**SECTION 5 REFERENCES**


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<td>5</td>
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<td>Fatigue</td>
<td>Host Factors</td>
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<td>Resources</td>
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<td>Female sex</td>
<td>Pulmonary radiation</td>
<td>Psychosocial assessment</td>
<td>'Childhood Cancer Survivors' by Nancy Keene, Wendy Hobbie &amp; Kathy Ruccione, Childhood Cancer Guides, 2012</td>
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<td></td>
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<td>Depression</td>
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<td>See also: <a href="http://www.cancer.gov">www.cancer.gov</a> ('Facing Forward' series for survivors)</td>
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<td>Obesity</td>
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<td>Considerations for Further Testing and Intervention</td>
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<tr>
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<td></td>
<td>Central CNS tumor (e.g., craniopharyngioma)</td>
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<td>Screen for physical sources of fatigue, such as anemia, sleep disturbances, nutritional deficiencies, cardiomyopathy, pulmonary fibrosis, hypothyroidism, or other endocrinopathy.</td>
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<td>Unemployment</td>
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<td>Sleep disturbance</td>
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### ANY CANCER EXPERIENCE

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<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling/ Further Considerations</th>
</tr>
</thead>
</table>
| 6     | Any Cancer Experience| Limitations in healthcare and insurance access | Social Factors  
Lower household income  
Lower educational achievement  
Unemployment | HISTORY  
Psychosocial assessment with attention to healthcare and insurance access  
Yearly | Health Links  
Finding and Paying for Healthcare  
Considerations for Further Testing and Intervention  
Social work consultation | SYSTEM = Psychosocial  
SCORE = 2A |

### SECTION 6 REFERENCES


## BLOOD/SERUM PRODUCTS

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<th>Health Counseling/ Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>7</td>
<td>Diagnosed prior to 1972</td>
<td>Chronic hepatitis B</td>
<td>Living in hyperendemic area</td>
<td>Chronic immunosuppression</td>
<td><strong>SCREENING</strong>&lt;br&gt; Hepatitis B surface antigen (HBsAg)&lt;br&gt; Hepatitis B core antibody (anti HBc or HBCab)</td>
<td>Once in patients who received treatment for cancer prior to 1972.&lt;br&gt;Note: Date may vary for international patients.</td>
</tr>
</tbody>
</table>

**Info Link**
- 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 concentrates, and allogeneic marrow, cord blood, or stem cells.

**SYSTEM** = Immune<br>**SCORE** = 1

### SECTION 7 REFERENCES

### BLOOD/SERUM PRODUCTS (cont)

<table>
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<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling/ Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>8</td>
<td>Diagnosed prior to 1993</td>
<td>Chronic hepatitis C</td>
<td>Host Factors: Living in hyperendemic area</td>
<td>Host Factors: Chronic immunosuppression</td>
<td>SCREENING: Hepatitis C antibody</td>
<td>Health Links: Hepatitis \nConsiderations for Further Testing and Intervention: \nScreen for viral hepatitis in patients with persistently abnormal liver function regardless of transfusion history. Consider HCV PCR screening in transfused at-risk HCV-antibody negative patients with abnormal liver function and/or persistent immunosuppression (e.g., HCT recipients with chronic GVHD). Gastroenterology or hepatology consultation for management of patients with chronic hepatitis. Hepatitis A and B immunization in patients lacking immunity.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Info Link</th>
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</thead>
<tbody>
<tr>
<td>Exposure to blood/serum products prior to initiation of Hepatitis C screening of blood supply (1993 in the United States, considering more reliable EIA generation 2 released in the United States 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.</td>
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</tbody>
</table>

### SECTION 8 REFERENCES


### BLOOD/SERUM PRODUCTS

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<thead>
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<th>Periodic Evaluation</th>
<th>Health Counseling/ Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>9</td>
<td>Diagnosed between 1977 and 1985</td>
<td>HIV infection</td>
<td>Treatment Factors Blood products between 1977 and 1985</td>
<td>Medical Conditions HPV infection Health Behaviors IV drug use Unprotected sex Multiple partners High-risk sexual behavior Sexually transmitted diseases Tattoos Body piercing</td>
<td>SCREENING</td>
<td>HIV testing Once in patients who received treatment for cancer between 1977 and 1985. <strong>Note:</strong> Date may vary for international patients. Counseling Standard counseling regarding safe sex, universal precautions and high-risk behaviors that exacerbate risk, Considerations for Further Testing and Intervention HIV/infectious diseases specialist consultation for patients with chronic infection.</td>
</tr>
</tbody>
</table>

#### Info Link
- 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.

#### SECTION 9 REFERENCES
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<td>Dental abnormalities</td>
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<td>Dry mouth</td>
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<td></td>
<td>Tooth/root agenesis</td>
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<td>Yearly</td>
<td>Considerations for Further Testing and Intervention</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Root thinning/shortening</td>
<td></td>
<td></td>
<td></td>
<td>Regular dental care including fluoride applications. Baseline panorex prior to dental procedures to evaluate root development.</td>
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<td></td>
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<td>Enamel dysplasia</td>
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**SECTION 10 REFERENCES**


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<td>Busulfan</td>
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<td>Carmustine (BCNU)</td>
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<td>Pubertal (onset, tempo)</td>
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<td>Chlorambucil</td>
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<td>Sexual function (erectile, nocturnal emissions, libido)</td>
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<td>Cyclophosphamide</td>
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<td></td>
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<td>Medication use</td>
<td>Extensive information regarding infertility for patients and healthcare professionals is available on the following websites: American Society for Reproductive Medicine (<a href="http://www.asrm.org">www.asrm.org</a>); Fertile Hope (<a href="http://www.fertilehope.org">www.fertilehope.org</a>)</td>
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<td></td>
<td>- abdomen/pelvis</td>
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<td>- brain, cranium (neuroendocrine axis)</td>
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<td>- Genitourinary surgery</td>
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<td>Higher cumulative doses of alkylators or combinations of alkylators</td>
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<td>- brain, cranium (neuroendocrine axis)</td>
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<td>- Genitourinary surgery</td>
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<td>Health Behaviors</td>
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<td>Tobacco/marijuana use</td>
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<td></td>
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<td></td>
<td>History of sexually transmitted diseases</td>
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<td></td>
<td></td>
<td></td>
<td>Info Link</td>
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<td></td>
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<td></td>
<td>- Doses that cause gonadal dysfunction show individual variation.</td>
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<td></td>
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<td></td>
<td>- Germ cell function (spermatogenesis) is impaired at lower doses compared to Leydig cell (testosterone production) function.</td>
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<td>- Prepubertal status does not protect from gonadal injury in males.</td>
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<td>SYSTEM = Reproductive (male)</td>
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<td>SCORE =</td>
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<td>Alkylating Agents = 1</td>
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<td>Heavy Metals = 2A</td>
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<td>Non-Classical Alkylators = 2A</td>
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**SECTION 11 REFERENCES**


### CHEMOTHERAPY

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<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling/ Further Considerations</th>
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<tbody>
<tr>
<td>12</td>
<td><strong>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;Meclathamine&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;<strong>NON-CLASSICAL ALKYLATORS</strong>&lt;br&gt;Dacarbazine (DTIC)&lt;br&gt;Temozolomide</td>
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<tr>
<td></td>
<td><strong>Gonadal dysfunction (testicular)</strong>&lt;br&gt;Testosterone deficiency/ insufficiency&lt;br&gt;Delayed/arrested puberty</td>
<td>Host Factors: Testicular cancer&lt;br&gt;Aging</td>
<td>Treatment Factors:&lt;br&gt;MOPP&lt;br&gt;Cyclophosphamide cumulative dose ≥ 20 gm/m²&lt;br&gt;Conditioning for HCT:&lt;br&gt;Ifosfamide ≥ 60 gm/m²&lt;br&gt;Any alkylators combined with&lt;br&gt;- Testicular radiation&lt;br&gt;- Pelvic radiation&lt;br&gt;- Neuroaxis radiation</td>
<td>Treatment Factors:&lt;br&gt;MOPP&lt;br&gt;Cyclophosphamide cumulative dose ≥ 20 gm/m²&lt;br&gt;Conditioning for HCT:&lt;br&gt;Ifosfamide ≥ 60 gm/m²&lt;br&gt;Any alkylators combined with&lt;br&gt;- Testicular radiation&lt;br&gt;- Pelvic radiation&lt;br&gt;- Neuroaxis radiation</td>
<td><strong>HISTORY</strong>&lt;br&gt;Pubertal (onset, tempo)&lt;br&gt;Sexual function (erections, nocturnal emissions, libido)&lt;br&gt;Medication use&lt;br&gt;Yearly</td>
<td><strong>PHYSICAL</strong>&lt;br&gt;Tanner staging until sexually mature&lt;br&gt;Testicular volume by Prader orchiometer&lt;br&gt;Yearly</td>
</tr>
<tr>
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<td>Health Behaviors: Smoking</td>
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<td><strong>Info Link</strong>&lt;br&gt;- Doses that cause gonadal dysfunction show individual variation.&lt;br&gt;- Germ cell function (spermatogenesis) is impaired at lower doses compared to Leydig cell (testosterone production) function.&lt;br&gt;- Prepubertal status does not protect from gonadal injury in males.</td>
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<tr>
<td></td>
<td></td>
<td><strong>Health Links</strong>&lt;br&gt;Male Health Issues&lt;br&gt;Considerations for Further Testing and Intervention&lt;br&gt;Bone density evaluation in hypogonadal patients. Refer to endocrinology/urology for delayed puberty, persistently abnormal hormone levels or hormonal replacement for hypogonadal patients. Males with low normal testosterone should have periodic re-evaluation of testosterone as they age or if they become symptomatic. Testosterone insufficiency requiring hormone replacement therapy is rare after treatment with alkylating agents only.</td>
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</table>

### SECTION 12 REFERENCES


## CHEMOTHERAPY

### ALKYLATING AGENTS (cont)

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<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling/ Further Considerations</th>
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<tr>
<td>13 (female)</td>
<td><strong>ALKYLATING AGENTS</strong>&lt;br&gt;Busulfan&lt;br&gt;Carmustine (BCNU)&lt;br&gt;Chlorambucil&lt;br&gt;Cyclophosphamide&lt;br&gt;Ilotinamide&lt;br&gt;Lomustine (CCNU)&lt;br&gt;Mechlorethamine&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;<strong>NON-CLASSICAL ALKYLATORS</strong>&lt;br&gt;Dacarbazine (DTIC)&lt;br&gt;Temozolomide</td>
<td><strong>Gonadal dysfunction</strong>&lt;br&gt;Delayed/arrested puberty&lt;br&gt;Premature menopause&lt;br&gt;Infertility</td>
<td>Treatment Factors&lt;br&gt;Higher cumulative doses of alkylators or combinations of alkylators&lt;br&gt;Combined with radiation to:&lt;br&gt;- Abdomen/pelvis&lt;br&gt;- Lumbar or sacral spine (from ovarian scatter)&lt;br&gt;- Brain, cranium (neuroendocrine axis)</td>
<td>Treatment Factors&lt;br&gt;Any alkylators combined with:&lt;br&gt;- Pelvic radiation&lt;br&gt;- TBI&lt;br&gt;Host Factors&lt;br&gt;Older age at treatment</td>
<td><strong>HISTORY</strong>&lt;br&gt;Pubertal (onset, tempo), menstrual, pregnancy history&lt;br&gt;Sexual function (vaginal dryness, libido)&lt;br&gt;Medication use&lt;br&gt;Yearly</td>
<td><strong>PHYSICAL</strong>&lt;br&gt;Tanner staging&lt;br&gt;Yearly until sexually mature</td>
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</table>

### SECTION 13 REFERENCES


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**SECTION 13 REFERENCES—CONTINUED**


### ALKYLATING AGENTS (cont)

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<tbody>
<tr>
<td>14</td>
<td>ALKYLATING AGENTS</td>
<td>Acute myeloid leukemia, Myelodysplasia</td>
<td>Treatment Factors</td>
<td>Treatment Factors</td>
<td>HISTORY</td>
<td>Health Links</td>
</tr>
<tr>
<td></td>
<td>Busulfan</td>
<td></td>
<td>Less than 10 years since exposure to agent</td>
<td>Autologous HCT</td>
<td>Fatigue, Bleeding, Easy bruising</td>
<td>Reducing the Risk of Second Cancers</td>
</tr>
<tr>
<td></td>
<td>Carmustine (BCNU)</td>
<td></td>
<td>Higher cumulative alkylator dose or combination of alkylators</td>
<td></td>
<td>Yearly, up to 10 years after exposure to agent</td>
<td>Counseling</td>
</tr>
<tr>
<td></td>
<td>Chlorambucil</td>
<td></td>
<td>Note: Melphalan and mechlorethamine are more potent leukemogens than cyclophosphamide</td>
<td></td>
<td></td>
<td>Counsel to promptly report fatigue, pallor, petechiae or bone pain.</td>
</tr>
<tr>
<td></td>
<td>Cyclophosphamide</td>
<td></td>
<td>Medical Conditions</td>
<td></td>
<td>PHYSICAL</td>
<td>Counseling</td>
</tr>
<tr>
<td></td>
<td>Ifosfamide</td>
<td></td>
<td>Splenectomy (conflicting evidence)</td>
<td></td>
<td>Dermatologic exam (pallor, petechiae, purpura)</td>
<td>CBC and bone marrow exam as clinically indicated.</td>
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<td></td>
<td>Lomustine (CCNU)</td>
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<td></td>
<td>Mechlorethamine</td>
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<td>Melphalan</td>
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<td>Procarbazine</td>
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<td></td>
<td>Thiotaenia</td>
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<td>HEAVY METALS</td>
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<tr>
<td></td>
<td>Carboplatin</td>
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<td></td>
<td>Cisplatin</td>
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<td></td>
<td>NON-CLASSICAL ALKYLATORS</td>
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<td></td>
<td>Dacarbazine (DTIC)</td>
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<td></td>
<td>Temozolomide</td>
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**SECTION 14 REFERENCES**


### CHEMOTHERAPY

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<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling/ Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>15</td>
<td>ALKYLATING AGENTS</td>
<td>Pulmonary fibrosis</td>
<td>Treatment Factors Higher cumulative doses Combined with bleomycin Medical Conditions Atopic history Health Behaviors Smoking Inhaled illicit drug use</td>
<td>Treatment Factors BCNU ≥ 600 mg/m² Busulfan ≥ 500 mg (transplant doses) Combined with: - Chest radiation - TBI</td>
<td>HISTORY Cough SOB DOE Wheezing 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 Resources Extensive information regarding smoking cessation is available for patients on the NCI’s website: <a href="http://www.smokefree.gov">www.smokefree.gov</a> Counseling Counsel regarding tobacco avoidance/smoking cessation. Due to the potential pulmonary toxicity of this therapy, patients who desire to SCUBA dive should be advised to obtain medical clearance from a pulmonologist. Considerations for Further Testing and Intervention In patients with abnormal PFTs, consider repeat evaluation prior to general anesthesia. Pulmonary consultation for symptomatic pulmonary dysfunction. Influenza and pneumococcal vaccines.</td>
</tr>
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</table>

### SECTION 15 REFERENCES

### CHEMOTHERAPY

<table>
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<th>Sec #</th>
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<th>Potential Late Effects</th>
<th>Risk Factors</th>
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<th>Periodic Evaluation</th>
<th>Health Counseling/ Further Considerations</th>
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<tr>
<td>16</td>
<td>ALKYLATING AGENTS</td>
<td>Cataracts</td>
<td>Treatment Factors Combined with corticosteroids</td>
<td>Treatment Factors Combined with cranial, orbital, or eye radiation TBI Longer interval since treatment</td>
<td>HISTORY Visual changes (decreased acuity, halos, diplopia) Yearly</td>
<td>PHYSICAL Eye exam (visual acuity, funduscopic exam for lens opacity) Yearly</td>
</tr>
</tbody>
</table>

**Health Links**

Cataracts

**Considerations for Further Testing and Intervention**

Ophthalmology consultation if problem identified. 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 = 2B**

### SECTION 16 REFERENCES

### CHEMOTHERAPY

#### ALKYLATING AGENTS (cont)

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<tr>
<th>Sec #</th>
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<th>Potential Late Effects</th>
<th>Risk Factors</th>
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<tr>
<td>17</td>
<td>ALKYLATING AGENTS</td>
<td>Urinary tract toxicity</td>
<td>Treatment Factors</td>
<td>Cyclophosphamide dose ≥ 3 gm/m²</td>
<td>HISTORY</td>
<td>Health Links</td>
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<td></td>
<td>Cyclophosphamide</td>
<td>Hemorrhagic cystitis</td>
<td>Higher cumulative doses (decreased incidence with Mesna)</td>
<td>Pelvic radiation dose ≥ 30 Gy</td>
<td>Urinary urgency/frequency</td>
<td>Bladder Health</td>
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<td></td>
<td>Ifosfamide</td>
<td>Bladder fibrosis</td>
<td>Combined with pelvic radiation</td>
<td></td>
<td>Urinary incontinence/retention</td>
<td>Counseling</td>
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<td></td>
<td></td>
<td>Dysfunctional voiding</td>
<td>Health Behaviors</td>
<td></td>
<td>Dysuria</td>
<td>Counsel to promptly report dysuria or gross hematuria.</td>
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<tr>
<td></td>
<td></td>
<td>Vesicoureteral reflux</td>
<td>Alcohol use</td>
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<td>Nocturia</td>
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<td></td>
<td>Hydronephrosis</td>
<td>Smoking</td>
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<td>Abnormal urinary stream</td>
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<td>Yearly</td>
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</table>

**SYSTEM = Urinary**

**SCORE = 1**

### SECTION 17 REFERENCES


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<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
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<th>Health Counseling/ Further Considerations</th>
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<tbody>
<tr>
<td>18</td>
<td>ALKYLATING AGENTS</td>
<td>Bladder malignancy</td>
<td>Treatment Factors Combined with pelvic radiation</td>
<td>HISTORY&lt;br&gt;Hematuria&lt;br&gt;Urinary urgency/frequency&lt;br&gt;Urinary incontinence/retention&lt;br&gt;Dysuria&lt;br&gt;Nocturia&lt;br&gt;Abnormal urinary stream&lt;br&gt;Yearly</td>
<td><strong>Health Links</strong>&lt;br&gt;Bladder Health&lt;br&gt;Counseling&lt;br&gt;Counsel to promptly report dysuria or gross hematuria.&lt;br&gt;&lt;br&gt;<strong>Considerations for Further Testing and Intervention</strong>&lt;br&gt;For patients with positive history, obtain urinalysis and consider urine culture, spot urine calcium/creatinine ratio, and ultrasound of kidneys and bladder for patients with microscopic hematuria (defined as &gt; 5 RBC/HFP 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.</td>
<td>SYSTEM = SMN&lt;br&gt;SCORE = 2A</td>
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**SECTION 18 REFERENCES**


## CHEMOTHERAPY

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<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
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<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling/ Further Considerations</th>
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<tbody>
<tr>
<td>19</td>
<td>ALKYLATING AGENTS</td>
<td>Ifosfamide</td>
<td>Renal toxicity Glomerular injury Hypertension Tubular injury (renal tubular acidosis, Fanconi’s syndrome, hypophosphatemic rickets)</td>
<td>Host Factors Younger age at treatment Mononephric Treatment Factors Higher cumulative dose Combined with other nephrotoxic agents such as: - Cisplatin - Carboplatin - Aminoglycosides Amphotericin - Immunosuppressants Methotrexate - Radiation impacting the kidney Medical Conditions Tumor infiltration of kidney(s) Pre-existing renal impairment Nephrectomy</td>
<td>Host Factors Age &lt; 4 years at time of treatment Treatment Factors Ifosfamide dose ≥ 60 grams/m² Renal radiation dose ≥ 15 Gy</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 Urinalysis Yearly</td>
</tr>
</tbody>
</table>

### ALKYLATING AGENTS (cont)

**Info Link**
Ifosfamide-related renal toxicity typically occurs during the acute treatment phase and improves or progresses over time.

**SYSTEM = Urinary**
**SCORE = 1**

### SECTION 19 REFERENCES


### CHEMOTHERAPY

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<th>Periodic Evaluation</th>
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<tr>
<td>20</td>
<td>HEAVY METALS</td>
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</tr>
<tr>
<td></td>
<td>Carboplatin (myeloablative doses OR any dose if age at diagnosis &lt; 1 year)</td>
<td>Ototoxicity</td>
<td>Host Factors</td>
<td>Host Factors</td>
<td>HISTORY</td>
<td>Health Links</td>
</tr>
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<td></td>
<td></td>
<td>Sensorineural hearing loss</td>
<td>Age &lt; 4 years at treatment</td>
<td>CNS neoplasm</td>
<td>Hearing difficulties (with/without background noise)</td>
<td>Hearing Loss</td>
</tr>
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<td>Tinnitus</td>
<td>Treatment Factors</td>
<td>Treatment Factors</td>
<td>Tinnitus</td>
<td>Educational Issues</td>
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<td></td>
<td>Vertigo</td>
<td>Combined with:</td>
<td>Cumulative cisplatin dose</td>
<td>Vertigo</td>
<td>Considerations for Further Testing and Intervention</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>- Cranial/ear radiation</td>
<td>≥ 360 mg/m²</td>
<td>Yearly</td>
<td>Audiology consultation for amplification in patients with hearing loss.</td>
</tr>
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<td></td>
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<td></td>
<td>- Ototoxic drugs (e.g., aminoglycosides, loop diuretics)</td>
<td>High dose cisplatin (i.e., 40 mg/m² per day × 5 days per course)</td>
<td>Yearly</td>
<td>Speech and language therapy for children with hearing loss.</td>
</tr>
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<td></td>
<td>Medical Conditions</td>
<td>Cisplatin administered AFTER cranial/ear radiation</td>
<td></td>
<td>Otolaryngology consultation in patients with chronic infection, cerumen impaction, or other anatomical problems exacerbating or contributing to hearing loss.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Chronic otitis</td>
<td>Chronic otitis</td>
<td>Cisplatin conditioning for HCT</td>
<td></td>
<td>Refer patients with auditory deficits to school liaison in community or cancer center (psychologist, social worker, school counselor) to facilitate provision of educational resources. Consider specific needs and/or preferential classroom seating, FM amplification system, and other educational assistance as indicated.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cerumen impaction</td>
<td>Renal dysfunction</td>
<td>Radiation involving ear</td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td>≥ 30 Gy</td>
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</tbody>
</table>

**Info Link**
- In general, patients who received carboplatin in nonmyeloablative doses do not appear to be at risk for clinically significant ototoxicity.
- Some studies have observed hearing loss among infants (with retinoblastoma) exposed to nonmyeloablative doses of carboplatin.

**HEAVY METALS**

**CARBOPlatin (myeloablative doses OR any dose if age at diagnosis < 1 year)**

- **Ototoxicity**
  - Sensorineural hearing loss
  - Tinnitus
  - Vertigo

- **Host Factors**
  - Age < 4 years at treatment
  - Treatment Factors
    - Cranial/ear radiation
    - Ototoxic drugs (e.g., aminoglycosides, loop diuretics)

- **Medical Conditions**
  - Chronic otitis
  - Cerumen impaction
  - Renal dysfunction

- **Treatment Factors**
  - Combined with:
    - Cranial/ear radiation
    - Ototoxic drugs (e.g., aminoglycosides, loop diuretics)

- **Highest Risk Factors**
  - CNS neoplasm
  - Cumulative cisplatin dose ≥ 360 mg/m²
  - High dose cisplatin (i.e., 40 mg/m² per day × 5 days per course)
  - Cisplatin administered AFTER cranial/ear radiation
  - Cisplatin conditioning for HCT
  - Radiation involving ear ≥ 30 Gy

- **Periodic Evaluation**
  - **HISTORY**
    - Hearing difficulties (with/without background noise)
  - **Tinnitus**
  - **Vertigo**

- **Health Counseling**
  - **Further Considerations**
    - Audiology consultation for amplification in patients with hearing loss.
    - Speech and language therapy for children with hearing loss.
    - Otolaryngology consultation in patients with chronic infection, cerumen impaction, or other anatomical problems exacerbating or contributing to hearing loss.
    - Refer patients with auditory deficits to school liaison in community or cancer center (psychologist, social worker, school counselor) to facilitate provision of educational resources. Consider specific needs and/or preferential classroom seating, FM amplification system, and other educational assistance as indicated.

**SYSTEM = Auditory**

**SCORE = 1**

### SECTION 20 REFERENCES


<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling/Further Considerations</th>
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<tbody>
<tr>
<td>HEAVY METALS (cont)</td>
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SECTION 20 REFERENCES—continued


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<th>Potential Late Effects</th>
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<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling/ Further Considerations</th>
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</thead>
<tbody>
<tr>
<td>21</td>
<td>HEAVY METALS Carboplatin Cisplatin</td>
<td>Peripheral sensory neuropathy Paresthesias Dysesthesias</td>
<td>Treatment Factors Combined with: - Vincristine - Taxanes - Gemcitabine</td>
<td>Treatment Factors Cumulative cisplatin dose ≥ 300 mg/m²</td>
<td>HISTORY Numbness Tingling Paresthesias Dysesthesia Yearly until 2 to 3 years after therapy, monitor yearly if symptoms persist</td>
<td>Health Links Peripheral Neuropathy Considerations for Further Testing and Intervention Physical therapy referral for patients with symptomatic neuropathy. Physical and occupational therapy assessment of hand function. Consider treatment with agent effective for neuropathic pain (e.g., gabapentin or amitriptyline).</td>
</tr>
</tbody>
</table>

**SECTION 21 REFERENCES**


HEAVY METALS (cont)

<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
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<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling/ Further Considerations</th>
</tr>
</thead>
</table>
| 22    | HEAVY METALS
Carboplatin
Cisplatin | Renal toxicity
Glomerular injury
Hypertension
Tubular injury
Renal insufficiency | Host Factors
Mononephric
Treatment Factors
Combined with other nephrotoxic agents, such as:
- Aminoglycosides
- Amphotericin
- Immunosuppressants
- Methotrexate
- Radiation impacting the kidney | Treatment Factors
Cisplatin dose ≥ 200 mg/m²
Renal radiation dose ≥ 15 Gy | PHYSICAL
Blood pressure
Yearly |
| | | | | SCREENING
BUN
Creatinine
Na, K, Cl, CO₂
Ca, Mg, PO₄ | |
| | | Medical Conditions
Diabetes mellitus
Hypertension
Nephrectomy | | Urinalysis
Yearly | |
| | | | | | Health Links
Kidney Health
Cardiovascular Risk Factors |
| | | | | | Counseling
In patients with salt-wasting tubular dysfunction, educate that low magnesium levels potentiate coronary atherosclerosis. |
| | | | | | Considerations for Further Testing and Intervention
Electrolyte supplements for patients with persistent electrolyte wasting. Nephrology consultation for patients with hypertension, proteinuria, or progressive renal insufficiency. |

SECTION 22 REFERENCES


## SECTION 23 REFERENCES


<table>
<thead>
<tr>
<th>Section #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling/ Further Considerations</th>
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**ANTIMETABOLITES (cont)**

**SECTION 23 REFERENCES (continued)**

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<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling/ Further Considerations</th>
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<tbody>
<tr>
<td><strong>ANTIMETABOLITES</strong></td>
<td><strong>Cytarabine (high dose IV)</strong></td>
<td><strong>Clinical leukoencephalopathy</strong></td>
<td><strong>Host Factors</strong></td>
<td><strong>Treatment Factors</strong></td>
<td><strong>HISTORY</strong></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Spasticity</td>
<td>Younger age at treatment</td>
<td>Radiation dose ≥ 24 Gy</td>
<td>Cognitive, motor and/or sensory deficits</td>
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<tr>
<td></td>
<td></td>
<td>Ataxia</td>
<td>CNS leukemia/lymphoma</td>
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<td>Seizures</td>
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<td></td>
<td></td>
<td>Dysarthria</td>
<td>Relapsed leukemia/lymphoma treated with CNS-directed therapy</td>
<td></td>
<td>Other neurologic symptoms</td>
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<td>Dysphagia</td>
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<td>Yearly</td>
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<td>Hemiparesis</td>
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<td><strong>PHYSICAL</strong></td>
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<td>Seizures</td>
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<td>Neurologic exam</td>
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<td>Yearly</td>
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<td><strong>Info Link</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td><strong>Considerations for Further Testing and Intervention</strong></td>
</tr>
<tr>
<td></td>
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<td></td>
<td></td>
<td></td>
<td>Brain CT; Brain MRI with MR angiography as clinically indicated with referred study based on intracranial lesion to be evaluated:</td>
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<td></td>
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<td>- Calcifications: CT</td>
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<td>- White matter: MRI with diffusion-tensor imaging (DTI)</td>
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<td></td>
<td>- Microvascular injury: Gadolinium-enhanced MRI with diffusion-weighted imaging (DWI)</td>
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<td></td>
<td></td>
<td></td>
<td>Neurology consultation and follow-up as clinically indicated.</td>
</tr>
</tbody>
</table>

**Info Link**

- 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. Note: new deficits may emerge over time.

**SECTION 24 REFERENCES**

### SECTION 24 REFERENCES (continued)

<table>
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<th>Health Counseling/ Further Considerations</th>
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<tr>
<td>25</td>
<td><strong>ANTIMETABOLITES</strong></td>
<td>No known late effects</td>
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<td>SCREENING</td>
<td><strong>SYSTEM = No Known Late Effects</strong></td>
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<td>Cytarabine (low dose IV)</td>
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<td>No Known Late Effects</td>
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<tr>
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<td>Cytarabine IO</td>
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<td>Cytarabine IT</td>
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<td>Cytarabine SQ</td>
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*Info Link*
Acute toxicities predominate, from which the majority of patients recover without sequelae.

Low-dose IV is defined as any single dose < 1000 mg/m².
## ANTIMETABOLITES (cont)

<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
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<th>Health Counseling/ Further Considerations</th>
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<tbody>
<tr>
<td>26</td>
<td><strong>ANTIMETABOLITES</strong></td>
<td>Mercaptopurine (6MP)</td>
<td>Hepatic dysfunction</td>
<td>Medical Conditions</td>
<td><strong>PHYSICAL</strong></td>
<td>Health Links</td>
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<tr>
<td></td>
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<td>Thioguanine (6TG)</td>
<td>Veno-occlusive disease</td>
<td>Viral hepatitis</td>
<td>Scleral icterus</td>
<td>Liver Health</td>
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<td></td>
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<td></td>
<td>(VOD)</td>
<td>Previous VOD</td>
<td>Jaundice</td>
<td>Considerations for Further Testing and Intervention</td>
</tr>
<tr>
<td></td>
<td>Info Link</td>
<td></td>
<td></td>
<td></td>
<td>Hepatomegaly</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Acute hepatotoxicity reported with thioguanine used in CCG 1952 (regimens B1 and B2) for ALL maintenance therapy requires longer follow-up to determine long-term sequelae.</td>
<td></td>
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<td></td>
<td>Splenomegaly</td>
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<td>Yearly</td>
<td>SYSTEM = GI/Hepatic</td>
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<tr>
<td></td>
<td>Info Link</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>SCORE = 2A</td>
</tr>
<tr>
<td></td>
<td>• Acute toxicities predominate from which the majority of patients recover without sequelae.</td>
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<td></td>
<td>• Delayed hepatic dysfunction may occur after a history of acute VOD, presenting as portal hypertension with liver biopsy indicating nodular regenerative hyperplasia, fibrosis, or siderosis.</td>
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</tr>
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</table>

### SECTION 26 REFERENCES


<table>
<thead>
<tr>
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<th>Potential Late Effects</th>
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<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling/ Further Considerations</th>
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</thead>
<tbody>
<tr>
<td>27</td>
<td><strong>ANTIMETABOLITES</strong> Methotrexate (high dose IV) Methotrexate (low dose IV) Methotrexate IM Methotrexate PO</td>
<td>Reduced bone mineral density (BMD) Defined as Z-score &gt; 2.0 SD below the mean in survivors &lt; 20 years old or T-score &gt;1.0 SD below the mean in survivors ≥ 20 years old</td>
<td>Host Factors Both genders are at risk Younger age at diagnosis Caucasian Lower weight and BMI</td>
<td>Host Factors Older age at time of treatment Treatment Factors Methotrexate cumulative dose ≥ 40 gm/m² Prolonged corticosteroid therapy (e.g., for chronic GVHD)</td>
<td><strong>SCREENING</strong> Bone density evaluation (DEXA or quantitative CT) Baseline at entry into long-term follow-up, repeat as clinically indicated</td>
<td><strong>Health Links</strong> Bone Health <strong>Resources</strong> National Osteoporosis Foundation Website: <a href="http://www.nof.org">www.nof.org</a> <strong>Considerations for Further Testing and Intervention</strong> Ensure the AAP recommended minimum daily intake of Vitamin D (400 IU/day) for children, with possible considerations for high doses in selected patients (e.g., kidney disease or Vitamin D deficiency). Many experts recommend higher Vitamin D intake in adults as well. Also 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. Advocate for regular weight-bearing exercises such as running and jumping. Use caution regarding calcium supplementation in patients with history of renal lithiasis. Treatment of exacerbating or predisposing conditions (e.g., hormonal replacement therapy for hypogonadism, growth hormone 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).</td>
</tr>
</tbody>
</table>

### Info Link
- High-dose IV is defined as any single dose ≥ 1000 mg/m².

### Info Link
- The World Health Organization definition of osteoporosis in adults is based on comparison of a measured bone mineral density (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.

**SYSTEM = Musculoskeletal**
**SCORE = 2B**
### CHERMOTherapy

<table>
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<th>Periodic Evaluation</th>
<th>Health Counseling/ Further Considerations</th>
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### Section 27 References

# ANTIMETABOLITES (cont)

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<td>Methotrexate (high dose IV)</td>
<td>Renal toxicity</td>
<td>Host Factors</td>
<td>Treatment Factors</td>
<td>PHYSICAL</td>
<td>Health Links</td>
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<td>Methotrexate (low dose IV)</td>
<td>Glomerular injury</td>
<td>Mononephric</td>
<td>Combined with other</td>
<td>Blood pressure</td>
<td>Kidney Health</td>
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<td>Methotrexate IM</td>
<td>Hypertension</td>
<td>Treatment</td>
<td>nephrotoxic agents</td>
<td>Yearly</td>
<td>Cardiovascular Risk Factors</td>
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<td>Methotrexate PO</td>
<td></td>
<td>Factors</td>
<td>such as:</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- Cisplatin/carboplatin</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>- Ifosfamide</td>
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<td>- Aminoglycosides</td>
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<td>- Amphotericin</td>
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<td>- Radiation impacting the kidneys</td>
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<td>Nephrectomy</td>
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<td>Info Link</td>
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<td>Acute toxicities predominate, from which the majority of patients recover without sequelae.</td>
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<tr>
<td>Info Link</td>
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<td>High-dose IV is defined as any single dose ≥ 1000 mg/m².</td>
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**SECTION 28 REFERENCES**


### Section 29: Antimetabolites (cont)

<table>
<thead>
<tr>
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<th>Potential Late Effects</th>
<th>Risk Factors</th>
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<th>Health Counseling/ Further Considerations</th>
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<tbody>
<tr>
<td>29</td>
<td>Antimetabolites</td>
<td>Hepatic dysfunction</td>
<td>Treatment Factors: Abdominal radiation, Medical Conditions: Viral hepatitis</td>
<td>Treatment Factors: Treatment before 1970, Medical Conditions: Chronic viral hepatitis</td>
<td><strong>Physical</strong>&lt;br&gt;- Scleral icterus&lt;br&gt;- Jaundice&lt;br&gt;- Ascites&lt;br&gt;- Hepatomegaly&lt;br&gt;- Splenomegaly&lt;br&gt;<strong>Screening</strong>&lt;br&gt;- ALT&lt;br&gt;- AST&lt;br&gt;- Bilirubin&lt;br&gt;Baseline at entry into long-term follow-up. Repeat as clinically indicated.</td>
<td><strong>Health Links</strong>&lt;br&gt;- Liver Health&lt;br&gt;<strong>Considerations for Further Testing and Intervention</strong>&lt;br&gt;- Prothrombin time for evaluation of 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. Gastroenterology/hepatology consultation in patients with persistent liver dysfunction. Hepatitis A and B immunization in patients lacking immunity. <strong>System = GI/Hepatic</strong>&lt;br&gt;<strong>Score = 2A</strong></td>
</tr>
</tbody>
</table>

### Antimetabolites

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

**Info Link**<br>High-dose IV is defined as any single dose ≥ 1000 mg/m².

### Section 29 References

<table>
<thead>
<tr>
<th>Section</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
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<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling/ Further Considerations</th>
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<tbody>
<tr>
<td>30</td>
<td>ANTIMETABOLITES Methotrexate (high dose IV) Methotrexate (IO) Methotrexate (IT)</td>
<td>Neurocognitive deficits Functional deficits in: - Executive function (planning and organizing) - 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>Host Factors Younger age at treatment CNS leukemia/lymphoma Relapsed leukemia/lymphoma treated with CNS-directed therapy Female sex Treatment Factors In combination with: - Corticosteroids - TBI - Cranial radiation - Cytarabine (high-dose IV) - Longer elapsed time since therapy - Hyperthyroidism</td>
<td>Host Factors Age &lt; 3 years old at time of treatment Premorbid or family history of learning or attention problems Treatment Factors Radiation dose ≥ 24 Gy Single fraction TBI (10 Gy)</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 Educational Issues Considerations for Further Testing and Intervention Formal neuropsychological evaluation to include tests of processing speed, computer-based attention, visual motor integration, memory, comprehension of verbal instructions, verbal fluency, executive function and planning. Refer patients with neurocognitive deficits to school liaison in community or cancer center (psychologist, social worker, school counselor) to facilitate acquisition of educational resources and/or social skills training. Consider use of psychotropic medication (e.g., stimulants) or evidence-based rehabilitation training. Caution—lower starting dose and assessment of increased sensitivity when initiating therapy is recommended. Refer to community services for vocational rehabilitation or for services for developmentally disabled.</td>
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</table>

**SYSTEM = CNS **
SCORE = 1

---

**SECTION 30 REFERENCES**

### ANTIMETABOLITES (cont)

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<th>Sec #</th>
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#### SECTION 30 REFERENCES—continued


### ANTIMETABOLITES (cont)

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<th>Risk Factors</th>
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</tr>
</thead>
<tbody>
<tr>
<td>31</td>
<td>ANTIMETABOLITES</td>
<td>Methotrexate (high dose IV) Methotrexate (IO) Methotrexate (IT)</td>
<td>Clinical leukoencephalopathy Spasticity Ataxia Dysarthria Dysphagia Hemiparesis Seizures</td>
<td>Host Factors Younger age at treatment CNS leukemia/lymphoma Relapsed leukemia/lymphoma treated with CNS-directed therapy</td>
<td>Treatment Factors Radiation dose ≥ 24 Gy</td>
<td>HISTORY Cognitive, motor and/or sensory deficits Seizures Other neurologic symptoms Yearly Physical Neurological exam Yearly</td>
</tr>
</tbody>
</table>

**Info Link**
- High-dose IV is defined as any single dose ≥ 1000 mg/m².
- 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.

**Considerations for Further Testing and Intervention**
- Brain CT, Brain MRI with MR angiography as clinically indicated with preferred study based on intracranial lesion to be evaluated:
  - Calcifications: CT
  - White matter: MRI with diffusion-tensor imaging (DTI)
  - Microvascular injury: Gadolinium-enhanced MRI with diffusion-weighted imaging (DWI)
- Neurology consultation and follow-up as clinically indicated.

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

### SECTION 31 REFERENCES


### Section 32 References

## Anthracycline Antibiotics (cont)

<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling/Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>33 (male)</td>
<td>Anthracycline Antibiotics</td>
<td>Daunorubicin, Doxorubicin, Epirubicin, Idarubicin, Mitoxantrone</td>
<td>Cardiac toxicity, Cardiomyopathy, Arrhythmias, Subclinical left ventricular dysfunction</td>
<td>Host Factors: Black/or African descent, Younger than age 5 years at time of treatment</td>
<td>History: SOB, DOE, Orthopnea, Chest pain, Palpitations. If under 25 yrs: abdominal symptoms (nausea, vomiting). Yearly</td>
<td>Counseling: Counsel patients with prolonged QTc interval about use of medications that may further prolong the QTc interval (e.g., tricyclic anti-depressants, antifungals, macrolide antibiotics, metronidazole). Counsel regarding maintaining appropriate weight, blood pressure and heart-healthy diet. Counsel regarding appropriate exercise. Aerobic exercise is generally safe and should be encouraged for most patients. Intensive isometric activities (e.g., heavy weight lifting, wrestling) should generally be avoided. High repetition weight lifting involving lighter weights is more likely to be safe. The number of repetitions should be limited to that which the survivor can perform with ease. Patients who choose to engage in strenuous or varsity team sports should discuss appropriate guidelines and a plan for ongoing monitoring with a cardiologist.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Treatment Factors: Combined with radiation involving the heart, Combined with other cardiotoxic chemotherapy - Cyclophosphamide conditioning for HCT - Amsacrine</td>
<td>Treatment Factors: Higher cumulative anthracycline doses: - ≥ 550 mg/m² in patients 18 years or older at time of treatment - ≥ 300 mg/m² in patients younger than 18 years at time of treatment - Any dose in infancy - Chest radiation ≥ 30 Gy Longer time elapsed</td>
<td></td>
<td>Considerations for Further Testing and Intervention: Cardiology consultation in patients with subclinical abnormalities on screening evaluations, left ventricular dysfunction, dysrhythmia, or prolonged QTc interval. Consider excess risk of intensive isometric exercise program in any high-risk patient (defined as needing screening every 1 or 2 years).</td>
</tr>
</tbody>
</table>

### Info Link (Mitoxantrone)

- Although Mitoxantrone technically belongs to the anthracenedione class of antitumor antibiotics, it is related to the anthracycline family and is included here because of its cardiotoxic potential.

### Info Link (Dose Conversion)

- Pediatric studies of anthracycline cardiotoxicity typically describe risks based on combined cumulative doses of doxorubicin. There is a paucity of literature to support isotoxic dose conversion.
- To gauge the frequency of screening, use the following formulas to convert to doxorubicin isotoxic equivalents prior to calculating total cumulative anthracycline dose:
  - Doxorubicin: Multiply total dose x 1
  - Daunorubicin: Multiply total dose x 1
  - Epirubicin: Multiply total dose x 0.67
  - Idarubicin: Multiply total dose x 5
  - Mitoxantrone: Multiply total dose x 4
- Clinical judgment should ultimately be used to determine indicated screening for individual patients.

### Clinical Judgment

- Follow-up after anthracycline dosage of doxorubicin isotoxic equivalent.
- Multiply total dose
- Doxorubicin: x 1
- Daunorubicin: x 1
- Epirubicin: x 0.67
- Idarubicin: x 5
- Mitoxantrone: x 4

### Potential Late Effects

- **Cardiac toxicity:**
  - Cardiomyopathy
  - Arrhythmias

- **Subclinical left ventricular dysfunction**

### Risk Factors

#### Host Factors

- Black/or African descent
- Younger than age 5 years at time of treatment

#### Treatment Factors

- Combined with radiation involving the heart
- Combined with other cardiotoxic chemotherapy
- Cyclophosphamide conditioning for HCT
- Amsacrine

### Highest Risk Factors

- Higher cumulative anthracycline doses:
  - ≥ 550 mg/m² in patients 18 years or older at time of treatment
  - ≥ 300 mg/m² in patients younger than 18 years at time of treatment
  - Any dose in infancy
  - Chest radiation ≥ 30 Gy
  - Longer time elapsed

### Periodic Evaluation

- **History:**
  - SOB
  - DOE
  - Orthopnea
  - Chest pain
  - Palpitations
  - If under 25 yrs: abdominal symptoms (nausea, vomiting)

- **Yearly:**
  - Exertional intolerance is uncommon in patients younger than 25 years old.
  - Abdominal symptoms (nausea, emesis) may be observed more frequently than exertional dyspnea or chest pain in younger patients.

### Physical

- Cardiac murmur
- S3, S4
- Increased P2 sound
- Pericardial rub
- Rales
- Wheezes
- Jugular venous distension
- Peripheral edema

### Screening

- **ECHO (or comparable imaging to evaluate cardiac function):**
  - Baseline at entry into long-term follow-up, then periodically based on age at treatment, radiation dose, and cumulative anthracycline dose.
  - EKG (include evaluation of QTc interval)
  - Baseline at entry into long-term follow-up, repeat as clinically indicated.
**ANTHRACYCLINE ANTIBIOTICS (cont)**

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**SECTION 33 REFERENCES**


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<table>
<thead>
<tr>
<th>Age at Treatment</th>
<th>Radiation with Potential Impact to the Heart</th>
<th>Anthracycline Dose</th>
<th>Recommended Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1 year old</td>
<td>Yes</td>
<td>Any</td>
<td>Every year</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>&lt;200 mg/m²</td>
<td>Every 2 years</td>
</tr>
<tr>
<td></td>
<td></td>
<td>≥200 mg/m²</td>
<td>Every year</td>
</tr>
<tr>
<td>1-4 years old</td>
<td>Yes</td>
<td>Any</td>
<td>Every year</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>&lt;100 mg/m²</td>
<td>Every 5 years</td>
</tr>
<tr>
<td></td>
<td></td>
<td>≥100 mg/m² to &lt;300 mg/m²</td>
<td>Every 2 years</td>
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<tr>
<td></td>
<td></td>
<td>≥300 mg/m²</td>
<td>Every year</td>
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<tr>
<td>≥5 years old</td>
<td>Yes</td>
<td>&lt;300 mg/m²</td>
<td>Every 2 years</td>
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<tr>
<td></td>
<td></td>
<td>≥300 mg/m²</td>
<td>Every year</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>&lt;200 mg/m²</td>
<td>Every 5 years</td>
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<tr>
<td></td>
<td></td>
<td>≥200 mg/m² to &lt;300 mg/m²</td>
<td>Every 2 years</td>
</tr>
<tr>
<td></td>
<td></td>
<td>≥300 mg/m²</td>
<td>Every year</td>
</tr>
<tr>
<td>Any age with decrease in serial function</td>
<td></td>
<td></td>
<td>Every year</td>
</tr>
</tbody>
</table>

*Age at time of first cardiotoxic therapy (anthracycline or radiation [see Section 80], whichever was given first)

†Based on doxorubicin isotoxic equivalent dose [see conversion factors on previous page, “Info Link (Dose Conversion)”]
<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling/ Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>34</td>
<td>ANTHRACYCLINE ANTIBIOTICS</td>
<td></td>
<td>Cardiac toxicity</td>
<td>Combined with radiation involving the heart</td>
<td>Host Factors</td>
<td>HISTORY</td>
</tr>
<tr>
<td></td>
<td>Daunorubicin</td>
<td>Cardiomyopathy</td>
<td>Arhythmiyas</td>
<td>Combined with other cardiotoxic chemotherapy</td>
<td>Female sex</td>
<td>S0B</td>
</tr>
<tr>
<td></td>
<td>Doxorubicin</td>
<td>Subclinical left ventricular dysfunction</td>
<td>- Cyclophosphamide conditioning for HCT</td>
<td>Black/of African descent</td>
<td>Orthopnea</td>
<td>DOE</td>
</tr>
<tr>
<td></td>
<td>Epirubicin</td>
<td></td>
<td>- Amsacine</td>
<td>Younger than age 5 years at time of treatment</td>
<td>Chest pain</td>
<td>Chest pain</td>
</tr>
<tr>
<td></td>
<td>Idarubicin</td>
<td></td>
<td>Medical Conditions</td>
<td>Over 300 mg/m² in patients younger than 18 years at time of treatment</td>
<td>Palpitations</td>
<td>Cardiac dysfunction</td>
</tr>
<tr>
<td></td>
<td>Mitoxantrone</td>
<td></td>
<td>Health Behaviors</td>
<td>Any dose in infant</td>
<td>If under 25 yrs: abdominal symptoms</td>
<td>If under 25 yrs: abdominal symptoms</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Isometric exercise</td>
<td>- Chest radiation ≥ 30 Gy</td>
<td>(nausea, vomiting)</td>
<td>(nausea, vomiting)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Drug use</td>
<td>Drug use (e.g., cocaine, diet pills, ephedra, mahuang)</td>
<td>Longer time elapsed</td>
<td>Yearly</td>
<td>Yearly</td>
</tr>
</tbody>
</table>

**Info Link (Mitoxantrone):** Although Mitoxantrone technically belongs to the anthracenedione class of anti-tumor antibiotics, it is related to the anthracycline family and is included here because of its cardiotoxic potential.

**Info Link (Dose Conversion):**
- Pediatric studies of anthracycline cardiotoxicity typically describe risks based on combined cumulative doses of doxorubicin. There is a paucity of literature to support isotropic dose conversion.
- To gauge the frequency of screening, use the following formulas to convert to doxorubicin isotopic equivalents prior to calculating total cumulative anthracycline dose.
  - Doxorubicin: Multiply total dose x 1
  - Daunorubicin: Multiply total dose x 1
  - Epirubicin: Multiply total dose x 0.67
  - Idarubicin: Multiply total dose x 5
  - Mitoxantrone: Multiply total dose x 4
  - Clinical judgment should ultimately be used to determine indicated screening for individual patients.

**Info Link:**
- Dose levels correlating with cardiotoxicity are derived from adult studies.
- Childhood cancer patients exhibit clinical and subclinical toxicity at lower levels.
- Certain conditions (such as isometric exercise, pregnancy, 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.
### SECTION 34 REFERENCES


### RECOMMENDED FREQUENCY OF ECHOCARDIOGRAM (or comparable cardiac imaging)

<table>
<thead>
<tr>
<th>Age at Treatment&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Radiation with Potential Impact to the Heart&lt;sup&gt;b&lt;/sup&gt;</th>
<th>Anthracycline Dose&lt;sup&gt;c&lt;/sup&gt;</th>
<th>Recommended Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1 year old</td>
<td>Yes</td>
<td>Any</td>
<td>Every year</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>&lt; 200 mg/m²</td>
<td>Every 2 years</td>
</tr>
<tr>
<td></td>
<td></td>
<td>≥ 200 mg/m²</td>
<td>Every year</td>
</tr>
<tr>
<td>1-4 years old</td>
<td>Yes</td>
<td>Any</td>
<td>Every year</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>&lt;100 mg/m²</td>
<td>Every 5 years</td>
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<tr>
<td></td>
<td></td>
<td>100 to &lt;300 mg/m²</td>
<td>Every 2 years</td>
</tr>
<tr>
<td></td>
<td></td>
<td>≥300 mg/m²</td>
<td>Every year</td>
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<tr>
<td>≥5 years old</td>
<td>Yes</td>
<td>&lt;300 mg/m²</td>
<td>Every 2 years</td>
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<tr>
<td></td>
<td></td>
<td>≥300 mg/m²</td>
<td>Every year</td>
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<tr>
<td></td>
<td>No</td>
<td>&lt;200 mg/m²</td>
<td>Every 5 years</td>
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<tr>
<td></td>
<td></td>
<td>200 to &lt;300 mg/m²</td>
<td>Every 2 years</td>
</tr>
<tr>
<td></td>
<td></td>
<td>≥300 mg/m²</td>
<td>Every year</td>
</tr>
</tbody>
</table>

<sup>a</sup>Age at time of first cardiotoxic therapy (anthracycline or radiation [see Section 81], whichever was given first)

<sup>b</sup>See Section 81

<sup>c</sup>Based on doxorubicin isotoxic equivalent dose [see conversion factors on previous page, “Info Link (Dose Conversion)”]
<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling/ Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>35</td>
<td>ANTI-TUMOR ANTIBIOTICS Bleomycin</td>
<td>Pulmonary toxicity - Interstitial pneumonitis - Pulmonary fibrosis - Acute respiratory distress syndrome (very rare)</td>
<td>Treatment Factors - Bleomycin dose: 400 U/m² (injury observed in doses 60–100 U/m² in children) Combined with: - Chest radiation - TBI</td>
<td>HISTORY - Cough - SOB - DOE - Wheezing - Yearly</td>
<td>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>
</tr>
</tbody>
</table>

- **SYSTEM** = Pulmonary  
- **SCORE** =  
  - Interstitial pneumonitis = 1  
  - Pulmonary fibrosis = 1  
  - ARDS = 2B  

### SECTION 35 REFERENCES


### SECTION 35 REFERENCES—continued

<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling/ Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>36</td>
<td>ANTI-TUMOR ANTIBIOTICS (cont) Dactinomycin</td>
<td>No known late effects</td>
<td>SCREENING</td>
<td>No Known Late Effects</td>
<td></td>
<td>Health Links</td>
</tr>
</tbody>
</table>

**Info Link**
Dactinomycin has been associated with acute veno-occlusive disease, from which the majority of patients recover without sequelae.

**SECTION 36 REFERENCES**
### CORTICOSTEROIDS

<table>
<thead>
<tr>
<th>Section</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling/ Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>37</td>
<td>CORTICOSTEROIDS</td>
<td>Reduced bone mineral density (BMD) Defined as Z-score &gt; 2.0 SD below the mean in survivors &lt; 20 years old or T-score &gt; 1.0 SD below the mean in survivors ≥ 20 years old</td>
<td>Host Factors Both genders are at risk Younger age at diagnosis Caucasian Lower weight and BMI</td>
<td>Host Factors Older age at time of treatment Treatment Factors Dexamethasone effect is more potent than prednisone Glucocorticoid cumulative dose ≥ 9 gm/m² prednisone equivalent</td>
<td>SCREENING Bone density evaluation (DEXA or quantitative CT) Baseline at entry into long-term follow-up, repeat as clinically indicated</td>
<td><strong>Health Links</strong> Bone Health <strong>Resources</strong> National Osteoporosis Foundation Website (<a href="http://www.nof.org">www.nof.org</a>) <strong>Considerations for Further Testing and Intervention</strong> Ensure the AAP recommended minimum daily intake of Vitamin D (400 IU/day) for children, with possible considerations for higher doses in selected patients (e.g., kidney disease or Vitamin D deficiency). Many experts recommend higher Vitamin D intake in adults as well. Also 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. Advocate for regular weight-bearing exercises such as running and jumping. Use caution regarding calcium supplementation in patients with history of renal lithiasis. Treatment of exacerbating or predisposing conditions (e.g., hormonal replacement therapy for hypogonadism, growth hormone 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).</td>
</tr>
</tbody>
</table>

**Info Link**
- The World Health Organization definition of osteoporosis in adults is based on comparison of a measured bone mineral density (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.
<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling/Further Considerations</th>
</tr>
</thead>
</table>

### CORTICOSTEROIDS (cont)

#### SECTION 37 REFERENCES


### CHEMOTHERAPY

<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling/ Further Considerations</th>
</tr>
</thead>
</table>

**Info Link**  
- Osteonecrosis typically occurs during the acute treatment phase, may progress over time or resolve.  
- Multifocal osteonecrosis is significantly more common (3:1) than unifocal.

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

### SECTION 38 REFERENCES

<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling/ Further Considerations</th>
</tr>
</thead>
</table>
| 39    | CORTICOSTEROIDS      | Cataracts              | Treatment Factors Combined with: - TBI - Busulfan | Treatment Factors TBI Cranial, orbital, or eye radiation Longer interval since treatment | HISTORY Visual changes (decreased acuity, halos, diplopia) Yearly | HEALTH CARE HEALTH CARE HEALTH CARE HEALTH CARE HEALTH CARE HEALTH CARE HEALTH CARE HEALTH CARE HEALTH CARE HEALTH CARE HEALTH CARE HEALTH CARE HEALTH CARE HEALTH CARE HEALTH CARE HEALTH CARE HEALTH CARE HEALTH CARE HEALTH CARE HEALTH CARE HEALTH CARE HEALTH CARE HEALTH CARE HEALTH CARE HEALTH CARE HEALTH CARE HEALTH CARE HEALTH CARE HEALTH CARE HEALTH CARE HEALTH CARE HEALTH CARE HEALTH CARE HEALTH CARE HEALTH CARE HEALTH CARE HEALTH CARE HEALTH CARE HEALTH CARE HEALTH CARE HEALTH CARE HEALTH CARE HEALTH CARE HEALTH CARE HEALTH CARE HEALTH CARE HEALTH CARE HEALTH CARE HEALTH CARE HEALTH CARE HEALTH CARE HEALTH CARE HEALTH CARE HEALTH CARE HEALTH CARE HEALTH CARE HEALTH CARE HEALTH CARE HEALTH CARE HEALTH CARE HEALTH CARE 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**SECTION 39 REFERENCES**


## Chemotherapy

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<tr>
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<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling/Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>40</td>
<td>ENZYMES Asparaginase</td>
<td>No known late effects</td>
<td></td>
<td></td>
<td>HISTORY</td>
<td>SYSTEM = No Known Late Effects SCORE = 1</td>
</tr>
</tbody>
</table>

### Info Link

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

### Section 40 References


## Chemotherapy

<table>
<thead>
<tr>
<th>Sec #</th>
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<th>Potential Late Effects</th>
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<th>Periodic Evaluation</th>
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</thead>
<tbody>
<tr>
<td>41</td>
<td>PLANT ALKALOIDS</td>
<td>Vinblastine Vincristine</td>
<td>Peripheral sensory or motor neuropathy</td>
<td>Treatment Factors Combined with platinum chemotherapy, gemcitabine or taxanes</td>
<td>Medical Conditions Charcot-Marie-Tooth disease</td>
<td>HISTORY: Areflexia Weakness Foot drop Paresthesias Dysesthesias Yearly until 2 to 3 years after therapy, monitor yearly if symptoms persist</td>
</tr>
</tbody>
</table>

### Info Link
- 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.

### System = PNS

### Score = 2A

## Plant Alkaloids

### Section 41 References


## PLANT ALKALOIDS (cont)

<table>
<thead>
<tr>
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<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
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</thead>
<tbody>
<tr>
<td>42</td>
<td>PLANT ALKALOIDS</td>
<td>Vinblastine Vincristine</td>
<td>Vasospastic attacks (Raynaud’s phenomenon)</td>
<td>Health Behaviors Smoking Illicit drug use</td>
<td>HISTORY Vasospasms of hands, feet, nose, lips, cheeks, or earlobes related to stress or cold temperatures Yearly</td>
<td>PHYSICAL Physical exam of affected area As indicated</td>
</tr>
</tbody>
</table>

### SECTION 42 REFERENCES


## CHEMOTHERAPY

<table>
<thead>
<tr>
<th>Sec #</th>
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<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling/ Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>43 EPIPODOPHYLLOTOXINS</td>
<td>Etoposide (VP16) Teniposide (VM26)</td>
<td>Acute myeloid leukemia</td>
<td>Medical Conditions Splenectomy (conflicting evidence)</td>
<td>Treatment Factors Weekly or twice weekly administration Less than 5 years since exposure to agent Autologous HCT</td>
<td>HISTORY Fatigue Bleeding Easy bruising Yearly, up to 10 years after exposure to agent PHYSICAL Dermatologic exam (pallor, petechiae, purpura) Yearly, up to 10 years after exposure to agent</td>
<td>Health Links Reducing the Risk of Second Cancers Counseling Counsel to promptly report fatigue, pallor, petechiae, or bone pain. Considerations for Further Testing and Intervention CBC and bone marrow exam as clinically indicated.</td>
</tr>
</tbody>
</table>

### Info Link
Epipodophyllotoxin administration schedules since approximately 1990; have been modified to reduce the risk of this complication.

### SECTION 43 REFERENCES


DETERMINING APPLICABILITY OF RADIATION SECTIONS FOR SPECIFIC PATIENTS BASED ON EXPOSURE

GENERAL CONSIDERATIONS

- The radiation sections of the COG Long-Term Follow-Up Guidelines (Sections 44–102) are organized by anatomic region from the head downward. For specifics regarding relevant exposures to each anatomic region and radiation field, refer to the applicable pages of the “Radiation Reference Guide” in Appendix I and to the figures in this section.

- To determine specific screening guidelines by section number for an individual patient, use the “Patient-Specific Guideline Identification Tool” in Appendix I together with the “Radiation Reference Guide.”

RADIATION DOSE CALCULATIONS

Some sections of the COG Long-Term Follow-Up Guidelines relevant to radiation exposure include 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 (see Appendix I—“Radiation Reference Guide”—for examples).

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

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.

§Whole lung radiation, if given, should be included in minimum dose calculations for Sections 75–77, 83, 102.

GENERAL FACTORS INFLUENCING RADIATION TOXICITY

Include: daily fraction size, cumulative dose, age of patient at irradiation and type of radiation used. Toxicity may not be manifest until growth is completed or patient ages.
NOTES

- This diagram provides an overview of the organization of the radiation sections of the COG Long-Term Follow-Up Guidelines.
- Radiation sections are arranged by anatomic region beginning with the cranium and proceeding downward.
- Arrows traversing multiple anatomic areas indicate body systems or organs (i.e., oral cavity, neck/thyroid, heart, esophagus, and bowel) that may be affected by radiation to any of the indicated anatomic regions.
- Additional detailed information, including examples of radiation dose calculations and diagrams of each body region are provided in the “Radiation Reference Guide” (Appendix I).
- Use the “Patient-Specific Guideline Identification Tool” in Appendix I together with the “Radiation Reference Guide” to determine specific screening guidelines by section number for individual patients.

\[\text{Screening may be indicated for patients who received TBI alone—see Info Link in indicated section(s).}\]
### Section 44: RADIATION ALL FIELDS (INCLUDING TBI)

#### Therapeutic Agent(s)

All Radiation Fields (Including TBI)

#### Potential Late Effects

Secondary benign or malignant neoplasm  
Occurring in or near radiation field

#### Risk Factors

**Host Factors**
- Cancer predisposing mutation (e.g., p53, RB1, NF1)  
- Younger age at treatment  

**Treatment Factors**
- High cumulative radiation dose  
- Large radiation treatment volumes  
- Alkylating agent exposure

#### Highest Risk Factors

**Treatment Factors**
- Orthovoltage radiation (commonly used before 1970) due to delivery of greater dose to skin and bones

#### Periodic Evaluation

**PHYSICAL**
- Inspection and palpation of skin and soft tissues in irradiated field(s)

**SCREENING**
- Other evaluations based on treatment volumes

**Yearly**

**Further Considerations**

Health Counseling:

- Reducing the Risk of Second Cancers

- Considerations for Further Testing and Intervention
  
  Surgical and/or oncology consultation as clinically indicated.

### See Section 44 References

**RADIATION**

<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling/ Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>45</td>
<td>All Radiation Fields (Including TBI)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- **Dysplastic nevi Skin cancer**
- **Basal cell carcinoma**
- **Squamous cell carcinoma**
- **Melanoma**

**Host Factors**
- Gorlin’s syndrome (nevoid basal cell carcinoma syndrome)

**Health Behaviors**
- Sun exposure
- Tanning booths

**Treatment Factors**
- Orthovoltage radiation (commonly used before 1970) due to delivery of greater dose to skin and bones

**HISTORY**
- Skin lesions
- Changing moles (asymmetry, bleeding, increasing size, indistinct borders)

**PHYSICAL**
- Dermatologic exam of irradiated fields

**Health Links**
- Skin Health
- Reducing the Risk of Second Cancers

**Considerations for Further Testing and Intervention**
- Dermatology consultation for evaluation and monitoring of atypical nevi. Oncology consultation as clinically indicated.

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

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**SECTION 45 REFERENCES**

## RADIATION

<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>46</td>
<td>All Radiation Fields (Except TBI)</td>
<td>Dermatologic changes Fibrosis Telangiectasias Permanent alopecia Altered skin pigmentation</td>
</tr>
</tbody>
</table>

### Risk Factors
- **Host Factors**
  - Younger age at treatment
- **Treatment Factors**
  - Total radiation dose $\geq 40$ Gy
  - Large dose fractions (e.g., $\geq 2$ Gy per fraction)

### Highest Risk Factors
- Treatment Factors
  - Radiation dose $\geq 50$ Gy
  - Orthovoltage radiation (commonly used before 1970) due to delivery of greater dose to skin and bones

### Periodic Evaluation
- **PHYSICAL**
  - Dermatologic exam of irradiated fields
  - Yearly

### Health Counseling/Further Considerations
- **Health Links**
  - Skin Health
  - System = Dermatologic
  - Score = 1

---

### SECTION 46 REFERENCES

<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling/ Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>47</td>
<td>All Radiation Fields (Except TBI)</td>
<td>Bone malignancies</td>
<td>Host Factors: Adolescent at treatment Cancer-predisposing mutation (e.g., p53, RB1, NF1) Treatment Factors: Higher radiation dose Combined with alkylating agents</td>
<td>Treatment Factors: Radiation dose ≥ 30 Gy Orthovoltage radiation (commonly used before 1970) due to delivery of greater dose to skin and bones</td>
<td>HISTORY: Bone pain (especially in irradiated field) Yearly PHYSICAL: Palpation of bones in irradiated field Yearly</td>
<td>Counseling: Counsel patient to report symptoms promptly (e.g., bone pain, bone mass, persistent fevers) Considerations for Further Testing and Intervention: X-ray or other diagnostic imaging in patients with clinical symptoms. Oncology consultation as clinically indicated.</td>
</tr>
</tbody>
</table>

**SECTION 47 REFERENCES**


### RADIATION

<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
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<th>Health Counseling/ Further Considerations</th>
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*See “Patient-Specific Guideline Identification Tool” in Appendix I to determine specific screening guidelines by section number for individual patients.*

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### SECTION 48 REFERENCES


<table>
<thead>
<tr>
<th>Sec #</th>
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<th>Health Counseling/ Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>49</td>
<td>Cranial Ear/Infratemporal Total Body Irradiation (TBI)</td>
<td>Neurocognitive deficits Functional deficits in: - Executive function (planning and organization) - Sustained attention - Memory (particularly visual, sequential, temporal memory) - Processing speed - Visual-motor integration - Fine motor dexterity - Language Learning deficits in math and reading (particularly reading comprehension) Diminished IQ Behavioral change</td>
<td>Host Factors Younger age at treatment Primary CNS tumor CNS leukemia/lymphoma Relapsed leukemia/lymphoma treated with CNS-directed therapy Head/neck tumors with brain in radiation field</td>
<td>Host Factors Age &lt; 3 years at time of treatment Female sex Temporal lobe field Premorbid or family history of learning or attention problems</td>
<td>HISTORY Educational and/or vocational progress Yearly</td>
<td>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>
</tr>
</tbody>
</table>

**Info Link**
- Neurocognitive deficits in survivors of leukemia and lymphoma are more frequently related to information processing (e.g., learning disability).
- 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 deficits may emerge over time.

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

**SECTION 49 REFERENCES**

## RADIATION

<table>
<thead>
<tr>
<th>Sec #</th>
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</table>

### POTENTIAL IMPACT TO BRAIN/CRANIUM (cont)

### SECTION 49 REFERENCES–continued


<table>
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<th>Periodic Evaluation</th>
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</tr>
</thead>
<tbody>
<tr>
<td>50</td>
<td>Cranial Ear/Infratemporal Total Body Irradiation (TBI)</td>
<td>Clinical leuкоencephalopathy Spasticity Ataxia Dysarthria Dysphagia Hemi pari esis Seizures</td>
<td>Host Factors Younger age at treatment CNS leukemia/lymphoma Relapsed leukemia/lymphoma treated with CNS-directed therapy Treatment Factors In combination with: - Dexamethasone - Methotrexate (IT, IO, high-dose IV) - Cytarabine (high-dose IV) - Higher radiation dose Larger radiation field Greater cortical volumes Longer elapsed time since therapy</td>
<td>Host Factors Radiation dose ≥ 24 Gy Treatment Factors Fraction dose ≥ 3 Gy</td>
<td>HISTORY Cognitive, motor and/or sensory deficits Seizures Other neurologic symptoms Yearly PHYSICAL Neurologic exam Yearly</td>
<td>Considerations for Further Testing and Intervention Brain CT, Brain MRI with MR angiography as clinically indicated with preferred study based on intracranial lesion to be evaluated: - Calcifications: CT - White matter: MRI with diffusion-tensor imaging (DTI) - Microvascular injury: Gadolinium-enhanced MRI with diffusion-weighted imaging (DWI) Neurology consultation and follow-up as clinically indicated.</td>
</tr>
</tbody>
</table>

**Info Link**
- Clinical leuкоencephalopathy may present with or without imaging abnormalities (e.g., leuкоencephalopathy, 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.

**SECTION 50 REFERENCES**


<table>
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<tr>
<th>Sec #</th>
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<tbody>
<tr>
<td></td>
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**SECTION 50 REFERENCES—continued**

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<th>Health Counseling/Further Considerations</th>
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</thead>
<tbody>
<tr>
<td>51</td>
<td>≥ 18 Gy to: Cranial Ear/Infratemporal Nasopharyngeal Orbital/Eye Waldeyer’s Ring TBI*</td>
<td>Cerebrovascular complications Stroke Moyamoya Occlusive cerebral vasculopathy Cavernomas</td>
<td>Host Factors Down syndrome Treatment Factors Suprasellar radiation Medical Conditions Sickle cell disease Neurofibromatosis</td>
<td>Host Factors Parasellar tumor Treatment Factors Radiation dose ≥ 50 Gy Circle of Willis in radiation field</td>
<td>HISTORY Hemiparesis Hemiplegia Weakness Aphasia PHYSICAL Neurologic exam Yearly</td>
<td>Considerations for Further Testing and Intervention Brain MRI with diffusion-weighted imaging with MR angiography as clinically indicated. Neurology/neurosurgery consultation and follow-up. Physical and occupational therapy as clinically indicated. Note: Revascularization procedures are likely helpful for moyamoya. Aspirin prophylaxis has not yet been shown to be beneficial for moyamoya or occlusive cerebral vasculopathy.</td>
</tr>
</tbody>
</table>

**Info Link**

- Moyamoya syndrome is the complete occlusion of one or more of the three major cerebral vessels with the development of small, immature collateral vessels.
- This condition 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.

- This section is only applicable to patients who:
  1) Received radiation to any of the specified fields at ≥ 18 Gy
  2) Received a combination of radiation to any of the specified fields and TBI, the sum of which is ≥ 18 Gy
- See dose calculation rules on page 56 for patients who received: (a) radiation to more than one of the specified fields, or (b) more than one planned course of treatment to the same field.
- See “Patient-Specific Guideline Identification Tool” in Appendix I to determine specific screening guidelines by section number for individual patients.

---

**SECTION 51 REFERENCES**


## RADIATION

<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling/Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>52</td>
<td>Cranial Ear/Infratemporal Nasopharyngeal Orbital/Eye Waldeyer's Ring</td>
<td>Craniofacial abnormalities</td>
<td>Host Factors</td>
<td>Host Factors</td>
<td>HISTORY</td>
<td>Resources</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Younger age at treatment Age &lt; 5 years at time of treatment Radiation dose ≥ 30 Gy</td>
<td>Treatment Factors</td>
<td>Treatment Factors</td>
<td>Psychosocial assessment, with attention to: Educational and/or vocational progress Depression Anxiety Post-traumatic stress Social withdrawal</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Higher radiation dose</td>
<td>Radiation dose ≥ 30 Gy</td>
<td>Yearly</td>
<td>Considerations for Further Testing and Intervention</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Reconstructive craniofacial surgical consultation. Consultation with psychologist in patients with adjustment disorders related to facial asymmetry/deformity.</td>
</tr>
</tbody>
</table>

### SYSTEM = Musculoskeletal

### SCORE = 1

---

### SECTION 52 REFERENCES


* See “Patient-Specific Guideline Identification Tool” in Appendix I to determine specific screening guidelines by section number for individual patients.
### RADIATION

<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling/ Further Considerations</th>
</tr>
</thead>
</table>
| 53    | Cranial Ear/Infratemporal Nasopharyngeal Orbital/Eye Waldeyer's Ring | Chronic sinusitis | Treatment Factors  
Radiation dose to sinuses  
≥ 30 Gy  
Radiomimetic chemotherapy  
(e.g., doxorubicin, dactinomycin) | Medical Conditions  
Atopic history  
Hypogammaglobulinemia | HISTORY  
Rhinorrhea, postnasal discharge  
Yearly | PHYSICAL  
Sinuses  
Yearly  
Nasal exam  
Yearly | SYSTEM = Immune  
SCORE = 1  
Considerations for Further Testing and Intervention  
CT scan of sinuses as clinically indicated. Otolaryngology consultation as clinically indicated. |

### SECTION 53 REFERENCES


*See “Patient-Specific Guideline Identification Tool” in Appendix I to determine specific screening guidelines by section number for individual patients.*
### RADIATION

**Therapeutic Agent(s):** Cranial Ear/Infratemporal Nasopharyngeal Orbital/Eye Waldeyer's Ring

**Potential Late Effects:** Overweight Obesity

**Host Factors:**
- Younger at treatment
- Higher cranial radiation dose
- Combined with corticosteroids

**Medical Conditions:**
- Familial dyslipidemia
- Growth hormone deficiency
- Hypothyroidism
- Hypogonadism

**Risk Factors:**
- Overweight: Age 2–20 years: BMI for age ≥ 85th – < 95th percentile
  - Age ≥ 21 years: BMI ≥ 25–29.9
  - Obesity: Age 2–20 years: BMI for age ≥ 95th percentile
  - Age ≥ 21 years: BMI ≥ 30

**Highest Risk Factors:**
- Age < 4 years old at time of treatment
- Female sex
- Cranial radiation dose ≥ 18 Gy

**Periodic Evaluation:**
- Height
- Weight
- BMI
- Blood pressure

**Health Counseling/Further Considerations:**
- Counsel regarding obesity-related health risks
- Consider evaluation for other co-morbid conditions, including dyslipidemia, hypertension, or impaired glucose metabolism.

---

**SECTION 54 REFERENCES**


### SECTION 54 REFERENCES—continued

### SECTION 55 REFERENCES


### SECTION 55 REFERENCES – continued


<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling/Further Considerations</th>
</tr>
</thead>
</table>
| 56    | Cranial Ear/Infratemporal Nasopharyngeal Orbital/Eye Waldeyer's Ring | Precocious puberty | Host Factors  
Younger age at treatment  
Treatment Factors  
Radiation doses $\geq$ 18 Gy | PHYSICAL  
Height  
Weight  
Tanner staging  
Testicular volume by Prader orchidometry  
Yearly until sexually mature | | |

**Potential Late Effects (cont)**

**SYSTEM = Endocrine/Metabolic**

**SCORE = 1**

**SECTION 56 REFERENCES**


• See “Patient-Specific Guideline Identification Tool” in Appendix I to determine specific screening guidelines by section number for individual patients.
<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling/ Further Considerations</th>
</tr>
</thead>
</table>
| 57    | Cranial Ear/Infratemporal Nasopharyngeal Orbital/Eye Waldeyer's Ring | Precocious puberty | Host Factors
Female sex
Younger age at treatment | Treatment Factors
Radiation doses ≥ 18 Gy | PHYSICAL
Height
Weight
Tanner staging
Yearly until sexually mature | Health Links
Precocious Puberty
Resources
www.magicfoundation.org
Considerations for Further Testing and Intervention
Obtain FSH, LH, estradiol as clinically indicated in patients with signs of accelerated pubertal progression and growth. Obtain x-ray for bone age in rapidly growing children. Endocrine consultation for accelerated puberty (puberty in girl < 8 years old). |

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

---

**SECTION 57 REFERENCES**


---

• See “Patient-Specific Guideline Identification Tool” in Appendix I to determine specific screening guidelines by section number for individual patients.
<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling/ Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>58</td>
<td>≥ 40 Gy to: Cranial Ear/Infratemporal Nasopharyngeal Orbital/Eye Waldeyer’s Ring TBI*</td>
<td>Hyperprolactinemia</td>
<td>Treatment Factors Higher radiation dose Surgery or tumor in hypothalamic area</td>
<td>Treatment Factors Radiation dose ≥ 50 Gy</td>
<td>HISTORY Decreased libido Galactorrhea Yearly</td>
<td>Health Links Hyperprolactinemia</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>SCREENING Prolactin level</td>
<td>Resources <a href="http://www.magicfoundation.org">www.magicfoundation.org</a></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>In patients with galactorrhea or decreased libido.</td>
<td>Considerations for Further Testing and Intervention CT evaluation of sella turcica for pituitary adenoma in patients with hyperprolactinemia. Endocrine consultation for patients with hyperprolactinemia or galactorrhea.</td>
</tr>
</tbody>
</table>

*This section is only applicable to patients who:
1) Received radiation to any of the specified fields at ≥ 40 Gy OR
2) Received a combination of radiation to any of the specified fields and TBI, the sum of which is ≥ 40 Gy

See dose calculation rules on page 56 for patients who received: (a) radiation to more than one of the specified fields, or (b) more than one planned course of treatment to the same field.

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

**SECTION 58 REFERENCES**


## RADIATION

<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling/ Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>59</td>
<td>&gt;= 40 Gy to: Cranial Ear/Infratemporal Nasopharyngeal Orbital/Eye Waldeyer’s Ring TBI*</td>
<td>Hyperprolactinemia</td>
<td>Treatment Factors: Higher radiation dose Surgery or tumor in hypothalamic area</td>
<td>Treatment Factors: Radiation dose &gt;= 50 Gy</td>
<td>HISTORY: Galactorrhea Menstrual history Yearly</td>
<td>SYSTEM = Endocrine/Metabolic Score = 1</td>
</tr>
</tbody>
</table>

### Hyperprolactinemia

- **HISTORY**
  - Galactorrhea
  - Menstrual history
- **SCREENING**
  - Prolactin level
  - In patients with galactorrhea or amenorrhea.

- **Treatment Factors**
  - Radiation dose >= 50 Gy

- **Screening Considerations**
  - CT evaluation of sella turcica for pituitary adenoma in patients with hyperprolactinemia.
  - Endocrine consultation for patients with hyperprolactinemia or galactorrhea.

### System Score
- **SYSTEM** = Endocrine/Metabolic
- **Score** = 1

---

### SECTION 59 REFERENCES


### RADIATION

<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling/ Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>60</td>
<td>≥ 40 Gy to: Cranial Ear/Infratemporal Nasopharyngeal Orbital/Eye Waldeyer's Ring TBI*</td>
<td>Central hypothyroidism</td>
<td>Treatment Factors Higher radiation dose</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Info Link*
Central hypothyroidism includes thyroid-releasing and thyroid-stimulating hormone deficiency

• This section is only applicable to patients who:
  1) Received radiation to any of the specified fields at ≥ 40 Gy
  2) Received a combination of radiation to any of the specified fields and TBI, the sum of which is ≥ 40 Gy

• See dose calculation rules on page 56 for patients who received: (a) radiation to more than one of the specified fields, or (b) more than one planned course of treatment to the same field.

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

*TBI is included for dose calculation purposes only; this section is not applicable to patients who received TBI alone.

### POTENTIAL IMPACT TO NEUROENDOCRINE AXIS (cont)

### SECTION 60 REFERENCES


**RADIATION**

**Therapeutic Agent(s)**
- Cranial
- Ear/Infratemporal
- Nasopharyngeal
- Orbital/Eye
- Waldeyer's Ring

**Potential Late Effects**
- Gonadotropin deficiency

**Risk Factors**
- Treatment Factors
-Higher radiation dose

**Highest Risk Factors**
- Gonadotropin deficiency
- Includes LH and FSH deficiency.

**Periodic Evaluation**
- **HISTORY**
  - Pubertal (onset, tempo)
  - Sexual function (erections, nocturnal emissions, libido)
  - Medication use
  - Yearly

- **PHYSICAL**
  - Tanner staging until sexually mature
  - Testicular volume by Prader orchiometer

- **SCREENING**
  - Semen analysis
  - At request of sexually mature patient
  - FSH
  - LH
  - Testosterone (ideally morning)
  - Baseline at age 14 and as clinically indicated in patients with delayed/arrested puberty and/or clinical signs and symptoms of testosterone deficiency

**Health Counseling/Further Considerations**
- **Health Links**
  - Male Health Issues
    - See also: Hypopituitarism

- **Resources**
  - American Society for Reproductive Medicine: [www.asrm.org](http://www.asrm.org)
  - Fertile Hope: [www.fertilehope.org](http://www.fertilehope.org)

- **Considerations for Further Testing and Intervention**
  - Refer to endocrinologist for delayed puberty or persistently abnormal hormone levels. Hormonal replacement therapy for hypogonadal patients. Reproductive endocrinology referral for infertility evaluation and consultation regarding assisted reproductive technologies. Spermatogenesis can be induced with gonadotropins in men with hypogonadotropic hypogonadism. Consider bone density testing in patients who are gonadotropin deficient.

**System = Reproductive (male)**
**Score = 1**

---

**SECTION 61 REFERENCES**

### RADIATION

<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling/ Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>62</td>
<td>≥ 30 Gy to: Cranial Ear/Infratemporal Nasopharyngeal Orbital/Eye Waldeyer's Ring</td>
<td><strong>Gonadotropin deficiency</strong></td>
<td>Treatment Factors: Higher radiation dose</td>
<td><strong>HISTORY</strong> Pubertal (onset, tempo) Menstrual/pregnancy history Sexual function (vaginal dryness, libido) Medication use</td>
<td>Yearly</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(female)</td>
<td><strong>Info Link</strong> Gonadotropin deficiency includes LH and FSH deficiency.</td>
<td></td>
<td><strong>PHYSICAL</strong> Tanner staging Yearly until sexually mature</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
|       |                      | *This section is only applicable to patients who:  
1) Received radiation to any of the specified fields at ≥ 30 Gy OR  
2) Received a combination of radiation to any of the specified fields and TBI, the sum of which is ≥ 30 Gy  
See dose calculation rules on page 56 for patients who received: (a) radiation to more than one of the specified fields, or (b) more than one planned course of treatment to the same field.  
See “Patient-Specific Guideline Identification Tool” in Appendix I to determine specific screening guidelines by section number for individual patients. | | |
|       |                      | *TBI is included for dose calculation purposes only; this section is not applicable to patients who received TBI alone. | | | |

• **SYSTEM** = Reproductive (female)  
**SCORE** = 1

### POTENTIAL IMPACT TO NEUROENDOCRINE AXIS (cont)

- **HISTORY**
  - Pubertal (onset, tempo)
  - Menstrual/pregnancy history
  - Sexual function (vaginal dryness, libido)
  - Medication use
- **PHYSICAL**
  - Tanner staging
  - Yearly until sexually mature
- **SCREENING**
  - FSH
  - LH
  - Estradiol
  - Baseline at age 13, and as clinically indicated in patients with delayed puberty, irregular menses, primary or secondary amenorrhea, or clinical signs and symptoms of estrogen deficiency

### SECTION 62 REFERENCES


- **Health Links**
  - Female Health Issues
  - See also: Hypopituitarism
- **Resources**
  - American Society for Reproductive Medicine: [www.asrm.org](http://www.asrm.org)
  - Fertile Hope: [www.fertilehope.org](http://www.fertilehope.org)
- **Considerations for Further Testing and Intervention**
  - Refer to endocrinologist for delayed puberty or persistently abnormal hormone levels. Hormonal replacement therapy for hypogonadal patients. Reproductive endocrinology referral for infertility evaluation and consultation regarding assisted reproductive technologies. Consider bone density testing in patients who are gonadotropin deficient.
## RADIATION

<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling/ Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>63</td>
<td>≥ 30 Gy to: Cranial Ear/Infratemporal Nasopharyngeal Orbital/Eye Waldeyer's Ring TBI*</td>
<td>Central adrenal insufficiency</td>
<td>Treatment Factors Higher radiation dose Surgery or tumor in the suprasellar region</td>
<td>Treatment Factors Prior development of another hypothalamic-pituitary endocrinopathy</td>
<td>HISTORY</td>
<td>Health Links</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Failure to thrive Anorexia Dehydration Hypoglycemia Lethargy Unexplained hypotension Yearly</td>
<td>Central Adrenal Insufficiency See also: Hypopituitarism</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>SCREENING</td>
<td>Resources</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Refer for yearly endocrinology evaluation if dose to hypothalamic-pituitary axis ≥30 Gy</td>
<td><a href="http://www.magicfoundation.org">www.magicfoundation.org</a></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Counseling</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Counsel regarding corticosteroid replacement therapy and stress dosing. Counsel regarding Medical Alert bracelet.</td>
</tr>
</tbody>
</table>

* TBI is included for dose calculation purposes only; this section is not applicable to patients who received TBI alone.

### SECTION 63 REFERENCES


### RADIATION

<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling/ Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>64</td>
<td>Cranial/Orbital/Eye Total Body Irradiation (TBI)</td>
<td>Cataracts</td>
<td>Treatment Factors: Radiation dose $\geq$ 10 Gy TBI $\geq$ 2 Gy in single fraction or $\geq$ 5 Gy fractionated Radiation combined with: - Corticosteroids - Busulfan - Longer interval since treatment</td>
<td>Treatment Factors: Radiation dose $\geq$ 15 Gy Fraction dose $\geq$ 2 Gy TBI $\geq$ 5 Gy in single fraction or $\geq$ 10 Gy fractionated Cranial/orbital/eye radiation combined with TBI</td>
<td>HISTORY: Visual changes (decreased acuity, halos, diplopia) Yearly</td>
<td>PHYSICAL: Eye exam (visual acuity, funduscopic exam for lens opacity) Yearly</td>
</tr>
</tbody>
</table>

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

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

### SECTION 64 REFERENCES


<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling/ Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>65</td>
<td>≥ 30 Gy to: Cranial Orbital/Eye TBI*</td>
<td>Ocular toxicity Orbital hypoplasia Lacrimal duct atrophy Xerophthalmia (keratoconjunctivitis sicca) Keratitis Telangiectasias Retinopathy Optic chiasm neuropathy Enophthalmos Chronic painful eye Maculopathy Papillopathy Glaucoma</td>
<td>Treatment Factors Higher radiation dose Higher daily fraction dose Radiomimetic chemotherapy (e.g., doxorubicin, dacarbazine) [problems related to tearing] Host Factors Chronic GVHD (xerophthalmia only)</td>
<td>Treatment Factors Total dose ≥ 50 Gy Fraction dose ≥ 2 Gy</td>
<td>HISTORY Visual changes (decreased acuity, halos, diplopia) Dry eye Persistent eye irritation Excessive tearing Light sensitivity Poor night vision Painful eye Yearly</td>
<td>SYSTEM = Ocular SCORE = 1</td>
</tr>
</tbody>
</table>

*TBI is included for dose calculation purposes only; this section is not applicable to patients who received TBI alone.

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

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

• This section is only applicable to patients who:
  1) Received radiation to any of the specified fields at ≥ 30 Gy OR
  2) Received a combination of radiation to any of the specified fields and TBI, the sum of which is ≥ 30 Gy
• See dose calculation rules on page 56 for patients who received: (a) radiation to more than one of the specified fields, or (b) more than one planned course of treatment to the same field.
• See “Patient-Specific Guideline Identification Tool” in Appendix I to determine specific screening guidelines by section number for individual patients.

SECTION 65 REFERENCES


## RADIATION

<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling/ Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>66</td>
<td>≥ 30 Gy to: Cranial Ear/Infratemporal Nasopharyngeal Waldeyer's Ring TBI*</td>
<td>Ototoxicity Tymanosclerosis Otosclerosis Eustachian tube dysfunction Conductive hearing loss</td>
<td>Host Factors Younger age at treatment Treatment Factors Higher radiation dose Medical Conditions Chronic otitis Chronic cerumen impaction</td>
<td>Treatment Factors Dose ≥ 50 Gy</td>
<td>HISTORY Hearing difficulties (with/without background noise) Tinnitus Vertigo Yearly PHYSICAL Otoscopic exam Yearly SCREENING Complete audiological evaluation Yearly after completion of therapy for 5 years (for patients &lt; 10 years old, continue yearly until age 10), then every 5 years If hearing loss is detected, test at least yearly or as recommended by audiologist If clinical suspicion of hearing loss at any time, test as clinically indicated If audiogram is inconclusive or unevaluable, refer to audiologist for consideration of electrophysiologic testing e.g., otoacoustic emissions [OAEs]</td>
<td>Health Links Hearing Loss Educational Issues Considerations for Further Testing and Intervention Audiology consultation for patients with hearing loss. Otolaryngology consultation for patients with chronic infection, cerumen impaction, or other anatomical problems exacerbating or contributing to hearing loss. Speech and language therapy for children with hearing loss. Refer patients with auditory deficits to school liaison in community or cancer center (psychologist, social worker, school counselor) to facilitate provision of educational resources. Consider specialized evaluation for specific needs and/or preferential classroom seating, FM amplification system, and other educational assistance as indicated.</td>
</tr>
</tbody>
</table>

*This section is only applicable to patients who:
1) Received radiation to any of the specified fields at ≥ 30 Gy OR
2) Received a combination of radiation to any of the specified fields and TBI, the sum of which is ≥ 30 Gy

• See dose calculation rules on page 56 for patients who received: (a) radiation to more than one of the specified fields, or (b) more than one planned course of treatment to the same field.

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

### SECTION 66 REFERENCES


## RADIATION

<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling/ Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>67</td>
<td>≥ 30 Gy to: Cranial Ear/Infratemporal Nasopharyngeal Waldeyer's Ring TBI*</td>
<td>Ototoxicity Sensorineural hearing loss Tinnitus</td>
<td>Host Factors Younger age at treatment CNS tumor Treatment Factors Higher radiation dose Conventional (non-conformal) radiation Medical Conditions CSF shunting</td>
<td>Treatment Factors Radiation administered prior to platinum chemotherapy Combined with other ototoxic agents such as: - Cisplatin - Carboplatin in myeloablative doses - Aminoglycosides</td>
<td>HISTORY Hearing difficulties (with/without background noise) Tinnitus Vertigo Yearly PHYSICAL Otoscopic exam Yearly SCREENING Complete audiological evaluation Yearly after completion of therapy for 5 years [for patients &lt;10 years old, continue yearly until age 10], then every 5 years If hearing loss is detected, test at least yearly or as recommended by audiologist If clinical suspicion of hearing loss at any time, test as clinically indicated If audiogram is inconclusive or unevaluable, refer to audiologist for consideration of electrophysiologic testing e.g., otoacoustic emissions [OAEs]</td>
<td>Health Links</td>
</tr>
</tbody>
</table>

- This section is only applicable to patients who:
  1. Received radiation to any of the specified fields at ≥ 30 Gy OR
  2. Received a combination of radiation to any of the specified fields and TBI, the sum of which is ≥ 30 Gy
- See dose calculation rules on page 56 for patients who received: (a) radiation to more than one of the specified fields, or (b) more than one planned course of treatment to the same field.
- See “Patient-Specific Guideline Identification Tool” in Appendix I to determine specific screening guidelines by section number for individual patients.

### SECTION 67 REFERENCES


### RADIATION

<table>
<thead>
<tr>
<th>Section #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling/ Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>68</td>
<td>Cranial Nasopharyngeal Oropharyngeal Waldeyer's Ring Cervical (neck) Supraclavicular Spine (cervical) Spine (whole) Subtotal Lymphoid Irradiation (STLI) Extended Mantle Mantle Mini-Mantle Total Lymphoid Irradiation (TLI)</td>
<td>Xerostomia Salivary gland dysfunction</td>
<td>Head and neck radiation involving the parotid gland Higher radiation doses Radiomimetic chemotherapy (e.g., doxorubicin, dactinomycin)</td>
<td>Treatment Factors Salivary gland dose ≥ 30 Gy Medical Conditions Chronic GVHD</td>
<td>HISTORY</td>
<td>Xerostomia Yearly</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>PHYSICAL</td>
<td>Oral exam Yearly</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>SCREENING</td>
<td>Dental exam and cleaning Every 6 months</td>
</tr>
</tbody>
</table>

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

### SECTION 68 REFERENCES

### RADIATION

<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling/ Further Considerations</th>
</tr>
</thead>
</table>

**SECTION 69 REFERENCES**


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

<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling/ Further Considerations</th>
</tr>
</thead>
</table>
| 70    | ≥ 40 Gy to: Cranial Nasopharyngeal Oropharyngeal Waldeyer's Ring Cervical (neck) Supraclavicular Spine (cervical) Spine (whole) Subtotal Lymphoid Irradiation (STLI) Extended Mantle Mantle Mini-Mantle Total Lymphoid Irradiation (TLI) TBI* | Osteoradionecrosis | Treatment Factors Radiation dose to bone ≥ 45 Gy | Treatment Factors Dose ≥ 50 Gy | HISTORY  
Impaired or delayed healing following dental work Persistent jaw pain or swelling Trismus As clinically indicated  
PHYSICAL  
Impaired wound healing Jaw swelling Trismus As clinically indicated |  
• This section is only applicable to patients who:  
1) Received radiation to any of the specified fields at ≥ 40 Gy OR  
2) Received a combination of radiation to any of the specified fields plus relevant spinal radiation and/or TBI, the sum of which is ≥ 40 Gy  
• See dose calculation rules on page 56 for patients who received: (a) radiation to more than one of the specified fields, or (b) more than one planned course of treatment to the same field.  
• See “Patient-Specific Guideline Identification Tool” in Appendix I to determine specific screening guidelines by section number for individual patients.  
  
**TBI is included for dose calculation purposes only; this section is not applicable to patients who received TBI alone.** |  
  
#### Health Links  
Osteoradionecrosis  
Considerations for Further Testing and Intervention  
Imaging studies (x-ray, CT scan and/or MRI) may assist in making diagnosis. Surgical biopsy may be needed to confirm diagnosis. Consider hyperbaric oxygen treatments.  
  
**SYSTEM = Dental  
SCORE = 1** |

---

### SECTION 70 REFERENCES

### POTENTIAL IMPACT TO NECK/THYROID

<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling/ Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>71</td>
<td>Cranial Nasopharyngeal Oropharyngeal Waldeyer's Ring Cervical (neck) Supraclavicular Spine (cervical) Spine (whole) Subtotal Lymphoid Irradiation (STLI) Extended Mantle Mantle Mediastinal Mini-Mantle Total Body Irradiation (TBI) Total Lymphoid Irradiation (TLI)</td>
<td>Thyroid nodules</td>
<td>Host Factors Younger age at treatment Female sex Treatment Factors Higher radiation dose Thyroid gland directly in radiation field</td>
<td>Treatment Factors Radiation dose ≥ 25 Gy</td>
<td>Physiological Thyroid exam Yearly</td>
<td>Health Links Thyroid Problems Considerations for Further Testing and Intervention Ultrasound and FNA for evaluation of palpable nodule(s). Endocrine and/or surgical consultation for diagnostic biopsy or thyroidectomy.</td>
</tr>
</tbody>
</table>

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

### SECTION 71 REFERENCES


## RADIATION

<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling/ Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>72</td>
<td>Cranial Nasopharyngeal Oropharyngeal Waldeyer's Ring Cervical (neck) Supraclavicular Spine (cervical) Spine (whole) Subtotal Lymphoid Irradiation (STLI) Extended Mantle Mantle Mediastinal Mini-Mantle Total Body Irradiation (TBI) Total Lymphoid Irradiation (TLI)</td>
<td>Thyroid cancer</td>
<td>Host Factors: Younger age at treatment Female sex Treatment Factors: &gt; 5 years after irradiation Thyroid gland directly in radiation field TBI Risk increased up to 30 Gy with a downturn of risk after 30 Gy</td>
<td></td>
<td>PHYSICAL Thyroid exam Yearly</td>
<td><strong>Health Links</strong> Thyroid Problems <strong>Considerations for Further Testing and Intervention</strong> Ultrasound and FNA for evaluation of palpable nodule(s). Surgical consultation for resection. Nuclear medicine consultation for ablation of residual disease. Endocrine consultation for postoperative medical management.</td>
</tr>
</tbody>
</table>

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

---

### SECTION 72 REFERENCES


---

*See “Patient-Specific Guideline Identification Tool” in Appendix I to determine specific screening guidelines by section number for individual patients.*
## RADIATION

<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling/ Further Considerations</th>
</tr>
</thead>
</table>
Female sex | Treatment Factors
Radiation dose ≥ 10 Gy Thyroid gland directly in radiation field TBI | Treatment Factors
Radiation dose ≥ 20 Gy | HISTORY
Fatigue
Weight gain
Cold intolerance
Constipation
Dry skin
Brittle hair
Depressed mood Yearly
Consider more frequent screening during periods of rapid growth |

**SCREENING**

| TSH | Yearly
Consider more frequent screening during periods of rapid growth |

**PHYSICAL**

| Height
Weight
Hair and skin
Thyroid exam Yearly | Consider more frequent screening during periods of rapid growth |

**SYSTEM = Endocrine/Metabolic**

**SCORE = 1**

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

### POTENTIAL IMPACT TO NECK/THYROID (cont)

- **Health Links**
  - Thyroid Problems

- **Counseling**
  - Counsel at-risk females of childbearing potential to have their thyroid levels checked prior to attempting pregnancy and periodically throughout pregnancy.

- **Considerations for Further Testing and Intervention**
  - Endocrine consultation for medical management.

### SECTION 73 REFERENCES

### RADIATION

<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling/Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cervical (neck)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>SYSTEM = Endocrine/Metabolic. SCORE = 1</td>
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<tr>
<td></td>
<td>Supraclavicular Spine (cervical)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Spine (whole)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Subtotal Lymphoid Irradiation (STLI)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Extended Mantle Mantle</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Mediastinal Mini-Mantle</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Total Lymphoid Irradiation (TLI)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>TBI*</td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

*This section is only applicable to patients who:*

1. Received radiation to any of the specified fields at ≥ 40 Gy
2. Received a combination of radiation to any of the specified fields plus relevant spinal radiation and/or TBI, the sum of which is ≥ 40 Gy.

*See dose calculation rules on page 56 for patients who received: (a) radiation to more than one of the specified fields, or (b) more than one planned course of treatment to the same field.

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

### SECTION 74 REFERENCES


### RADIATION

<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling/ Further Considerations</th>
</tr>
</thead>
</table>
| 75    | ≥ 40 Gy to: Cranial Nasopharyngeal Oropharyngeal Waldeyer's Ring Cervical (neck) Supraclavicular Spine (cervical) Spine (whole) Subtotal Lymphoid Irradiation (STLI) Chest (thorax) Extended Mantle Mantle Mediastinal Mini-Mantle Whole lung Total Lymphoid Irradiation (TLI) TBI* | Carotid artery disease | Medical Conditions | Hypertension Diabetes mellitus Hypercholesterolemia | HISTORY  
Memory impairment Yearly | PHYSICAL  
Diminished carotid pulses Carotid bruits Abnormal neurologic exam (compromise of blood flow to brain) Yearly |

- This section is only applicable to patients who:
  1. Received radiation to any of the specified fields at ≥ 40 Gy
  2. Received a combination of radiation to any of the specified fields plus relevant spinal radiation and/or TBI, the sum of which is ≥ 40 Gy

- See dose calculation rules on page 56 for patients who received:
  a. radiation to more than one of the specified fields, or
  b. more than one planned course of treatment to the same field.

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

*TBI is included for dose calculation purposes only; this section is not applicable to patients who received TBI alone.

### SECTION 75 REFERENCES

<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling/ Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>76</td>
<td>≥ 40 Gy to: Cervical (neck) Supraclavicular Spine (cervical) Spine (whole) Subtotal Lymphoid Irradiation (STLI) Chest (thorax) Extended Mantle Mantle Mediastinal Mini-Mantle Whole lung Total Lymphoid Irradiation (TLI) TBI*</td>
<td>Subclavian artery disease</td>
<td></td>
<td></td>
<td>PHYSICAL</td>
<td>Considerations for Further Testing and Intervention</td>
</tr>
</tbody>
</table>

- Diminished brachial and radial pulses
- Pallor of upper extremities
- Coolness of skin
- Unequal blood pressure
- Yearly

**SYSTEM = Cardiovascular**

**SCORE = 2A**

---

*This section is only applicable to patients who:

1) Received radiation to any of the specified fields at ≥ 40 Gy
2) Received a combination of radiation to any of the specified fields plus relevant spinal radiation and/or TBI, the sum of which is ≥ 40 Gy

See dose calculation rules on page 56 for patients who received: (a) radiation to more than one of the specified fields, or (b) more than one planned course of treatment to the same field.

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

---

**SECTION 76 REFERENCES**


<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling/ Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>77</td>
<td>10 Gy to: Subtotal Lymphoid Irradiation (STLI) Axilla Chest (thorax) Extended Mantle Mantle Mediastinal Mini–Mantle Whole lung Total Body Irradiation (TBI)* Total Lymphoid Irradiation (TLI)</td>
<td>Breast cancer</td>
<td>Host Factors Family history of breast cancer Treatment Factors Higher radiation dose Longer time since radiation (&gt; 5 years) Decreased risk in women treated with alkylating agents</td>
<td>Host Factors BRACA1, BRACA2, ATM mutation</td>
<td><strong>PHYSICAL</strong></td>
<td><strong>Health Links</strong></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td><strong>SCREENING</strong></td>
<td><strong>Breast Cancer</strong></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>≥ 20 Gy</td>
<td>Yearly, beginning at puberty until age 25, then every 6 months</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td><strong>Mammogram</strong></td>
<td>Yearly, beginning 8 years after radiation or at age 25, whichever occurs last.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td><strong>Breast MRI</strong></td>
<td>Yearly, as an adjunct to mammography beginning 8 years after radiation or at age 25, whichever occurs last.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Clinician to discuss benefits and risks/harms of screening with patient. If decision is made to screen, then follow screening recommendations for ≥ 20 Gy.</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Info Link</td>
<td>Mammography is currently limited in its ability to evaluate the premenopausal breast.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>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 gene mutation of known penetrance).</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>The upper age limit at which both modalities should be used for breast cancer surveillance has not been established.</td>
</tr>
</tbody>
</table>

**Info Link**

- *Important: The risk of breast cancer in patients who received 10–19 Gy of radiation with potential impact to the breast or those who received TBI alone is of a lower magnitude compared to those who received ≥ 20 Gy of radiation with potential impact to the breast (e.g., thorax, axilla).
- Monitoring of patients who received 10–19 Gy of radiation with potential impact to the breast, or those who received TBI without additional radiation, should be determined on an individual basis.
- After the clinician discusses the benefits and risks/harms of screening with the patient, if a decision is made to screen, then follow the recommendations for patients who received ≥ 20 Gy.

---

**SECTION 77 REFERENCES**


### RADIATION

<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling/ Further Considerations</th>
</tr>
</thead>
</table>

### POTENTIAL IMPACT TO BREAST (cont)

**SECTION 77 REFERENCES—continued**


### POTENTIAL IMPACT TO BREAST (cont)

<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling/ Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>78 (female)</td>
<td>Subtotal Lymphoid Irradiation (STLI) Axilla Chest (thorax) Extended Mantle Mantle Mediastinal Mini-Mantle Whole lung Total Body Irradiation (TBI) Total Lymphoid Irradiation (TLI)</td>
<td>Breast tissue hypoplasia</td>
<td>Host Factors Prepubertal at time of breast irradiation Treatment Factors</td>
<td>Treatment Factors Radiation dose ≥ 10 Gy to prepubertal breast bud may cause failure of development (hypoplasia)</td>
<td>PHYSICAL Breast exam Yearly</td>
<td>Considerations for Further Testing and Intervention Surgical consultation for breast reconstruction after completion of growth.</td>
</tr>
</tbody>
</table>

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

### SECTION 78 REFERENCES


## RADIATION

<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling/ Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>79</td>
<td>Subtotal Lymphoid Irradiation (STLI) Axilla Chest (thorax) Extended Mantle Mantle Mediastinal Mini-Mantle Whole lung Total Body Irradiation (TBI) Total Lymphoid Irradiation (TLI)</td>
<td>Pulmonary toxicity Pulmonary fibrosis Interstitial pneumonitis Restrictive lung disease Obstructive lung disease</td>
<td>Host Factors Younger age at irradiation Treatment Factors Radiation dose &gt; 10 Gy Radiation combined with: - Bleomycin - Busulfan - Carmustine (BCNU) - Lomustine (CCNU) - Radiomimetic chemotherapy (e.g., doxorubicin, daunomycin) Chest radiation combined with TBI Medical Conditions Atopic history Health Behaviors Smoking Inhaled illicit drug use</td>
<td>Treatment Factors Radiation dose ≥ 15 Gy TBI ≥ 6 Gy in single fraction or ≥ 12 Gy fractionated</td>
<td>HISTORY Cough SOB DOE Wheezing 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 Resources Extensive information regarding smoking cessation is available for patients on the NCI's website: <a href="http://www.smokefree.gov">www.smokefree.gov</a> Counseling Counsel regarding tobacco avoidance/ smoking cessation. Due to the potential pulmonary toxicity of this therapy, patients who desire to SCUBA dive should be advised to obtain medical clearance from a pulmonologist. Considerations for Further Testing and Intervention In patients with abnormal PFTs, consider repeat evaluation prior to general anesthesia. Pulmonary consultation for patients with symptomatic pulmonary dysfunction. Influenza and Pneumococcal vaccinations.</td>
</tr>
</tbody>
</table>

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

### SECTION 79 REFERENCES


<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling/Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>80</td>
<td>Chest (thorax)</td>
<td>Cardiac toxicity</td>
<td>Host Factors</td>
<td>Host Factors</td>
<td>HISTORY</td>
<td>Health Links</td>
</tr>
<tr>
<td></td>
<td>Extended Mantle</td>
<td>Congestive heart failure</td>
<td>Younger age at irradiation</td>
<td>Black/ of African descent</td>
<td>SOB</td>
<td>Heart Health</td>
</tr>
<tr>
<td></td>
<td>Mantle</td>
<td>Cardiomyopathy</td>
<td>Family history of dyslipidemia</td>
<td>Younger than age 5 years at treatment</td>
<td>DOE</td>
<td>Cardiovascular Risk Factors</td>
</tr>
<tr>
<td></td>
<td>Mediastinal</td>
<td>Pericarditis</td>
<td>Coronary artery disease</td>
<td>Treatment Factors</td>
<td>Chest pain</td>
<td>Diet and Physical Activity</td>
</tr>
<tr>
<td></td>
<td>Whole lung</td>
<td>Pericardial fibrosis</td>
<td>Radiation dose ≥ 20 Gy to chest</td>
<td>Anteriorly-weighted radiation fields</td>
<td>Palpitations</td>
<td>Dental Health</td>
</tr>
<tr>
<td></td>
<td>Hepatic</td>
<td>Valvular disease</td>
<td>TBI</td>
<td>Combined with radiomimetic chemotherapy (e.g., doxorubicin, daunorubicin)</td>
<td>If under 25 yrs: abdominal symptoms (nausea, vomiting)</td>
<td>Counseling</td>
</tr>
<tr>
<td></td>
<td>Inverted Y</td>
<td>Myocardial infarction</td>
<td>Combined with other cardiotoxic chemotherapy:</td>
<td>Lack of subcarinal shielding</td>
<td>Yearly</td>
<td>Counsel patients with prolonged QTc interval about use of medications that may further prolong the QTc interval (e.g., tricyclic anti-depressants, antifungals, macrolide antibiotics, metronidazole). Counsel regarding maintaining appropriate weight, blood pressure and heart-healthy diet. Counsel regarding endocarditis prophylaxis if at highest risk. Note: 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) 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. Counsel regarding appropriate exercise. Aerobic exercise is generally safe and should be encouraged for most patients. Intensive isometric activities (e.g., heavy weight lifting, wrestling) should generally be avoided. High repetition weight lifting involving lighter weights is more likely to be safe. The number of repetitions should be limited to that which the survivor can perform with ease. Patients who choose to engage in strenuous or varsity team sports should discuss appropriate guidelines and a plan for ongoing monitoring with a cardiologist.</td>
</tr>
<tr>
<td></td>
<td>Left Flank/Hemiabdomen</td>
<td>Arhythmia</td>
<td>Medical Conditions</td>
<td>Hypertension</td>
<td>Obesity</td>
<td>PHYSICAL</td>
</tr>
<tr>
<td></td>
<td>Left upper quadrant</td>
<td>Atherosclerotic heart disease</td>
<td>Dyslipidemia</td>
<td>Diabetes mellitus</td>
<td>Cardiac murmur</td>
<td>Cardiac murmur</td>
</tr>
<tr>
<td></td>
<td>Paraaoptic</td>
<td></td>
<td>Congenital heart disease</td>
<td>Congenital heart disease</td>
<td>S3, S4</td>
<td>Increased P2 sound</td>
</tr>
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<td></td>
<td>Renal</td>
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<td>Febrile illness</td>
<td>Febrile illness</td>
<td>Pericardial rub</td>
<td>Pericardial rub</td>
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<td></td>
<td>Right Flank/Hemiabdomen</td>
<td></td>
<td>Health Behaviors</td>
<td>Smoking</td>
<td>年</td>
<td>Yearly</td>
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<tr>
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<td>Right Upper quadrant</td>
<td></td>
<td>Isometric exercise</td>
<td>Drug use (e.g., cocaine, diet pills, ephedra)</td>
<td>Yearly</td>
<td>Physical exercise is generally safe and should be encouraged for most patients. Intensive isometric activities (e.g., heavy weight lifting, wrestling) should generally be avoided. High repetition weight lifting involving lighter weights is more likely to be safe. The number of repetitions should be limited to that which the survivor can perform with ease. Patients who choose to engage in strenuous or varsity team sports should discuss appropriate guidelines and a plan for ongoing monitoring with a cardiologist.</td>
</tr>
<tr>
<td></td>
<td>Spleen (entire)</td>
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<tr>
<td></td>
<td>Spleen (partial)</td>
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<tr>
<td></td>
<td>Whole abdomen</td>
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<tr>
<td></td>
<td>Spine (thoracic)</td>
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<td></td>
<td>Spine (whole)</td>
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<tr>
<td></td>
<td>Subtotal Lymphoid</td>
<td></td>
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<td></td>
</tr>
<tr>
<td></td>
<td>Irradiation (STLI)</td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td></td>
<td>Total Body Irradiation (TBI)</td>
<td></td>
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<td></td>
<td></td>
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<tr>
<td></td>
<td>Total Lymphoid</td>
<td></td>
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</tr>
<tr>
<td></td>
<td>Irradiation (TLI)</td>
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</tr>
</tbody>
</table>

### SEC #80 (Male)

#### Chest (thorax) Extended Mantle

- **Potential Late Effects**: Cardiac toxicity (congestive heart failure, cardiomyopathy, pericarditis, pericardial fibrosis, valvular disease, myocardial infarction, arrhythmia, atherosclerotic heart disease)
- **Risk Factors**: Younger age at irradiation, family history of dyslipidemia, coronary artery disease
- **Host Factors**: Black or African descent, younger than age 5 years at treatment
- **Treatment Factors**: Radiation dose ≥ 20 Gy to chest
- **Highest Risk Factors**: Combined with radiomimetic chemotherapy (e.g., doxorubicin, daunorubicin) combined with other cardiotoxic chemotherapy: anthracyclines, cyclophosphamide conditioning for HCT, amrascin
- **Medical Conditions**: Hypertension, obesity, dyslipidemia, diabetes mellitus, congenital heart disease, febrile illness
- **Health Behaviors**: Smoking, isometric exercise, drug use (e.g., cocaine, diet pills, ephedra)
- **Periodic Evaluation**: Yearly

### RECOMMENDED FREQUENCY OF ECHOCARDIOGRAM

<table>
<thead>
<tr>
<th>Age at Treatment*</th>
<th>Radiation Dose</th>
<th>Anthracycline Dose†</th>
<th>Recommended Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 5 years old</td>
<td>Any</td>
<td>None</td>
<td>Every 2 years</td>
</tr>
<tr>
<td>≥ 5 years old</td>
<td>&lt; 30 Gy²</td>
<td>None</td>
<td>Every 5 years</td>
</tr>
<tr>
<td></td>
<td>≥ 30 Gy²</td>
<td>None</td>
<td>Every 2 years</td>
</tr>
<tr>
<td></td>
<td>Any</td>
<td>&lt; 300 mg/m²²</td>
<td>Every 2 years</td>
</tr>
<tr>
<td></td>
<td>Any</td>
<td>≥ 300 mg/m²²</td>
<td>Every year</td>
</tr>
</tbody>
</table>

- **Note**: See “Patient-Specific Guideline Identification Tool” in Appendix I to determine specific screening guidelines by section number for individual patients.

### Health Counseling/Further Considerations

- **Medical**: Cardiac murmur, S3, S4, increased P2 sound, pericardial rub, wheezes, jugular venous distension, peripheral edema
- **Physical**: Fasting blood glucose or HbA1c and lipid profile
- **Screening**: Fasting blood glucose OR HbA1c and lipid profile
- **Periodic Evaluation**: Every 2 years
- **Considerations for Further Testing and Intervention**: Cardiology consultation for patients with subclinical abnormalities on screening evaluations or with left ventricular dysfunction, dysrhythmia or prolonged QTc interval. Consider cardiology consultation (5 to 10 years after radiation) to evaluate risk for coronary artery disease in patients who received ≥ 40 Gy chest radiation alone or ≥ 30 Gy chest radiation plus anthracycline. Consider excess risk of intensive isometric exercise program in any high risk patient defined as needing screening every 1 or 2 years.

---

**SYSTEM = Cardiovascular**

**SCORE = 1**
**SECTION 80 REFERENCES**


### RADIATION

**Therapeutic Agent(s)**
- Hepatic
- Inverted Y
- Left Flank/Hemiabdomen
- Left upper quadrant
- Paraortic
- Renal
- Right Flank/Hemiabdomen
- Right Upper quadrant
- Spleen (entire)
- Spleen (partial)
- Whole abdomen
- Spine (thoracic)
- Spine (whole)
- Subtotal Lymphoid Irradiation (STLI)
- Chest (thorax)
- Extended Mantle
- Mantle
- Mediastinal
- Whole lung
- Total Body Irradiation (TBI)
- Total Lymphoid Irradiation (TLI)

**Potential Late Effects**
- Cardiac toxicity
- Congestive heart failure
- Cardiomyopathy
- Pericarditis
- Pericardial fibrosis
- Valvular disease
- Myocardial infarction
- Arrhythmia
- Atherosclerotic heart disease

**Host Factors**
- Younger age at irradiation
- Family history of dyslipidemia
- Coronary artery disease

**Treatment Factors**
- Radiation dose ≥ 20 Gy to chest TBI
- Combined with radiomimetic chemotherapy (e.g., doxorubicin, dactinomycin)
- Combined with other cardiotoxic chemotherapy:
  - Anthracyclines
  - Cyclophosphamide conditioning for HCT
  - Amrubicine

**Medical Conditions**
- Hypertension
- Obesity
- Dyslipidemia
- Diabetes mellitus
- Congenital heart disease
- Febrile illness
- Pregnancy
- Premature ovarian failure
- (untreated)

**Host Factors**
- Female sex
- Black/or African descent
- Younger than age 5 years at treatment

**Treatment Factors**
- Anteriorly-weighted radiation fields
- Lack of subcardial shielding
- Doses ≥ 30 Gy in patients who have received anthracyclines
- Doses ≥ 40 Gy in patients who have not received anthracyclines
- Longer time since treatment

**Recommended Frequency of Echocardiogram**

<table>
<thead>
<tr>
<th>Age at Treatment</th>
<th>Radiation Dose</th>
<th>Anthracycline Dose</th>
<th>Recommended Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 5 years old</td>
<td>Any</td>
<td>None</td>
<td>Every 2 years</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Any</td>
<td>Every year</td>
</tr>
<tr>
<td>≥ 5 years old</td>
<td>&lt; 30 Gy</td>
<td>None</td>
<td>Every 5 years</td>
</tr>
<tr>
<td></td>
<td>≥ 30 Gy</td>
<td>None</td>
<td>Every 2 years</td>
</tr>
<tr>
<td></td>
<td>Any</td>
<td>&lt; 300 mg/m²</td>
<td>Every 2 years</td>
</tr>
<tr>
<td></td>
<td></td>
<td>≥ 300 mg/m²</td>
<td>Every year</td>
</tr>
</tbody>
</table>

**Further Considerations**
- See “Patient-Specific Guideline Identification Tool” in Appendix I to determine specific screening guidelines by section number for individual patients.

---

### POTENTIAL IMPACT TO HEART (cont)

**HISTORY**
- SOB
- DOE
- Orthopaea
- Chest pain
- Palpitations
- If under 25 yrs: abdominal symptoms (nausea, vomiting)

**Perioperative Evaluation**

- **Yearly**
  - Exertional intolerance is uncommon in patients younger than 25 years old.
  - Abdominal symptoms (nausea, emesis) may be observed more frequently than exertional dyspnea or chest pain in younger patients.

**PHYSICAL**

- Cardiac murmur
- S3, S4
- Increased P2 sound
- Pericardial rub
- Rales
- Wheezes
- Jugular venous distension
- Peripheral edema
- Yearly

**SCREENING**

- Fasting blood glucose OR HbA1c and lipid profile
  - Every 2 years
  - If abnormal, refer for ongoing management

- EKG (including evaluation of QTc interval)
  - Baseline at entry into long-term follow-up, repeat as clinically indicated

- ECHO (or comparable imaging to evaluate cardiac anatomy and function)
  - Baseline at entry into long-term follow-up, then periodically based on age at treatment, radiation dose, and cumulative anthracycline dose.

**Counseling**

Counsel patients with prolonged QTc interval about use of medications that may further prolong the QTc interval (e.g., tricyclic antidepressants, antifungals, macrolide antibiotics, metronidazole). Counsel regarding maintenance of appropriate weight, blood pressure, and heart-healthy diet. Counsel regarding endocarditis prophylaxis if at highest risk.

**Note:** 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. Counsel regarding appropriate exercise. Aerobic exercise is generally safe and should be encouraged for most patients. Intensive isometric activities (e.g., heavy weight lifting, wrestling) should generally be avoided. High repetition weight lifting involving lighter weights is more likely to be safe. The number of repetitions should be limited to that which the survivor can perform with ease. Patients who choose to engage in strenuous or varsity team sports should discuss appropriate guidelines and a plan for ongoing monitoring with a cardiologist.

**Considerations for Further Testing and Intervention**

Cardiology consultation for patients with subclinical abnormalities on screening evaluations or with left ventricular dysfunction, dysrhythmia or prolonged QTc interval. Additional cardiology evaluation for patients who are pregnant or planning pregnancy who: (1) received ≥ 30 Gy chest radiation, or (2) received chest radiation in combination with cardiotoxic chemotherapy (anthracyclines or high-dose cyclophosphamide). Evaluation to include echocardiogram before and periodically during pregnancy (especially during third trimester) and monitoring during labor and delivery due to risk of cardiac failure. Consider cardiology consultation (5 to 10 years after radiation) to evaluate risk for coronary artery disease in patients who received ≥ 40 Gy chest radiation alone or ≥ 30 Gy chest radiation plus anthracycline. Consider excess risk of intensive isometric exercise program in any high-risk patient defined as needing screening every 1 or 2 years.

**Health Links**
- Heart Health
- Cardiovascular Risk Factors
- Diet and Physical Activity
- Dental Health

**Health Counseling/Further Considerations**

**SYSTEM**

**SCORE = 1**

---

**Notes:***
- If patient received radiation to more than one specified field, see dose calculation rules on page 56.
RADIATION

<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling/Further Considerations</th>
</tr>
</thead>
</table>

**SECTION 81 REFERENCES**


### RADIATION

<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling/ Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>82</td>
<td>≥ 40 Gy to: Inverted Y Left Flank/Hemiabdomen Left upper quadrant Paraaortic Spleen (entire) Whole abdomen Subtotal Lymphoid Irradiation (STLI) Total Lymphoid Irradiation (TLI) TBI*</td>
<td>Functional asplenia At risk for life-threatening infection with encapsulated organisms (e.g., <em>Haemophilus influenzae</em>, <em>Streptococcus pneumoniae</em>, meningococcus)</td>
<td>Treatment Factors Higher radiation dose to entire spleen</td>
<td></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</td>
<td><strong>Health Links</strong> Splenic Precautions <strong>Counseling</strong> Medical alert bracelet/card noting functional asplenia Counsel regarding risk of life-threatening infections with encapsulated organisms. Also counsel regarding risk associated with malaria and tick-borne diseases if living in or visiting endemic areas. <strong>Considerations for Further Testing and Intervention</strong> In patients with T ≥ 101°F (38.3°C) or other signs of serious illness, administer a long-acting, broad-spectrum parenteral antibiotic (e.g., ceftriaxone), and continue close medical monitoring while awaiting blood culture results. 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 ≥ 104°F meningitis, pneumonia, or other serious focus of infection signs of septic shock or previous history of serious infection. Immunize with Pneumococcal, Meningococcal, and HIB vaccines according to current ACIP recommendations. Discuss with dental provider potential need for antibiotic prophylaxis based on planned procedure.</td>
</tr>
</tbody>
</table>

* TBI is included for dose calculation purposes only; this section is not applicable to patients who received TBI alone.

**Info Link**
- Not all paraaortic and inverted Y treatment fields include the spleen.
- Survivors are at risk for functional asplenia only if the spleen was included in the radiation field.

**• This section is only applicable to patients who:**

1. Received radiation to any of the specified fields at ≥ 40 Gy OR
2. Received a combination of radiation to any of the specified fields and TBI, the sum of which is ≥ 40 Gy

 **See dose calculation rules on page 56 for patients who received:**
- (a) radiation to more than one of the specified fields, or
- (b) more than one planned course of treatment to the same field.

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

### SECTION 82 REFERENCES

### SECTION 82 REFERENCES–continued


### RADIATION

<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling/ Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>83</td>
<td>≥ 30 Gy to:</td>
<td>Esophageal stricture</td>
<td>Treatment Factors: Higher radiation dose</td>
<td>Treatment Factors: Radiation dose ≥ 40 Gy</td>
<td>HISTORY: Dysphagia, Heartburn</td>
<td>Health Links: Gastrointestinal Health</td>
</tr>
<tr>
<td></td>
<td>Hepatic</td>
<td></td>
<td>Radiomimetic chemotherapy (e.g., doxorubicin, actinomycin)</td>
<td>Medical Conditions: Gastroesophageal reflux, History of Candida esophagitis</td>
<td>Yearly</td>
<td>Considerations for Further Testing and Intervention: Surgical and/or gastroenterology consultation for symptomatic patients.</td>
</tr>
<tr>
<td></td>
<td>Inverted Y</td>
<td></td>
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</tr>
<tr>
<td></td>
<td>Left Flank/Hemiabdomen</td>
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<tr>
<td></td>
<td>Left upper quadrant</td>
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<tr>
<td></td>
<td>Paraortic</td>
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<tr>
<td></td>
<td>Renal</td>
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<tr>
<td></td>
<td>Right Flank/Hemiabdomen</td>
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<tr>
<td></td>
<td>Right Upper quadrant</td>
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<tr>
<td></td>
<td>Spleen (entire)</td>
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<td>Spleen (partial)</td>
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<td></td>
<td>Whole abdomen</td>
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<td>Cervical (neck)</td>
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<tr>
<td></td>
<td>Supraclavicular</td>
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<tr>
<td></td>
<td>Spine (cervical)</td>
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<tr>
<td></td>
<td>Spine (thoracic)</td>
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<td></td>
<td>Spine (whole)</td>
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<tr>
<td></td>
<td>Subtotal Lymphoid Irradiation (STLI)</td>
<td></td>
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<tr>
<td></td>
<td>Chest (thorax)</td>
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<td></td>
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<tr>
<td></td>
<td>Extended Mantle</td>
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<tr>
<td></td>
<td>Mantle</td>
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<tr>
<td></td>
<td>Mediastinal</td>
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<tr>
<td></td>
<td>Mini-Mantle</td>
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<td></td>
<td>Whole lung</td>
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</tr>
<tr>
<td></td>
<td>Total Lymphoid Irradiation (TLI)</td>
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<td></td>
</tr>
<tr>
<td></td>
<td>TBI*</td>
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</tbody>
</table>

*This section is only applicable to patients who:
1) Received radiation to any of the specified fields at ≥ 30 Gy
   OR
2) Received a combination of radiation to any of the specified fields plus relevant spinal radiation and/or TBI, the sum of which is ≥ 30 Gy

See dose calculation rules on page 56 for patients who received: (a) radiation to more than one of the specified fields, or (b) more than one planned course of treatment to the same field.

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

---

### SECTION 83 REFERENCES


### SECTION 84 REFERENCES


### RADIATION

<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling/ Further Considerations</th>
</tr>
</thead>
</table>
| 85    | Total Body Irradiation (TBI) | Dyslipidemia | Host Factors
Family history of dyslipidemia | Medical Conditions | SCREENING
Fasting lipid profile
Every 2 years and as clinically indicated | | |

**Note:** For all guideline sections relevant to patients who received TBI please see page 129.

---

### SECTION 85 REFERENCES


---

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

<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling/ Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>86</td>
<td>≥ 30 Gy to: Hepatic Inverted Y Left Flank/Hemiabdomen Left upper quadrant Paraaoctic Renal Right Flank/Hemiabdomen Right Upper quadrant Spleen (entire) Spleen (partial) Whole abdomen Subtotal Lymphoid Irradiation (STLI) Extended Mantle Total Lymphoid Irradiation (TLI) TBI*</td>
<td>Hepatic fibrosis Cirrhosis Focal nodular hyperplasia</td>
<td>Treatment Factors Higher radiation dose Medical Conditions Chronic hepatitis History of VOD Health Behaviors Alcohol use</td>
<td>Treatment Factors Dose ≥ 40 Gy to at least 1/3 of liver volume Dose 20-30 Gy to entire liver</td>
<td>PHYSICAL Jaundice Spider angiomomas Palmar erythema Xanthomata Hepatomegaly Splenomegaly</td>
<td>YEARLY SCREENING ALT AST Bilirubin Baseline at entry into long-term follow-up, repeat as clinically indicated</td>
</tr>
</tbody>
</table>

*This section is only applicable to patients who:
1) Received radiation to any of the specified fields at ≥ 30 Gy
2) Received a combination of radiation to any of the specified fields and TBI, the sum of which is ≥ 30 Gy

- See dose calculation rules on page 56 for patients who received: (a) radiation to more than one of the specified fields, or (b) more than one planned course of treatment to the same field.
- See “Patient-Specific Guideline Identification Tool” in Appendix I to determine specific screening guidelines by section number for individual patients.

---

### SECTION 86 REFERENCES

## RADIATION

### POTENTIAL IMPACT TO GI/HEPATIC SYSTEM (cont)

<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling/ Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>87</td>
<td>≥ 30 Gy to:</td>
<td></td>
<td></td>
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</tr>
<tr>
<td></td>
<td>Hepatic Inverted Y</td>
<td>Cholelithiasis</td>
<td>Host Factors</td>
<td></td>
<td>HISTORY</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Colicky abdominal pain related to fatty food intake</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Left Flank/Hemiabdomen</td>
<td></td>
<td></td>
<td></td>
<td>Excessive flatulence</td>
<td>Yearly and as clinically indicated</td>
</tr>
<tr>
<td></td>
<td>Left upper quadrant</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Paaortic Renal</td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td></td>
<td>Right Flank/Hemiabdomen</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Right Upper quadrant</td>
<td></td>
<td></td>
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</tr>
<tr>
<td></td>
<td>Spleen (entire)</td>
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<tr>
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<td>Spleen (partial)</td>
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<tr>
<td></td>
<td>Whole abdomen</td>
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<td></td>
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<td></td>
<td>Subtotal Lymphoid Irradiation (STLI)</td>
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<td></td>
<td>Extended Mantle</td>
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<td></td>
<td>Total Lymphoid Irradiation (TLI)</td>
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<tr>
<td></td>
<td>TBI*</td>
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</tr>
</tbody>
</table>

*This section is only applicable to patients who:
1) Received radiation to any of the specified fields at ≥ 30 Gy
2) Received a combination of radiation to any of the specified fields and TBI, the sum of which is ≥ 30 Gy

- See dose calculation rules on page 56 for patients who received: (a) radiation to more than one of the specified fields, or (b) more than one planned course of treatment to the same field.
- See “Patient-Specific Guideline Identification Tool” in Appendix I to determine specific screening guidelines by section number for individual patients.

<table>
<thead>
<tr>
<th>Health Links</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gastrointestinal Health</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Considerations for Further Testing and Intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>Consider gallbladder ultrasound in patients with chronic abdominal pain</td>
</tr>
</tbody>
</table>

**SYSTEM = GI/Hepatic**

**SCORE = 2B**

### SECTION 87 REFERENCES

## RADIATION

<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling/ Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>88</td>
<td>&gt; 30 Gy to: Hepatic Inverted Y Left Flank/Hemiabdomen Left upper quadrant Paraaortic Renal Right Flank/Hemiabdomen Right Upper quadrant Spleen (entire) Spleen (partial) Whole abdomen Bladder Femoral Iliac Inguinal Pelvic Prostate Vaginal Spine (lumbar) Spine (sacral) Spine (thoracic) Spine (whole) Subtotal Lymphoid Irradiation (STLI) Extended Mantle Total Lymphoid Irradiation (TLI) TBI*</td>
<td>Bowel obstruction</td>
<td>Treatment Factors Higher radiation dose to bowel Abdominal surgery</td>
<td>Treatment Factors Radiation dose ≥ 45 Gy (Obstruction may occur in people who received lower doses of abdominal radiation during childhood)</td>
<td>HISTORY Abdominal pain Distention Vomiting Constipation With clinical symptoms of obstruction PHYSICAL Tenderness Abdominal guarding Distension With clinical symptoms of obstruction</td>
<td>SYSTEM = GI/Hepatic SCORE = 1</td>
</tr>
</tbody>
</table>

*In this section, bowel obstruction and other symptoms are assessed for patients treated with abdominal radiation who have not had abdominal surgery. Additional evaluation is suggested for those with a history of abdominal surgery, abdominal pain, or a radiation dose of ≥ 45 Gy. The potential impact of radiation on the gastrointestinal (GI) and hepatic systems is discussed below.*

**INFO LINK**

1. This section is only applicable to patients who:
   1. Received radiation to any of the specified fields at ≥ 30 Gy OR
   2. Received a combination of radiation to any of the specified fields plus relevant spinal radiation and/or TBI, the sum of which is ≥ 30 Gy

2. See dose calculation rules on page 56 for patients who received: (a) radiation to more than one of the specified fields, or (b) more than one planned course of treatment to the same field.

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

**EVALUATION**

- HISTORY Abdominal pain Distention Vomiting Constipation With clinical symptoms of obstruction
- PHYSICAL Tenderness Abdominal guarding Distension With clinical symptoms of obstruction

**HEALTH CONSIDERATIONS**

- Bowel obstruction is rarely seen in individuals treated with abdominal radiation who have not had abdominal surgery.
- Bowel obstruction may occur in people who received lower doses of abdominal radiation during childhood.

**SPECIAL CONSIDERATIONS**

- Surgical consultation in patients unresponsive to medical management.
- Obtain KUB in patients with clinical symptoms of obstruction.

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

---

**SECTION 88 REFERENCES**

### RADIATION

<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling/ Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>89</td>
<td>≥ 30 Gy to:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Health Links: Gastrointestinal Health</td>
</tr>
<tr>
<td></td>
<td>Hepatic Inverted Y</td>
<td>Chronic enterocolitis</td>
<td>Treatment Factors</td>
<td>Treatment Factors</td>
<td>HISTORY</td>
<td>System = GI/Hepatic</td>
</tr>
<tr>
<td></td>
<td>Left Flank/Hemiabdomen</td>
<td>Fistula</td>
<td>Higher radiation dose to bowel</td>
<td>Radiation dose ≥ 45 Gy</td>
<td>Nausea</td>
<td>Score = 1</td>
</tr>
<tr>
<td></td>
<td>Left upper quadrant</td>
<td>Strictures</td>
<td>Abdominal surgery</td>
<td></td>
<td>Vomiting</td>
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<tr>
<td></td>
<td>Parasitic</td>
<td></td>
<td></td>
<td></td>
<td>Abdominal pain</td>
<td></td>
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<tr>
<td></td>
<td>Renal</td>
<td></td>
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<td></td>
<td>Diarrhea</td>
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<td></td>
<td>Right Flank/Hemiabdomen</td>
<td></td>
<td></td>
<td></td>
<td>Yearly</td>
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<tr>
<td></td>
<td>Right Upper quadrant</td>
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<td></td>
<td>Spleen (entire)</td>
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<td></td>
<td>Spleen (partial)</td>
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<td></td>
<td>Whole abdomen</td>
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<td></td>
<td>Bladder</td>
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<td>Femoral</td>
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<td>Iliac</td>
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<td>Inguinal</td>
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<td></td>
<td>Pelvic</td>
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<td>Prostate</td>
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<td></td>
<td>Vaginal</td>
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<tr>
<td></td>
<td>Spine (lumbar)</td>
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<td></td>
<td>Spine (sacral)</td>
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<td></td>
<td>Spine (thoracic)</td>
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<td></td>
<td>Spine (whole)</td>
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<td></td>
<td>Subtotal Lymphoid Irradiation (STLI)</td>
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<td></td>
<td>Extended Mantle</td>
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<td></td>
<td>Total Lymphoid Irradiation (TLI)</td>
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<tr>
<td></td>
<td>TBI*</td>
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</tbody>
</table>

* TBI is included for dose calculation purposes only; this section is not applicable to patients who received TBI alone.

**This section is only applicable to patients who:**  
1) Received radiation to any of the specified fields at ≥ 30 Gy  
OR  
2) Received a combination of radiation to any of the specified fields plus relevant spinal radiation and/or TBI, the sum of which is ≥ 30 Gy

- See dose calculation rules on page 56 for patients who received: (a) radiation to more than one of the specified fields, or (b) more than one planned course of treatment to the same field.
- See “Patient-Specific Guideline Identification Tool” in Appendix I to determine specific screening guidelines by section number for individual patients.

### POTENTIAL IMPACT TO GI/HEPATIC SYSTEM (cont)

#### SECTION 89 REFERENCES


### RADIATION

<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling/ Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>90</td>
<td>≥ 30 Gy to: Hepatic Inverted Y Left Flank/Hemiabdomen Left upper quadrant Paraaortic Renal Right Flank/Hemiabdomen Right Upper quadrant Spleen (entire) Spleen (partial) Whole abdomen Bladder Femoral Iliac Inguinal Pelvic Prostate Vaginal Spine (lumbar) Spine (sacral) Spine (thoracic) Spine (whole) Subtotal Lymphoid Irradiation (STLI) Extended Mantle Total Body Irradiation (TBI) Total Lymphoid Irradiation (TLI)</td>
<td>Colorectal cancer</td>
<td>Host Factors Current age ≥ 50 years Treatment Factors Higher radiation dose to bowel Higher daily dose fraction Combined with chemotherapy (especially alkylators) Medical Conditions Obesity Health Behaviors High fat/low fiber diet</td>
<td>Host Factors Personal history of ulcerative colitis, gastrointestinal malignancy, adenomatous polyps, or hepatoblastoma Familial polyposis Family history of colorectal cancer or polyps in first degree relative</td>
<td>SCREENING Colonoscopy Every 5 years [minimum] beginning at 10 years after radiation or at age 35 years [whichever occurs last] More frequently if indicated based on colonoscopy results Per the ACS, begin screening earlier for the following high-risk groups—HNPCC: at puberty FAP: at age 21 years IBD: 8 years after diagnosis of IBD Information from the first colonoscopy will inform frequency of follow-up testing</td>
<td></td>
</tr>
</tbody>
</table>

**Info Link**

- Reports of colorectal cancer in cohorts of long-term survivors suggest that radiation likely increases risk but the median age of onset is not as well established as that of secondary breast cancer following chest radiation.
- The expert panel agreed that early onset of screening is likely beneficial and that a prudent course would be to initiate screening for colorectal cancer for those at highest risk (abdominal pelvic and/or spinal radiation ≥ 30 Gy) at age 35 or 10 years post radiation whichever occurs last.
- Surveillance should be done via colonoscopy as per recommendations for populations at highest risk with information from the first colonoscopy informing the frequency of follow-up testing.

**Screening**

- Colonoscopy: Every 5 years [minimum] beginning at 10 years after radiation or at age 35 years [whichever occurs last].
- More frequently if indicated based on colonoscopy results.
- Per the ACS, begin screening earlier for the following high-risk groups:—HNPCC: at puberty.
- FAP: at age 21 years.
- IBD: 8 years after diagnosis of IBD.
- Information from the first colonoscopy will inform frequency of follow-up testing.

**Colonoscopy**

- Every 5 years [minimum] beginning at 10 years after radiation or at age 35 years [whichever occurs last].
- More frequently if indicated based on colonoscopy results.
- Per the ACS, begin screening earlier for the following high-risk groups:—HNPCC: at puberty.
- FAP: at age 21 years.
- IBD: 8 years after diagnosis of IBD.
- Information from the first colonoscopy will inform frequency of follow-up testing.

**Health Counseling/ Further Considerations**

- Surgical and/or oncology consultation as needed.

**SCORING**

- SYSTEM = SMN
- SCORE = 2A

**Info Link**

- Reports of colorectal cancer in cohorts of long-term survivors suggest that radiation likely increases risk however the risk related to TBI alone has not been established.

- Monitoring of patients who received TBI without additional radiation potentially impacting the colon/rectum should be determined on an individual basis. (See Info Link in next column.)

- This section is only applicable to patients who:
  1. Received radiation to any of the specified fields at ≥ 30 Gy
   OR
  2. Received a combination of radiation to any of the specified fields plus relevant spinal radiation and/or TBI, the sum of which is ≥ 30 Gy

- See dose calculation rules on page 56 for patients who received: (a) radiation to more than one of the specified fields, or (b) more than one planned course of treatment to the same field.

- See “Patient-Specific Guideline Identification Tool” in Appendix I to determine specific screening guidelines by section number for individual patients.
<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling/Further Considerations</th>
</tr>
</thead>
</table>

**RADIATION**

**POTENTIAL IMPACT TO GI/HEPATIC SYSTEM (cont)**

**SECTION 90 REFERENCES**


### RADIATION

<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling/ Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>91</td>
<td>Hepatic Inverted Y</td>
<td>Renal toxicity</td>
<td>Host Factors</td>
<td>Treatment Factors</td>
<td>PHYSICAL</td>
<td>Health Links</td>
</tr>
<tr>
<td></td>
<td>Left Flank/Hemiabdomen</td>
<td>Renal insufficiency</td>
<td>Bilateral Wilms tumor</td>
<td>Radiation dose ≥ 15 Gy</td>
<td>Blood pressure</td>
<td>Kidney Health</td>
</tr>
<tr>
<td></td>
<td>Left upper quadrant</td>
<td>Hypertension</td>
<td>Mononephric</td>
<td>TBI ≥ 6 Gy in single fraction or ≥ 12 Gy fractionated</td>
<td>Yearly</td>
<td>Cardiovascular Risk Factors</td>
</tr>
<tr>
<td></td>
<td>Paraaoctic Renal</td>
<td></td>
<td>Radiomimetic chemotherapy</td>
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<td></td>
<td>Right Flank/Hemiabdomen</td>
<td></td>
<td>(e.g., doxorubicin, daclomycin)</td>
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<tr>
<td></td>
<td>Right Upper quadrant</td>
<td></td>
<td>Radiation dose ≥ 10 Gy</td>
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<tr>
<td></td>
<td>Spleen (entire)</td>
<td></td>
<td>TBI combined with radiation to the kidney</td>
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<tr>
<td></td>
<td>Whole abdomen</td>
<td></td>
<td>Combined with other nephrotoxic agents, such as:</td>
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<tr>
<td></td>
<td>Subtotal Lymphoid Irradiation (STLI)</td>
<td></td>
<td>- Cisplatin</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>Extended Mantle</td>
<td></td>
<td>- Carboplatin</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Total Body Irradiation (TBI)</td>
<td></td>
<td>- Ifosfamide</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Total Lymphoid Irradiation (TLI)</td>
<td></td>
<td>- Aminoglycosides</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>- Amphotericin</td>
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<td></td>
<td></td>
<td></td>
<td>- Immunosuppressants</td>
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</tr>
</tbody>
</table>

**Medical Conditions**
- Diabetes mellitus
- Hypertension
- Nephrectomy

**Treatment Factors**

- Radiation dose ≥ 15 Gy
- TBI ≥ 6 Gy in single fraction or ≥ 12 Gy fractionated

**Host Factors**
- Bilateral Wilms tumor
- Mononephric

**Risk Factors**
- Radiomimetic chemotherapy (e.g., doxorubicin, dacarbazine)
- Radiation dose ≥ 10 Gy
- TBI combined with radiation to the kidney
- Combined with other nephrotoxic agents, such as:
  - Cisplatin
  - Carboplatin
  - Ifosfamide
  - Aminoglycosides
  - Amphotericin
  - Immunosuppressants

**Periodic Evaluation**
- Baseline at entry into long-term follow-up
- Urinalysis

**Health Counseling/ Further Considerations**
- Yearly

---

### SECTION 91 REFERENCES

<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling/ Further Considerations</th>
</tr>
</thead>
</table>
| 92   | ≥ 30 Gy to: Inverted Y Left Flank/Hemiabdomen Right Flank/Hemiabdomen Whole abdomen Bladder Iliac Inguinal Pelvic Prostate Vaginal Spine (sacral) Spine (whole) Total Lymphoid Irradiation (TLI) TBI* | Hemorrhagic cystitis   | Treatment Factors Higher radiation dose (≥ 30 Gy to entire bladder, ≥ 60 Gy to portion of bladder) | Treatment Factors Combined with cyclophosphamide and/or ifosfamide | HISTORY | Health Links
Urinary urgency/frequency
Urinary incontinence/retention
Dysuria
Nocturia
Abnormal urinary stream
Yearly

**This section is only applicable to patients who:**
1) Received radiation to any of the specified fields at ≥ 30 Gy
OR
2) Received a combination of radiation to any of the specified fields plus relevant spinal radiation and/or TBI, the sum of which is ≥ 30 Gy

See dose calculation rules on page 56 for patients who received: (a) radiation to more than one of the specified fields, or (b) more than one planned course of treatment to the same field.

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

*TBI is included for dose calculation purposes only; this section is not applicable to patients who received TBI alone.

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

### POTENTIAL IMPACT TO URINARY TRACT (cont)

**References**


## RADIATION

### POTENTIAL IMPACT TO URINARY TRACT (cont)

<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling/ Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>93</td>
<td>≥ 30 Gy to: Inverted Y Left Flank/Hemiabdomen Right Flank/Hemiabdomen Whole abdomen Bladder Iliac Inguinal Pelvic Prostate Vaginal Spine (sacral) Spine (whole) Total Lymphoid Irradiation (TLI) TBI*</td>
<td>Urinary tract toxicity Bladder fibrosis Dysfunctional voiding Vesicoureteral reflux Hydronephrosis</td>
<td>Treatment Factors Higher cumulative radiation dose (≥ 45 Gy) Radiation to entire bladder Combined with: - Cyclophosphamide - Ifosfamide - Vincristine</td>
<td><strong>Highest Risk Factors</strong></td>
<td><strong>Periodic Evaluation</strong></td>
<td><strong>Health Counseling/ Further Considerations</strong></td>
</tr>
<tr>
<td></td>
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<td></td>
<td>HISTORY</td>
<td>Hematuria Urinary urgency/frequency Urinary incontinence/retention Dysuria Nocturia Abnormal urinary stream</td>
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<td>SCREENING</td>
<td>Urinanalysis</td>
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</tbody>
</table>

*This section is only applicable to patients who:
1) Received radiation to any of the specified fields at ≥ 30 Gy OR
2) Received a combination of radiation to any of the specified fields plus relevant spinal radiation and/or TBI, the sum of which is ≥ 30 Gy

See dose calculation rules on page 56 for patients who received: (a) radiation to more than one of the specified fields, or (b) more than one planned course of treatment to the same field.

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

### SECTION 93 REFERENCES


### RADIATION

<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling/ Further Considerations</th>
</tr>
</thead>
</table>
| 94    | Inverted Y Left Flank/Hemiabdomen | Bladder malignancy | Treatment Factors Radiation to pelvis Combined with:  - Cyclophosphamide  - Ifosfamide | | HISTORY:  - Hematuria  - Urinary urgency/frequency  - Urinary incontinence/retention  - Dysuria  - Nocturia  Abnormal urinary stream | Yearly  
|       | Right Flank/Hemiabdomen Whole abdomen Bladder Iliac Inguinal Pelvic Prostate Vaginal Spine (sacral) Spine (whole) Total Lymphoid Irradiation (TLI) | | Health Behaviors Alcohol use Smoking | | HEALTH LINKS:  - Bladder Health | 

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

**SECTION 94 REFERENCES**


• See “Patient-Specific Guideline Identification Tool” in Appendix I to determine specific screening guidelines by section number for individual patients.
<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling/Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>95 (female)</td>
<td>Inverted Y Left Flank/Hemiabdomen Right Flank/Hemiabdomen Whole abdomen Bladder Vaginal Spine (lumbar) Spine (sacral) Spine (whole) Total Body Irradiation (TBI) Total Lymphoid Irradiation (TLI)</td>
<td>Uterine vascular insufficiency Resulting in adverse pregnancy outcomes, such as spontaneous abortion, neonatal death, low-birth weight infant, fetal malposition, and premature labor</td>
<td>Host Factors Females with Wilms tumor and associated Müllerian anomalies Treatment Factors Higher radiation dose to pelvis</td>
<td>Host Factors Prepubertal at treatment Treatment Factors Radiation dose ≥ 30 Gy TBI</td>
<td>HISTORY Pregnancy Yearly and as clinically indicated Childbirth history Yearly and as clinically indicated</td>
<td><strong>Health Links</strong> Female Health Issues <strong>Resources</strong> American Society for Reproductive Medicine: <a href="http://www.asrm.org">www.asrm.org</a> Fertile Hope: <a href="http://www.fertilehope.org">www.fertilehope.org</a> <strong>Considerations for Further Testing and Intervention</strong> Consider high-level ultrasound evaluation of genitourinary tract after pubertal development as clinically indicated in patients contemplating pregnancy. High-risk obstetrical care during pregnancy.</td>
</tr>
</tbody>
</table>

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


### SECTION 95 REFERENCES

## RADIATION

<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Treatment Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling/ Further Considerations</th>
</tr>
</thead>
</table>
| 96 (female) | Inverted Y Left Flank/Hemiabdomen Right Flank/Hemiabdomen Whole abdomen Bladder Pelvic Vaginal Spine (lumbar) Spine (sacral) Spine (whole) Total Body Irradiation (TBI) Total Lymphoid Irradiation (TLI) | Gonadal dysfunction (ovarian) Delayed/arrested puberty Premature menopause Infertility | Host Factors Older age at irradiation | Treatment Factors Radiation dose ≥ 5 Gy if pubertal, ≥ 10 Gy if prepubertal Combined with cyclophosphamide conditioning for IRT | thernal onset, tempo, menstrual, pregnancy history | ESTRADIOL | Health Links

### POTENTIAL IMPACT TO FEMALE REPRODUCTIVE SYSTEM (cont)

- **Infertility**
- Premature menopause
- Delayed/arrested puberty
- Gonadal dysfunction (ovarian)

### Risk Factors

- Older age at irradiation
- Combined with alkylating agent chemotherapy
- Radiation dose ≥ 15 Gy if prepubertal

### Highest Risk Factors

- Radiation dose ≥ 10 Gy if pubertal, ≥ 15 Gy if prepubertal Combined with cyclophosphamide conditioning for IRT

### Periodic Evaluation

- History
  - Pubertal onset, tempo, menstrual, pregnancy history
  - Sexual function (vaginal dryness, libido)
  - Medication use
  - Yearly

- Physical
  - Tanner staging
  - Yearly until sexually mature

- Screening
  - FSH
  - LH
  - Estradiol
  - Baseline at age 13 AND as clinically indicated in patients with delayed or arrested puberty, irregular menses, primary or secondary amenorrhea, and/or clinical signs and symptoms of estrogen deficiency

### Health Counseling/ Further Considerations

- American Society for Reproductive Medicine: [www.asrm.org](http://www.asrm.org)
- Fertile Hope: [www.fertilehope.org](http://www.fertilehope.org)

### Counseling

Counsel regarding the need for contraception, since there is tremendous individual variability in gonadal toxicity after exposure to radiation. Recovery of fertility may occur years after therapy. Counsel regarding risks and benefits of HRT.

### Considerations for Further Testing and Intervention

Bone density evaluation in hypogonadal patients. Refer to endocrinology/gynecology for delayed puberty, persistently abnormal hormone levels or hormonal replacement for hypogonadal patients. Reproductive endocrinology referral for infertility evaluation and consultation regarding assisted reproductive technologies.

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### SECTION 96 REFERENCES


### SECTION 96 REFERENCES—CONTINUED

### RADIATION

<table>
<thead>
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</thead>
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<tr>
<td>97</td>
<td>Inverted Y Left Flank/Hemiabdomen Right Flank/Hemiabdomen Whole abdomen Bladder Iliac Pelvic Vaginal Total Lymphoid Irradiation (TLI)</td>
<td>Vaginal fibrosis/stenosis</td>
<td>Host Factors</td>
<td>Treatment Factors</td>
<td>HISTORY</td>
<td>Considerations for Further Testing and Intervention</td>
</tr>
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</table>

### SECTION 97 REFERENCES


*See “Patient-Specific Guideline Identification Tool” in Appendix I to determine specific screening guidelines by section number for individual patients.*
### RADIATION

<table>
<thead>
<tr>
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<th>Therapeutic Agent(s)</th>
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<th>Risk Factors</th>
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<tbody>
<tr>
<td>98</td>
<td>Inverted Y Left Flank/Hemiabdomen Right Flank/Hemiabdomen Whole abdomen Bladder Femenal Iliac Inguinal Pelvic Prostate Testicular Total Body Irradiation (TBI) Total Lymphoid Irradiation (TLI)</td>
<td>Gonadal dysfunction (testicular) Reduced fertility Oligospermia Azospermia Infertility</td>
<td>Host Factors Testicular cancer Obesity Ejaculatory dysfunction Medications Occupational exposures (pesticides, heavy metals, solvents)</td>
<td>Treatment Factors Radiation dose to testes ≥ 6 Gy—azoospermia likely permanent</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Info Link**
The testes are included in the left and right flank/hemiabdomen only if the fields extended below iliac crest.

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

### POTENTIAL IMPACT TO MALE REPRODUCTIVE SYSTEM

| History of sexually transmitted diseases Tobacco/marijuana use Chronic GVHD Medical Conditions Genitourinary surgery Occupational exposures Medications | Host Factors Radiation dose to testes: - 1 to 3 Gy—azoospermia may be reversible - 3 to 6 Gy—azoospermia possibly reversible (but unlikely) - 8 to 10 Gy—azoospermia likely permanent Fractionated small doses greater risk than single large doses Combined with alkylating agents | Treatment Factors Radiation dose to testes: - 1 to 3 Gy—azoospermia may be reversible - 3 to 6 Gy—azoospermia possibly reversible (but unlikely) - 8 to 10 Gy—azoospermia likely permanent Fractionated small doses greater risk than single large doses Combined with alkylating agents | Treatment Factors Radiation dose to testes: - 1 to 3 Gy—azoospermia may be reversible - 3 to 6 Gy—azoospermia possibly reversible (but unlikely) - 8 to 10 Gy—azoospermia likely permanent Fractionated small doses greater risk than single large doses Combined with alkylating agents | Periodic Evaluation Yearly | Health Counseling/Further Considerations |

### SECTION 98 REFERENCES


<table>
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<tbody>
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### SECTION 98 REFERENCES–CONTINUED

## Radiation

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<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling/ Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>99 (male)</td>
<td>≥ 20 Gy to: Inverted Y Left Flank/Hemiabdomen Right Flank/Hemiabdomen Whole abdomen Bladder Femoral Iliac Inguinal Pelvic Prostate Testicular Total Lymphoid Irradiation (TLI) TBI*</td>
<td>Gonadal dysfunction (testicular): Testosterone deficiency/insufficiency Delayed/arrested puberty</td>
<td>Host Factors Testicular cancer Aging Treatment Factors Testicular irradiation combined with head/brain irradiation Combined with unilateral orchietomy</td>
<td>Treatment Factors Combined with alkylating agents Combined with cyclophosphamide conditioning for HCT</td>
<td><strong>HISTORY</strong> Pubertal (onset, tempo) Sexual function (erections, nocturnal emissions, libido) Medication use <strong>PHYSICAL</strong> Tanner staging until sexually mature Testicular volume by Prader orchiodiometry <strong>SCREENING</strong> Testosterone (ideally morning) Baseline at age 14 AND as clinically indicated in patients with delayed or arrested puberty and/or clinical signs and symptoms of testosterone deficiency</td>
<td><strong>Health Links</strong> Male Health Issues <strong>Considerations for Further Testing and Intervention</strong> Bone density evaluation in hypogonadal patients. Refer to endocrinology/urology for delayed puberty, persistently abnormal hormone levels or hormonal replacement for hypogonadal patients. Males with low normal testosterone should have periodic repeat measurements of testosterone as they age or if they become symptomatic.</td>
</tr>
</tbody>
</table>

* TBI is included for dose calculation purposes only; this section is not applicable to patients who received TBI alone.

**Info Link**

The testes are included in the left and right flank/ hiaabdomen only if the fields extended below iliac crest.

- This section is only applicable to patients who:
  1) Received radiation to any of the specified fields at ≥ 20 Gy
  2) Received a combination of radiation to any of the specified fields and TBI, the sum of which is ≥ 20 Gy

- See dose calculation rules on page 56 for patients who received: (a) radiation to more than one of the specified fields, or (b) more than one planned course of treatment to the same field.

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

### Section 99 References


### RADIATION

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<thead>
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<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling/ Further Considerations</th>
</tr>
</thead>
</table>
| 100   | All Radiation Fields (including TBI) | Musculoskeletal growth problems, Hypoplasia, Fibrosis, Reduced or uneven growth, Shortened trunk height (trunk radiation), Limb length discrepancy (extremity radiation) | **Host Factors**  
Younger age at treatment  
**Treatment Factors**  
Higher cumulative radiation dose  
Larger radiation treatment field  
Higher radiation dose per fraction | **Host Factors**  
Prepubertal at treatment  
**Treatment Factors**  
Orthovoltage radiation (commonly used before 1970) due to delivery of greater dose to skin and bones  
Epiphysis in treatment field  
Dose ≥ 20 Gy | **PHYSICAL**  
Limb lengths  
Yearly for patients who had extremity radiation  
Height  
Yearly  
Weight  
Yearly  
Sitting height  
Yearly for patients who had trunk radiation | Counseling  
Counsel regarding increased risk of fractures in weight-bearing irradiated bones  
Considerations for Further Testing and Intervention  
Orthopedic consultation for any deficit noted in growing child. Consider plastic surgery consult for reconstruction. |

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

---

### SECTION 100 REFERENCES


<table>
<thead>
<tr>
<th>Section</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling/Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>101</td>
<td>Hepatic Inverted Y Left Flank/Hemiabdomen Left upper quadrant Paraaoartic Renal Right Flank/Hemiabdomen Right Upper quadrant Spleen (entire) Spleen (partial) Whole abdomen Spine (thoracic) Spine (whole) Subtotal Lymphoid Irradiation (STLI) Chest (thorax) Extended Mantle Mantle Mediastinal Whole lung Total Lymphoid Irradiation (TLI)</td>
<td>Scoliosis/Kyphosis</td>
<td>Host Factors Younger age at irradiation Paraspinal malignancies Neurofibromatosis Treatment Factors Hemithoracic or abdominal radiation Hemithoracic, abdominal or spinal surgery Radiation of only a portion of (rather than whole) vertebral body</td>
<td>Treatment Factors Radiation doses ≥ 20 Gy (lower doses for infants) Orthovoltage radiation (commonly used before 1970) due to delivery of greater dose to skin and bones</td>
<td>PHYSICAL Spine exam for scoliosis and kyphosis Yearly until growth completed, may need more frequent assessment during puberty or if curve detected</td>
<td>Health Links Scoliosis and Kyphosis Considerations for Further Testing and Intervention Spine films in patients with clinically apparent curve. Orthopedic consultation as indicated based on radiographic exam. SYSTEM = Musculoskeletal SCORE = 1</td>
</tr>
</tbody>
</table>

**SECTION 101 REFERENCES**


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

<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
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</thead>
<tbody>
<tr>
<td>102</td>
<td>≥ 40 Gy to:</td>
<td>Radiation-induced fracture</td>
<td>Treatment Factors: History of surgery to cortex of bone</td>
<td>Treatment Factors: Radiation dose ≥ 50 Gy to bone</td>
<td>PHYSICAL Pain, swelling, deformity of bone As indicated</td>
<td>Considerations for Further Testing and Intervention Radiograph of affected bone as clinically indicated. Orthopedic evaluation as clinically indicated.</td>
</tr>
</tbody>
</table>

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

*This section is only applicable to patients who:
1. Received radiation to any of the specified fields at ≥ 40 Gy
   OR
2. Received a combination of radiation to any of the specified fields plus relevant spinal radiation and/or TBI, the sum of which is ≥ 40 Gy

*See dose calculation rules on page 56 for patients who received: (a) radiation to more than one of the specified fields, or (b) more than one planned course of treatment to the same field.

*See “Patient-Specific Guideline Identification Tool” in Appendix I to determine specific screening guidelines by section number for individual patients.
### SECTION 102 REFERENCES

HEMATOPOIETIC CELL TRANSPLANT

HEMATOPOIETIC CELL TRANSPLANT INTRODUCTORY INFORMATION/TBI-RELATED POTENTIAL LATE EFFECTS

Info Link: Hematopoietic Cell Transplant Introductory Information

- Complications after hematopoietic cell transplantation have multifactorial etiology: 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, complication of transplant process (immunosuppression and GVHD), complications in the post-transplant period, underlying disease, host genetic factors, 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.


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 these Guidelines.

<table>
<thead>
<tr>
<th>Section #</th>
<th>Gender</th>
<th>Potential Late Effect</th>
</tr>
</thead>
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<tr>
<td>44</td>
<td>Both</td>
<td>Secondary benign or malignant neoplasms</td>
</tr>
<tr>
<td>45</td>
<td>Both</td>
<td>Dysplastic nevi/skin cancer</td>
</tr>
<tr>
<td>48</td>
<td>Both</td>
<td>Brain tumor (benign or malignant)</td>
</tr>
<tr>
<td>49</td>
<td>Both</td>
<td>Neurocognitive deficits</td>
</tr>
<tr>
<td>50</td>
<td>Both</td>
<td>Clinical leukoencephalopathy</td>
</tr>
<tr>
<td>55</td>
<td>Both</td>
<td>Growth hormone deficiency</td>
</tr>
<tr>
<td>64</td>
<td>Both</td>
<td>Cataracts</td>
</tr>
<tr>
<td>69</td>
<td>Both</td>
<td>Dental abnormalities</td>
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<tr>
<td>71</td>
<td>Both</td>
<td>Thyroid nodules</td>
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<tr>
<td>72</td>
<td>Both</td>
<td>Thyroid cancer</td>
</tr>
<tr>
<td>73</td>
<td>Both</td>
<td>Hypothyroidism</td>
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<tr>
<td>77*</td>
<td>Female</td>
<td>Breast cancer</td>
</tr>
<tr>
<td>78</td>
<td>Female</td>
<td>Breast tissue hypoplasia</td>
</tr>
<tr>
<td>79</td>
<td>Both</td>
<td>Pulmonary toxicity</td>
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<tr>
<td>80</td>
<td>Male</td>
<td>Cardiac toxicity</td>
</tr>
<tr>
<td>81</td>
<td>Female</td>
<td>Cardiac toxicity</td>
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<tr>
<td>84</td>
<td>Both</td>
<td>Impaired glucose metabolism/diabetes mellitus</td>
</tr>
<tr>
<td>85</td>
<td>Both</td>
<td>Dyslipidemia</td>
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<tr>
<td>90*</td>
<td>Both</td>
<td>Colorectal cancer</td>
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<td>91</td>
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<td>Renal toxicity</td>
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<td>95</td>
<td>Female</td>
<td>Uterine vascular insufficiency</td>
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<td>96</td>
<td>Female</td>
<td>Gonadal dysfunction (ovarian)</td>
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<tr>
<td>98</td>
<td>Male</td>
<td>Gonadal dysfunction (testicular)</td>
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<tr>
<td>100</td>
<td>Both</td>
<td>Musculoskeletal growth problems</td>
</tr>
</tbody>
</table>

*Screening may be indicated for patients who received TBI alone – see Info Link in this section
<table>
<thead>
<tr>
<th>Sec</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
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</thead>
<tbody>
<tr>
<td>103</td>
<td>Autologous Hematopoietic Cell Transplant (HCT)</td>
<td>Myelodysplasia Acute myeloid leukemia</td>
<td>Treatment Factors Radiation therapy Stem cell mobilization with etoposide Alkylating agent chemotherapy Epipodophyllotoxins Anthracyclines Autologous transplant</td>
<td>Host Factors Older age Treatment Factors Autologous transplant for non-Hodgkin and Hodgkin lymphoma Peripheral blood stem cells</td>
<td>HISTORY Fatigue Bleeding Easy bruising Yearly, up to 10 years after transplant</td>
<td>Health Links Reducing the Risk of Second Cancers Counseling Counsel to promptly report fatigue, pallor, petechiae or bone pain. Considerations for Further Testing and Intervention CBC and bone marrow exam as clinically indicated.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>SYSTEM = SMN</td>
<td>SCORE = 1</td>
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</tbody>
</table>

**SECTION 103 REFERENCES**


HEMATOPOIETIC CELL TRANSPLANT (cont)

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<td>104</td>
<td>Hematopoietic Cell Transplant (HCT)</td>
<td>Solid tumors</td>
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<td>Younger age at transplant</td>
<td>TBI</td>
<td>PHYSICAL Evaluation for benign or malignant neoplasms</td>
<td>Yearly</td>
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<td>Fanconi’s anemia</td>
<td>Radiotherapy</td>
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<td></td>
<td></td>
<td></td>
<td>Treatment Factors</td>
<td>Medical Conditions</td>
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<tr>
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<td></td>
<td>Radiation therapy</td>
<td>Hepatitis C infection</td>
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<td>Chronic GVHD</td>
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<td>Human Papillomavirus (HPV) infection</td>
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</table>

SYSTEM = SMN
SCORE = 1

SECTION 104 REFERENCES

## HEMATOPOIETIC CELL TRANSPLANT

<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling/ Further Considerations</th>
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</thead>
</table>
| 105 (female) | Hematopoietic Cell Transplant (HCT) | Solid tumors | Host Factors  
Younger age at transplant  
Fanconi's anemia | Treatment Factors  
Radiation therapy  
Medical Conditions  
Hepatitis C infection  
Chronic GVHD  
Human Papillomavirus (HPV) infection | Treatment Factors  
TBI | PHYSICAL  
Evaluation for benign or malignant neoplasms  
Yearly | |

### SECTION 105 REFERENCES


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<td>Hematopoietic Cell Transplant (HCT)</td>
<td>Lymphoma</td>
<td>Medical Conditions</td>
<td>Host Factors</td>
<td>PHYSICAL</td>
<td>Considerations for Further Testing and Intervention</td>
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<td></td>
<td>Chronic GVHD</td>
<td>Diagnosis of primary immune deficiency</td>
<td>Lymphadenopathy</td>
<td>Oncology consultation as clinically indicated.</td>
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<td>Host Factors</td>
<td>Yearly</td>
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<td>Treatment Factors</td>
<td>HLA mismatch</td>
<td>Splenomegaly</td>
<td>SCORE = 1</td>
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<td></td>
<td>Yearly</td>
<td>Unrelated donor transplant</td>
<td>Yearly</td>
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<td>ATG</td>
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### SECTION 106 REFERENCES


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<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling/ Further Considerations</th>
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</thead>
<tbody>
<tr>
<td>107</td>
<td>Hematopoietic Cell Transplant (HCT)</td>
<td>Hepatic toxicity</td>
<td>Treatment Factors</td>
<td>Medical Conditions</td>
<td>SCREENING</td>
<td>Health Links</td>
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<td></td>
<td>Chronic hepatitis</td>
<td>History of multiple transusions</td>
<td>Chronic hepatitis C with siderosis and steatosis</td>
<td>ALT, AST, Bilirubin, Ferritin</td>
<td>Liver Health</td>
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<td></td>
<td></td>
<td>Cirrhosis</td>
<td>Radiation to the liver</td>
<td></td>
<td>Baseline at entry into long-term follow-up, repeat as clinically indicated</td>
<td>Gastrointestinal Health</td>
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<td>Iron overload</td>
<td>Antimetabolite therapy</td>
<td></td>
<td></td>
<td>Considerations for Further Testing and Intervention</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Medical Conditions</td>
<td></td>
<td></td>
<td>Prothrombin time for evaluation of 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.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Chronic GHD</td>
<td></td>
<td></td>
<td>Note: PCR testing for HCV may be required in immunosuppressed patients who are negative for antibody. Gastroenterology/hepatology consultation in patients with persistent liver dysfunction or known hepatitis. Hepatitis A and B immunizations in patients lacking immunity. Consider liver biopsy in patients with persistent elevation of ferritin (based on clinical context and magnitude of elevation). Consider phlebotomy or chelation therapy for treatment of iron overload.</td>
</tr>
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<td></td>
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<td></td>
<td>Viral hepatitis</td>
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<td></td>
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<td></td>
<td>History of VOD</td>
<td></td>
<td></td>
<td>SCORE = 1</td>
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<td></td>
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<td>Health Behaviors</td>
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<td></td>
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<td></td>
<td>Alcohol use</td>
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<tbody>
<tr>
<td>108</td>
<td>Hematopoietic Cell Transplant (HCT)</td>
<td>Osteonecrosis (Avascular Necrosis)</td>
<td>Treatment Factors: Corticosteroids (dexamethasone effect is more potent than prednisone) Other immunosuppressants TBI High-dose radiation to any bone Allogeneic HCT &gt; autologous</td>
<td>Host Factors: Pubertal or pre-pubertal at time of transplant Treatment Factors: Prolonged immune-suppressive therapy (e.g., for chronic GVHD) Medical Conditions: Chronic GVHD</td>
<td>HISTORY: Joint pain, Swelling, Immobility Limited range of motion Yearly</td>
<td>Health Links: Osteonecrosis Considerations for Further Testing and Intervention: MRI as clinically indicated in patients with history suggestive of osteonecrosis (should be done soon after symptom onset). Orthopedic consultation in patients with positive imaging and/or symptoms of osteonecrosis. Symptomatic lesions confer the greatest risk for collapse. Physical therapy evaluation (for non-pharmacologic pain management, range of motion, strengthening, stretching, functional mobility).</td>
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**SECTION 108 REFERENCES**


### Hematopoietic Cell Transplant (HCT) (cont)

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</table>
| 109   | Hematopoietic Cell Transplant (HCT) | Reduced bone mineral density (BMD) Defined as Z-score > 2.0 SD below the mean in survivors < 20 years old or T-score > 1.0 SD below the mean in survivors ≥ 20 years old | Host Factors Both genders are at risk Younger age at diagnosis Caucasian Lower weight and BMI | Host Factors Older age at time of treatment Treatment Factors Prolonged corticosteroid therapy (e.g., for chronic GVHD) | Screening Bone density evaluation (DEXA or quantitative CT) Baseline at entry into long-term follow-up, repeat as clinically indicated | **Info Link**  
- The World Health Organization definition of osteoporosis in adults is based on comparison of a measured bone mineral density (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.  

### Info Link
- The optimal method of measuring bone health in children is controversial. Existing technologies have limitations.  
- Dual energy x-ray absorptiometry (DEXA) provides an estimate of total bone mass at a given site.  
- Quantitative CT provides distinct measures of trabecular and cortical bone dimension and density.  

### Considerations for Further Testing and Intervention
- Ensure the AAP recommended minimum daily intake of Vitamin D (400 IU/day) for children, with possible considerations for high doses in selected patients (e.g., kidney disease or Vitamin D deficiency). Many experts recommend higher Vitamin D intake in adults as well. Also 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. Advocate for regular weight-bearing exercises such as running and jumping. Use caution regarding calcium supplementation in patients with history of renal lithiasis. Treatment of exacerbating or predisposing conditions (e.g., hormonal replacement therapy for hypogonadism, growth hormone 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).
**HEMATOPOIETIC CELL TRANSPLANT (cont)**

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### HEMATOPOIETIC CELL TRANSPLANT (cont)

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<tr>
<td>110</td>
<td>Hematopoietic Cell Transplant (HCT)</td>
<td>Renal toxicity Glomerular injury Tubular injury Hypertension</td>
<td>Treatment Factors Chronic cyclosporine use</td>
<td>Host Factors Older age at transplant Treatment Factors TBI Medical Conditions Acute kidney injury within 6 months of HCT History of cGVHD</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 Urinalysis Yearly</td>
<td>Health Links Kidney Health Cardiovascular Risk Factors Considerations for Further Testing and Intervention Nephrology consultation for patients with hypertension, proteinuria, or progressive renal insufficiency</td>
</tr>
</tbody>
</table>

### SECTION 110 REFERENCES


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</thead>
</table>
| 111   | HCT with *any history of Chronic GVHD* | Dermatologic toxicity  
Permanent alopecia  
Nail dysplasia  
Vitiligo  
Scleroderma  
Squamous cell carcinoma of the skin |  |  | PHYSICAL  
Hair (alopecia)  
Nails (hypoplasia)  
Skin (vitiligo, scleroderma)  
Yearly |  |

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

Health Links  
Skin Health  
SYSTEM = Dermatologic  
SCORE = 1

### SECTION 111 REFERENCES


### HEMATOPOIETIC CELL TRANSPLANT WITH CHRONIC GVHD (cont)

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</thead>
<tbody>
<tr>
<td>112</td>
<td>HCT with any history of Chronic GVHD</td>
<td>Xerophthalmia (keratoconjunctivitis sicca)</td>
<td>Treatment Factors: Cranial radiation, Eye radiation, Radiomimetic chemotherapy (e.g., doxorubicin, dactinomycin)</td>
<td>Treatment Factors: Radiation dose to eye ≥ 30 Gy, Radiation fraction ≥ 2 Gy</td>
<td>HISTORY: Dry eyes (burning, itching, foreign body sensation, inflammation) Yearly</td>
<td>Health Links: Eye Health, Considerations for Further Testing and Intervention: Supportive care with artificial tears. Schirmer’s testing as clinically indicated. Ongoing ophthalmology follow-up for identified problems. Consider every six month ophthalmology evaluation for patients with corneal damage.</td>
</tr>
</tbody>
</table>

**SYSTEM = Ocular, SCORE = 1**

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</thead>
<tbody>
<tr>
<td>HCT with any history of Chronic GVHD</td>
<td>Xerostomia</td>
<td>Salivary gland dysfunction</td>
<td>Head and neck radiation involving the parotid gland</td>
<td>Salivary gland radiation dose ≥ 30 Gy Use of azathioprine for cGVHD management</td>
<td>HISTORY Xerostomia Yearly</td>
<td>Health Links Dental Health</td>
</tr>
<tr>
<td></td>
<td>Dental caries</td>
<td></td>
<td>Higher radiation doses Radiomimetic chemotherapy (e.g., doxorubicin, daclomycin)</td>
<td>Medical Conditions High grade of cGVHD Fanconi anemia</td>
<td>PHYSICAL Oral exam Yearly</td>
<td>Considerations for Further Testing and Intervention Supportive care with saliva substitutes, moistening agents, and sialogogues (pilocarpine). Regular dental care including fluoride applications and regular screening for intraoral malignancy.</td>
</tr>
<tr>
<td></td>
<td>Periodontal disease</td>
<td></td>
<td></td>
<td></td>
<td>SCREENING Dental exam and cleaning Every 6 months</td>
<td>SYSTEM = Dental SCORE = 1</td>
</tr>
<tr>
<td></td>
<td>Oral cancer (squamous cell carcinoma)</td>
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</tbody>
</table>

**Info Link**

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

**SECTION 113 REFERENCES**


### SECTION 114 REFERENCES—continued


## HEMATOPOIETIC CELL TRANSPLANT WITH CHRONIC GVHD (cont)

### Sec # 115

**Therapeutic Agent(s):** HCT with any history of Chronic GVHD

**Potential Late Effects:** Immunologic complications

- Secretory IgA deficiency
- Hypogammaglobulinemia
- Decreased B cells
- T cell dysfunction
- Chronic infections (e.g., conjunctivitis, sinusitis, and bronchitis associated with chronic GVHD)

**Risk Factors:**
- Host Factors
  - Active cGVHD
- Medical Conditions
  - Prolonged immunosuppression related to cGVHD and its treatment

**Highest Risk Factors:**
- Host Factors: Active cGVHD
- Medical Conditions: Prolonged immunosuppression related to cGVHD and its treatment

**Periodic Evaluation:**
- HISTORY
  - Chronic conjunctivitis
  - Chronic sinusitis
  - Chronic bronchitis
  - Recurrent or unusual infections
  - Sepsis
- PHYSICAL
  - Pulmonary exam
  - Eye exam
  - Nasal exam

**Health Counseling/Further Considerations:**
- Considerations for Further Testing and Intervention
  - Host Factors: Active cGVHD
  - Medical Conditions: Prolonged immunosuppression related to cGVHD and its treatment

### Info Link

Immunologic complications related to cGVHD may persist or resolve over time.

### SECTION 115 REFERENCES


### HEMATOPOIETIC CELL TRANSPLANT WITH CHRONIC GVHD (cont)

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<th>Periodic Evaluation</th>
<th>Health Counseling/ Further Considerations</th>
</tr>
</thead>
</table>
| 116   | HCT with currently active chronic GVHD | Functional asplenia At risk for life-threatening infection with encapsulated organisms (e.g., Haemophilus influenzae, Streptococcus pneumoniae, meningococcus) | Treatment Factors Splenic radiation Ongoing immunosuppression | Host Factors Hypogammaglobulinemia | **PHYSICAL**
Physical exam at time of febrile illness to evaluate degree of illness and potential source of infection
When febrile T ≥ 101°F as indicated for patients with active chronic GVHD |
**SCREENING**
Blood culture When febrile T ≥ 101°F as indicated for patients with active chronic GVHD |

### Info Link
This section applies only to patients who have active cGVHD.

### Health Links
**Splenic Precautions**
- Advise obtaining medical alert bracelet/card noting functional asplenia. Counsel regarding risk of life-threatening infections with encapsulated organisms. Also counsel regarding risk associated with malaria and tick-borne diseases if living in or visiting endemic areas

### Considerations for Further Testing and Intervention
- Consider antibiotic prophylaxis for encapsulated organisms and bacteremia/endocarditis prophylaxis for duration of immunosuppressive therapy for chronic GVHD (see: American Academy of Pediatric Dentistry, Guideline on Antibiotic Prophylaxis for Dental Patients at Risk for Infection). In patients with T ≥ 101°F (38.3°C) or other signs of serious illness, administer a long-acting, broad-spectrum parenteral antibiotic (e.g., ceftriaxone), and continue close medical monitoring while awaiting blood culture results. 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 ≥ 104°F; meningitis, pneumonia, or other serious focus of infection; signs of septic shock; or previous history of serious infection.
- Immunize with Pneumococcal, Meningococcal, and Hib vaccines according to current ACIP recommendations.

### Info Link
- See current edition of AAP Red Book for current recommendations regarding antibiotic prophylaxis and immunizations

### SYSTEM = Immune
### SCORE = 1

### SECTION 116 REFERENCES
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**SECTION 116 REFERENCES—continued**


### HEMATOPOIETIC CELL TRANSPLANT WITH CHRONIC GVHD (cont)

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<th>Highest Risk Factors</th>
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</thead>
</table>
| 117   | HCT with *any history of chronic GVHD* | Esophageal stricture | Treatment Factors
Radiation involving the esophagus
Radiomimetic chemotherapy (e.g., doxorubicin, daunomycin) | Medical Conditions
Gastroesophageal reflux
History of Candida esophagitis | Treatment Factors
Radiation dose ≥ 40 Gy | HISTORY
Dysphagia
Heartburn | Yearly | Health Links
Gastrointestinal Health
Considerations for Further Testing and Intervention
Surgery and/or gastroenterology consultation for symptomatic patients. |

**Info Link**
Esophageal stricture related to cGVHD is generally not reversible over time.

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

### SECTION 117 REFERENCES


### HEMATOPOIETIC CELL TRANSPLANT WITH CHRONIC GVHD (cont)

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<th>Periodic Evaluation</th>
<th>Health Counseling/ Further Considerations</th>
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<tbody>
<tr>
<td>118</td>
<td>HCT with any history of chronic GVHD</td>
<td>Vaginal fibrosis/stenosis</td>
<td>Treatment Factors Pelvic radiation</td>
<td>HISTORY Psychosocial assessment Dyspareunia Vulvar pain Post-coital bleeding Difficulty with tampon insertion Yearly</td>
<td>PHYSICAL Examine genitalia for lichen planus-like features as well as erosions, fissures, and ulcers Yearly SCREENING Gynecologic consultation when age appropriate</td>
<td>Considerations for Further Testing and Intervention Psychological consultation in patients with emotional difficulties.</td>
</tr>
</tbody>
</table>

#### SYSTEM = Reproductive (female) 
**SCORE = 1**

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### SECTION 118 REFERENCES


### HEMATOPOIETIC CELL TRANSPLANT WITH CHRONIC GVHD (cont)

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<tr>
<td>119</td>
<td>HCT with <em>any history of chronic GVHD</em></td>
<td>Joint contractures</td>
<td></td>
<td></td>
<td>Musculoskeletal exam yearly</td>
<td>Consultation with physical therapy, rehabilitation medicine/ physiatrist.</td>
</tr>
</tbody>
</table>

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

**SECTION 119 REFERENCES**


**SYSTEM = Musculoskeletal**
**SCORE = 1**
### SURGERY

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<td>Amputation</td>
<td>Amputation-related complications</td>
<td>Host Factors</td>
<td>Phantom pain</td>
<td>History</td>
<td>Phantom pain</td>
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<tr>
<td></td>
<td></td>
<td>Impaired cosmos</td>
<td>Skeletally immature/growing children</td>
<td>Functional and activity limitations</td>
<td>Functional and activity limitations</td>
<td>Amputation</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Functional and activity limitations</td>
<td>Residual limb integrity problems</td>
<td>Yearly</td>
<td>Physical</td>
<td>Residual limb integrity</td>
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<td></td>
<td></td>
<td>Phantom pain</td>
<td>Trans-femur amputation</td>
<td>Yearly</td>
<td>Screen</td>
<td>Prosthetic evaluation</td>
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<td></td>
<td></td>
<td>Neuropathic pain</td>
<td>Trans-tibia amputation</td>
<td>Every 6 months until skeletally mature, then yearly</td>
<td>Considerations for Further Testing and Intervention</td>
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<td></td>
<td>Musculoskeletal pain</td>
<td>Medical Conditions</td>
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<td>Increased energy expenditure</td>
<td>Obesity</td>
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<td></td>
<td>Impaired quality of life and functional status</td>
<td>Diabetes</td>
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<td></td>
<td></td>
<td>Psychological maladjustment</td>
<td>Poor residual limb healing</td>
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### AMPUTATION

<table>
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<td>SCORE = 1</td>
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### SECTION 120 REFERENCES


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<tr>
<td>121</td>
<td>Central venous catheter</td>
<td>Thrombosis, Vascular insufficiency, Infection of retained cuff or line tract</td>
<td></td>
<td></td>
<td>HISTORY&lt;br&gt;Tenderness or swelling at previous catheter site&lt;br&gt;Yearly</td>
<td>PHYSICAL&lt;br&gt;Venous stasis&lt;br&gt;Swelling&lt;br&gt;Tenderness at previous catheter site&lt;br&gt;Yearly and as clinically indicated</td>
</tr>
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**SECTION 121 REFERENCES**


### SURGERY CYSTECTOMY

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<tr>
<td>122</td>
<td>Cystectomy</td>
<td>Cystectomy-related complications</td>
<td>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)</td>
<td>Screening: Vitamin B12 level&lt;br&gt;Yearly starting 5 years after cystectomy (patients with ileal enterocystoplasty only)&lt;br&gt;Urology evaluation&lt;br&gt;Yearly</td>
<td>System: Urinary&lt;br&gt;Score: Asymptomatic bacteriuria: 1&lt;br&gt;Chronic urinary tract infection: 1&lt;br&gt;Renal dysfunction: 1&lt;br&gt;Vesicoureteral reflux: 1&lt;br&gt;Hydronephrosis: 1&lt;br&gt;Spontaneous neobladder perforation: 1&lt;br&gt;Reservoir calculi: 2A&lt;br&gt;Vitamin B12/folate/carotene deficiency: 2B</td>
<td>Health Links: Cystectomy, Kidney Health</td>
</tr>
</tbody>
</table>

**Info Link**

- All potential late effects for pelvic surgery apply to Cystectomy (see also Sections 145–148).  
- Reservoir calculi are stones in the neobladder (a reservoir for urine usually constructed of ileum/colon)

### SECTION 122 REFERENCES


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</thead>
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<tr>
<td>123</td>
<td>Enucleation</td>
<td>Impaired cosmesis</td>
<td>Host Factors</td>
<td>Younger age at enucleation</td>
<td>SCREENING Evaluation by ocularist Yearly</td>
<td>Health Links Eye Health Considerations for Further Testing and Intervention Psychological consultation in patients with emotional difficulties related to cosmetic and visual impairment. Vocational rehabilitation referral as indicated.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Poor prosthetic fit</td>
<td>Treatment Factors</td>
<td>Combined with radiation</td>
<td>Evaluation by ophthalmologist Yearly</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Orbital hypoplasia</td>
<td></td>
<td></td>
<td></td>
<td>SYSTEM = Ocular SCORE = 1</td>
</tr>
</tbody>
</table>

**SECTION 123 REFERENCES**

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<tr>
<td>124</td>
<td>Hysterectomy</td>
<td>Pelvic floor dysfunction</td>
<td>Treatment Factors</td>
<td>Pelvic radiation</td>
<td>HISTORY</td>
<td>Health Links</td>
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<tr>
<td></td>
<td></td>
<td>Urinary incontinence</td>
<td>Urinary leakage</td>
<td>Abdominal pain</td>
<td>Urinary leakage</td>
<td>Female Health Issues</td>
</tr>
<tr>
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<td></td>
<td>Sexual dysfunction</td>
<td>Dyspareunia</td>
<td>Psychosocial assessment</td>
<td>Abdominal pain</td>
<td>Counseling</td>
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<tr>
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<td></td>
<td></td>
<td>Yearly</td>
<td>Dyspareunia</td>
<td>Considerations for Further Testing and Intervention</td>
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<td></td>
<td></td>
<td>Psychosocial assessment</td>
<td>Reproductive endocrinology consultation for patients wishing to pursue pregnancy via gestational surrogate.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Yearly</td>
<td></td>
</tr>
</tbody>
</table>

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<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling/ Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>125</td>
<td>Laparotomy</td>
<td>Adhesions, Bowel obstruction</td>
<td>Treatment Factors Combined with radiation</td>
<td>HISTORY Abdominal pain, Distention, Vomiting, Constipation With clinical symptoms of obstruction</td>
<td>PHYSICAL Tenderness, Abdominal guarding, Distention With clinical symptoms of obstruction</td>
<td>Health Links Gastrointestinal Health Considerations for Further Testing and Intervention KUB as clinically indicated for suspected obstruction. Surgical consultation for patients unresponsive to medical management. SYSTEM = GI/Hepatic SCORE = 1</td>
</tr>
</tbody>
</table>

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<table>
<thead>
<tr>
<th>Sec #</th>
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</tr>
</thead>
<tbody>
<tr>
<td>126</td>
<td>Limb sparing procedure</td>
<td>Complications related to limb sparing procedure&lt;br&gt;Functional and activity limitations&lt;br&gt;Contractures&lt;br&gt;Chronic infection&lt;br&gt;Chronic pain&lt;br&gt;Limb length discrepancy&lt;br&gt;Musculoskeletal pain&lt;br&gt;Increased energy expenditure&lt;br&gt;Fibrosis&lt;br&gt;Prosthetic malfunction (loosening, non-union, fracture) requiring revision, replacement or amputation&lt;br&gt;Prosthetic revision required due to growth&lt;br&gt;Impaired quality of life&lt;br&gt;Complications with pregnancy/delivery (in female patients with internal hemipelvectomy)</td>
<td>Host Factors&lt;br&gt;Younger age at surgery&lt;br&gt;Rapid growth spurt&lt;br&gt;Skeletally immature</td>
<td>Treatment Factors&lt;br&gt;Radiation to extremity&lt;br&gt;Medical Conditions&lt;br&gt;Poor healing; Infection of reconstruction</td>
<td>HISTORY&lt;br&gt;Functional and activity limitations&lt;br&gt;Yearly and as clinically indicated</td>
<td>Health Links&lt;br&gt;Limb Sparing Procedures&lt;br&gt;Counseling&lt;br&gt;Counsel regarding need for antibiotic prophylaxis prior to dental and invasive procedures if applicable.</td>
</tr>
</tbody>
</table>

**SYSTEM = Musculoskeletal**

**SCORE = 1**

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**SECTION 126 REFERENCES**


### SECTION 126 REFERENCES


### SURGERY

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<tbody>
<tr>
<td>127</td>
<td>Nephrectomy</td>
<td>Hydrocele</td>
<td>Host Factors</td>
<td>Denys-Drash syndrome</td>
<td>PHYSICAL</td>
<td>Health Links</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Renal toxicity</td>
<td>WAGR syndrome</td>
<td></td>
<td>Blood pressure</td>
<td>Single Kidney Health</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Proteinuria</td>
<td>Hypospadias</td>
<td></td>
<td>Yearly</td>
<td>See also: Kidney Health</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Hyperfiltration</td>
<td>Cryptorchidism</td>
<td></td>
<td>Testicular exam to</td>
<td>Cardiovascular Risk Factors</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Renal insufficiency</td>
<td>Bilateral Wilms tumor</td>
<td></td>
<td>evaluate for</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>hydrocele</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Yearly</td>
<td></td>
</tr>
</tbody>
</table>

**Info Link**
- 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.

**Treatment Factors**
- Combined with other nephrotoxic therapy such as:
  - Cisplatin
  - Carboplatin
  - Ifosfamide
  - Aminoglycosides
  - Amphotericin
  - Immunosuppressants
  - Methotrexate
  - Radiation impacting the kidneys

**Screening**
- BUN
- Creatinine
- Na, K, Cl, CO₂
- Ca, Mg, PO₄

Baseline at entry into long-term follow-up. Repeat as clinically indicated.

**Urinalysis**
- Yearly

**Considerations for Further Testing and Intervention**
- Nephrology consultation for patients with hypertension, proteinuria or progressive renal insufficiency.

---

### SECTION 127 REFERENCES


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<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling/ Further Considerations</th>
</tr>
</thead>
</table>
| 128 (female) | Nephrectomy | Renal toxicity  
Proteinuria  
Hyperfiltration  
Renal insufficiency | Host Factors  
Denys-Drash syndrome  
WAGR syndrome  
Bilateral Wilms tumor | Treatment Factors  
Combined with other nephrotoxic therapy such as:  
Cisplatin  
Carboplatin  
Ifosfamide  
Aminoglycosides  
Amphotericin  
Immunosuppressants  
Methotrexate  
Radiation impacting the kidneys | 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  
Urinalysis  
Yearly | Health Links  
Single Kidney Health  
See also: Kidney Health  
Cardiovascular Risk Factors  
Counseling  
Counsel mononephric survivors regarding sports and activity safety, stressing the importance of physical fitness, and proper use of seatbelts (i.e., wearing lapbelts around hips, not waist). Consideration should be given to survivor health status, current kidney health (position, size, function), and acceptability of unlikely risk of renal injury to the survivor and/or family. Counsel to use NSAIDS with caution. Documentation of this discussion is recommended.  
Considerations for Further Testing and Intervention  
Nephrology consultation for patients with hypertension, proteinuria, or progressive renal insufficiency. |

**Info Link**  
- 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.

**SECTION 128 REFERENCES**


## Section 129 References


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<thead>
<tr>
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<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling/ Further Considerations</th>
</tr>
</thead>
</table>
| 130   | Neurosurgery–Brain   | Motor and/or sensory deficits.  
Paralysis  
Movement disorders  
Ataxia  
Eye problems (ocular nerve palsy, gaze paresis, nystagmus, papilledema, optic atrophy) | Host Factors  
Primary CNS tumor  
Medical Conditions  
Hydrocephalus | Host Factors  
Optic pathway tumor;  
Hypothalamic tumor;  
Suprasellar tumor (eye problems) | SCREENING  
Evaluation by neurologist  
Yearly, until 2 to 3 years after surgery or stable; Continue to monitor if symptoms persist  
Evaluation by physiatrist/rehabilitation medicine specialist  
Yearly, or more frequently as clinically indicated in patients with motor dysfunction | Considerations for Further Testing and Intervention  

**SECTION 130 REFERENCES**


<table>
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<th>Therapeutic Agent(s)</th>
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</thead>
<tbody>
<tr>
<td>131</td>
<td>Neurosurgery–Brain</td>
<td>Seizures</td>
<td>Host Factors</td>
<td>Primary CNS tumor</td>
<td>SCREENING</td>
<td>SYSTEM = CNS</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Treatment Factors</td>
<td>Methotrexate (IV, IT, IO)</td>
<td>Evaluation by neurologist</td>
<td>SCORE = 1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>As clinically indicated</td>
<td></td>
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</table>

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<table>
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<tr>
<th>Sec #</th>
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<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling/ Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>132</td>
<td>Neurosurgery–Brain</td>
<td>Hydrocephalus</td>
<td>Host Factors</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Shunt malfunction</td>
<td>Primary CNS tumor</td>
<td></td>
<td></td>
<td>Education patient/family regarding potential symptoms of shunt malfunction.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>SCREENING</td>
<td>Per the American Academy of Pediatric Dentistry endocarditis prophylaxis guidelines, antibiotics are not indicated prior to dental work for patients with V-P shunts (indicated for V-A and V-V shunts only).</td>
</tr>
<tr>
<td></td>
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<td></td>
<td></td>
<td></td>
<td>Abdominal x-ray</td>
<td>System = CNS</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>After pubertal growth spurt for patients with shunts to assure distal shunt tubing in peritoneum</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Evaluation by neurologist</td>
<td>Yearly for patients with shunts</td>
</tr>
</tbody>
</table>

**SECTION 132 REFERENCES**


<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling/ Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>133</td>
<td>Neurosurgery–Brain</td>
<td>Overweight/obesity</td>
<td>Treatment Factors Surgery in suprasellar region</td>
<td>Host Factors Extension of tumor into hypothalamus Pre-treatment obesity Craniopharyngioma</td>
<td>PHYSICAL Height Weight BMI Yearly</td>
<td>Health Links Diet and Physical Activity Cardiovascular Risk Factors Counseling Nutritional counseling. Counsel regarding obesity-related health risks Considerations for Further Testing and Intervention Consider evaluation for central endocrinopathies, including growth hormone deficiency, central hypothyroidism, central adrenal insufficiency, precocious puberty, and gonadotropin deficiency. Refer to endocrine to manage hormonal dysfunction. Consider evaluation for other co-morbid conditions, including dyslipidemia, hypertension, and impaired glucose metabolism/diabetes mellitus.</td>
</tr>
</tbody>
</table>

**Info Link**

Overweight
- Age 2–20 years: BMI for age ≥ 85th–< 95th percentile
- Age ≥ 21 years: BMI ≥ 25–29.9
- Obesity
- Age 2–20 years: BMI for age ≥ 95th percentile
- Age ≥ 21 years: BMI ≥ 30

BMI = wt(kg)/ht(M²)


Growth charts for patients < 21 years of age available on-line at: [www.cdc.gov/growthcharts](http://www.cdc.gov/growthcharts)

**SECTION 133 REFERENCES**


## SURGERY

<table>
<thead>
<tr>
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<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling/Further Considerations</th>
</tr>
</thead>
</table>
SCREENING: Na, K, Cl, CO₂, Serum Osmolality, Urine Osmolality  
As clinically indicated if history consistent with excessive thirst and/or polyuria | SYSTEM = Endocrine/Metabolic  
SCORE = 1 |

### SECTION 134 REFERENCES


<table>
<thead>
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<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
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</thead>
<tbody>
<tr>
<td>135</td>
<td>Neurosurgery–Spinal cord</td>
<td>Neurogenic bladder Urinary incontinence</td>
<td>Host Factors Tumor adjacent to or compressing spinal cord or cauda equina</td>
<td>Host Factors Injury above the level of the sacrum</td>
<td>HISTORY Hematuria Urinary urgency/frequency Urinary incontinence/retention Dysuria Nocturia Abnormal urinary stream Yearly</td>
<td>Health Links Neurogenic Bladder Counseling Counsel regarding adequate fluid intake, regular voiding, seeking medical attention for symptoms of voiding dysfunction or urinary tract infection and compliance with recommended bladder catheterization regimen. Considerations for Further Testing and Intervention Urologic consultation for patients with dysfunctional voiding or recurrent urinary tract infections.</td>
</tr>
</tbody>
</table>

**NEUROSURGERY—SPINAL CORD**

**SECTION 135 REFERENCES**


<table>
<thead>
<tr>
<th>Sec #</th>
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<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling/ Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>136</td>
<td>Neurosurgery–Spinal cord</td>
<td>Neurogenic bowel</td>
<td>Host Factors</td>
<td>Host Factors</td>
<td>HISTORY</td>
<td>Counseling</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Fecal incontinence</td>
<td>Tumor adjacent to or compressing spinal cord or cauda equina</td>
<td>Injury above the level of the sacrum</td>
<td>Chronic constipation</td>
<td>Counsel regarding benefits of adherence to bowel regimen, including adequate hydration, fiber, laxatives/enemas as clinically indicated.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Treatment Factors</td>
<td>Radiation dose ≥ 50 Gy to bladder, pelvis, or spine</td>
<td>Fecal soiling</td>
<td>Yearly</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>PHYSICAL</td>
<td>Considerations for Further Testing and Intervention</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Rectal exam</td>
<td>GI consultation to establish bowel regimen for patients with chronic impaction or fecal soiling.</td>
</tr>
<tr>
<td></td>
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<td></td>
<td></td>
<td></td>
<td>As clinically indicated</td>
<td></td>
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<tr>
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<th>Health Counseling/ Further Considerations</th>
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</thead>
<tbody>
<tr>
<td>137 (male)</td>
<td>Neurosurgery–Spinal cord</td>
<td>Psychosexual dysfunction&lt;br&gt;Erectile dysfunction&lt;br&gt;Ejaculatory dysfunction</td>
<td>Host Factors&lt;br&gt;Tumor adjacent to or compressing spinal cord or cauda equina</td>
<td>Host Factors&lt;br&gt;Injury above the level of the sacrum&lt;br&gt;Treatment Factors&lt;br&gt;Radiation dose ≥ 55 Gy to penile bulb in adult and ≥ 45 Gy in prepubertal child</td>
<td>HISTORY&lt;br&gt;Sexual function (erections, nocturnal emissions, libido)&lt;br&gt;Yearly&lt;br&gt;Medication use&lt;br&gt;Yearly</td>
<td>HEALTH LINKS&lt;br&gt;Male Health Issues&lt;br&gt;Counseling&lt;br&gt;Men with erectile/ejaculatory dysfunction desiring paternity can consider assisted reproductive technology for sperm retrieval Resources: <a href="http://www.urologychannel.com">www.urologychannel.com</a>&lt;br&gt;Considerations for Further Testing and Intervention&lt;br&gt;Urologic consultation in patients with positive history.&lt;br&gt;SYSTEM = CNS&lt;br&gt;SCORE = 2A</td>
</tr>
</tbody>
</table>

**SECTION 137 REFERENCES**


### Section 138: Neurosurgery—Spinal Cord (cont)

<table>
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<tr>
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<th>Periodic Evaluation</th>
<th>Health Counseling/ Further Considerations</th>
</tr>
</thead>
</table>
| 138 (female) | Neurosurgery–Spinal cord | Psychosexual dysfunction | Host Factors  
Tumor adjacent to or compressing spinal cord or cauda equina  
Treatment Factors  
Radiation to bladder, pelvis, or spine  
Medical Conditions  
Hypogonadism  
Vaginal fibrosis/stenosis  
Chronic GVHD | Host Factors  
Injury above the level of the sacrum | **HISTORY**  
Altered or diminished sensation, loss of sensation  
Dyspareunia  
Medication use | Yearly | **SYSTEM = CNS**  
**SCORE = 2A**

### Section 138 References

### SURGERY

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<th>Periodic Evaluation</th>
<th>Health Counseling/ Further Considerations</th>
</tr>
</thead>
</table>
| 139   | Neurosurgery—Spinal cord | Scoliosis/Kyphosis | Host Factors  
Preoperative deformity  
Young age (deformity can still develop even if skeletally mature at time of surgery) | Treatment Factors  
Radiation to the spine  
Increasing number of laminae removed  
Facetectomy  
Laminectomy (versus laminotomy)  
Laminectomy without fusion | Treatment Factors  
> 3 laminae removed;  
Increasing number of resections  
Surgery of thoracolumbar junction | PHYSICAL  
Spine exam for scoliosis and kyphosis  
Yearly until growth completed, may need more frequent assessment during puberty or if curve detected | Health Links  
Scoliosis and Kyphosis  
Considerations for Further Testing and Intervention  
Spine films in patients with clinically apparent curve. Orthopedic consultation as indicated based on radiographic exam. |

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### SECTION 139 REFERENCES

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</thead>
</table>
| 140 (female) | Oophoropexy | Oophoropexy-related complications  
Inability to conceive despite normal ovarian function  
Dyspareunia  
Symptomatic ovarian cysts  
Bowel obstruction  
Pelvic adhesions | Treatment Factors  
Ovarian radiation  
Tubo-ovarian dislocation, especially with lateral ovarian transposition | HISTORY  
Inability to conceive despite normal ovarian function  
Dyspareunia  
Abdominal pain  
Pelvic pain | Yearly  
Considerations for Further Testing and Intervention  
Gynecologic consultation for patients with positive history and/or physical findings. |

**SECTION 140 REFERENCES**


<table>
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<tbody>
<tr>
<td>141</td>
<td>Oophorectomy (unilateral)</td>
<td>Premature menopause</td>
<td>Health Behaviors Smoking</td>
<td>Treatment Factors - Combined with: - Pelvic radiation - Alkylating agents - TBI</td>
<td>SCREENING FSH LH Estradiol Baseline at age 13 AND as clinically indicated in patients with delayed or arrested puberty, irregular menses, primary or secondary amenorrhea, and/or clinical signs and symptoms of estrogen deficiency</td>
<td>Health Links Female Health Issues Resources American Society for Reproductive Medicine (<a href="http://www.asrm.org">www.asrm.org</a>) Fertile Hope (<a href="http://www.fertilehope.org">www.fertilehope.org</a>) Counseling Counsel currently menstruating women to be cautious about delaying childbearing. Counsel regarding need for contraception. Considerations for Further Testing and Intervention Refer to reproductive endocrinology for counseling regarding oocyte cryopreservation in patients wishing to preserve options for future fertility.</td>
</tr>
</tbody>
</table>

**Info Link**
Evidence for premature menopause following unilateral oophorectomy is limited and has been extrapolated from the adult literature.

**SECTION 141 REFERENCES**


## SURGERY

### OOPHORECTOMY (BILATERAL)

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<tbody>
<tr>
<td>142 (female)</td>
<td>Oophorectomy (bilateral)</td>
<td>Hypogonadism</td>
<td>Infertility</td>
<td></td>
<td>SCREENING</td>
<td>Health Links</td>
</tr>
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<td></td>
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<td></td>
<td>Female Health Issues</td>
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<td></td>
<td>Resources</td>
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<td></td>
<td>American Society for Reproductive Medicine (<a href="http://www.asrm.org">www.asrm.org</a>)</td>
</tr>
<tr>
<td></td>
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<td></td>
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<td></td>
<td>Fertile Hope (<a href="http://www.fertilehope.org">www.fertilehope.org</a>)</td>
</tr>
<tr>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Counseling</td>
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<td></td>
<td></td>
<td>Counsel regarding benefits of HRT in promoting pubertal progression, bone and cardiovascular health. Counsel women regarding pregnancy potential with donor eggs (if uterus is intact).</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Considerations for Further Testing and Intervention</td>
</tr>
<tr>
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<td></td>
<td></td>
<td>Bone density evaluation in hypogonadal patients. Reproductive endocrinology referral regarding assisted reproductive technologies. Monitor cardiovascular health.</td>
</tr>
</tbody>
</table>

### SECTION 142 REFERENCES

### SURGERY

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<tr>
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<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling/ Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>143 (male)</td>
<td>Orchiectomy unilateral</td>
<td>Gonadal dysfunction (testicular) Reduced fertility Testosterone insufficiency</td>
<td>Host Factors Testicular cancer Obesity Ejaculatory dysfunction Medications Occupational exposures (pesticides, heavy metals, solvents) Treatment Factors Orchiectomy combined with pelvic or testicular radiation and/or alkylating agents</td>
<td>History Pubertal (onset, tempo) Sexual function (erections, nocturnal emissions, libido) Medication use Yearly Physical Tanner staging Until sexually mature Testicular volume by Prader orchimeter; Testicular examination (including prosthesis) Yearly Screening Screening for reduced fertility: Semen analysis As requested by sexually mature patient FSH In sexually mature patient if unable to obtain semen analysis Screening for testosterone insufficiency: Testosterone (ideally morning) As clinically indicated in patients with delayed or arrested puberty and/or clinical signs and symptoms of testosterone deficiency</td>
<td>Health Links Male Health Issues Counseling Counsel to wear athletic supporter with protective cup during athletic activities. Considerations for Further Testing and Intervention Consider surgical placement of testicular prosthesis and ongoing monitoring for surgical complications after prosthesis placement. Orchiectomy can be associated with psychological distress related to altered body image.</td>
<td></td>
</tr>
</tbody>
</table>

### SECTION 143 REFERENCES

### ORCHIECTOMY (BILATERAL)

<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling/ Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>144</td>
<td>Orchiectomy (bilateral)</td>
<td>Gonadal dysfunction (testicular)</td>
<td></td>
<td></td>
<td>PHYSICAL</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Infertility</td>
<td></td>
<td></td>
<td>Examination of testicular prostheses</td>
<td>Health Links</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Testosterone Deficiency</td>
<td></td>
<td></td>
<td>Yearly</td>
<td>Male Health Issues</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>SCREENING</td>
<td>Considerations for Further Testing and Intervention</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Refer to endocrinology at age 11 for</td>
<td>Consider surgical placement of testicular prostheses and ongoing monitoring for surgical complications after prostheses placement. Orchiectomy can be associated with psychological distress related to altered body image.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>initiation of hormonal replacement therapy to induce puberty (or immediately for post-pubertal patients)</td>
<td>SCORE = 1</td>
</tr>
</tbody>
</table>

**SYSTEM = Reproductive (male)**

### SECTION 144 REFERENCES


<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling/Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>145</td>
<td>Pelvic surgery Cystectomy</td>
<td>Urinary incontinence Urinary tract obstruction</td>
<td>Host Factors: Tumor adjacent to or compressing spinal cord or cauda equina</td>
<td>Treatment Factors: Retroperitoneal node dissection, extensive pelvic dissection (e.g., bilateral ureteral reimplantation, retroperitoneal tumor resection), radiation to the bladder, pelvis, and/or lumbar-sacral spine</td>
<td>HISTORY: Hematuria, Urinary urgency/frequency, Urinary incontinence/retention, Dysuria, Nocturia, Abnormal urinary stream</td>
<td>Periodically, consider counseling regarding adequate fluid intake, regular voiding, seeking medical attention for symptoms of voiding dysfunction or urinary tract infection and compliance with recommended bladder catheterization regimen. Consider urologic consultation for patients with dysfunctional voiding or recurrent urinary tract infections.</td>
</tr>
</tbody>
</table>

**SECTION 145 REFERENCES**


<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling/ Further Considerations</th>
</tr>
</thead>
</table>
| 146   | Pelvic surgery Cystectomy | Fecal incontinence | Host Factors  
Tumor adjacent to or compressing spinal cord or cauda equina  
Treatment Factors  
Radiation to the bladder, pelvis, or spine | Historic  
Chronic constipation  
Fecal soiling  
Yearly  
Physical  
Rectal exam  
As clinically indicated | | Counseling  
Counsel regarding benefits of adherence to bowel regimen, including adequate hydration, fiber, laxatives/enemas as clinically indicated.  
Considerations for Further Testing and Intervention  
GI consultation to establish bowel regimen for patients with chronic impaction or fecal soiling. |

**SECTION 146 REFERENCES**


### Section 147: Pelvic Surgery (cont)

<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling/Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>147</td>
<td>Pelvic surgery</td>
<td>Sexual dysfunction (male)</td>
<td>Treatment Factors</td>
<td>Extensive presacral tumor resection or dissection; Radiation dose ≥ 55 Gy to penile bulb in adult and ≥ 45 Gy in prepubertal child</td>
<td>HISTORY</td>
<td>HEALTH LINKS</td>
</tr>
<tr>
<td></td>
<td>Cystectomy</td>
<td>Retrograde ejaculation</td>
<td>Retropitoneal node dissection</td>
<td>Sexual function (erectons, nocturnal emissions, libido)</td>
<td><strong>Health Issues</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Anejaculation</td>
<td>Retropitoneal tumor resection</td>
<td>Medication use</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Erectile dysfunction</td>
<td>Cystectomy</td>
<td>Quality of ejaculate (frothy white urine with first void after intercourse suggests retrograde ejaculation)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Radical prostatectomy</td>
<td>Yearly</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Tumor adjacent to spine; Radiation to bladder, pelvis, or spine</td>
<td><strong>Resources</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Medical Conditions</td>
<td><a href="http://www.urologychannel.com">www.urologychannel.com</a></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Hypogonadism</td>
<td><strong>Counseling</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Men with erectile/ejaculatory dysfunction desiring paternity can consider assisted reproductive technology for sperm retrieval.</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td><strong>Considerations for Further Testing and Intervention</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Urologic consultation in patients with positive history and/or physical exam findings.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Section 147 References


<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling/Further Considerations</th>
</tr>
</thead>
</table>
| 148 (female) | Pelvic surgery Cystectomy | Sexual dysfunction (female) | Host Factors  
Chronic GVHD  
Hypogonadism  
Tumor adjacent to spine  
Medical Conditions  
Radiation to bladder, pelvis, or spine | HISTORY  
Altered or diminished sensation, loss of sensation  
Dyspareunia  
Medication use  
Yearly | SYSTEM = Reproductive (female)  
SCORE = 2A |

**SECTION 148 REFERENCES**


<table>
<thead>
<tr>
<th>Section #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling/ Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>149</td>
<td>Splenectomy</td>
<td>Asplenia</td>
<td>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</td>
<td>SCREENING Blood culture When febrile T ≥ 101°F</td>
<td>Health Links Splenic Precautions Counseling Advise obtaining medical alert bracelet/card noting asplenia. Counsel regarding risk of life-threatening infections with encapsulated organisms. Also counsel regarding risk associated with malaria and tick-borne diseases if living in or visiting endemic areas. Considerations for Further Testing and Intervention In patients with T ≥ 101° (38.3° C) or other signs of serious illness, administer a long-acting, broad-spectrum parenteral antibiotic (e.g., ceftriaxone), and continue close medical monitoring while awaiting blood culture results. 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 ≥ 104°F; meningitis, pneumonia, or other serious focus of infection; signs of septic shock; or previous history of serious infection. Immunize with Pneumococcal, Meningococcal, and Hib vaccines according to current ACIP recommendations. Discuss with dental provider potential need for antibiotic prophylaxis based on planned procedure. Info Link See current edition of AAP Red Book for recommendations regarding antibiotic prophylaxis and immunizations</td>
</tr>
</tbody>
</table>

**SECTION 149 REFERENCES**


SECTION 149 REFERENCES


<table>
<thead>
<tr>
<th>Section #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling/Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>150</td>
<td>Thoracic surgery (includes thoracotomy, chest wall surgery, rib resection, pulmonary lobectomy, pulmonary metastasectomy, pulmonary wedge resection)</td>
<td>Pulmonary dysfunction</td>
<td>Treatment Factors Combined with pulmonary toxic therapy: - Bleomycin - Busulfan - Carmustine (BCNU) - Lomustine (CCNU)</td>
<td>Treatment Factors Combined with: - Chest radiation - TBI</td>
<td>HISTORY</td>
<td>Health Links</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Medical Conditions Atopic history</td>
<td></td>
<td>Cough</td>
<td>Pulmonary Health</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Health Behaviors Smoking</td>
<td></td>
<td>SOB</td>
<td>Resources</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Inhaled illicit drug use</td>
<td></td>
<td>Wheezing</td>
<td>Extensive information regarding smoking cessation is available for patients on the NCI's website: <a href="http://www.smokefree.gov">www.smokefree.gov</a></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(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>
<td>Yearly</td>
<td>Counseling</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Counsel regarding tobacco avoidance/smoking cessation. Patients who desire to SCUBA dive should be advised to obtain medical clearance from a pulmonologist.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Considerations for Further Testing and Intervention</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>In patients with abnormal PFTs, consider repeat evaluation prior to general anesthesia. Pulmonary consultation for patients with symptomatic pulmonary dysfunction; Influenza and pneumococcal vaccinations.</td>
</tr>
</tbody>
</table>

**SECTION 150 REFERENCES**


### 151 Thoracic surgery (includes thoracotomy, chest wall surgery, rib resection, pulmonary lobectomy, pulmonary metastasectomy, pulmonary wedge resection)

<table>
<thead>
<tr>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling/ Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Scoliosis/Kyphosis</td>
<td>Host Factors</td>
<td>Treatment Factors</td>
<td>PHYSICAL</td>
<td>Health Links</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Young age (deformity can still develop even if skeletally mature at time of surgery) Preoperative deformity</td>
<td>Greater number of ribs resected</td>
<td>Spine exam for scoliosis and kyphosis</td>
<td>Scoliosis and Kyphosis</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Yearly until growth completed, may need more frequent assessment during puberty or if curve detected</td>
<td>Considerations for Further Testing and Intervention</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Spine films in patients with clinically apparent curve. Orthopedic consultation as indicated based on radiographic exam</td>
</tr>
</tbody>
</table>

**SYSTEM = Musculoskeletal**  
**SCORE = 2A**

### SECTION 151 REFERENCES


### Surgery

<table>
<thead>
<tr>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling/Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thyroidectomy</td>
<td>Hypothyroidism</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Info Link**
- Total thyroidectomy is uncommon, but if done 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).

### Section 152 References


<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling/ Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>153</td>
<td>Radioiodine therapy (I-131 thyroid ablation)</td>
<td>Lacrimal duct atrophy</td>
<td></td>
<td></td>
<td>HISTORY Excessive tearing Yearly</td>
<td>Considerations for Further Testing and Intervention&lt;br&gt;Ophthalmology consultation as clinically indicated.</td>
</tr>
</tbody>
</table>

**SECTION 153 REFERENCES**


### OTHER THERAPEUTIC MODALITIES

<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling/ Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>154</td>
<td>Radioiodine therapy (I-131 thyroid ablation)</td>
<td>Hypothyroidism</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</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 and 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

**SYSTEM = Endocrine/Metabolic**
**SCORE = 2A**

### SECTION 154 REFERENCES


## OTHER THERAPEUTIC MODALITIES

<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling/ Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>155</td>
<td>Systemic MIBG (in therapeutic doses)</td>
<td>Hypothyroidism</td>
<td></td>
<td></td>
<td></td>
<td>Health Links</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Thyroid Problems</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Counseling</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Counsel at-risk females of childbearing potential to have their thyroid levels checked prior to attempting pregnancy and periodically throughout pregnancy.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Considerations for Further Testing and Intervention</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Endocrine consultation for medical management.</td>
</tr>
</tbody>
</table>

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

### SECTION 155 REFERENCES


<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling/ Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>156</td>
<td>Bioimmunotherapy (e.g., G-CSF, IL-2, erythropoietin)</td>
<td>Insufficient information currently available regarding late effects of biological agents.</td>
<td></td>
<td></td>
<td>SCREENING</td>
<td>SYSTEM = No Known Late Effects SCORE = N/A</td>
</tr>
</tbody>
</table>

**SECTION 156 REFERENCES**


### CANCER SCREENING GUIDELINES

<table>
<thead>
<tr>
<th>Sec #</th>
<th>Organ</th>
<th>Population Risk Factors</th>
<th>Highest Risk Factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>157</td>
<td>Breast</td>
<td>Over age 40</td>
<td>Chest radiation with potential impact to the breast (see Section 77), including ≥ 20 Gy to the following fields: - Chest (torax) - Whole lung - Mediastinal - Axilla - Mini-Mantle - Mantle - Extended Mantle - TLI - STLI - TBI* - BRCA1, BRCA2, ATM mutation</td>
</tr>
</tbody>
</table>

#### Breast Cancer

<table>
<thead>
<tr>
<th>PATIENTS AT STANDARD RISK (ACS Recommendation)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PHYSICAL</strong></td>
</tr>
<tr>
<td>Clinical breast exam</td>
</tr>
<tr>
<td>Every 3 years between ages 20–39, then yearly beginning at age 40</td>
</tr>
</tbody>
</table>

| **SCREENING**                                 |
| Mammogram                                    |
| Yearly, beginning at age 40                  |

<table>
<thead>
<tr>
<th>PATIENTS AT HIGHEST RISK (≥ 20 Gy radiation with potential impact to the breast)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PHYSICAL</strong></td>
</tr>
<tr>
<td>Breast self exam</td>
</tr>
<tr>
<td>Monthly, beginning at puberty</td>
</tr>
</tbody>
</table>

| Clinical breast exam |
| Yearly, beginning at puberty until age 25, then every 6 months |

| **SCREENING** |
| Mammogram |
| Yearly, beginning 8 years after radiation or at age 25, whichever occurs last. |

| Breast MRI |
| Yearly, as an adjunct to mammography beginning 8 years after radiation or at age 25, whichever occurs last. |

#### Health Counseling/ Further Considerations

| Health Links |
| Breast Cancer (for patients at highest risk only) |

| Counseling |
| For patients at highest risk, counsel to perform breast self-examination monthly, beginning at puberty. For standard risk patients, provide general guidance regarding routine screening beginning at age 40 per current ACS guidelines. |

| Considerations for Further Testing and Interventions |
| Surgery and/or oncology consultation as clinically indicated |

#### Info Link

- *Important*: The risk of breast cancer in patients who received 10–19 Gy of radiation with potential impact to the breast or those who received TBI alone is of a lower magnitude compared to those who received ≥20 Gy of radiation with potential impact to the breast (e.g., thorax, axilla).
- Monitoring of patients who received 10–19 Gy of radiation with potential impact to the breast or those who received TBI without additional radiation should be determined on an individual basis.
- After the clinician discusses the benefits and risks/harms of screening with the patient, if a decision is made to screen, then follow the recommendations for patients who received ≥ 20 Gy.

### SECTION 157 REFERENCES


### SECTION 157 REFERENCES (continued)


### CANCER SCREENING GUIDELINES

<table>
<thead>
<tr>
<th>Sec #</th>
<th>Organ</th>
<th>Population Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling/ Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>158 (female)</td>
<td>Cervical</td>
<td>Early age at first intercourse, Multiple lifetime sex partners, Smoking, Sexually transmitted diseases</td>
<td>Personal history of cervical dysplasia, Prenatal DES exposure, HPV infection, Immunosuppression, Chronic steroid use, HIV positive, Chronic GVHD</td>
<td><strong>PATIENTS AT STANDARD RISK (ACS Recommendation)</strong>&lt;br&gt;<strong>PHYSICAL</strong>&lt;br&gt;Pelvic exam Every 3–5 years beginning at age 21 (see “Screening” below for specific recommendations)&lt;br&gt;<strong>SCREENING</strong>&lt;br&gt;Cervical PAP smear • Cervical cancer screening should begin at age 21 y.&lt;br&gt;• For women aged 21–29 y, screening should be done every 3 y with conventional or liquid-based Pap tests.&lt;br&gt;• For women aged 30–65 y, screening should be done every 5 y with the HPV test and the Pap test (preferred), or every 3 y with the Pap test alone (acceptable).&lt;br&gt;• Women aged &gt; 65 y who have had &gt; 3 consecutive negative Pap tests or &gt; 2 consecutive negative HPV and Pap tests within the last 10 y, with the most recent test occurring within the last 5 y, and women who have had a total hysterectomy should stop cervical cancer screening.&lt;br&gt;• Women at any age should not be screened annually by any screening method.</td>
<td><strong>Health Links</strong>&lt;br&gt;Reducing the Risk of Second Cancers&lt;br&gt;<strong>Counseling</strong>&lt;br&gt;Counsel regarding risk/benefits of HPV vaccination.&lt;br&gt;<strong>Info Link</strong>&lt;br&gt;• Human papillomavirus virus (HPV) is the leading cause of cervical cancer in women. HPV vaccination protects against 70% of cervical cancers and the quadrivalent form the vaccine reduces the incidence of genital warts.&lt;br&gt;• The Centers for Disease Control Advisory Committee on Immunization Practices (CDC/ACIP) and American Cancer Society (ACS) both recommend routine HPV immunization of girls when they are 11–12 years old.&lt;br&gt;• Females as young as 9 years can receive HPV vaccination at the discretion of their health care provider. HPV vaccination is also recommended for females 13–26 (CDC/ACIP) years to catch up missed vaccines or to complete the series.&lt;br&gt;• For optimal protection, the vaccine should be administered before the onset of sexual activity. Females who are sexually active may still benefit from vaccination through protection against strains to which they have not been exposed.&lt;br&gt;• HPV vaccination does not change recommendations for cervical cancer PAP screening since the vaccine does not protect against all cancer-causing types of HPV. See Markowitz LE et al. (2007) and Centers for Disease Control and Prevention (2010), for further information.&lt;br&gt;<strong>Considerations for Further Testing and Interventions</strong>&lt;br&gt;Gynecology and/or oncology consultation as clinically indicated.</td>
</tr>
</tbody>
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### SECTION 158 REFERENCES

<table>
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<tr>
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<tbody>
<tr>
<td>159</td>
<td>Colorectal</td>
<td>High fat/low fiber diet</td>
<td>Radiation with potential impact to the colon/rectum (see Section 90), including ≥ 30 Gy to the following fields:</td>
<td>PATIENTS AT STANDARD RISK (ACS Recommendation)</td>
<td>Health Links</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Age ≥ 50 years Obesity</td>
<td>- Spleen (thoracic, lumbar, sacral, whole)</td>
<td><strong>SCREENING</strong></td>
<td>Colorectal Cancer</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>- Extended Mantle</td>
<td>Option 1</td>
<td>Considerations for Further Testing and Interventions</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>- Hepatic</td>
<td>Fecal occult blood (minimum of 3 cards) Yearly, beginning at age 50</td>
<td>Gastroenterology, surgery and/or oncology consultation as clinically indicated.</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>- Renal</td>
<td><strong>AND/OR</strong></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>- Upper quadrant (right, left)</td>
<td>Flexible sigmoidoscopy Every 5 years, beginning at age 50</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>- Spleen (partial, entire)</td>
<td><strong>Note:</strong> The combination of yearly fecal occult blood testing and every 5 year flexibile sigmoidoscopy is preferable to either test done alone.</td>
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<td></td>
<td></td>
<td></td>
<td>- Paraaortic</td>
<td>Option 2</td>
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<td></td>
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<td></td>
<td>- Flank/Hemiabdomen (right, left)</td>
<td>Double contrast barium enema Every 5 years, beginning at age 50</td>
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<td></td>
<td></td>
<td></td>
<td>- Whole abdomen</td>
<td>Option 3</td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td>- Inverted Y</td>
<td>Colonoscopy Every 10 years, beginning at age 50</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>- Pelvic</td>
<td><strong>PATIENTS AT HIGHEST RISK</strong></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>- Vaginal</td>
<td><strong>SCREENING</strong></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>- Prostate</td>
<td>Colonoscopy Every 5 years (minimum); more frequently if indicated based on colonoscopy results. Begin monitoring 10 years after radiation or at age 35, whichever occurs last. Monitor more frequently if clinically indicated. Per the ACS, begin screening earlier for the following high-risk groups: HNPCC (at puberty), FAP (at age 21 years), IBD (8 years after diagnosis of IBD). Information from the first colonoscopy will inform frequency of follow-up testing.</td>
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<td></td>
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<td></td>
<td>- Bladder</td>
<td><strong>Info Link</strong></td>
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<td></td>
<td></td>
<td></td>
<td>- Iliac</td>
<td>- Reports of gastrointestinal malignancies in cohorts of long-term survivors suggest that radiation likely increases risk, but the median age of onset is not as well established as that of secondary breast cancer following chest radiation.</td>
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</tr>
<tr>
<td></td>
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<td></td>
<td>- Inguinal</td>
<td>- The expert panel agreed that early onset of screening likely was beneficial, and that a prudent course would be to initiate screening for colorectal cancer for those at highest risk (abdominal, pelvic, and/or spinal radiation ≥ 30 Gy) at age 35, or 10 years post radiation, whichever occurs last.</td>
<td></td>
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<tr>
<td></td>
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<td></td>
<td>- Femoral</td>
<td>- Surveillance should be done via colonoscopy as per recommendations for populations at highest risk, with information from the first colonoscopy informing the frequency of follow-up testing.</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>- TLI</td>
<td>- While the American Cancer Society recently added computed tomographic colonography (CTC) (AKA “Virtual Colonoscopy”) as an acceptable option for colorectal cancer screening of average-risk adults, the National Comprehensive Cancer Network and United States Preventive Services Task Force concluded that data was too premature to warrant its use in screening.</td>
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<tr>
<td></td>
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<td></td>
<td>- STLI</td>
<td>- Colonoscopy remains the preferred screening modality for survivors at highest risk of colorectal cancer.</td>
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<td></td>
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<td>- TBI*</td>
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<td></td>
<td></td>
<td></td>
<td>Personal history of ulcerative colitis, gastrointestinal malignancy, adenomatous polyps or hepatoblastoma</td>
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<td></td>
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<td></td>
<td>Familial polyposis</td>
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<td></td>
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<td></td>
<td>Family history of colorectal cancer or polyps in first degree relative</td>
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</tbody>
</table>

**Info Link**
- Monitoring of patients who received TBI without additional radiation potentially impacting the colon/rectum should be determined on an individual basis. (See Info Link in next column.)
- Important: Reports of colorectal cancer in cohorts of long-term survivors suggest that radiation likely increases risk; however, the risk related to TBI alone has not been established.
### SECTION 159 REFERENCES


### CANCER SCREENING GUIDELINES

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</thead>
<tbody>
<tr>
<td>160</td>
<td>Female</td>
<td>Endometrial</td>
<td>Obesity, Older age, Unopposed estrogen therapy, Tamoxifen, Diabetes, Hypertension, High fat diet, Early menopause, Late menopause, Nulliparity, Infertility, Failure to ovulate</td>
<td>History of/at risk for hereditary nonpolyposis colon cancer (HNPCC)</td>
<td><strong>PATIENTS AT STANDARD RISK (ACS Recommendation)</strong>&lt;br&gt;Endometrial biopsy&lt;br&gt;Yearly, beginning at age 35 for patients at highest risk</td>
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### SECTION 160 REFERENCES

### CANCER SCREENING GUIDELINES

<table>
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<tr>
<th>Sec #</th>
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</thead>
<tbody>
<tr>
<td>161</td>
<td>Lung</td>
<td>Chest radiation with potential impact to the lung Smoking Workplace exposures to asbestos, arsenic, radiation Second hand smoke (in non-smokers)</td>
<td>Chest radiation with potential impact to the lung combined with smoking</td>
<td><strong>PATIENTS AT HIGHEST RISK</strong>&lt;br&gt;<strong>HISTORY</strong>&lt;br&gt;Cough Wheezing SOB DOE&lt;br&gt;Yearly, and as clinically indicated</td>
<td><strong>Health Links</strong>&lt;br&gt;Reducing the Risk of Second Cancers <strong>Considerations for Further Testing and Intervention</strong>&lt;br&gt;Imaging and surgery and/or oncology consultation as clinically indicated</td>
</tr>
</tbody>
</table>

### LUNG CANCER

**SCREENING**<br>Clinicians should discuss the benefits and risks/harms of spiral CT scanning for patients at highest risk

### SECTION 161 REFERENCES

### CANCER SCREENING GUIDELINES

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### ORAL CANCER

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<tr>
<td>163</td>
<td>Prostate</td>
<td>Older age, with steadily increasing risk after age 40 years.</td>
<td>African-American race Family history of prostate cancer in first degree relative</td>
<td>ALL PATIENTS Clinicians should be prepared to discuss prostate cancer testing with patients</td>
<td>Health Links Reducing the Risk of Second Cancers</td>
</tr>
<tr>
<td></td>
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<td></td>
<td></td>
<td></td>
<td>Considerations for Further Testing and Intervention</td>
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<td></td>
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<td></td>
<td>Urology and/or oncology consultation as clinically indicated.</td>
</tr>
</tbody>
</table>

**SECTION 163 REFERENCES**


Info Link
- The USPSTF found good evidence that PSA screening can detect early-stage prostate cancer but mixed and inconclusive evidence that early detection improves health outcomes.
- Screening is associated with important harms, including frequent false-positive results and unnecessary anxiety, biopsies, and potential complications of treatment of some cancers that may never have affected a patient’s health.
- The USPSTF concludes that evidence is insufficient to determine whether the benefits outweigh the harms for a screened population. ACS concurs with this conclusion.
## CANCER SCREENING GUIDELINES

### SKIN CANCER

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</thead>
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<tr>
<td>164</td>
<td>Skin</td>
<td>Light skin color</td>
<td>Any history of radiation</td>
<td>PATIENTS AT STANDARD RISK</td>
<td>Health Links</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Chronic exposure to sun</td>
<td>Personal history of melanoma or skin cancer</td>
<td></td>
<td>Reducing the Risk of Second Cancers</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Atypical moles or ≥ 50 moles</td>
<td>Dysplastic nevi</td>
<td></td>
<td>Skin Health</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Family history of melanoma or skin cancer</td>
<td></td>
<td>Considerations for Further Testing and Intervention</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>History of severe sunburn at young age</td>
<td></td>
<td>Surgery, dermatology, and/or oncology consultation as clinically indicated</td>
</tr>
</tbody>
</table>

### PATIENTS AT STANDARD RISK

**Info Link**
- The U.S. Preventive Services Task Force (USPSTF) concludes that the evidence is insufficient to recommend for or against routine screening for skin cancer using a total-body skin examination for the early detection of cutaneous melanoma, basal cell cancer, or squamous cell skin cancer.
- There are no randomized trials or case-control studies that directly examine whether screening by clinicians is associated with improved clinical outcomes such as reduced morbidity or mortality from skin cancer. No studies were found that evaluated whether screening improves the outcomes of these cancers.
- The American Cancer Society recommends skin examination as part of a cancer-related checkup, which should occur on the occasion of the patient's periodic health examination. Self-examination of skin is recommended once a month.

### PATIENTS AT HIGHEST RISK

#### PHYSICAL
- Skin self exam
- Monthly
- Dermatologic exam with attention to skin lesions and pigmented nevi in radiation field
- Yearly

### SECTION 164 REFERENCES


**TESTICULAR CANCER**

<table>
<thead>
<tr>
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</thead>
</table>
| 165   | Testicular  | Young males             | History of cryptorchidism<br>History of testicular cancer or carcinoma in-situ in contralateral testis<br>History of gonadal dysgenesis<br>Klinefelter’s syndrome<br>Family history of testicular cancer | **Info Link**<br>- For standard and high risk populations, the USPSTF recommends against routine screening for testicular cancer in asymptomatic adolescent and adult males.<br>- In 2004, the USPSTF found no new evidence that screening with clinical examination or testicular self-examination is effective in reducing mortality from testicular cancer. Even in the absence of screening, the current treatment interventions provide very favorable health outcomes.<br>- Given the low prevalence of testicular cancer, limited accuracy of screening tests, and no evidence for the incremental benefits of screening, the USPSTF concluded that the harms of screening exceed any potential benefits.<br>- ACS also no longer recommends clinical testicular cancer screening or testicular self-examination. | **CANCER SCREENING GUIDELINES**

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### GENERAL HEALTH SCREENING

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<tr>
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<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling/Further Considerations</th>
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</thead>
<tbody>
<tr>
<td>166</td>
<td>General Health Screening</td>
<td></td>
<td></td>
<td>SCREENING Refer to United States Preventive Services Task Force recommendations at <a href="http://www.ahrq.gov/clinic/uspstfix.htm">www.ahrq.gov/clinic/uspstfix.htm</a></td>
<td>Childhood cancer survivors should receive general health maintenance per standard recommendations for age. Recommended preventive services per the USPSTF include screening for hypertension, obesity, depression, tobacco use, and alcohol misuse. In addition, certain subpopulations require screening for lipid disorders, sexually transmitted diseases, and diabetes mellitus. Others require counseling regarding the prevention of cardiovascular disease, osteoporosis, and other disorders. See <a href="http://www.ahrq.gov/clinic/uspstfix.htm">www.ahrq.gov/clinic/uspstfix.htm</a> for specific recommendations. Assess immunization status on all patients; reimmunize as indicated. See <a href="http://www.cdc.gov/vaccines/">www.cdc.gov/vaccines/</a> for current immunization schedules. For all HCT patients, reimmunization per current recommendations (Ljungman et al, 2009: <a href="http://www.nature.com/bmt/journal/v44/n8/full/bmt2009263a.html">www.nature.com/bmt/journal/v44/n8/full/bmt2009263a.html</a>).</td>
</tr>
</tbody>
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