

**Children's Oncology Group**  
**Long-Term Follow-Up Guidelines**  
**for Survivors of Childhood, Adolescent,**  
**and Young Adult Cancer**

**Version 4.0 – October 2013**

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**CHILDREN'S  
ONCOLOGY  
GROUP**

The world's childhood  
cancer experts



# Long-Term Follow-Up Guidelines

for Survivors of Childhood, Adolescent, and Young Adult Cancers

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3	5		<b>Risky behaviors</b>
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5	7		<b>Fatigue</b>
6	8		<b>Limitations in healthcare and insurance access</b>
<b>Blood/Serum Products</b>			
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15	18		<b>Pulmonary fibrosis</b>
16	19		<b>Cataracts</b>
17	20		<b>Urinary tract toxicity</b>
18	21		<b>Bladder malignancy</b>
19	22		<b>Renal toxicity</b>
20	23		<b>Ototoxicity</b>
21	25		<b>Peripheral sensory neuropathy;</b>
22	26		<b>Renal toxicity</b>
(n/a)			[Removed from v4: Dyslipidemia]
23	27		<b>Neurocognitive deficits</b>
24	29		<b>Clinical leukoencephalopathy</b>
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26	32		<b>Hepatic dysfunction; veno-occlusive disease (VOD)</b>
27	33		<b>Reduced bone mineral density (BMD)</b>
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29	36		<b>Hepatic dysfunction</b>
30	37		<b>Neurocognitive deficits</b>
31	39		<b>Clinical leukoencephalopathy</b>
32	40		<b>Acute myeloid leukemia</b>
33	41	Male	<b>Cardiac toxicity</b>
34	43	Female	<b>Cardiac toxicity</b>
35	45		<b>Pulmonary toxicity</b>
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(n/a)			[Removed from v4: Metabolic syndrome]
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Section #	Page	Gender	Potential Late Effect
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71	89		<b>Thyroid nodules</b>
72	90		<b>Thyroid cancer</b>
73	91		<b>Hypothyroidism</b>
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88	110		<b>Bowel obstruction</b>
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## Contents (cont)

Section #	Page	Gender	Potential Late Effect
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101	126		<i>Scoliosis/kyphosis</i>
(n/a)			[Removed from v4: Kyphosis]
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	129		<b>TBI-related Potential Late Effects</b>
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120	150		<i>Amputation-related complications</i>
121	151		<i>Thrombosis; vascular insufficiency; infection of retained cuff or line tract</i>
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Section #	Page	Gender	Potential Late Effect
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146	177		<i>Fecal incontinence</i>
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(n/a)			[Removed from v4: Hydrocele]
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## Contents (cont)

Section #	Page	Gender	Potential Late Effect
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## COG Long-Term Follow-Up Guidelines Content Outline

### Long-Term Follow-Up Guidelines

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- Disclaimer
- Contributors
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  - 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

- Reference Materials
  - Abbreviations
  - Chemotherapy Agents
  - Radiation Fields Defined
- Summary of Cancer Treatment
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  - Template for Summary of Cancer Treatment (Abbreviated)
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- 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

Children's Oncology Group. *Long-Term Follow-Up Guidelines for Survivors of Childhood, Adolescent and Young Adult Cancers, Version 4.0*. Monrovia, CA: Children's Oncology Group; October 2013; Available on-line: [www.survivorshipguidelines.org](http://www.survivorshipguidelines.org).

#### Guidelines Methodology

Landier W, Bhatia S, Eshelman DA, Forte KJ, Sweeney T, Hester AL, Darling J, Armstrong FD, Blatt J, Constine LS, Freeman CR, Friedman DL, Green DM, Marina N, Meadows AT, Neglia JP, Oeffinger KC, Robison LL, Ruccione KS, Sklar CA, Hudson MM. Development of risk-based guidelines for pediatric cancer survivors: the Children's Oncology Group long-term follow-up guidelines from the Children's Oncology Group Late Effects Committee and Nursing Discipline. *J Clin Oncol* 2004; 22(24):4979-90.

#### Health Links Background and Application

Eshelman D, Landier W, Sweeney T, Hester AL, Forte K, Darling J & Hudson MM. Facilitating care for childhood cancer survivors: integrating Children's Oncology Group long-term follow-up guidelines and health links in clinical practice. *J Pediatr Oncol Nurs* 2004; 21(5): 271-280.

## 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](http://www.survivorshipguidelines.org).



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**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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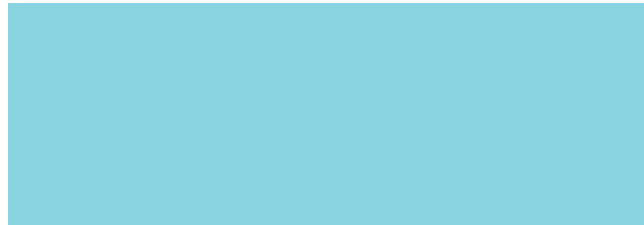
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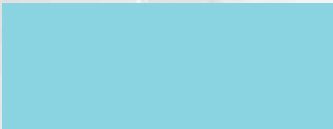
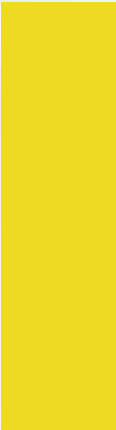
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Gastrointestinal Hepatic Oral/Dental	Soraya Beiraghi, DDS Sharon Castellino, MD, MSH, <i>Chair</i> Joan Darling, PhD Andrew Davidoff, MD Karen Effinger, MD Cherry Estilo, DMD Melissa M. Hudson, MD Sue Kaste, DO Jennifer Magee, DMD Kevin McMullen, MD Cesar Migliorati, DDS, MS, PhD Andrew Muir, MD, MSH Man Wai Ng, DDS, MPH John Petty, MD Melissa Rayburg Jefferson, MD Kathy Ruble, PhD, RN, CPNP Marie-Ellen Sarvida, MD Sheila Shope, RN, FNP	University of Minnesota Wake Forest University Health Sciences Children's Oncology Group St. Jude Children's Research Hospital Lucile Packard Children's Hospital Stanford University Memorial Sloan-Kettering Cancer Center St. Jude Children's Research Hospital St. Jude Children's Research Hospital Brigham & Women's Hospital Riley Hospital for Children University of Tennessee Health Science Center Duke University Medical Center Children's Hospital Boston Wake Forest University Health Sciences Children's Mercy Hospitals and Clinics Johns Hopkins University Loyola University Medical Center St. Jude Children's Research Hospital	Pediatric dentistry Pediatric oncology Patient advocacy Surgery Pediatric oncology Pediatric dentistry Pediatric oncology Pediatric radiology Pediatric dentistry Radiation oncology Pediatric dentistry Pediatric GI/hepatology Pediatric dentistry Surgery Pediatric oncology Nursing Pediatric oncology Family medicine

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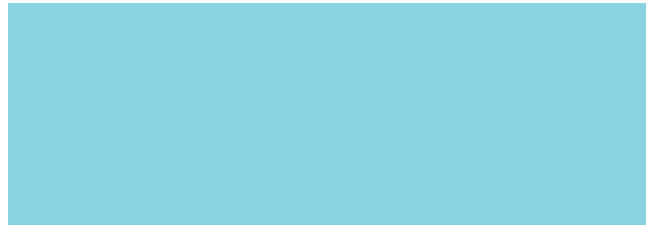
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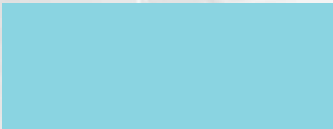
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# Introductory Material



**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

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<b>Overview</b>	<p>The Children's Oncology Group <i>Long-Term Follow-Up Guidelines for Survivors of Childhood, Adolescent, and Young Adult Cancers</i> (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&amp;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&amp;P, with 80 (51%) relying solely on the H&amp;P and 31 (20%) relying on the H&amp;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.</p>
<b>Goal</b>	<p>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.</p>
<b>Target Population</b>	<p>The recommendations for periodic screening evaluations provided in the Children's Oncology Group <i>Long-Term Follow-Up Guidelines for Survivors of Childhood, Adolescent, and Young Adult Cancers</i> 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.</p>
<b>Focus</b>	<p>These guidelines are intended for use <b><i>beginning two or more years following the completion of cancer therapy</i></b>, and provide a framework for ongoing late effects monitoring in childhood cancer survivors; <b><i>however, these guidelines are not intended to provide guidance for follow-up of the pediatric cancer survivor's primary disease.</i></b></p>

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## Introduction (cont)

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<b>Intended Users</b>	<p>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.</p> <p>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.</p>
<b>Developer</b>	<p>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.</p>
<b>Funding Source</b>	<p>This work was supported by the Children's Oncology Group Chair's Grant U10 CA098543 from the National Cancer Institute.</p>
<b>Evidence Collection</b>	<p>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.</p>

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## Introduction (cont)

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<b>Methods</b>	<p>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.</p> <p>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.</p> <p>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).</p>
<b>Grading Criteria</b>	<p>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.</p>
<b>Pre-Release Review</b>	<p>The initial version of the guidelines (Version 1.0 – Children's Oncology Group <i>Late Effects Screening Guidelines</i>) 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.</p>

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## Introduction (cont)

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<b>Revisions</b>	<p>The guidelines were initially released to the public (Version 1.1 – <i>Childhood Cancer Survivor Long-Term Follow-Up Guidelines</i>) 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 – <i>Long-Term Follow-Up Guidelines for Survivors of Childhood, Adolescent, and Young Adult Cancers</i>) was released to the public on the Children’s Oncology Group Website in March 2004.</p> <p>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).</p> <p>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.</p>
<b>Plan for Updates</b>	<p>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 <a href="http://www.survivorshipguidelines.org">www.survivorshipguidelines.org</a>.</p>
<b>Definitions</b>	<p>“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.</p>
<b>Recommendations and Rationale:</b>	<p>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.</p>

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## Introduction (cont)

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<b>Potential Benefits and Harms</b>	<p>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.</p> <p>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.</p>
<b>Patient Preferences</b>	<p>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.</p>
<b>Implementation Considerations:</b>	<p>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.</p> <p>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, (<a href="mailto:mehorowi@txch.org">mehorowi@txch.org</a>) or Susan Krause (<a href="mailto:skrause@txch.org">skrause@txch.org</a>).</p>

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## 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:

Category	Statement of Consensus
1	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.
2A	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.
2B	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.
3	There is major disagreement that the recommendation is appropriate

**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.

## Instructions for Use – Version 4.0

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

### 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:

<b>Section Number</b>	Unique identifier for each guideline section.
<b>Therapeutic Agent</b>	Therapeutic intervention for malignancy, including chemotherapy, radiation, surgery, blood/serum products, hematopoietic cell transplant, and other therapeutic modalities.
<b>Potential Late Effects</b>	Most common late treatment complications associated with specified therapeutic intervention.
<b>Risk Factors</b>	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.
<b>Highest Risk Factors</b>	Conditions (host factors, treatment factors, medical conditions and/or health behaviors) associated with the highest risk for developing the complication.
<b>Periodic Evaluations</b>	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.
<b>Health Counseling/ Further Considerations</b>	<p><b>Health Links:</b> 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>.</p> <p><b>Counseling:</b> Suggested patient counseling regarding measures to prevent/reduce risk or promote early detection of the potential treatment complication.</p> <p><b>Resources:</b> Books and websites that may provide the clinician with additional relevant information.</p> <p><b>Considerations for Further Testing and Intervention:</b> 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.</p>

## Instructions for Use (cont)

<b>System Score</b>	<p>Body system (e.g., auditory, musculoskeletal) most relevant to each guideline section.</p> <p>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.</p>
<b>Cancer Screening Recommendations</b>	<p>Sections 157–166 contain preventive screening recommendations for common adult-onset cancers, organized by column as follows:</p> <p><b>Organ:</b> The organ at risk for developing malignancy.</p> <p><b>Population Risk Factors:</b> Risk factors such as age, gender, genetic susceptibility, personal or family history, health-related behaviors or co-morbidities generally associated with increased risk for the specified malignancy in general populations.</p> <p><b>Highest Risk Factors:</b> 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).</p> <p><b>Periodic Evaluations:</b></p> <p><b>Standard Risk:</b> 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 (<a href="http://www.ahrq.gov/clinic/serfiles.htm">www.ahrq.gov/clinic/serfiles.htm</a>).</p> <p><b>Highest Risk:</b> 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</p>
<b>References</b>	<p>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.</p>
<p><b><i>The following documents are also included to further assist with application of these guidelines:</i></b></p>	
<b>Explanation of Scoring</b>	<p>Elucidation of the process used by the panel of experts to assign scores to each guideline section.</p>
<b>Patient-Specific Guideline Identification Tool</b>	<p>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, <b><i>use of the Patient-Specific Guideline Identification Tool is imperative</i></b> in order to determine each potential late effect associated with each therapeutic agent within this document (<i>see Appendix I</i>).</p>

### 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-*



## Instructions for Use (cont)

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  $\geq 1000$  mg/m<sup>2</sup>) versus “standard dose” (all single doses  $< 1000$  mg/m<sup>2</sup>)
  - 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 1972, 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 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](mailto:mehorowi@txch.org)) or Susan Krause ([skrause@txch.org](mailto: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:

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## 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 psychosocial/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; otosclerosis, 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  $\geq 40$  Gy to  $\geq 30$  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/Quality of Life 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  $\geq 30$  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  $\geq 20$  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)

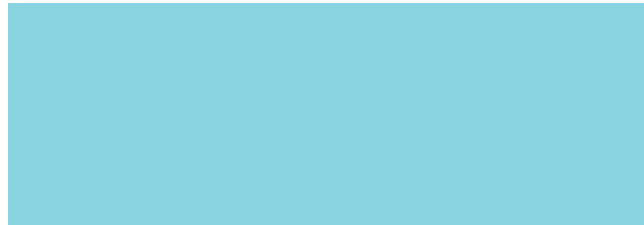
- Added importance of monitoring cardiovascular health in hypogonadal females for
  - Bilateral oophorectomy and hypogonadism/infertility (Section 142)
- Added importance of monitoring for surgical complications after prosthesis placement and cautioned that orchiectomy can be associated with psychological 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)



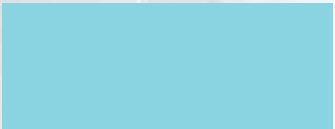
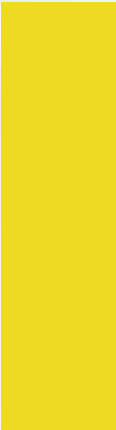
- The text that introduces the hematopoietic cell transplant sections (103–119) now precedes Section 103, since it is relevant to all hematopoietic cell transplant sections
- “Risk Factors” and “Highest Risk Factors” have been updated, based on current literature as reviewed by the Task Forces
- Links 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

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
1	<p><b>Any Cancer Experience</b></p> <p><b>Info Link</b> The Children's Oncology Group Long-Term Follow-Up Guidelines apply to patients who have been off therapy for a minimum of 2 years.</p>	<p><b>Adverse Psychosocial/QoL Effects</b></p> <p>Social withdrawal Educational problems Dysfunctional marital relationships Under-employment/ Unemployment Dependent living</p>	<p><b>Host Factors</b></p> <p>Female sex Family history of depression, anxiety, or mental illness Younger age at diagnosis Neurocognitive problems Physical limitations</p> <p><b>Social Factors</b></p> <p>Lower household income Lower educational achievement</p> <p><b>Treatment Factors</b></p> <p>Hematopoietic Cell Transplant</p>	<p><b>Host Factors</b></p> <p>CNS tumor CNS-directed therapy Hearing loss Premorbid learning or emotional difficulties</p> <p><b>Social Factors</b></p> <p>Failure to graduate from high school</p>	<p><b>HISTORY</b></p> <p>Psychosocial assessment with attention to:</p> <ul style="list-style-type: none"> <li>- Educational and/or vocational progress</li> <li>- Social withdrawal</li> </ul> <p>Yearly</p>	<p><b>Health Links</b></p> <p>Introduction to Long-Term Follow-Up Emotional Issues Educational Issues</p> <p><b>Resources</b></p> <p>'Childhood Cancer Survivors' by Nancy Keene, Wendy Hobbie &amp; Kathy Ruccione, Childhood Cancer Guides, 2012; 'Educating the Child with Cancer' edited by Nancy Keene, Candlelighters Childhood Cancer Foundation, Bethesda, MD, 2003. See also: <a href="http://www.cancer.gov">www.cancer.gov</a> ('Facing Forward' series for survivors)</p> <p><b>Considerations for Further Testing and Intervention</b></p> <p>Consider psychological consultation in patients with emotional difficulties related to cancer experience, including physical deformities or chronic disabilities. Consider social work consultation. Refer as indicated to school liaison in community or cancer center (psychologist, social worker, school counselor) to facilitate acquisition of educational resources.</p> <div style="text-align: center; border: 1px solid black; padding: 5px; margin-top: 20px;"> <p><b>SYSTEM = Psychosocial</b></p> <p><b>SCORE = 2A</b></p> </div>

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# ANY CANCER EXPERIENCE

(CONT)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
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# ANY CANCER EXPERIENCE

(CONT)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
2	Any Cancer Experience	<b>Mental health disorders</b> Depression Anxiety Post-traumatic stress Suicidal ideation	<b>Host Factors</b> Female sex Family history of depression, anxiety, or mental illness  <b>Social Factors</b> Lower household income Lower educational achievement  <b>Treatment Factors</b> Hematopoietic Cell Transplant  <b>Medical Conditions</b> Chronic pain	<b>Host Factors</b> CNS tumor CNS-directed therapy Premorbid learning or emotional difficulties Perceived poor physical health  <b>Social Factors</b> Failure to graduate from high school	<b>HISTORY</b> <b>Psychosocial assessment with attention to:</b> - Depression - Anxiety - Post-traumatic stress - Suicidal ideation Yearly	<b>Health Links</b> <b>Emotional Issues</b>  <b>Resources</b> 'Childhood Cancer Survivors' by Nancy Keene, Wendy Hobbie & Kathy Ruccione, Childhood Cancer Guides, 2012  <b>Considerations for Further Testing and Intervention</b> Consider psychological consultation in patients with emotional difficulties related to cancer experience, including physical deformities or chronic disabilities. Consider appropriate psychotropic medications. Consider evaluation of parent for post-traumatic stress syndrome  <div style="border: 1px solid black; padding: 5px; text-align: center;"><b>SYSTEM = Psychosocial</b> <b>SCORE = 2A</b></div>

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# ANY CANCER EXPERIENCE

(CONT)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
3	Any Cancer Experience	<b>Risky behaviors</b> Behaviors known to increase the likelihood of subsequent illness or injury	<b>Social Factors</b> Lower household income	<b>Host Factors</b> Older age at diagnosis  <b>Social Factors</b> Lower educational achievement	<b>HISTORY</b> <b>Psychosocial assessment</b> Yearly	<b>Health Links</b> <b>Emotional Issues</b>  <b>Resources</b> 'Childhood Cancer Survivors' by Nancy Keene, Wendy Hobbie & 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)
						<b>SYSTEM = Psychosocial</b>  <b>SCORE = 2A</b>

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# ANY CANCER EXPERIENCE

(CONT)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
4	Any Cancer Experience	Psychosocial disability due to pain	<b>Treatment Factors</b> Amputation Radiation to bone/joint Limb-sparing surgery Vincristine exposure  <b>Medical Conditions</b> Osteonecrosis	<b>Host Factors</b> CNS tumor Hodgkin lymphoma	<b>HISTORY</b> Psychosocial assessment Yearly	<b>Health Links</b> Chronic Pain after Childhood Cancer  <b>Resources</b> ‘Childhood Cancer Survivors’ by Nancy Keene, Wendy Hobbie & Kathy Ruccione, Childhood Cancer Guides, 2012 See also: <a href="http://www.nccn.org">www.nccn.org</a> (chronic pain)  <b>Considerations for Further Testing and Intervention</b> Consider psychological consultation in patients with emotional difficulties related to cancer experience, including physical deformities or chronic disabilities. Consider appropriate psychotropic medications. Consider referral to pain rehabilitation clinic.  <div style="border: 1px solid black; padding: 5px; text-align: center;">                         SYSTEM = Psychosocial                          SCORE = 2A                     </div>

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# ANY CANCER EXPERIENCE

(CONT)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
5	Any Cancer Experience	<p><b>Fatigue</b></p> <p><b>Info Link</b> Risk of sleep disturbance is increased for patients with CNS tumors and craniopharyngiomas.</p>	<p><b>Host Factors</b> Female sex Depression Obesity Central CNS tumor (e.g., craniopharyngioma)</p> <p><b>Social Factors</b> Unemployment</p> <p><b>Medical Conditions</b> Sleep disturbance</p>	<p><b>Host Factors</b> Pulmonary radiation</p>	<p><b>HISTORY</b></p> <p><b>Psychosocial assessment</b> Yearly</p>	<p><b>Resources</b></p> <p>'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)</p> <p><b>Considerations for Further Testing and Intervention</b></p> <p>Screen for physical sources of fatigue, such as anemia, sleep disturbances, nutritional deficiencies, cardiomyopathy, pulmonary fibrosis, hypothyroidism, or other endocrinopathy.</p> <div style="border: 1px solid black; padding: 5px; text-align: center;"> <p><b>SYSTEM = Psychosocial</b></p> <p><b>SCORE = 2A</b></p> </div>

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# ANY CANCER EXPERIENCE

(CONT)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
6	Any Cancer Experience	Limitations in healthcare and insurance access	<b>Social Factors</b> Lower household income Lower educational achievement Unemployment		<b>HISTORY</b> Psychosocial assessment with attention to healthcare and insurance access Yearly	<b>Health Links</b> Finding and Paying for Healthcare  <b>Considerations for Further Testing and Intervention</b> Social work consultation  <div style="border: 1px solid black; padding: 5px; text-align: center;">                         SYSTEM = Psychosocial                          SCORE = 2A                     </div>

## SECTION 6 REFERENCES

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# BLOOD/SERUM PRODUCTS

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
7	<p><b>Diagnosed prior to 1972</b></p> <p><b>Info Link</b></p> <ul style="list-style-type: none"> <li>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.</li> <li>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.</li> <li>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.</li> </ul>	Chronic hepatitis B	<p><b>Host Factors</b> Living in hyperendemic area</p> <p><b>Treatment Factors</b> Blood products before 1972</p> <p><b>Health Behaviors</b> IV drug use Unprotected sex Multiple partners High-risk sexual behavior Sexually transmitted diseases Tattoos Body piercing</p>	<p><b>Host Factors</b> Chronic immunosuppression</p>	<p><b>SCREENING</b></p> <p><b>Hepatitis B surface antigen (HBsAg)</b> <b>Hepatitis B core antibody (anti HBc or HBcAb)</b></p> <p>Once in patients who received treatment for cancer prior to 1972.</p> <p><b>Note:</b> Date may vary for international patients.</p>	<p><b>Health Links</b></p> <p>Hepatitis</p> <p><b>Considerations for Further Testing and Intervention</b></p> <p>Gastroenterology or hepatology consultation for patients with chronic hepatitis. Hepatitis A immunization in patients lacking immunity.</p> <div style="border: 1px solid black; padding: 5px; text-align: center;"> <p><b>SYSTEM = Immune</b></p> <p><b>SCORE = 1</b></p> </div>

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# BLOOD/SERUM PRODUCTS

(cont)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
8	<p><b>Diagnosed prior to 1993</b></p> <p><b>Info Link</b></p> <ul style="list-style-type: none"> <li>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.</li> <li>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.</li> <li>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.</li> </ul>	Chronic hepatitis C	<p><b>Host Factors</b> Living in hyperendemic area</p> <p><b>Treatment Factors</b> Blood products before 1993</p> <p><b>Health Behaviors</b> IV drug use Unprotected sex Multiple partners High-risk sexual behavior Sexually transmitted diseases Tattoos Body piercing</p>	<p><b>Host Factors</b> Chronic immunosuppression</p> <p><b>Treatment Factors</b> Blood products prior to 1986 (when surrogate screening of blood donors with ALT was initiated and donors with self-reported high-risk behaviors were deferred)</p>	<p><b>SCREENING</b></p> <p><b>Hepatitis C antibody</b> Once in patients who received treatment for cancer prior to 1993.</p> <p><b>Note:</b> Date may vary for international patients.</p> <p><b>Hepatitis C PCR (to establish chronic infection)</b> Once in patients with positive Hepatitis C antibody.</p>	<p><b>Health Links</b> Hepatitis</p> <p><b>Considerations for Further Testing and Intervention</b></p> <p>Screen 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.</p> <div style="text-align: center; border: 1px solid black; padding: 5px; margin-top: 20px;"> <p><b>SYSTEM = Immune</b></p> <p><b>SCORE = 1</b></p> </div>

## SECTION 8 REFERENCES

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# BLOOD/SERUM PRODUCTS

(cont)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
9	<p><b>Diagnosed between 1977 and 1985</b></p> <p><b>Info Link</b></p> <ul style="list-style-type: none"> <li>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.</li> <li>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.</li> <li>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.</li> </ul>	HIV infection	<p><b>Treatment Factors</b> Blood products between 1977 and 1985</p> <p><b>Medical Conditions</b> HPV infection</p> <p><b>Health Behaviors</b> IV drug use Unprotected sex Multiple partners High-risk sexual behavior Sexually transmitted diseases Tattoos Body piercing</p>		<p><b>SCREENING</b></p> <p><b>HIV testing</b> Once in patients who received treatment for cancer between 1977 and 1985.</p> <p><b>Note:</b> Date may vary for international patients.</p>	<p><b>Counseling</b> Standard counseling regarding safe sex, universal precautions and high-risk behaviors that exacerbate risk</p> <p><b>Considerations for Further Testing and Intervention</b> HIV/infectious diseases specialist consultation for patients with chronic infection.</p> <div style="border: 1px solid black; padding: 5px; text-align: center;"> <p><b>SYSTEM = Immune</b></p> <p><b>SCORE = 1</b></p> </div>

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# CHEMOTHERAPY

# ANY CHEMOTHERAPY

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
10	Any Chemotherapy	<b>Dental abnormalities</b> Tooth/root agenesis Root thinning/shortening Enamel dysplasia Microdontia	<b>Host Factors</b> Any patient who had not developed permanent dentition at time of cancer therapy  <b>Treatment Factors</b> Any radiation treatment involving the oral cavity or salivary glands	<b>Host Factors</b> Younger age at treatment, especially < 5 years old	<b>HISTORY</b> Dry mouth Yearly  <b>PHYSICAL</b> Oral exam Yearly  <b>SCREENING</b> Dental exam and cleaning Every 6 months	<b>Health Links</b> Dental Health  <b>Considerations for Further Testing and Intervention</b> Regular dental care including fluoride applications. Baseline panorex prior to dental procedures to evaluate root development.  <div style="border: 1px solid black; padding: 5px; text-align: center;">                         SYSTEM = Dental                          SCORE = 1                     </div>

## SECTION 10 REFERENCES

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# CHEMOTHERAPY

# ALKYLATING AGENTS

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
11 (male)	<p><b>ALKYLATING AGENTS</b></p> <p>Busulfan Carmustine (BCNU) Chlorambucil Cyclophosphamide Ifosfamide Lomustine (CCNU) Mechlorethamine Melphalan Procarbazine Thiotepa</p> <p><b>HEAVY METALS</b></p> <p>Carboplatin Cisplatin</p> <p><b>NON-CLASSICAL ALKYLATORS</b></p> <p>Dacarbazine (DTIC) Temozolomide</p>	<p><b>Gonadal dysfunction (testicular)</b></p> <p>Reduced fertility Oligospermia Azoospermia Infertility</p>	<p><b>Host Factors</b></p> <p>Testicular cancer Obesity Ejaculatory dysfunction Medications Occupational exposures (pesticides, heavy metals, solvents)</p> <p><b>Treatment Factors</b></p> <p>Higher cumulative doses of alkylators or combinations of alkylators</p> <p>Combined with radiation to:</p> <ul style="list-style-type: none"> <li>- abdomen/pelvis</li> <li>- testes</li> <li>- brain, cranium (neuroendocrine axis)</li> <li>- Genitourinary surgery</li> </ul> <p><b>Health Behaviors</b></p> <p>Tobacco/marijuana use History of sexually transmitted diseases</p>	<p><b>Treatment Factors</b></p> <p>MOPP ≥ 3 cycles Busulfan ≥ 600 mg/m<sup>2</sup> Cyclophosphamide cumulative dose ≥ 7.5 gm/m<sup>2</sup> or as conditioning for HCT Ifosfamide ≥ 60 gm/m<sup>2</sup> Any alkylators combined with:</p> <ul style="list-style-type: none"> <li>- testicular radiation</li> <li>- pelvic radiation</li> <li>- TBI</li> </ul>	<p><b>HISTORY</b></p> <p><b>Pubertal (onset, tempo)</b> <b>Sexual function (erections, nocturnal emissions, libido)</b> <b>Medication use</b> Yearly</p> <p><b>PHYSICAL</b></p> <p><b>Tanner staging until sexually mature</b> <b>Testicular volume by Prader orchimeter</b> Yearly</p> <p><b>SCREENING</b></p> <p><b>Semen analysis</b> At request of sexually mature patient Periodic evaluation over time is recommended as resumption of spermatogenesis can occur up to 10 years post therapy</p> <p><b>FSH</b> In sexually mature patient if unable to obtain semen analysis</p>	<p><b>Health Links</b></p> <p><b>Male Health Issues</b></p> <p><b>Resources</b></p> <p>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>)</p> <p><b>Counseling</b></p> <p>Counsel regarding the need for contraception, since there is tremendous individual variability in gonadal toxicity after exposure to alkylating agents. Recovery of fertility may occur years after therapy.</p> <p><b>Considerations for Further Testing and Intervention</b></p> <p>Reproductive endocrinology/urology referral for infertility evaluation and consultation regarding assisted reproductive technologies.</p> <div style="border: 1px solid black; padding: 5px; margin-top: 10px;"> <p><b>SYSTEM = Reproductive (male)</b></p> <p><b>SCORE =</b></p> <p><b>Alkylating Agents = 1</b></p> <p><b>Heavy Metals = 2A</b></p> <p><b>Non-Classical Alkylators = 2A</b></p> </div>

## SECTION 11 REFERENCES

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# CHEMOTHERAPY

# ALKYLATING AGENTS (cont)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
12 (male)	<b>ALKYLATING AGENTS</b> Busulfan Carmustine (BCNU) Chlorambucil Cyclophosphamide Ifosfamide Lomustine (CCNU) Mechlorethamine Melphalan Procarbazine Thiotepea  <b>HEAVY METALS</b> Carboplatin Cisplatin  <b>NON-CLASSICAL ALKYLATORS</b> Dacarbazine (DTIC) Temozolomide	<b>Gonadal dysfunction (testicular)</b> Testosterone deficiency/insufficiency Delayed/arrested puberty	<b>Host Factors</b> Testicular cancer Aging  <b>Treatment Factors</b> Higher cumulative doses of alkylators or combinations of alkylators Combined with radiation to: - Abdomen/pelvis - Testes - Brain, cranium (neuroendocrine axis) Unilateral orchiectomy  <b>Health Behaviors</b> Smoking	<b>Treatment Factors</b> MOPP Cyclophosphamide cumulative dose $\geq 20 \text{ gm/m}^2$ Conditioning for HCT; Ifosfamide $\geq 60 \text{ gm/m}^2$ Any alkylators combined with - Testicular radiation - Pelvic radiation - Neuroaxis radiation	<b>HISTORY</b> Pubertal (onset, tempo) Sexual function (erections, nocturnal emissions, libido) Medication use Yearly  <b>PHYSICAL</b> Tanner staging until sexually mature Testicular volume by Prader orchimeter Yearly  <b>SCREENING</b> 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	<b>Health Links</b> Male Health Issues  <b>Considerations for Further Testing and Intervention</b> 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.

**SYSTEM = Reproductive (male)**

**SCORE =**

Alkylating Agents = 1

Heavy Metals = 2A

Non-Classical Alkylators = 2A

## SECTION 12 REFERENCES

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# CHEMOTHERAPY

# ALKYLATING AGENTS (cont)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
13 (female)	<p><b>ALKYLATING AGENTS</b></p> <p>Busulfan Carmustine (BCNU) Chlorambucil Cyclophosphamide Ifosfamide Lomustine (CCNU) Mechlorethamine Melfhalan Procarbazine Thiotepa</p> <p><b>HEAVY METALS</b></p> <p>Carboplatin Cisplatin</p> <p><b>NON-CLASSICAL ALKYLATORS</b></p> <p>Dacarbazine (DTIC) Temozolomide</p>	<p><b>Gonadal dysfunction (ovarian)</b></p> <p>Delayed/arrested puberty Premature menopause Infertility</p>	<p><b>Treatment Factors</b></p> <p>Higher cumulative doses of alkylators or combinations of alkylators</p> <p>Combined with radiation to:</p> <ul style="list-style-type: none"> <li>- Abdomen/pelvis</li> <li>- Lumbar or sacral spine (from ovarian scatter)</li> <li>- Brain, cranium (neuroendocrine axis)</li> </ul> <p><b>Health Behaviors</b></p> <p>Smoking</p>	<p><b>Treatment Factors</b></p> <p>Any alkylators combined with:</p> <ul style="list-style-type: none"> <li>- pelvic radiation</li> <li>- TBI</li> </ul> <p><b>Host Factors</b></p> <p>Older age at treatment</p>	<p><b>HISTORY</b></p> <p>Pubertal (onset, tempo), menstrual, pregnancy history</p> <p><b>Sexual function (vaginal dryness, libido)</b></p> <p><b>Medication use</b></p> <p>Yearly</p> <p><b>PHYSICAL</b></p> <p><b>Tanner staging</b></p> <p>Yearly until sexually mature</p> <p><b>SCREENING</b></p> <p><b>FSH</b></p> <p><b>LH</b></p> <p><b>Estradiol</b></p> <p>Baseline at age 13 <b>AND</b> 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</p>	<p><b>Health Links</b></p> <p><b>Female Health Issues</b></p> <p><b>Resources</b></p> <p>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>)</p> <p><b>Counseling</b></p> <p>Counsel currently menstruating women at increased risk of early menopause to be cautious about delaying childbearing. Counsel regarding the need for contraception, since there is tremendous individual variability in gonadal toxicity after exposure to alkylating agents. Recovery of fertility may occur years after therapy.</p> <p><b>Considerations for Further Testing and Intervention</b></p> <p>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</p> <div style="border: 1px solid black; padding: 5px; margin-top: 20px;"> <p><b>SYSTEM = Reproductive (female)</b></p> <p><b>SCORE =</b></p> <p>Alkylating Agents = 1</p> <p>Heavy Metals = 2A</p> <p>Non-Classical Alkylators = 2A</p> </div>

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# CHEMOTHERAPY

# ALKYLATING AGENTS (cont)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
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# CHEMOTHERAPY

# ALKYLATING AGENTS (cont)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
14	<b>ALKYLATING AGENTS</b> Busulfan Carmustine (BCNU) Chlorambucil Cyclophosphamide Ifosfamide Lomustine (CCNU) Mechlorethamine Melphalan Procarbazine Thiotepa  <b>HEAVY METALS</b> Carboplatin Cisplatin  <b>NON-CLASSICAL ALKYLATORS</b> Dacarbazine (DTIC) Temozolomide	<b>Acute myeloid leukemia</b> <b>Myelodysplasia</b>	<b>Treatment Factors</b> Less than 10 years since exposure to agent Higher cumulative alkylator dose or combination of alkylators  <b>Note:</b> Melphalan and mechlorethamine are more potent leukemogens than cyclophosphamide  <b>Medical Conditions</b> Splenectomy (conflicting evidence)	<b>Treatment Factors</b> Autologous HCT	<b>HISTORY</b> <b>Fatigue</b> <b>Bleeding</b> <b>Easy bruising</b> Yearly, up to 10 years after exposure to agent  <b>PHYSICAL</b> <b>Dermatologic exam (pallor, petechiae, purpura)</b> Yearly, up to 10 years after exposure to agent	<b>Health Links</b> <b>Reducing the Risk of Second Cancers</b>  <b>Counseling</b> Counsel to promptly report fatigue, pallor, petechiae or bone pain.  <b>Counseling</b> CBC and bone marrow exam as clinically indicated .  <div style="border: 1px solid black; padding: 5px; text-align: center;"> <b>SYSTEM = SMN</b>   <b>SCORE =</b>                      Alkylating Agents = 1                      Heavy Metals = 2A                      Non-Classical Alkylators = 2A                 </div>

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# CHEMOTHERAPY

# ALKYLATING AGENTS (cont)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
15	<b>ALKYLATING AGENTS</b> Busulfan Carmustine (BCNU) Lomustine (CCNU)	<b>Pulmonary fibrosis</b>	<b>Treatment Factors</b> Higher cumulative doses Combined with bleomycin  <b>Medical Conditions</b> Atopic history  <b>Health Behaviors</b> Smoking Inhaled illicit drug use	<b>Treatment Factors</b> BCNU ≥ 600 mg/m <sup>2</sup> Busulfan ≥ 500 mg (transplant doses) Combined with: - Chest radiation - TBI	<b>HISTORY</b>  Cough SOB DOE Wheezing Yearly  <b>PHYSICAL</b>  Pulmonary exam Yearly  <b>SCREENING</b>  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.	<b>Health Links</b> <b>Pulmonary Health</b>  <b>Resources</b> Extensive information regarding smoking cessation is available for patients on the NCI's website: <a href="http://www.smokefree.gov">www.smokefree.gov</a>  <b>Counseling</b> 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.  <b>Considerations for Further Testing and Intervention</b> In patients with abnormal PFTs, consider repeat evaluation prior to general anesthesia. Pulmonary consultation for symptomatic pulmonary dysfunction. Influenza and pneumococcal vaccines.  <b>SYSTEM = Pulmonary</b> <b>SCORE = 1</b>

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# ALKYLATING AGENTS (cont)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
16	<b>ALKYLATING AGENTS</b> Busulfan	Cataracts	<b>Treatment Factors</b> Combined with corticosteroids	<b>Treatment Factors</b> Combined with cranial, orbital, or eye radiation TBI Longer interval since treatment	<b>HISTORY</b> <b>Visual changes (decreased acuity, halos, diplopia)</b> Yearly  <b>PHYSICAL</b> <b>Eye exam (visual acuity, funduscopic exam for lens opacity)</b> Yearly	<b>Health Links</b> <b>Cataracts</b>  <b>Considerations for Further Testing and Intervention</b> 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.  <b>SYSTEM = Ocular</b> <b>SCORE = 2B</b>

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# CHEMOTHERAPY

# ALKYLATING AGENTS (cont)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
17	<b>ALKYLATING AGENTS</b> Cyclophosphamide Ifosfamide	<b>Urinary tract toxicity</b> Hemorrhagic cystitis Bladder fibrosis Dysfunctional voiding Vesicoureteral reflux Hydronephrosis	<b>Treatment Factors</b> Higher cumulative doses (decreased incidence with Mesna) Combined with pelvic radiation  <b>Health Behaviors</b> Alcohol use Smoking	<b>Treatment Factors</b> Cyclophosphamide dose $\geq 3$ gm/m <sup>2</sup> Pelvic radiation dose $\geq 30$ Gy	<b>HISTORY</b> <b>Hematuria</b> <b>Urinary urgency/frequency</b> <b>Urinary incontinence/retention</b> <b>Dysuria</b> <b>Nocturia</b> <b>Abnormal urinary stream</b> Yearly	<b>Health Links</b> <b>Bladder Health</b>  <b>Counseling</b> Counsel to promptly report dysuria or gross hematuria.  <b>Considerations for Further Testing and Intervention</b> 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 $\geq 5$ 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.  <b>SYSTEM = Urinary</b> <b>SCORE = 1</b>

## SECTION 17 REFERENCES

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# CHEMOTHERAPY

## ALKYLATING AGENTS (cont)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
18	<b>ALKYLATING AGENTS</b> Cyclophosphamide	Bladder malignancy	<b>Treatment Factors</b> Combined with pelvic radiation  <b>Health Behaviors</b> Alcohol use Smoking		<b>HISTORY</b> Hematuria Urinary urgency/frequency Urinary incontinence/retention Dysuria Nocturia Abnormal urinary stream Yearly	<b>Health Links</b> Bladder Health  <b>Counseling</b> Counsel to promptly report dysuria or gross hematuria.  <b>Considerations for Further Testing and Intervention</b> 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 > 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.  <div style="border: 1px solid black; padding: 5px; text-align: center;">                         SYSTEM = SMN                          SCORE = 2A                     </div>

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# CHEMOTHERAPY

# ALKYLATING AGENTS (cont)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
19	<b>ALKYLATING AGENTS</b> Ifosfamide	<p><b>Renal toxicity</b> Glomerular injury Hypertension Tubular injury (renal tubular acidosis, Fanconi's syndrome, hypophosphatemic rickets)</p> <p><b>Info Link</b> Ifosfamide-related renal toxicity typically occurs during the acute treatment phase and improves or progresses over time</p>	<p><b>Host Factors</b> Younger age at treatment Mononephric</p> <p><b>Treatment Factors</b> Higher cumulative dose Combined with other nephrotoxic agents such as: - Cisplatin - Carboplatin - Aminoglycosides - Amphotericin - Immunosuppressants - Methotrexate - Radiation impacting the kidney</p> <p><b>Medical Conditions</b> Tumor infiltration of kidney(s) Pre-existing renal impairment Nephrectomy</p>	<p><b>Host Factors</b> Age &lt; 4 years at time of treatment</p> <p><b>Treatment Factors</b> Ifosfamide dose ≥ 60 grams/m<sup>2</sup> Renal radiation dose ≥ 15 Gy</p>	<p><b>PHYSICAL</b> Blood pressure Yearly</p> <p><b>SCREENING</b> <b>BUN</b> <b>Creatinine</b> <b>Na, K, Cl, CO<sub>2</sub></b> <b>Ca, Mg, PO<sub>4</sub></b> Baseline at entry into long-term follow-up, repeat as clinically indicated</p> <p><b>Urinalysis</b> Yearly</p>	<p><b>Health Links</b> <b>Kidney Health</b> <b>Cardiovascular Risk Factors</b></p> <p><b>Considerations for Further Testing and Intervention</b> Electrolyte supplements for patients with persistent electrolyte wasting. Nephrology consultation for patients with hypertension, proteinuria, or progressive renal insufficiency</p> <p><b>SYSTEM = Urinary</b> <b>SCORE = 1</b></p>

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# CHEMOTHERAPY

# HEAVY METALS

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
20	<p><b>HEAVY METALS</b> Carboplatin (myeloablative doses OR any dose if age at diagnosis &lt; 1 year) Cisplatin</p> <p><b>Info Link</b></p> <ul style="list-style-type: none"> <li>• In general, patients who received carboplatin in nonmyeloablative doses do not appear to be at risk for clinically significant ototoxicity.</li> <li>• Some studies have observed hearing loss among infants (with retinoblastoma) exposed to nonmyeloablative doses of carboplatin.</li> </ul>	<p><b>Ototoxicity</b> Sensorineural hearing loss Tinnitus Vertigo</p>	<p><b>Host Factors</b> Age &lt; 4 years at treatment</p> <p><b>Treatment Factors</b> Combined with: - Cranial/ear radiation - Ototoxic drugs (e.g., aminoglycosides, loop diuretics)</p> <p><b>Medical Conditions</b> Chronic otitis Cerumen impaction Renal dysfunction</p>	<p><b>Host Factors</b> CNS neoplasm</p> <p><b>Treatment Factors</b> Cumulative cisplatin dose ≥ 360 mg/m<sup>2</sup> High dose cisplatin (i.e., 40 mg/m<sup>2</sup> per day × 5 days per course) Cisplatin administered AFTER cranial/ear radiation Carboplatin conditioning for HCT Radiation involving ear ≥ 30 Gy</p>	<p><b>HISTORY</b> <b>Hearing difficulties (with/without background noise)</b> <b>Tinnitus</b> <b>Vertigo</b> Yearly</p> <p><b>PHYSICAL</b> <b>Otosopic exam</b> Yearly</p> <p><b>SCREENING</b> <b>Complete audiological evaluation</b> Baseline at entry into long-term followup. 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].</p> <p><b>Info Link</b></p> <ul style="list-style-type: none"> <li>• A “complete audiological evaluation” includes pure tone air and bone conduction, speech audiometry, and tympanometry for both ears.</li> <li>• Frequency-specific auditory brainstem response (ABR) can be performed if the above is inconclusive.</li> </ul>	<p><b>Health Links</b> <b>Hearing Loss</b> <b>Educational Issues</b></p> <p><b>Considerations for Further Testing and Intervention</b></p> <p>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.</p> <p><b>SYSTEM = Auditory</b> <b>SCORE = 1</b></p>

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# CHEMOTHERAPY

# HEAVY METALS (cont)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
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# CHEMOTHERAPY

# HEAVY METALS (cont)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
21	<b>HEAVY METALS</b> Carboplatin Cisplatin	<p><b>Peripheral sensory neuropathy</b> Paresthesias Dysesthesias</p> <p><b>Info Link</b></p> <ul style="list-style-type: none"> <li>Acute toxicities most commonly occur and usually improve or resolve prior to patients entering long-term follow-up.</li> <li>Neuropathy can persist after treatment and is typically not late in onset.</li> </ul>	<p><b>Treatment Factors</b> Combined with:</p> <ul style="list-style-type: none"> <li>Vincristine</li> <li>Taxanes</li> <li>Gemcitabine</li> </ul>	<p><b>Treatment Factors</b> Cumulative cisplatin dose <math>\geq 300 \text{ mg/m}^2</math></p>	<p><b>HISTORY</b></p> <p><b>Numbness</b> <b>Tingling</b> <b>Paresthesias</b> <b>Dysesthesia</b></p> <p>Yearly until 2 to 3 years after therapy, monitor yearly if symptoms persist</p> <p><b>PHYSICAL</b></p> <p><b>Neurologic exam</b> Yearly</p>	<p><b>Health Links</b></p> <p><b>Peripheral Neuropathy</b></p> <p><b>Considerations for Further Testing and Intervention</b></p> <p>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).</p> <div style="border: 1px solid black; padding: 5px; text-align: center;"> <p><b>SYSTEM = PNS</b></p> <p><b>SCORE = 2A</b></p> </div>

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# CHEMOTHERAPY

# HEAVY METALS (cont)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
22	<b>HEAVY METALS</b> Carboplatin Cisplatin	<b>Renal toxicity</b> Glomerular injury Hypertension Tubular injury Renal insufficiency	<b>Host Factors</b> Mononephric  <b>Treatment Factors</b> Combined with other nephrotoxic agents, such as: - Aminoglycosides - Amphotericin - Immunosuppressants - Methotrexate - Radiation impacting the kidney  <b>Medical Conditions</b> Diabetes mellitus Hypertension Nephrectomy	<b>Treatment Factors</b> Cisplatin dose $\geq$ 200 mg/m <sup>2</sup> Renal radiation dose $\geq$ 15 Gy	<b>PHYSICAL</b> <b>Blood pressure</b> Yearly  <b>SCREENING</b> <b>BUN</b> <b>Creatinine</b> <b>Na, K, Cl, CO<sub>2</sub></b> <b>Ca, Mg, PO<sub>4</sub></b> Baseline at entry into long-term follow-up, repeat as clinically indicated  <b>Urinalysis</b> Yearly	<b>Health Links</b> <b>Kidney Health</b> <b>Cardiovascular Risk Factors</b>  <b>Counseling</b> In patients with salt-wasting tubular dysfunction, educate that low magnesium levels potentiate coronary atherosclerosis.  <b>Considerations for Further Testing and Intervention</b> Electrolyte supplements for patients with persistent electrolyte wasting. Nephrology consultation for patients with hypertension, proteinuria, or progressive renal insufficiency.  <b>SYSTEM = Urinary</b> <b>SCORE = 2A</b>

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# CHEMOTHERAPY

# ANTIMETABOLITES

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
23	<b>ANTIMETABOLITES</b> Cytarabine (high dose IV)	<b>Neurocognitive deficits</b> Functional deficits in: - Executive function (planning and organization) - Sustained attention - Memory (particularly visual, sequencing, temporal memory) - Processing speed - Visual-motor integration - Fine motor dexterity Learning deficits in math and reading (particularly reading comprehension) Diminished IQ Behavioral change	<b>Host Factors</b> Younger age at treatment CNS leukemia/lymphoma Relapsed leukemia/lymphoma treated with CNS-directed therapy  <b>Treatment Factors</b> In combination with: - Corticosteroids - TBI - Cranial radiation - Methotrexate (IT, IO, high-dose IV) - Longer elapsed time since therapy	<b>Host Factors</b> Age < 3 years old at time of treatment Female sex Premorbid or family history of learning or attention problems  <b>Treatment Factors</b> Radiation dose ≥ 24 Gy Single fraction TBI (10 Gy)	<b>HISTORY</b> <b>Educational and/or vocational progress</b> Yearly  <b>SCREENING</b> <b>Referral for formal neuropsychological evaluation</b> Baseline at entry into long-term follow-up, then periodically as clinically indicated for patients with evidence of impaired educational or vocational progress	<b>Health Links</b> <b>Educational Issues</b>  <b>Considerations for Further Testing and Intervention</b> 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.
	<b>Info Link</b> High-dose IV is defined as any single dose ≥ 1000 mg/m <sup>2</sup> .					

**SYSTEM = CNS**  
**SCORE = 2A**

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# CHEMOTHERAPY

# ANTIMETABOLITES (cont)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
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## SECTION 23 REFERENCES (continued)

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# CHEMOTHERAPY

# ANTIMETABOLITES (cont)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
24	<b>ANTIMETABOLITES</b> Cytarabine (high dose IV)	<b>Clinical leukoencephalopathy</b> Spasticity Ataxia Dysarthria Dysphagia Hemiparesis Seizures	<b>Host Factors</b> Younger age at treatment CNS leukemia/lymphoma Relapsed leukemia/lymphoma treated with CNS-directed therapy  <b>Treatment Factors</b> Combined with - Methotrexate (IT, IO, high-dose IV) - Dexamethasone - Cranial radiation	<b>Treatment Factors</b> Radiation dose ≥ 24 Gy	<b>HISTORY</b> <b>Cognitive, motor and/or sensory deficits</b> <b>Seizures</b> <b>Other neurologic symptoms</b> Yearly  <b>PHYSICAL</b> <b>Neurologic exam</b> Yearly	<b>Considerations for Further Testing and Intervention</b> Brain CT; Brain MRI with MR angiography as clinically indicated with referred 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.
	<b>Info Link</b> High-dose IV is defined as any single dose ≥ 1000 mg/m <sup>2</sup>	<b>Info Link</b> <ul style="list-style-type: none"> <li>Clinical leukoencephalopathy may present with or without imaging abnormalities (e.g., leukoencephalopathy, cerebral lacunes, cerebral atrophy, dystrophic calcifications, mineralizing microangiopathy).</li> <li>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.</li> <li>Neuroimaging changes do not always correlate with degree of cognitive dysfunction.</li> <li>Prospective studies are needed to define the dose/effect relationship of neurotoxic agents. Note: new deficits may emerge over time.</li> </ul>				

**SYSTEM = CNS**  
**SCORE = 2A**

## SECTION 24 REFERENCES

Baker WJ, Royer GL, Jr., Weiss RB. Cytarabine and neurologic toxicity. *J Clin Oncol.* Apr 1991;9(4):679-693.

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# CHEMOTHERAPY

# ANTIMETABOLITES (cont)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
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## SECTION 24 REFERENCES (continued)

Vera P, Rohrlich P, Stievenart JL, et al. Contribution of single-photon emission computed tomography in the diagnosis and follow-up of CNS toxicity of a cytarabine-containing regimen in pediatric leukemia. *J Clin Oncol.* Sep 1999;17(9):2804-2810.

# CHEMOTHERAPY

# ANTIMETABOLITES (cont)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
25	<b>ANTIMETABOLITES</b> Cytarabine (low dose IV) Cytarabine IO Cytarabine IT Cytarabine SQ  <b>Info Link</b> Low-dose IV is defined as any single dose < 1000 mg/m <sup>2</sup> .	No known late effects  <b>Info Link</b> Acute toxicities predominate, from which the majority of patients recover without sequelae.			<b>SCREENING</b> No Known Late Effects	<div style="border: 1px solid black; padding: 5px; text-align: center;">                         SYSTEM = No Known Late Effects                          SCORE = 1                     </div>



# CHEMOTHERAPY

# ANTIMETABOLITES (cont)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
26	<b>ANTIMETABOLITES</b> Mercaptopurine (6MP) Thioguanine (6TG)	<b>Hepatic dysfunction</b> <b>Veno-occlusive disease (VOD)</b>	<b>Medical Conditions</b> Viral hepatitis Previous VOD Siderosis	<b>Medical Conditions</b> Chronic viral hepatitis	<b>PHYSICAL</b> Scleral icterus Jaundice Ascites Hepatomegaly Splenomegaly Yearly  <b>SCREENING</b> ALT AST Bilirubin Baseline at entry into long-term follow-up. Repeat as clinically indicated	<b>Health Links</b> <b>Liver Health</b>  <b>Considerations for Further Testing and Intervention</b> 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.
	<b>Info Link</b> • 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. • See COG Website (CCG 1952 protocol page) for updated advisories.	<b>Info Link</b> • Acute toxicities predominate from which the majority of patients recover without sequelae. • 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.				

**SYSTEM = GI/Hepatic**  
**SCORE = 2A**

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# CHEMOTHERAPY

# ANTIMETABOLITES (cont)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
27	<b>ANTIMETABOLITES</b> Methotrexate (high dose IV) Methotrexate (low dose IV) Methotrexate IM Methotrexate PO	<b>Reduced bone mineral density (BMD)</b> 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	<b>Host Factors</b> Both genders are at risk Younger age at diagnosis Caucasian Lower weight and BMI  <b>Treatment Factors</b> Corticosteroids Cyclosporine Tacrolimus Cranial radiation Craniospinal radiation HCT/TBI  <b>Medical Conditions</b> Growth hormone deficiency Hypogonadism/delayed puberty Hyperthyroidism  <b>Health Behaviors</b> Inadequate intake of calcium and vitamin D Lack of weight bearing exercise Smoking Alcohol use Carbonated beverages	<b>Host Factors</b> Older age at time of treatment  <b>Treatment Factors</b> Methotrexate cumulative dose ≥ 40 gm/m <sup>2</sup> Prolonged corticosteroid therapy (e.g., for chronic GVHD)	<b>SCREENING</b> <b>Bone density evaluation (DEXA or quantitative CT)</b> Baseline at entry into long-term follow-up, repeat as clinically indicated	<b>Health Links</b> <b>Bone Health</b>  <b>Resources</b> National Osteoporosis Foundation Website: <a href="http://www.nof.org">www.nof.org</a>
	<b>Info Link</b> High-dose IV is defined as any single dose ≥ 1000 mg/m <sup>2</sup> .	<b>Info Link</b> <ul style="list-style-type: none"> <li>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.</li> <li>Current definitions of osteopenia (T-scores between 1.0 and 2.5 SD below the mean) and osteoporosis (T-scores &gt; 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.</li> <li>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.</li> <li>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.</li> <li>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.</li> </ul>	<b>Info Link</b> <ul style="list-style-type: none"> <li>The optimal method of measuring bone health in children is controversial. Existing technologies have limitations.</li> <li>Dual energy x-ray absorptiometry (DEXA) provides an estimate of total bone mass at a given site.</li> <li>Quantitative CT provides distinct measures of trabecular and cortical bone dimension and density.</li> </ul>	<b>Considerations for Further Testing and Intervention</b> 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).		

**SYSTEM = Musculoskeletal**  
**SCORE = 2B**

# CHEMOTHERAPY

# ANTIMETABOLITES (cont)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
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# CHEMOTHERAPY

# ANTIMETABOLITES (cont)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
28	<b>ANTIMETABOLITES</b> Methotrexate (high dose IV) Methotrexate (low dose IV) Methotrexate IM Methotrexate PO	<b>Renal toxicity</b> Glomerular injury Hypertension	<b>Host Factors</b> Mononephric  <b>Treatment Factors</b> Combined with other nephrotoxic agents such as: - Cisplatin/carboplatin - Ifosfamide - Aminoglycosides - Amphotericin - Immunosuppressants - Radiation impacting the kidneys	<b>Treatment Factors</b> Treatment before 1970	<b>PHYSICAL</b> <b>Blood pressure</b> Yearly  <b>SCREENING</b> <b>BUN</b> <b>Creatinine</b> <b>Na, K, Cl, CO<sub>2</sub></b> <b>Ca, Mg, PO<sub>4</sub></b> Baseline at entry into long-term follow-up, repeat as clinically indicated  <b>Urinalysis</b> Yearly	<b>Health Links</b> <b>Kidney Health</b> <b>Cardiovascular Risk Factors</b>  <b>Considerations for Further Testing and Intervention</b> Nephrology consultation for patients with hypertension, proteinuria, or progressive renal insufficiency.  <b>SYSTEM = Urinary</b> <b>SCORE = 2A</b>
	<b>Info Link</b> High-dose IV is defined as any single dose $\geq 1000$ mg/m <sup>2</sup> .	<b>Info Link</b> Acute toxicities predominate, from which the majority of patients recover without sequelae.				
				<b>Medical Conditions</b> Diabetes mellitus Hypertension Nephrectomy		

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# CHEMOTHERAPY

# ANTIMETABOLITES (cont)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
29	<b>ANTIMETABOLITES</b> Methotrexate (high dose IV) Methotrexate (low dose IV) Methotrexate IM Methotrexate PO  <b>Info Link</b> High-dose IV is defined as any single dose $\geq 1000$ mg/m <sup>2</sup> .	<b>Hepatic dysfunction</b>  <b>Info Link</b> Acute toxicities predominate from which the majority of patients recover without sequelae.	<b>Treatment Factors</b> Abdominal radiation  <b>Medical Conditions</b> Viral hepatitis	<b>Treatment Factors</b> Treatment before 1970  <b>Medical Conditions</b> Chronic viral hepatitis	<b>PHYSICAL</b> Scleral icterus Jaundice Ascites Hepatomegaly Splenomegaly Yearly  <b>SCREENING</b> ALT AST Bilirubin Baseline at entry into long-term follow-up. Repeat as clinically indicated.	<b>Health Links</b> Liver Health  <b>Considerations for Further Testing and Intervention</b> 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.  <div style="border: 1px solid black; padding: 5px; text-align: center;"> <b>SYSTEM = GI/Hepatic</b>  <b>SCORE = 2A</b> </div>

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# CHEMOTHERAPY

# ANTIMETABOLITES (cont)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
30	<b>ANTIMETABOLITES</b> Methotrexate (high dose IV) Methotrexate (IO) Methotrexate (IT)	<b>Neurocognitive deficits</b> Functional deficits in: - Executive function (planning and organization) - Sustained attention - Memory (particularly visual, sequencing, temporal memory) - Processing speed - Visual-motor integration - Fine motor dexterity Learning deficits in math and reading (particularly reading comprehension) Diminished IQ Behavioral change	<b>Host Factors</b> Younger age at treatment CNS leukemia/lymphoma Relapsed leukemia/lymphoma treated with CNS-directed therapy Female sex  <b>Treatment Factors</b> In combination with: - Corticosteroids - TBI - Cranial radiation - Cytarabine (high-dose IV) - Longer elapsed time since therapy - Hyperthyroidism	<b>Host Factors</b> Age < 3 years old at time of treatment Premorbid or family history of learning or attention problems  <b>Treatment Factors</b> Radiation dose ≥ 24 Gy Single fraction TBI (10 Gy)	<b>HISTORY</b> <b>Educational and/or vocational progress</b> Yearly  <b>SCREENING</b> <b>Referral for formal neuropsychological evaluation</b> Baseline at entry into long-term follow-up, then periodically as clinically indicated for patients with evidence of impaired educational or vocational progress	<b>Health Links</b> <b>Educational Issues</b>  <b>Considerations for Further Testing and Intervention</b> 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.
	<b>Info Link</b> High-dose IV is defined as any single dose ≥ 1000 mg/m <sup>2</sup> .	<b>Info Link</b> <ul style="list-style-type: none"> <li>Neurocognitive deficits in survivors of leukemia and lymphoma are more frequently related to information processing (e.g., learning disability).</li> <li>Neurocognitive deficits in brain tumor survivors treated with higher doses of cranial radiation are more global (significant decline in IQ).</li> <li>Extent of deficit depends on age at treatment, intensity of treatment, and time since treatment.</li> <li>New deficits may emerge over time.</li> </ul>	<b>Health Behaviors</b> Inadequate intake of calcium and vitamin D; Lack of weight bearing exercise; Smoking; Alcohol use; Carbonated beverages			<div style="border: 1px solid black; background-color: #006699; color: white; padding: 5px; text-align: center;"> <b>SYSTEM = CNS</b>  <b>SCORE = 1</b> </div>

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# ANTIMETABOLITES (cont)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
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# CHEMOTHERAPY

# ANTIMETABOLITES (cont)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
31	<b>ANTIMETABOLITES</b> Methotrexate (high dose IV) Methotrexate (IO) Methotrexate (IT)	<b>Clinical leukoencephalopathy</b> Spasticity Ataxia Dysarthria Dysphagia Hemiparesis Seizures	<b>Host Factors</b> Younger age at treatment CNS leukemia/lymphoma Relapsed leukemia/lymphoma treated with CNS-directed therapy  <b>Treatment Factors</b> Combined with: - Cytarabine (high-dose IV) - Dexamethasone - Cranial radiation	<b>Treatment Factors</b> Radiation dose $\geq$ 24 Gy	<b>HISTORY</b> <b>Cognitive, motor and/or sensory deficits</b> <b>Seizures</b> <b>Other neurologic symptoms</b> Yearly  <b>PHYSICAL</b> <b>Neurological exam</b> Yearly	<b>Considerations for Further Testing and Intervention</b> 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.
	<b>Info Link</b> High-dose IV is defined as any single dose $\geq$ 1000 mg/m <sup>2</sup> .	<b>Info Link</b> <ul style="list-style-type: none"> <li>Clinical leukoencephalopathy may present with or without imaging abnormalities (e.g., leukoencephalopathy, cerebral lacunes, cerebral atrophy, dystrophic calcifications, mineralizing microangiopathy).</li> <li>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.</li> <li>Neuroimaging changes do not always correlate with degree of cognitive dysfunction. Prospective studies are needed to define the dose/effect relationship of neurotoxic agents.</li> <li>New deficits may emerge over time.</li> </ul>				

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# CHEMOTHERAPY

# ANTHRACYCLINE ANTIBIOTICS

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
32	<p><b>ANTHRACYCLINE ANTIBIOTICS</b> Daunorubicin Doxorubicin Epirubicin Idarubicin Mitoxantrone</p> <p><b>Info Link (Mitoxantrone):</b> Although Mitoxantrone technically belongs to the anthracenedione class of anti-tumor antibiotics, it is related to the anthracycline family.</p>	Acute myeloid leukemia	<p><b>Treatment Factors</b> Less than 5 years since exposure to agent</p>	<p><b>Treatment Factors</b> Autologous HCT</p>	<p><b>HISTORY</b> <b>Fatigue</b> <b>Bleeding</b> <b>Easy bruising</b> Yearly, up to 10 years after exposure to agent</p> <p><b>PHYSICAL</b> <b>Dermatologic exam (pallor, petechiae, purpura)</b> Yearly, up to 10 years after exposure to agent</p>	<p><b>Health Links</b> <b>Reducing the Risk of Second Cancers</b></p> <p><b>Counseling</b> Counsel to promptly report fatigue, pallor, petechiae or bone pain.</p> <p><b>Considerations for Further Testing and Intervention</b> CBC and bone marrow exam as clinically indicated.</p> <div style="text-align: center; border: 1px solid black; padding: 5px; margin-top: 10px;"> <p><b>SYSTEM = SMN</b></p> <p><b>SCORE = 1</b></p> </div>

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# CHEMOTHERAPY

# ANTHRACYCLINE ANTIBIOTICS (cont)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
33 (male)	<p><b>ANTHRACYCLINE ANTIBIOTICS</b> Daunorubicin Doxorubicin Epirubicin Idarubicin Mitoxantrone</p> <p><b>Info Link (Mitoxantrone)</b> 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.</p> <p><b>Info Link (Dose Conversion)</b>  <ul style="list-style-type: none"> <li>• 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.</li> <li>• To gauge the frequency of screening, use the following formulas to convert to doxorubicin isotoxic equivalents prior to calculating total cumulative anthracycline dose.</li> </ul> <b>Doxorubicin:</b> Multiply total dose x 1  <b>Daunorubicin:</b> Multiply total dose x 1  <b>Epirubicin:</b> Multiply total dose x 0.67  <b>Idarubicin:</b> Multiply total dose x 5  <b>Mitoxantrone:</b> Multiply total dose x 4  <ul style="list-style-type: none"> <li>• Clinical judgment should ultimately be used to determine indicated screening for individual patients.</li> </ul> </p>	<p><b>Cardiac toxicity</b> Cardiomyopathy Arrhythmias Subclinical left ventricular dysfunction</p> <p><b>Info Link</b>  <ul style="list-style-type: none"> <li>• Dose levels correlating with cardiotoxicity are derived from adult studies.</li> <li>• Childhood cancer patients exhibit clinical and subclinical toxicity at lower levels.</li> <li>• Certain conditions (such as isometric exercise and viral infections) have been anecdotally reported to precipitate cardiac decompensation.</li> <li>• Prospective studies are needed to better define the contribution of these factors to cardiac disease risk.</li> </ul> </p>	<p><b>Treatment Factors</b> Combined with radiation involving the heart Combined with other cardiotoxic chemotherapy - Cyclophosphamide conditioning for HCT - Amsacrine</p> <p><b>Medical Conditions</b> Obesity Congenital heart disease Febrile illness Hypertension Diabetes mellitus</p> <p><b>Health Behaviors</b> Isometric exercise Smoking Drug use (e.g., cocaine, diet pills, ephedra, mahuang)</p>	<p><b>Host Factors</b> Black/of African descent Younger than age 5 years at time of treatment</p> <p><b>Treatment Factors</b> Higher cumulative anthracycline doses: - <math>\geq 550</math> mg/m<sup>2</sup> in patients 18 years or older at time of treatment - <math>\geq 300</math> mg/m<sup>2</sup> in patients younger than 18 years at time of treatment - Any dose in infant Chest radiation <math>\geq 30</math> Gy Longer time elapsed</p>	<p><b>HISTORY</b> SOB DOE Orthopnea Chest pain Palpitations <b>If under 25 yrs: abdominal symptoms (nausea, vomiting)</b> Yearly</p> <p><b>Info Link</b>  <ul style="list-style-type: none"> <li>• Exertional intolerance is uncommon in patients younger than 25 years old.</li> <li>• Abdominal symptoms (nausea, emesis) may be observed more frequently than exertional dyspnea or chest pain in younger patients.</li> </ul> </p> <p><b>PHYSICAL</b> Cardiac murmur S3, S4 Increased P2 sound Pericardial rub Rales Wheezes Jugular venous distension Peripheral edema Yearly</p> <p><b>SCREENING</b> <b>ECHO (or comparable imaging to evaluate cardiac function)</b> Baseline at entry into long-term follow-up, then periodically based on age at treatment, radiation dose, and cumulative anthracycline dose. <b>EKG (include evaluation of QTc interval)</b> Baseline at entry into long-term follow-up, repeat as clinically indicated.</p>	<p><b>Health Links</b> <b>Heart Health</b> <b>Cardiovascular Risk Factors</b></p> <p><b>Counseling</b> 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.</p> <p><b>Considerations for Further Testing and Intervention</b> 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).</p> <p><b>SYSTEM = Cardiovascular</b> <b>SCORE = 1</b></p>

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# ANTHRACYCLINE ANTIBIOTICS (cont)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
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## SECTION 33 REFERENCES

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

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

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

<sup>§</sup>See Section 80

<sup>†</sup>Based on doxorubicin isotoxic equivalent dose [see conversion factors on previous page, "Info Link (Dose Conversion)"]

# CHEMOTHERAPY

# ANTHRACYCLINE ANTIBIOTICS (cont)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
34 (female)	<p><b>ANTHRACYCLINE ANTIBIOTICS</b> Daunorubicin Doxorubicin Epirubicin Idarubicin Mitoxantrone</p> <p><b>Info Link (Mitoxantrone):</b> 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.</p> <p><b>Info Link (Dose Conversion):</b>  <ul style="list-style-type: none"> <li>• 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.</li> <li>• To gauge the frequency of screening, use the following formulas to convert to doxorubicin isotoxic equivalents prior to calculating total cumulative anthracycline dose.</li> </ul> <b>Doxorubicin:</b> Multiply total dose x 1  <b>Daunorubicin:</b> Multiply total dose x 1  <b>Epirubicin:</b> Multiply total dose x 0.67  <b>Idarubicin:</b> Multiply total dose x 5  <b>Mitoxantrone:</b> Multiply total dose x 4  <ul style="list-style-type: none"> <li>• Clinical judgment should ultimately be used to determine indicated screening for individual patients.</li> </ul> </p>	<p><b>Cardiac toxicity</b> Cardiomyopathy Arrhythmias Subclinical left ventricular dysfunction</p> <p><b>Info Link</b>  <ul style="list-style-type: none"> <li>• Dose levels correlating with cardiotoxicity are derived from adult studies.</li> <li>• Childhood cancer patients exhibit clinical and subclinical toxicity at lower levels.</li> <li>• Certain conditions (such as isometric exercise, pregnancy, and viral infections) have been anecdotally reported to precipitate cardiac decompensation.</li> <li>• Prospective studies are needed to better define the contribution of these factors to cardiac disease risk.</li> </ul> </p>	<p><b>Treatment Factors</b> Combined with radiation involving the heart Combined with other cardiotoxic chemotherapy - Cyclophosphamide conditioning for HCT - Amsacrine</p> <p><b>Medical Conditions</b> Obesity Congenital heart disease Febrile illness Pregnancy Hypertension Diabetes mellitus</p> <p><b>Health Behaviors</b> Isometric exercise Smoking Drug use (e.g., cocaine, diet pills, ephedra, mahuang)</p>	<p><b>Host Factors</b> Female sex Black/of African descent Younger than age 5 years at time of treatment</p> <p><b>Treatment Factors</b> Higher cumulative anthracycline doses: - <math>\geq 550</math> mg/m<sup>2</sup> in patients 18 years or older at time of treatment - <math>\geq 300</math> mg/m<sup>2</sup> in patients younger than 18 years at time of treatment - Any dose in infant - Chest radiation <math>\geq 30</math> Gy Longer time elapsed</p>	<p><b>HISTORY</b> SOB DOE Orthopnea Chest pain Palpitations <b>If under 25 yrs: abdominal symptoms (nausea, vomiting)</b> Yearly</p> <p><b>Info Link</b>  <ul style="list-style-type: none"> <li>• Exertional intolerance is uncommon in patients younger than 25 years old.</li> <li>• Abdominal symptoms (nausea, emesis) may be observed more frequently than exertional dyspnea or chest pain in younger patients.</li> </ul> </p> <p><b>PHYSICAL</b> Cardiac murmur S3, S4 Increased P2 sound Pericardial rub Rales Wheezes Jugular venous distension Peripheral edema Yearly</p> <p><b>SCREENING</b> <b>ECHO (or comparable imaging to evaluate cardiac function))</b> Baseline at entry into long-term follow-up, then periodically based on age at treatment, radiation dose, and cumulative anthracycline dose. <b>EKG (include evaluation of QTc interval)</b> Baseline at entry into long-term follow-up, repeat as clinically indicated.</p>	<p><b>Health Links</b> <b>Heart Health</b> <b>Cardiovascular Risk Factors</b></p> <p><b>Counseling</b> 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.</p> <p><b>Considerations for Further Testing and Intervention</b> 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). Additional cardiology evaluation in patients who received <math>\geq 300</math> mg/m<sup>2</sup> or <math>&lt; 300</math> mg/m<sup>2</sup> plus chest radiation who are pregnant or planning pregnancy. Evaluation to include an echocardiogram before and periodically during pregnancy (especially during third trimester) and monitoring during labor and delivery due to risk of cardiac failure.</p> <p><b>SYSTEM = Cardiovascular</b> <b>SCORE = 1</b></p>

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
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### RECOMMENDED FREQUENCY OF ECHOCARDIOGRAM (or comparable cardiac imaging)

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

\*Age at time of first cardiotoxic therapy (anthracycline or radiation [see Section 81], whichever was given first)

<sup>§</sup>See Section 81

<sup>†</sup>Based on doxorubicin isotoxic equivalent dose [see conversion factors on previous page, "Info Link (Dose Conversion)"]

# CHEMOTHERAPY

# ANTI-TUMOR ANTIBIOTICS

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
35	<b>ANTI-TUMOR ANTIBIOTICS</b> Bleomycin	<b>Pulmonary toxicity</b> Interstitial pneumonitis Pulmonary fibrosis Acute respiratory distress syndrome (very rare)	<b>Host Factors</b> Younger age at treatment  <b>Treatment Factors</b> Higher cumulative dose Combined with: - Busulfan - Carmustine (BCNU) - Lomustine (CCNU)  <b>Medical Conditions</b> Renal dysfunction High dose oxygen support such as during general anesthesia  <b>Health Behaviors</b> Smoking Inhaled illicit drug use	<b>Treatment Factors</b> Bleomycin dose $\geq 400$ U/m <sup>2</sup> (injury observed in doses 60–100 U/m <sup>2</sup> in children) Combined with: Chest radiation TBI	<b>HISTORY</b>  Cough SOB DOE Wheezing Yearly  <b>PHYSICAL</b>  Pulmonary exam Yearly  <b>SCREENING</b>  <b>PFTs (including DLCO and spirometry)</b> Baseline at entry into long-term follow-up, repeat as clinically indicated in patients with abnormal results or progressive pulmonary dysfunction.	<b>Health Links</b>  <b>Pulmonary Health</b> <b>Bleomycin Alert</b>  <b>Resources</b> Extensive information regarding smoking cessation is available for patients on the NCI's website: <a href="http://www.smokefree.gov">www.smokefree.gov</a> .  <b>Counseling</b> Notify healthcare providers of history of bleomycin therapy and risk of worsening fibrosis with high oxygen exposure such as during general anesthesia. Administration of high concentrations of oxygen may result in chronic progressive pulmonary fibrosis. 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.  <b>Considerations for Further Testing and Intervention</b> In patients with abnormal PFTs consider repeat evaluation prior to general anesthesia. Pulmonary consultation in patients with symptomatic or progressive pulmonary dysfunction. Influenza and pneumococcal vaccines.  <div style="border: 1px solid black; padding: 5px; text-align: center;"> <p><b>SYSTEM = Pulmonary</b></p> <p><b>SCORE =</b></p> <p><b>Interstitial pneumonitis = 1</b></p> <p><b>Pulmonary fibrosis = 1</b></p> <p><b>ARDS = 2B</b></p> </div>

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# CHEMOTHERAPY

# ANTI-TUMOR ANTIBIOTICS (cont)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
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# CHEMOTHERAPY

# ANTI-TUMOR ANTIBIOTICS (cont)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
36	<b>ANTI-TUMOR ANTIBIOTICS</b> Dactinomycin	No known late effects  <b>Info Link</b> Dactinomycin has been associated with acute veno-occlusive disease, from which the majority of patients recover without sequelae.			<b>SCREENING</b> No Known Late Effects	<b>Health Links</b>  <b>SYSTEM = No Known Late Effects</b> <b>SCORE = 1</b>

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# CHEMOTHERAPY

# CORTICOSTEROIDS

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
37	<b>CORTICOSTEROIDS</b> Dexamethasone Prednisone	<p><b>Reduced bone mineral density (BMD)</b> 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</p> <p><b>Info Link</b></p> <ul style="list-style-type: none"> <li>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.</li> <li>Current definitions of osteopenia (T-scores between 1.0 and 2.5 SD below the mean) and osteoporosis (T-scores &gt; 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.</li> <li>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.</li> <li>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.</li> <li>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.</li> </ul>	<p><b>Host Factors</b> Both genders are at risk Younger age at diagnosis Caucasian Lower weight and BMI</p> <p><b>Treatment Factors</b> Corticosteroids Cyclosporine Tacrolimus Cranial radiation Craniospinal radiation HCT/TBI</p> <p><b>Medical Conditions</b> Growth hormone deficiency Hypogonadism/delayed puberty Hyperthyroidism</p> <p><b>Health Behaviors</b> Inadequate intake of calcium and vitamin D Lack of weight bearing exercise Smoking Alcohol use Carbonated beverages</p>	<p><b>Host Factors</b> Older age at time of treatment</p> <p><b>Treatment Factors</b> Dexamethasone effect is more potent than prednisone Glucocorticoid cumulative dose ≥ 9 gm/m<sup>2</sup> prednisone equivalent</p>	<p><b>SCREENING</b> <b>Bone density evaluation (DEXA or quantitative CT)</b> Baseline at entry into long-term follow-up, repeat as clinically indicated</p> <p><b>Info Link</b></p> <ul style="list-style-type: none"> <li>The optimal method of measuring bone health in children is controversial. Existing technologies have limitations.</li> <li>Dual energy x-ray absorptiometry (DEXA) provides an estimate of total bone mass at a given site.</li> <li>Quantitative CT provides distinct measures of trabecular and cortical bone dimension and density.</li> </ul>	<p><b>Health Links</b> <b>Bone Health</b></p> <p><b>Resources</b> National Osteoporosis Foundation Website (<a href="http://www.nof.org">www.nof.org</a>)</p> <p><b>Considerations for Further Testing and Intervention</b> 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).</p> <div style="text-align: center; background-color: #006699; color: white; padding: 5px; margin-top: 20px;"> <p><b>SYSTEM = Musculoskeletal</b></p> <p><b>SCORE = 2B</b></p> </div>

# CHEMOTHERAPY

# CORTICOSTEROIDS (cont)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
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# CHEMOTHERAPY

# CORTICOSTEROIDS (cont)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
38	<b>CORTICOSTEROIDS</b> Dexamethasone Prednisone	<p><b>Osteonecrosis (avascular necrosis)</b></p> <p><b>Info Link</b></p> <ul style="list-style-type: none"> <li>• Osteonecrosis typically occurs during the acute treatment phase, may progress over time or resolve.</li> <li>• Multifocal osteonecrosis is significantly more common (3:1) than unifocal.</li> </ul>	<p><b>Host Factors</b> Host polymorphisms may confer increased risk</p> <p><b>Treatment Factors</b> Combined with high-dose radiation to any bone Dexamethasone effect is more potent than prednisone</p> <p><b>Medical Conditions</b> Sickle cell disease</p>	<p><b>Host Factors</b> Pubertal/post-pubertal at time of treatment</p> <p><b>Treatment Factors</b> Orthovoltage radiation (commonly used before 1970) due to delivery of greater dose to skin and bones</p>	<p><b>HISTORY</b></p> <p>Joint pain Swelling Immobility Limited range of motion Yearly</p> <p><b>PHYSICAL</b></p> <p>Musculoskeletal exam Yearly</p>	<p><b>Health Links</b></p> <p><b>Osteonecrosis</b></p> <p><b>Considerations for Further Testing and Intervention</b></p> <p>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).</p> <p><b>SYSTEM = Musculoskeletal</b></p> <p><b>SCORE = 1</b></p>

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# CHEMOTHERAPY

# CORTICOSTEROIDS (cont)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
39	<b>CORTICOSTEROIDS</b> Dexamethasone Prednisone	Cataracts	<b>Treatment Factors</b> Combined with: - TBI - Busulfan	<b>Treatment Factors</b> TBI Cranial, orbital, or eye radiation Longer interval since treatment	<b>HISTORY</b> <b>Visual changes (decreased acuity, halos, diplopia)</b> Yearly  <b>PHYSICAL</b> <b>Eye exam (visual acuity, funduscopic exam for lens opacity)</b> Yearly	<b>Health Links</b> Cataracts  <b>Considerations for Further Testing and Intervention</b> 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.  <b>SYSTEM = Ocular</b> <b>SCORE = 1</b>

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# CHEMOTHERAPY

# ENZYMES

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
40	<b>ENZYMES</b> Asparaginase	No known late effects  <b>Info Link</b> Acute toxicities predominate, from which the majority of patients recover without sequelae.			<b>HISTORY</b> No Known Late Effects	<b>SYSTEM = No Known Late Effects</b> <b>SCORE = 1</b>

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# CHEMOTHERAPY

# PLANT ALKALOIDS

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
41	<b>PLANT ALKALOIDS</b> Vinblastine Vincristine	<p><b>Peripheral sensory or motor neuropathy</b></p> <p>Areflexia Weakness Foot drop Parasthesias</p> <p><b>Info Link</b></p> <ul style="list-style-type: none"> <li>• Acute toxicities most commonly occur and usually improve or resolve prior to patients entering long-term follow-up.</li> <li>• Neuropathy can persist after treatment and is typically not late in onset.</li> </ul>	<p><b>Treatment Factors</b></p> <p>Combined with platinum chemotherapy, gemcitabine or taxanes</p> <p><b>Medical Conditions</b></p> <p>Anorexia Severe weight loss</p>	<p><b>Medical Conditions</b></p> <p>Charcot-Marie-Tooth disease</p>	<p><b>HISTORY</b></p> <p><b>Areflexia</b> <b>Weakness</b> <b>Foot drop</b> <b>Paresthesias</b> <b>Dysesthesias</b></p> <p>Yearly until 2 to 3 years after therapy, monitor yearly if symptoms persist</p> <p><b>PHYSICAL</b></p> <p><b>Neurologic exam</b></p> <p>Yearly, until 2 to 3 years after therapy monitor yearly if symptoms persist</p>	<p><b>Health Links</b></p> <p><b>Peripheral Neuropathy</b></p> <p><b>Considerations for Further Testing and Intervention</b></p> <p>Physical therapy referral for patients with symptomatic neuropathy. Physical therapy and occupational therapy assessment of hand function. Consider treatment with an anticonvulsant effective for neuropathic pain (e.g., gabapentin and amitriptyline).</p> <div style="border: 1px solid black; padding: 5px; text-align: center;"> <p><b>SYSTEM = PNS</b></p> <p><b>SCORE = 2A</b></p> </div>

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# CHEMOTHERAPY

# PLANT ALKALOIDS (cont)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
42	<b>PLANT ALKALOIDS</b> Vinblastine Vincristine	<b>Vasospastic attacks (Raynaud's phenomenon)</b>	<b>Health Behaviors</b> Smoking Illicit drug use		<b>HISTORY</b> Vasospasms of hands, feet, nose, lips, cheeks, or earlobes related to stress or cold temperatures Yearly  <b>PHYSICAL</b> Physical exam of affected area As Indicated	<b>Health Links</b> Raynaud's Phenomenon  <b>Counseling</b> Counsel to wear appropriate protective clothing in cold environments and to not use tobacco or illicit drugs (vasoconstrictors such as cocaine).  <b>Considerations for Further Testing and Intervention</b> Consider vasodilating medications (calcium-channel blockers, alpha blockers) for patients with frequent, severe vasospastic attacks unresponsive to behavioral management.  <div style="border: 1px solid black; padding: 5px; text-align: center;">                         SYSTEM = PNS                          SCORE = 2A                     </div>

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# CHEMOTHERAPY

# EPIPODOPHYLLOTOXINS

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
43	<b>EPIPODOPHYLLOTOXINS</b> Etoposide (VP16) Teniposide (VM26)	Acute myeloid leukemia	<b>Medical Conditions</b> Splenectomy (conflicting evidence)	<b>Treatment Factors</b> Weekly or twice weekly administration Less than 5 years since exposure to agent Autologous HCT	<b>HISTORY</b> <b>Fatigue</b> <b>Bleeding</b> <b>Easy bruising</b> Yearly, up to 10 years after exposure to agent  <b>PHYSICAL</b> <b>Dermatologic exam (pallor, petechiae, purpura)</b> Yearly, up to 10 years after exposure to agent	<b>Health Links</b> <b>Reducing the Risk of Second Cancers</b>  <b>Counseling</b> Counsel to promptly report fatigue, pallor, petechiae, or bone pain.  <b>Considerations for Further Testing and Intervention</b> CBC and bone marrow exam as clinically indicated.  <div style="border: 1px solid black; padding: 5px; text-align: center;"> <b>SYSTEM = SMN</b>  <b>SCORE = 1</b> </div>
	<b>Info Link</b> Epipodophyllotoxin administration schedules since approximately 1990; have been modified to reduce the risk of this complication.					

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## 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:

- Patient received radiation to any field(s) relevant to the particular guideline section at  $\geq$  the specified minimum dose<sup>†</sup>

**OR**

- Patient received a combination of radiation to any relevant field(s)<sup>†</sup> **plus** relevant spinal radiation<sup>‡</sup> **and/or** TBI, the sum of which is  $\geq$  the specified minimum dose<sup>§</sup>

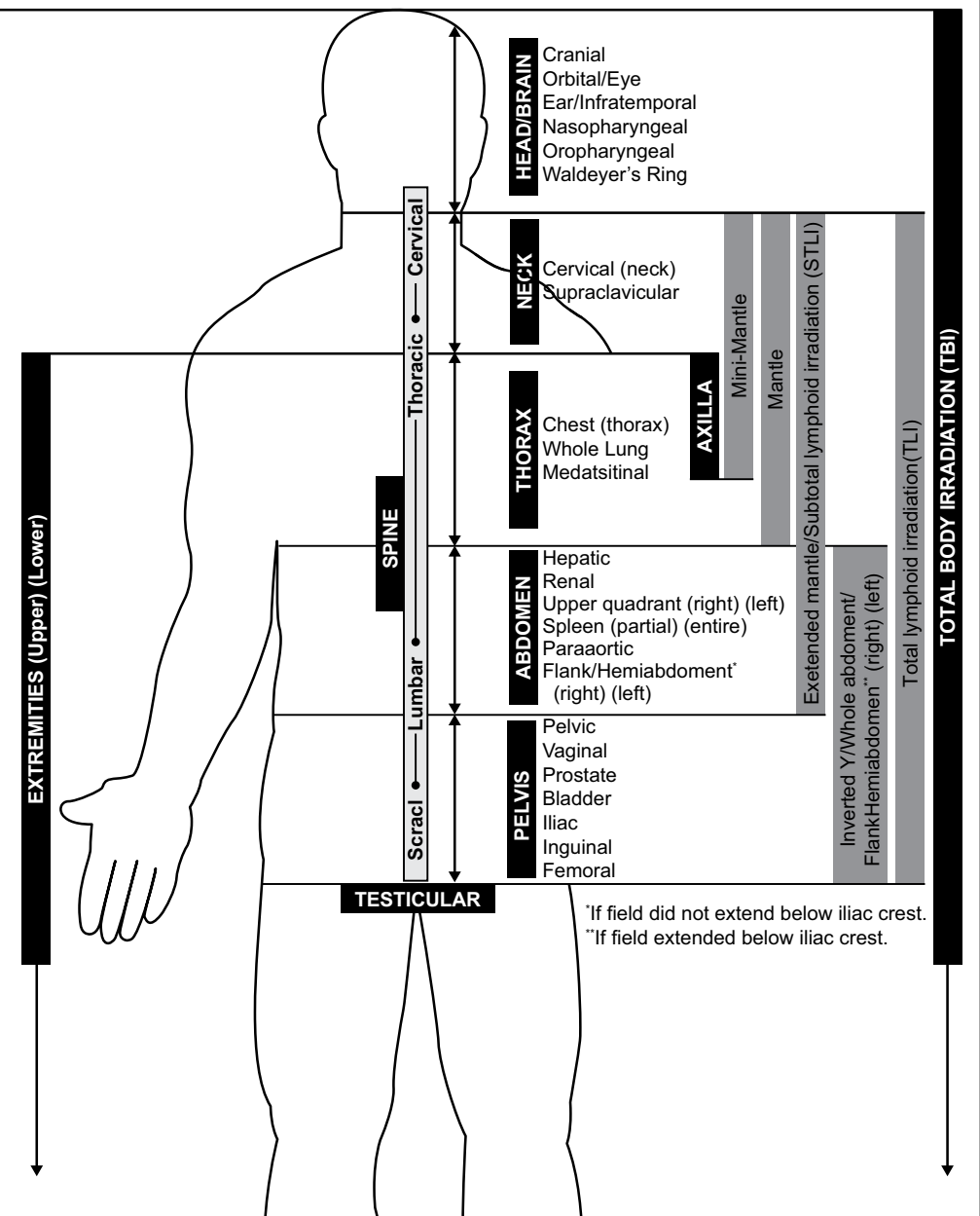
<sup>†</sup>Total dose to each field should include boost dose, if given. If patient received radiation to more than one field relevant to a particular guideline section during a single planned course of radiation treatment (excluding spinal radiation and TBI), **the field that received the largest radiation 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.

<sup>‡</sup>Use the **largest** dose of radiation delivered to the spinal field(s) specified in the guideline section.

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

### GENERAL FACTORS INFLUENCING RADIATION TOXICITY

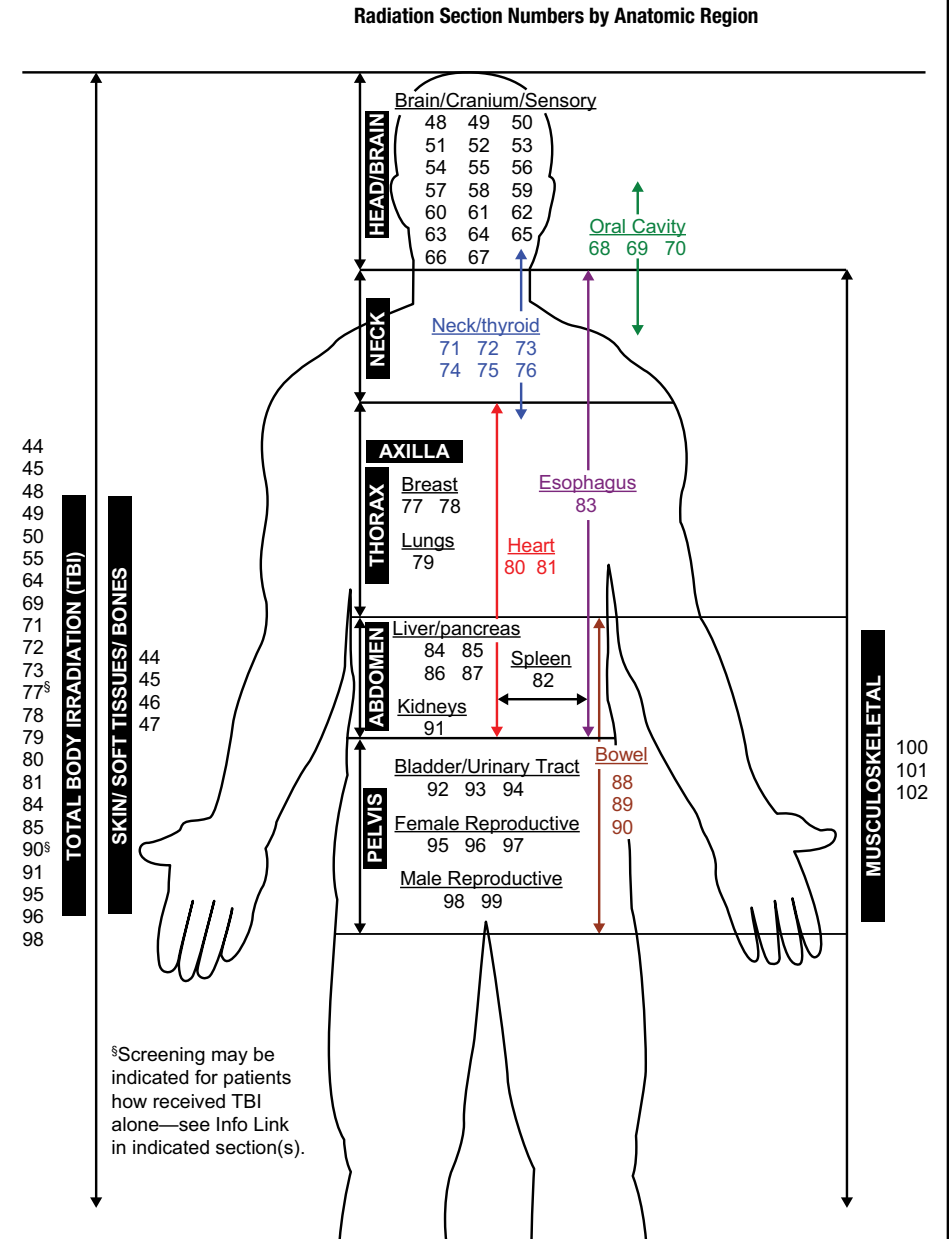
Include: daily fraction size, cumulative dose, age of patient at irradiation and type of radiation used. Toxicity may not be manifest until growth is completed or patient ages.



## GUIDE TO RADIATION SECTION NUMBERS BY ANATOMIC REGION

### 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.



# RADIATION

# ALL FIELDS (INCLUDING TBI)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
44	<b>All Radiation Fields (Including TBI)</b>	<p><b>Secondary benign or malignant neoplasm</b> Occurring in or near radiation field</p> <p><b>Info Link</b> Patients with bilateral or familial retinoblastoma (implying a germline mutation) are at increased risk for developing second malignant neoplasms.</p>	<p><b>Host Factors</b> Cancer predisposing mutation (e.g., p53, RB1, NF1) Younger age at treatment</p> <p><b>Treatment Factors</b> High cumulative radiation dose Large radiation treatment volumes Alkylating agent exposure</p>	<p><b>Treatment Factors</b> Orthovoltage radiation (commonly used before 1970) due to delivery of greater dose to skin and bones</p>	<p><b>PHYSICAL</b> <b>Inspection and palpation of skin and soft tissues in irradiated field(s)</b> Yearly</p> <p><b>SCREENING</b> <b>Other evaluations based on treatment volumes</b> See recommendations for specific fields</p>	<p><b>Health Links</b> <b>Reducing the Risk of Second Cancers</b></p> <p><b>Considerations for Further Testing and Intervention</b> Surgical and/or oncology consultation as clinically indicated.</p> <div style="border: 1px solid black; padding: 5px; text-align: center;"> <p><b>SYSTEM = SMN</b></p> <p><b>SCORE = 1</b></p> </div>
<div style="border: 1px solid black; padding: 5px;"> <ul style="list-style-type: none"> <li>• See “Radiation Reference Guide” in Appendix I for list of all radiation fields applicable to this section.</li> <li>• See “Patient-Specific Guideline Identification Tool” in Appendix I to determine specific screening guidelines by section number for individual patients.</li> </ul> </div>						

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# RADIATION

# ALL FIELDS (INCLUDING TBI) (cont)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
45	<b>All Radiation Fields (Including TBI)</b>	<b>Dysplastic nevi</b> <b>Skin cancer</b> Basal cell carcinoma Squamous cell carcinoma Melanoma	<b>Host Factors</b> Gorlin's syndrome (nevoid basal cell carcinoma syndrome)  <b>Health Behaviors</b> Sun exposure Tanning booths	<b>Treatment Factors</b> Orthovoltage radiation (commonly used before 1970) due to delivery of greater dose to skin and bones	<b>HISTORY</b> <b>Skin lesions</b> Changing moles (asymmetry, bleeding, increasing size, indistinct borders) Yearly  <b>PHYSICAL</b> <b>Dermatologic exam of irradiated fields</b> Yearly	<b>Health Links</b> <b>Skin Health</b> Reducing the Risk of Second Cancers  <b>Considerations for Further Testing and Intervention</b> Dermatology consultation for evaluation and monitoring of atypical nevi. Oncology consultation as clinically indicated.  <div style="border: 1px solid black; padding: 5px; text-align: center;"> <b>SYSTEM = SMN</b>  <b>SCORE = 1</b> </div>

- See "Radiation Reference Guide" in Appendix I for list of all radiation fields applicable to this section.
- See "Patient-Specific Guideline Identification Tool" in Appendix I to determine specific screening guidelines by section number for individual patients.

## SECTION 45 REFERENCES

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# RADIATION

# ALL FIELDS (EXCEPT TBI)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
46	<b>All Radiation Fields (Except TBI)</b>	<b>Dermatologic changes</b> Fibrosis Telangiectasias Permanent alopecia Altered skin pigmentation	<b>Host Factors</b> Younger age at treatment  <b>Treatment Factors</b> Total radiation dose $\geq$ 40 Gy Large dose fractions (e.g., $\geq$ 2 Gy per fraction)	<b>Treatment Factors</b> Radiation dose $\geq$ 50 Gy Orthovoltage radiation (commonly used before 1970) due to delivery of greater dose to skin and bones	<b>PHYSICAL</b> <b>Dermatologic exam of irradiated fields</b> Yearly	<b>Health Links</b> <b>Skin Health</b>  <b>SYSTEM = Dermatologic</b> <b>SCORE = 1</b>
<ul style="list-style-type: none"> <li>• See "Radiation Reference Guide" in Appendix I for list of all radiation fields applicable to this section.</li> <li>• See "Patient-Specific Guideline Identification Tool" in Appendix I to determine specific screening guidelines by section number for individual patients.</li> </ul>						

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# RADIATION

## ALL FIELDS (EXCEPT TBI) (cont)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
47	All Radiation Fields (Except TBI)	Bone malignancies	<b>Host Factors</b> Adolescent at treatment Cancer-predisposing mutation (e.g., p53, RB1, NF1)  <b>Treatment Factors</b> Higher radiation dose Combined with alkylating agents	<b>Treatment Factors</b> Radiation dose $\geq$ 30 Gy Orthovoltage radiation (commonly used before 1970) due to delivery of greater dose to skin and bones	<b>HISTORY</b> Bone pain (especially in irradiated field) Yearly  <b>PHYSICAL</b> Palpation of bones in irradiated field Yearly	<b>Counseling</b> Counsel patient to report symptoms promptly (e.g., bone pain, bone mass, persistent fevers)  <b>Considerations for Further Testing and Intervention</b> X-ray or other diagnostic imaging in patients with clinical symptoms. Oncology consultation as clinically indicated.  <div style="text-align: center; border: 1px solid black; padding: 5px;"> <b>SYSTEM = SMN</b>  <b>SCORE = 1</b> </div>

- See “Radiation Reference Guide” in Appendix I for list of all radiation fields applicable to this section.
- See “Patient-Specific Guideline Identification Tool” in Appendix I to determine specific screening guidelines by section number for individual patients.

### SECTION 47 REFERENCES

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# RADIATION

# POTENTIAL IMPACT TO BRAIN/CRANIUM

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
48	Cranial Ear/Infratemporal Nasopharyngeal Orbital/Eye Waldeyer's Ring Total Body Irradiation (TBI)	Brain tumor (benign or malignant)	<b>Host Factors</b> Younger age at treatment Neurofibromatosis  <b>Treatment Factors</b> Higher radiation dose (Risk of subsequent CNS tumor after cranial radiation increases in a dose-response relationship)	<b>Host Factors</b> Age < 6 years at time of treatment Ataxia telangiectasia	<b>HISTORY</b> Headaches Vomiting Cognitive, motor or sensory deficits Seizures and other neurologic symptoms Yearly  <b>PHYSICAL</b> Neurologic exam Yearly	<b>Considerations for Further Testing and Intervention</b> Brain MRI as clinically indicated for symptomatic patients. Consider brain MRI every other year for patients with neurofibromatosis beginning 2 years after radiation therapy. Neurosurgical consultation for tissue diagnosis and/or resection. Neuro-oncology consultation for medical management.  <b>SYSTEM = SMN</b> <b>SCORE = 1</b>
<p>• See "Patient-Specific Guideline Identification Tool" in Appendix I to determine specific screening guidelines by section number for individual patients.</p>						

## SECTION 48 REFERENCES

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# RADIATION

## POTENTIAL IMPACT TO BRAIN/CRANIUM (cont)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
49	<b>Cranial Ear/Infratemporal Total Body Irradiation (TBI)</b>	<p><b>Neurocognitive deficits</b> Functional deficits in:</p> <ul style="list-style-type: none"> <li>- Executive function (planning and organization)</li> <li>- Sustained attention</li> <li>- Memory (particularly visual, sequencing, temporal memory)</li> <li>- Processing speed</li> <li>- Visual-motor integration</li> <li>- Fine motor dexterity</li> <li>- Language</li> </ul> <p>Learning deficits in math and reading (particularly reading comprehension) Diminished IQ Behavioral change</p> <p><b>Info Link</b></p> <ul style="list-style-type: none"> <li>• Neurocognitive deficits in survivors of leukemia and lymphoma are more frequently related to information processing (e.g., learning disability).</li> <li>• Neurocognitive deficits in brain tumor survivors treated with higher doses of cranial radiation are more global (significant decline in IQ).</li> <li>• Extent of deficit depends on age at treatment, intensity of treatment, and time since treatment.</li> <li>• New deficits may emerge over time.</li> </ul>	<p><b>Host Factors</b> 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</p> <p><b>Treatment Factors</b> Radiation in combination with:</p> <ul style="list-style-type: none"> <li>- Corticosteroids</li> <li>- Methotrexate (IT, IO, high-dose IV)</li> <li>- Cytarabine (high-dose IV)</li> </ul> <p>Higher radiation dose Larger radiation field Greater cortical volumes Cranial radiation in combination with TBI Longer elapsed time since therapy</p>	<p><b>Host Factors</b> Age &lt; 3 years at time of treatment Female sex Temporal lobe field Premorbid or family history of learning or attention problems</p>	<p><b>HISTORY</b> Educational and/or vocational progress Yearly</p> <p><b>SCREENING</b> <b>Referral for formal neuropsychological evaluation</b> Baseline at entry into long-term follow-up, then periodically as clinically indicated for patients with evidence of impaired educational or vocational progress</p>	<p><b>Health Links</b> Educational Issues</p> <p><b>Considerations for Further Testing and Intervention</b> 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.</p> <div style="border: 1px solid black; padding: 5px; text-align: center;"> <p><b>SYSTEM = CNS</b> <b>SCORE = 1</b></p> </div>

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

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Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
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# RADIATION

## POTENTIAL IMPACT TO BRAIN/CRANIUM (cont)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
50	<b>Cranial Ear/Infratemporal Total Body Irradiation (TBI)</b>	<p><b>Clinical leukoencephalopathy</b></p> <p>Spasticity Ataxia Dysarthria Dysphagia Hemiparesis Seizures</p> <p><b>Info Link</b></p> <ul style="list-style-type: none"> <li>• Clinical leukoencephalopathy may present with or without imaging abnormalities (e.g., leukoencephalopathy, cerebral lacunes, cerebral atrophy, dystrophic calcifications, mineralizing microangiopathy).</li> <li>• 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.</li> <li>• Neuroimaging changes do not always correlate with degree of cognitive dysfunction. Prospective studies are needed to define the dose/effect relationship of neurotoxic agents.</li> <li>• New deficits may emerge over time.</li> </ul>	<p><b>Host Factors</b></p> <p>Younger age at treatment CNS leukemia/lymphoma Relapsed leukemia/lymphoma treated with CNS-directed therapy</p> <p><b>Treatment Factors</b></p> <p>In combination with:</p> <ul style="list-style-type: none"> <li>- Dexamethasone</li> <li>- Methotrexate (IT, IO, high-dose IV)</li> <li>- Cytarabine (high-dose IV)</li> <li>- Higher radiation dose</li> </ul> <p>Larger radiation field Greater cortical volumes Longer elapsed time since therapy</p>	<p><b>Host Factors</b></p> <p>Radiation dose <math>\geq</math> 24 Gy</p> <p><b>Treatment Factors</b></p> <p>Fraction dose <math>\geq</math> 3 Gy</p>	<p><b>HISTORY</b></p> <p><b>Cognitive, motor and/or sensory deficits</b> <b>Seizures</b> <b>Other neurologic symptoms</b> Yearly</p> <p><b>PHYSICAL</b></p> <p><b>Neurologic exam</b> Yearly</p>	<p><b>Considerations for Further Testing and Intervention</b></p> <p>Brain CT; Brain MRI with MR angiography as clinically indicated with preferred study based on intracranial lesion to be evaluated:</p> <ul style="list-style-type: none"> <li>- Calcifications: CT</li> <li>- White matter: MRI with diffusion-tensor imaging (DTI)</li> <li>- Microvascular injury: Gadolinium-enhanced MRI with diffusion-weighted imaging (DWI)</li> </ul> <p>Neurology consultation and follow-up as clinically indicated.</p> <div style="border: 1px solid black; padding: 5px; text-align: center;"> <p><b>SYSTEM = CNS</b></p> <p><b>SCORE = 1</b></p> </div>

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

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# RADIATION

## POTENTIAL IMPACT TO BRAIN/CRANIUM (cont)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
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# RADIATION

## POTENTIAL IMPACT TO BRAIN/CRANIUM (cont)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
51	<p>≥ 18 Gy to:  <b>Cranial</b>  <b>Ear/Infratemporal</b>  <b>Nasopharyngeal</b>  <b>Orbital/Eye</b>  <b>Waldeyer's Ring</b>  <b>TBI*</b></p> <p>*TBI is included for dose calculation purposes only; this section is not applicable to patients who received TBI alone.</p>	<p><b>Cerebrovascular complications</b>            Stroke            Moyamoya            Occlusive cerebral vasculopathy            Cavernomas</p> <p><b>Info Link</b></p> <ul style="list-style-type: none"> <li>• Moyamoya syndrome is the complete occlusion of one or more of the three major cerebral vessels with the development of small, immature collateral vessels.</li> <li>• This condition reflects an attempt to revascularize the ischemic portion of the brain.</li> <li>• Cavernomas are a common late effect of cranial radiation, but the majority of patients with cavernomas are asymptomatic.</li> </ul>	<p><b>Host Factors</b>            Down syndrome</p> <p><b>Treatment Factors</b>            Suprasellar radiation</p> <p><b>Medical Conditions</b>            Sickle cell disease            Neurofibromatosis</p>	<p><b>Host Factors</b>            Parasellar tumor</p> <p><b>Treatment Factors</b>            Radiation dose ≥ 50 Gy            Circle of Willis in radiation field</p>	<p><b>HISTORY</b>  <b>Hemiparesis</b>  <b>Hemiplegia</b>  <b>Weakness</b>  <b>Aphasia</b>            Yearly</p> <p><b>PHYSICAL</b>  <b>Neurologic exam</b>            Yearly</p>	<p><b>Considerations for Further Testing and Intervention</b>            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.</p> <p><b>SYSTEM = CNS</b>  <b>SCORE = 1</b></p>
<p>• This section is only applicable to patients who:</p> <ol style="list-style-type: none"> <li>1) Received radiation to any of the specified fields at ≥ 18 Gy                OR</li> <li>2) Received a combination of radiation to any of the specified fields <b>and</b> TBI, the sum of which is ≥ 18 Gy</li> </ol> <ul style="list-style-type: none"> <li>• 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.</li> <li>• See "Patient-Specific Guideline Identification Tool" in Appendix I to determine specific screening guidelines by section number for individual patients.</li> </ul>						

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# RADIATION

## POTENTIAL IMPACT TO BRAIN/CRANIUM (cont)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
52	<b>Cranial</b> <b>Ear/Infratemporal</b> <b>Nasopharyngeal</b> <b>Orbital/Eye</b> <b>Waldeyer's Ring</b>	<b>Craniofacial abnormalities</b>	<b>Host Factors</b> Younger age at treatment  <b>Treatment Factors</b> Higher radiation dose	<b>Host Factors</b> Age < 5 years at time of treatment  <b>Treatment Factors</b> Radiation dose ≥ 30 Gy	<b>HISTORY</b> <b>Psychosocial assessment, with attention to:</b> <b>Educational and/or vocational progress</b> <b>Depression</b> <b>Anxiety</b> <b>Post-traumatic stress</b> <b>Social withdrawal</b> Yearly  <b>PHYSICAL</b> <b>Craniofacial abnormalities</b> Yearly	<b>Resources</b> FACES—The National Craniofacial Association ( <a href="http://www.faces-cranio.org">www.faces-cranio.org</a> )  <b>Considerations for Further Testing and Intervention</b> Reconstructive craniofacial surgical consultation. Consultation with psychologist in patients with adjustment disorders related to facial asymmetry/deformity.  <div style="border: 1px solid black; padding: 5px; text-align: center;"> <b>SYSTEM = Musculoskeletal</b>  <b>SCORE = 1</b> </div>

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

### SECTION 52 REFERENCES

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# RADIATION

## POTENTIAL IMPACT TO BRAIN/CRANIUM (cont)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
53	Cranial Ear/Infratemporal Nasopharyngeal Orbital/Eye Waldeyer's Ring	Chronic sinusitis	<b>Treatment Factors</b> Radiation dose to sinuses ≥ 30 Gy Radiomimetic chemotherapy (e.g., doxorubicin, dactinomycin)  <b>Medical Conditions</b> Atopic history Hypogammaglobulinemia		<b>HISTORY</b> Rhinorrhea, postnasal discharge Yearly  <b>PHYSICAL</b> Sinuses Yearly Nasal exam Yearly	<b>Considerations for Further Testing and Intervention</b> CT scan of sinuses as clinically indicated. Otolaryngology consultation as clinically indicated.  <div style="border: 1px solid black; padding: 5px; text-align: center;">                         SYSTEM = Immune                          SCORE = 1                     </div>
<div style="border: 1px solid black; padding: 5px;">                     • See "Patient-Specific Guideline Identification Tool" in Appendix I to determine specific screening guidelines by section number for individual patients.                 </div>						

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# RADIATION

## POTENTIAL IMPACT TO BRAIN/CRANIUM (cont)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
54	Cranial Ear/Infratemporal Nasopharyngeal Orbital/Eye Waldeyer's Ring	<p><b>Overweight Obesity</b></p> <p><b>Info Link</b> Overweight: Age 2–20 years: BMI for age ≥ 85th–&lt; 95th percentile Age ≥ 21 years: BMI ≥ 25–29.9 Obesity: Age 2–20 years: BMI for age ≥ 95th percentile Age ≥ 21 years: BMI ≥ 30</p> <p>BMI=wt(kg)/ht(M<sup>2</sup>) BMI calculator available on-line at: <a href="http://www.nhlbi.nih.gov/guidelines/obesity/BMI/bmicalc.htm">www.nhlbi.nih.gov/guidelines/obesity/BMI/bmicalc.htm</a> Growth charts for patients &lt; 21 years of age available on-line at: <a href="http://www.cdc.gov/growthcharts">www.cdc.gov/growthcharts</a></p>	<p><b>Host Factors</b> Younger at treatment</p> <p><b>Treatment Factors</b> Higher cranial radiation dose Surgery in suprasellar region Combined with corticosteroids Prolonged corticosteroid therapy (e.g., for chronic GVHD)</p> <p><b>Medical Conditions</b> Familial dyslipidemia Growth hormone deficiency Hypothyroidism Hypogonadism</p>	<p><b>Host Factors</b> Age &lt; 4 years old at time of treatment Female sex</p> <p><b>Treatment Factors</b> Cranial radiation dose ≥ 18 Gy</p> <p><b>Medical Conditions</b> Inability to exercise</p>	<p><b>PHYSICAL</b></p> <p>Height Weight BMI Blood pressure Yearly</p>	<p><b>Health Links</b> <b>Diet and Physical Activity</b> <b>Cardiovascular Risk Factors</b></p> <p><b>Counseling</b> Counsel regarding obesity-related health risks</p> <p><b>Considerations for Further Testing and Intervention</b> Consider evaluation for other co-morbid conditions, including dyslipidemia, hypertension, or impaired glucose metabolism. Nutritional counseling.</p> <p><b>Info Link</b></p> <ul style="list-style-type: none"> <li>• Overweight/obesity may occur in a constellation of conditions known as the metabolic syndrome.</li> <li>• Definitions of the metabolic syndrome are evolving, but generally include a combination of central (abdominal) obesity with at least 2 or more of the following: <ul style="list-style-type: none"> <li>- hypertension</li> <li>- atherogenic dyslipidemia (elevated triglycerides, reduced HDL cholesterol), and</li> <li>- abnormal glucose metabolism (fasting hyperglycemia, hyperinsulinism, insulin resistance, diabetes mellitus type II).</li> </ul> </li> </ul>
			<p>• See "Patient-Specific Guideline Identification Tool" in Appendix I to determine specific screening guidelines by section number for individual patients.</p>			
						<p><b>SYSTEM = Endocrine/Metabolic</b></p> <p><b>SCORE = 1</b></p>

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Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
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# RADIATION

# POTENTIAL IMPACT TO NEUROENDOCRINE AXIS

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
55	Cranial Ear/Infratemporal Nasopharyngeal Orbital/Eye Waldeyer's Ring Total Body Irradiation (TBI)	Growth hormone deficiency  <b>Info Link</b> Growth charts available on-line at <a href="http://www.cdc.gov/growthcharts/">www.cdc.gov/growthcharts/</a>	<b>Host Factors</b> Younger age at treatment  <b>Treatment Factors</b> Higher radiation doses Surgery in suprasellar region Pretransplant radiation TBI ≥ 10 Gy in single fraction, ≥ 12 Gy fractionated	<b>Treatment Factors</b> Radiation dose ≥ 18 Gy Pretransplant cranial radiation TBI given in single fraction	<b>HISTORY</b> <b>Assessment of nutritional status</b> Every 6 months until growth is completed, then yearly.  <b>PHYSICAL</b> <b>Tanner staging</b> Every 6 months until sexually mature  <b>Height</b> <b>Weight</b> <b>BMI</b> Every 6 months until growth is completed, then yearly	<b>Health Links</b> <b>Growth Hormone Deficiency</b> See also: <b>Hypopituitarism</b>  <b>Resources</b> <a href="http://www.magicfoundation.org">www.magicfoundation.org</a>  <b>Considerations for Further Testing and Intervention</b> For skeletally immature children, refer to endocrinology if radiation dose ≥ 30 Gy. For those treated with < 30 Gy, obtain x-ray for bone age in poorly growing children. Endocrine consultation for: Poor growth for age or stage of puberty as evidenced by decline in growth velocity and change in percentile rankings on growth chart; weight below 3rd percentile on growth chart. Evaluate thyroid function in any poorly growing child. Consult with endocrinologist regarding risks/benefits of adult growth hormone replacement therapy. Consider bone density testing in patients who are growth hormone deficient.
<div style="border: 1px solid black; padding: 5px; margin: 10px auto; width: fit-content;"> <p>• See "Patient-Specific Guideline Identification Tool" in Appendix I to determine specific screening guidelines by section number for individual patients.</p> </div>						
						<div style="background-color: #00728f; color: white; padding: 5px; display: inline-block;"> <b>SYSTEM = Endocrine/Metabolic</b>   <b>SCORE = 1</b> </div>

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Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
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# RADIATION

## POTENTIAL IMPACT TO NEUROENDOCRINE AXIS (cont)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
56 (male)	Cranial Ear/Infratemporal Nasopharyngeal Orbital/Eye Waldeyer's Ring	Precocious puberty	<b>Host Factors</b> Younger age at treatment  <b>Treatment Factors</b> Radiation doses $\geq$ 18 Gy		<b>PHYSICAL</b> Height Weight Tanner staging Testicular volume by Prader orchidometry Yearly until sexually mature	<b>Health Links</b> Precocious Puberty  <b>Resources</b> <a href="http://www.magicfoundation.org">www.magicfoundation.org</a>  <b>Considerations for Further Testing and Intervention</b> Obtain FSH, LH, testosterone 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 boy < 9 years old).  <div style="border: 1px solid black; padding: 5px; width: fit-content; margin: 0 auto;"> <b>SYSTEM = Endocrine/Metabolic</b>  <b>SCORE = 1</b> </div>
<div style="border: 1px solid black; padding: 5px; width: fit-content; margin: 0 auto;">                     • See "Patient-Specific Guideline Identification Tool" in Appendix I to determine specific screening guidelines by section number for individual patients.                 </div>						

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# RADIATION

## POTENTIAL IMPACT TO NEUROENDOCRINE AXIS (cont)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
57 (female)	Cranial Ear/Infratemporal Nasopharyngeal Orbital/Eye Waldeyer's Ring	Precocious puberty	<b>Host Factors</b> Female sex Younger age at treatment  <b>Treatment Factors</b> Radiation doses ≥ 18 Gy		<b>PHYSICAL</b>  Height Weight Tanner staging Yearly until sexually mature	<b>Health Links</b> Precocious Puberty  <b>Resources</b> <a href="http://www.magicfoundation.org">www.magicfoundation.org</a>  <b>Considerations for Further Testing and Intervention</b> 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).  <div style="border: 1px solid black; padding: 5px; width: fit-content; margin: 0 auto;"> <b>SYSTEM = Endocrine/Metabolic</b>  <b>SCORE = 1</b> </div>
<div style="border: 1px solid black; padding: 5px; width: fit-content; margin: 0 auto;">                     • See "Patient-Specific Guideline Identification Tool" in Appendix I to determine specific screening guidelines by section number for individual patients.                 </div>						

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- Quigley C, Cowell C, Jimenez M, et al. Normal or early development of puberty despite gonadal damage in children treated for acute lymphoblastic leukemia. *N Engl J Med*. Jul 20 1989;321(3):143-151.
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- Sklar CA. Growth and neuroendocrine dysfunction following therapy for childhood cancer. *Pediatr Clin North Am*. Apr 1997;44(2):489-503.

# RADIATION

## POTENTIAL IMPACT TO NEUROENDOCRINE AXIS (cont)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
58 (male)	<p>≥ 40 Gy to:  <b>Cranial</b>  <b>Ear/Infratemporal</b>  <b>Nasopharyngeal</b>  <b>Orbital/Eye</b>  <b>Waldeyer's Ring</b>  <b>TBI*</b></p> <p>*TBI is included for dose calculation purposes only; this section is not applicable to patients who received TBI alone.</p>	<p><b>Hyperprolactinemia</b></p>	<p><b>Treatment Factors</b>            Higher radiation dose            Surgery or tumor in hypothalamic area</p>	<p><b>Treatment Factors</b>            Radiation dose ≥ 50 Gy</p>	<p><b>HISTORY</b>  <b>Decreased libido</b>  <b>Galactorrhea</b>            Yearly</p> <p><b>SCREENING</b>  <b>Prolactin level</b>            In patients with galactorrhea or decreased libido.</p>	<p><b>Health Links</b>  <b>Hyperprolactinemia</b></p> <p><b>Resources</b>  <a href="http://www.magicfoundation.org">www.magicfoundation.org</a></p> <p><b>Considerations for Further Testing and Intervention</b>            CT evaluation of sella turcica for pituitary adenoma in patients with hyperprolactinemia. Endocrine consultation for patients with hyperprolactinemia or galactorrhea.</p> <p><b>SYSTEM = Endocrine/Metabolic</b>  <b>SCORE = 1</b></p>

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# RADIATION

## POTENTIAL IMPACT TO NEUROENDOCRINE AXIS (cont)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
59 (female)	<p>≥ 40 Gy to:  <b>Cranial</b>  <b>Ear/Infratemporal</b>  <b>Nasopharyngeal</b>  <b>Orbital/Eye</b>  <b>Waldeyer's Ring</b>  <b>TBI*</b></p> <p>*TBI is included for dose calculation purposes only; this section is not applicable to patients who received TBI alone.</p>	<p><b>Hyperprolactinemia</b></p>	<p><b>Treatment Factors</b>            Higher radiation dose            Surgery or tumor in hypothalamic area</p>	<p><b>Treatment Factors</b>            Radiation dose ≥ 50 Gy</p>	<p><b>HISTORY</b>  <b>Galactorrhea</b>  <b>Menstrual history</b>            Yearly</p> <p><b>SCREENING</b>  <b>Prolactin level</b>            In patients with galactorrhea or amenorrhea.</p>	<p><b>Health Links</b>  <b>Hyperprolactinemia</b></p> <p><b>Resources</b>  <a href="http://www.magicfoundation.org">www.magicfoundation.org</a></p> <p><b>Considerations for Further Testing and Intervention</b>            CT evaluation of sella turcica for pituitary adenoma in patients with hyperprolactinemia. Endocrine consultation for patients with hyperprolactinemia or galactorrhea.</p> <p><b>SYSTEM = Endocrine/Metabolic</b>  <b>SCORE = 1</b></p>
<p>• This section is only applicable to patients who:</p> <ol style="list-style-type: none"> <li>Received radiation to any of the specified fields at ≥ 40 Gy OR</li> <li>Received a combination of radiation to any of the specified fields <b>and</b> TBI, the sum of which is ≥ 40 Gy</li> </ol> <p>• 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.</p> <p>• See “Patient-Specific Guideline Identification Tool” in Appendix I to determine specific screening guidelines by section number for individual patients.</p>						

### SECTION 59 REFERENCES

Constine LS, Woolf PD, Cann D, et al. Hypothalamic-pituitary dysfunction after radiation for brain tumors. *N Engl J Med.* Jan 14 1993;328(2):87-94.  
 Sklar CA, Constine LS. Chronic neuroendocrinological sequelae of radiation therapy. *Int J Radiat Oncol Biol Phys.* Mar 30 1995;31(5):1113-1121.

# RADIATION

## POTENTIAL IMPACT TO NEUROENDOCRINE AXIS (cont)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
60	<p>≥ 40 Gy to: Cranial Ear/Infratemporal Nasopharyngeal Orbital/Eye Waldeyer's Ring TBI*</p> <p>*TBI is included for dose calculation purposes only; this section is not applicable to patients who received TBI alone.</p>	<p><b>Central hypothyroidism</b></p> <p><b>Info Link</b> Central hypothyroidism includes thyroid-releasing and thyroid-stimulating hormone deficiency</p>	<p><b>Treatment Factors</b> Higher radiation dose</p>		<p><b>HISTORY</b></p> <p>Fatigue Weight gain Cold intolerance Constipation Dry skin Brittle hair Depressed mood Yearly, consider more frequent screening during periods of rapid growth</p> <p><b>PHYSICAL</b></p> <p>Height Weight Hair Skin Thyroid exam Yearly, consider more frequent screening during periods of rapid growth</p> <p><b>SCREENING</b></p> <p>TSH Free T4 Yearly, consider more frequent screening during periods of rapid growth</p>	<p><b>Health Links</b></p> <p>Thyroid Problems See also: Hypopituitarism</p> <p><b>Counseling</b></p> <p>Counsel at-risk females of childbearing potential to have their thyroid levels checked prior to attempting pregnancy and periodically throughout pregnancy.</p> <p><b>Considerations for Further Testing and Intervention</b></p> <p>Endocrine consultation for thyroid hormone replacement.</p> <p><b>SYSTEM = Endocrine/Metabolic</b> <b>SCORE = 1</b></p>
		<p>• This section is only applicable to patients who:</p> <ol style="list-style-type: none"> <li>Received radiation to any of the specified fields at ≥ 40 Gy OR</li> <li>Received a combination of radiation to any of the specified fields <b>and</b> TBI, the sum of which is ≥ 40 Gy</li> </ol> <p>• 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.</p> <p>• See "Patient-Specific Guideline Identification Tool" in Appendix I to determine specific screening guidelines by section number for individual patients.</p>				

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# RADIATION

## POTENTIAL IMPACT TO NEUROENDOCRINE AXIS (cont)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
61 (male)	<p>≥ 30 Gy to: Cranial Ear/Infratemporal Nasopharyngeal Orbital/Eye Waldeyer's Ring TBI*</p> <p>*TBI is included for dose calculation purposes only; this section is not applicable to patients who received TBI alone.</p>	<p><b>Gonadotropin deficiency</b></p> <p><b>Info Link</b> Gonadotropin deficiency includes LH and FSH deficiency.</p>	<p><b>Treatment Factors</b> Higher radiation dose</p>		<p><b>HISTORY</b></p> <p>Pubertal (onset, tempo) Sexual function (erections, nocturnal emissions, libido) Medication use Yearly</p> <p><b>PHYSICAL</b></p> <p>Tanner staging until sexually mature Testicular volume by Prader orchimeter Yearly</p> <p><b>SCREENING</b></p> <p>Semen analysis At request of sexually mature patient</p> <p><b>FSH</b> <b>LH</b> Testosterone (ideally morning) Baseline at age 14 <b>and</b> as clinically indicated in patients with delayed/arrested puberty and/or clinical signs and symptoms of testosterone deficiency</p>	<p><b>Health Links</b></p> <p>Male Health Issues See also: <b>Hypopituitarism</b></p> <p><b>Resources</b></p> <p>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></p> <p><b>Considerations for Further Testing and Intervention</b></p> <p>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.</p> <p><b>SYSTEM = Reproductive (male)</b> <b>SCORE = 1</b></p>
		<p>• This section is only applicable to patients who:</p> <ol style="list-style-type: none"> <li>Received radiation to any of the specified fields at ≥ 30 Gy OR</li> <li>Received a combination of radiation to any of the specified fields <b>and</b> TBI, the sum of which is ≥ 30 Gy</li> </ol> <p>• 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.</p> <p>• See "Patient-Specific Guideline Identification Tool" in Appendix I to determine specific screening guidelines by section number for individual patients.</p>				

### SECTION 61 REFERENCES

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- Quigley C, Cowell C, Jimenez M, et al. Normal or early development of puberty despite gonadal damage in children treated for acute lymphoblastic leukemia. *N Engl J Med.* Jul 20 1989;321(3):143-151.
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# RADIATION

## POTENTIAL IMPACT TO NEUROENDOCRINE AXIS (cont)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
62 (female)	<p>≥ 30 Gy to: Cranial Ear/Infratemporal Nasopharyngeal Orbital/Eye Waldeyer's Ring TBI*</p> <p>*TBI is included for dose calculation purposes only; this section is not applicable to patients who received TBI alone.</p>	<p><b>Gonadotropin deficiency</b></p> <p><b>Info Link</b> Gonadotropin deficiency includes LH and FSH deficiency.</p>	<p><b>Treatment Factors</b> Higher radiation dose</p>		<p><b>HISTORY</b></p> <p>Pubertal (onset, tempo) Menstrual/pregnancy history Sexual function (vaginal dryness, libido) Medication use Yearly</p> <p><b>PHYSICAL</b></p> <p>Tanner staging Yearly until sexually mature</p> <p><b>SCREENING</b></p> <p><b>FSH</b> <b>LH</b> <b>Estradiol</b> Baseline at age 13, <b>and</b> as clinically indicated in patients with delayed or arrested puberty, irregular menses, primary or secondary amenorrhea, or clinical signs and symptoms of estrogen deficiency</p>	<p><b>Health Links</b></p> <p><b>Female Health Issues</b> See also: <b>Hypopituitarism</b></p> <p><b>Resources</b> 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></p> <p><b>Considerations for Further Testing and Intervention</b> 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.</p> <p><b>SYSTEM = Reproductive (female)</b> <b>SCORE = 1</b></p>
<p>• This section is only applicable to patients who:</p> <ol style="list-style-type: none"> <li>Received radiation to any of the specified fields at ≥ 30 Gy OR</li> <li>Received a combination of radiation to any of the specified fields <b>and</b> TBI, the sum of which is ≥ 30 Gy</li> </ol> <p>• 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.</p> <p>• See "Patient-Specific Guideline Identification Tool" in Appendix I to determine specific screening guidelines by section number for individual patients.</p>						

### SECTION 62 REFERENCES

- Darzy KH. Radiation-induced hypopituitarism after cancer therapy: who, how and when to test. *Nat Clin Pract Endocrinol Metab.* Feb 2009 5(2):88-99.
- Chow EJ, Friedman DL, Yasui Y, et al. Timing of menarche among survivors of childhood acute lymphoblastic leukemia: a report from the Childhood Cancer Survivor Study. *Pediatr Blood Cancer.* Apr 2008;50(4):854-858.
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## POTENTIAL IMPACT TO NEUROENDOCRINE AXIS (cont)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
63	<p>≥ 30 Gy to: Cranial Ear/Infratemporal Nasopharyngeal Orbital/Eye Waldeyer's Ring TBI*</p> <p>*TBI is included for dose calculation purposes only; this section is not applicable to patients who received TBI alone.</p>	<p>Central adrenal insufficiency</p>	<p><b>Treatment Factors</b> Higher radiation dose Surgery or tumor in the suprasellar region</p>	<p><b>Treatment Factors</b> Prior development of another hypothalamic-pituitary endocrinopathy</p>	<p><b>HISTORY</b> Failure to thrive Anorexia Dehydration Hypoglycemia Lethargy Unexplained hypotension Yearly</p> <p><b>SCREENING</b> Refer for yearly endocrinology evaluation if dose to hypothalamic-pituitary axis ≥30 Gy</p>	<p><b>Health Links</b> Central Adrenal Insufficiency See also: Hypopituitarism</p> <p><b>Resources</b> <a href="http://www.magicfoundation.org">www.magicfoundation.org</a></p> <p><b>Counseling</b> Counsel regarding corticosteroid replacement therapy and stress dosing. Counsel regarding Medical Alert bracelet.</p> <p><b>SYSTEM = Endocrine/Metabolic</b> <b>SCORE = 1</b></p>

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# RADIATION

## POTENTIAL IMPACT TO EYE

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
64	<b>Cranial Orbital/Eye Total Body Irradiation (TBI)</b>  <b>Info Link</b> <ul style="list-style-type: none"> <li>• Radiation-related ocular complications other than cataracts are generally associated only with orbital/eye radiation or higher dose cranial radiation.</li> <li>• 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.</li> </ul>	Cataracts	<b>Treatment Factors</b> Radiation dose $\geq 10$ Gy TBI $\geq 2$ Gy in single fraction or $\geq 5$ Gy fractionated Radiation combined with: <ul style="list-style-type: none"> <li>- Corticosteroids</li> <li>- Busulfan</li> <li>- Longer interval since treatment</li> </ul>	<b>Treatment Factors</b> 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	<b>HISTORY</b> <b>Visual changes (decreased acuity, halos, diplopia)</b> Yearly  <b>PHYSICAL</b> <b>Eye exam (visual acuity, fundoscopic exam for lens opacity)</b> Yearly  <b>SCREENING</b> <b>Evaluation by ophthalmologist</b> Yearly for patients with ocular tumors [regardless of radiation dose] and for those who received TBI or $\geq 30$ Gy cranial/orbital/eye radiation Every 3 years for patients without ocular tumors who received $< 30$ Gy	<b>Health Links</b> <b>Cataracts</b>  <b>Considerations for Further Testing and Intervention</b> Ongoing ophthalmology follow-up for identified problems. Refer patients with visual deficits to school liaison in community or cancer center (psychologist, social worker, school counselor) to facilitate acquisition of educational resources  <div style="border: 1px solid black; padding: 5px; text-align: center;"> <b>SYSTEM = Ocular</b>  <b>SCORE = 1</b> </div>
			<div style="border: 1px solid black; padding: 5px;">           • See "Patient-Specific Guideline Identification Tool" in Appendix I to determine specific screening guidelines by section number for individual patients.         </div>			

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# RADIATION

## POTENTIAL IMPACT TO EYE (cont)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
65	<p>≥ 30 Gy to: <b>Cranial Orbital/Eye TBI*</b></p> <p>*TBI is included for dose calculation purposes only; this section is not applicable to patients who received TBI alone.</p> <p><b>Info Link</b></p> <ul style="list-style-type: none"> <li>• Radiation-related ocular complications other than cataracts are generally associated only with orbital/eye radiation or higher dose cranial radiation.</li> <li>• 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.</li> </ul>	<p><b>Ocular toxicity</b></p> <p>Orbital hypoplasia Lacrimal duct atrophy Xerophthalmia (keratoconjunctivitis sicca) Keratitis Telangiectasias Retinopathy Optic chiasm neuropathy Enophthalmos Chronic painful eye Maculopathy Papillopathy Glaucoma</p> <p><b>Info Link</b></p> <p>Reduced visual acuity may be associated with cataracts, retinal damage, and optic nerve damage.</p>	<p><b>Treatment Factors</b></p> <p>Higher radiation dose Higher daily fraction dose Radiomimetic chemotherapy (e.g., doxorubicin, dactinomycin) [problems related to tearing]</p>	<p><b>Host Factors</b></p> <p>Chronic GVHD (xerophthalmia only)</p> <p><b>Treatment Factors</b></p> <p>Total dose ≥ 50 Gy Fraction dose ≥ 2 Gy</p>	<p><b>HISTORY</b></p> <p><b>Visual changes (decreased acuity, halos, diplopia)</b></p> <p><b>Dry eye</b> <b>Persistent eye irritation</b> <b>Excessive tearing</b> <b>Light sensitivity</b> <b>Poor night vision</b> <b>Painful eye</b> Yearly</p> <p><b>PHYSICAL</b></p> <p><b>Visual acuity</b> <b>Funduscopy exam</b> Yearly</p> <p><b>SCREENING</b></p> <p><b>Evaluation by ophthalmologist</b> Yearly</p>	<p><b>Health Links</b></p> <p><b>Eye Health</b></p> <p><b>Resources</b></p> <p>FACES—The National Craniofacial Association website: <a href="http://www.faces-cranio.org/">www.faces-cranio.org/</a></p> <p><b>Considerations for Further Testing and Intervention</b></p> <p>Refer patients with visual deficits to school liaison in community or cancer center (psychologist, social worker, school counselor) to facilitate acquisition of educational resources.</p> <div style="border: 1px solid black; padding: 5px; text-align: center;"> <p><b>SYSTEM = Ocular</b></p> <p><b>SCORE = 1</b></p> </div>

• 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.

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# RADIATION

# POTENTIAL IMPACT TO EAR

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
66	<p>≥ 30 Gy to: <b>Cranial Ear/Infratemporal Nasopharyngeal Waldeyer's Ring TBI*</b></p> <p>*TBI is included for dose calculation purposes only; this section is not applicable to patients who received TBI alone.</p>	<p><b>Ototoxicity</b>                      Tympanosclerosis                      Otosclerosis                      Eustachian tube dysfunction                      Conductive hearing loss</p>	<p><b>Host Factors</b>                      Younger age at treatment</p> <p><b>Treatment Factors</b>                      Higher radiation dose</p> <p><b>Medical Conditions</b>                      Chronic otitis                      Chronic cerumen impaction</p>	<p><b>Treatment Factors</b>                      Dose ≥ 50 Gy</p>	<p><b>HISTORY</b>                      Hearing difficulties (with/without background noise)                      Tinnitus                      Vertigo                      Yearly</p> <p><b>PHYSICAL</b>                      Otoscopic exam                      Yearly</p> <p><b>SCREENING</b>  <b>Complete audiological evaluation</b>                      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]</p> <p><b>Info Link</b>                      • A “complete audiological evaluation” includes pure tone air and bone conduction, speech audiometry, and tympanometry for both ears.                      • Frequency-specific auditory brainstem response (ABR) can be performed if the above is inconclusive.</p>	<p><b>Health Links</b>                      Hearing Loss                      Educational Issues</p> <p><b>Considerations for Further Testing and Intervention</b>                      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.</p> <p><b>SYSTEM = Auditory</b>  <b>SCORE = 1</b></p>

• This section is only applicable to patients who:

- Received radiation to any of the specified fields at ≥ 30 Gy  
OR
- 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

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Hua C, Bass JK, Khan R et al. Hearing loss after radiotherapy for pediatric brain tumors: effect of cochlear dose. *Int J Biol Phys.* 2008;Nov 1 72(3):892-899.

Huang E, Teh BS, Strother DR, et al. Intensity-modulated radiation therapy for pediatric medulloblastoma: early report on the reduction of ototoxicity. *Int J Radiat Oncol Biol Phys.* Mar 1 2002;52(3):599-605.

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# RADIATION

## POTENTIAL IMPACT TO EAR (cont)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
67	<p>≥ 30 Gy to: <b>Cranial Ear/Infratemporal Nasopharyngeal Waldeyer's Ring TBI*</b></p> <p>*TBI is included for dose calculation purposes only; this section is not applicable to patients who received TBI alone.</p>	<p><b>Ototoxicity</b> Sensorineural hearing loss Tinnitus</p>	<p><b>Host Factors</b> Younger age at treatment CNS tumor</p> <p><b>Treatment Factors</b> Higher radiation dose Conventional (non-conformal) radiation</p> <p><b>Medical Conditions</b> CSF shunting</p>	<p><b>Treatment Factors</b> Radiation administered prior to platinum chemotherapy Combined with other ototoxic agents such as: - Cisplatin - Carboplatin in myeloablative doses - Aminoglycosides</p>	<p><b>HISTORY</b> <b>Hearing difficulties (with/without background noise)</b> <b>Tinnitus</b> <b>Vertigo</b> Yearly</p> <p><b>PHYSICAL</b> <b>Otoscopic exam</b> Yearly</p> <p><b>SCREENING</b> <b>Complete audiological evaluation</b> 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]</p> <p><b>Info Link</b> • A “complete audiological evaluation” includes pure tone air and bone conduction, speech audiometry, and tympanometry for both ears. • Frequency-specific auditory brainstem response (ABR) can be performed if the above is inconclusive.</p>	<p><b>Health Links</b> <b>Hearing Loss</b> <b>Educational Issues</b></p> <p><b>Considerations for Further Testing and Intervention</b> 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.</p> <p><b>SYSTEM = Auditory</b> <b>SCORE = 1</b></p>

• This section is only applicable to patients who:

- Received radiation to any of the specified fields at ≥ 30 Gy  
OR
- 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

Freilich RJ, Kraus DH, Budnick AS, Bayer LA, Finlay JL. Hearing loss in children with brain tumors treated with cisplatin and carboplatin-based high-dose chemotherapy with autologous bone marrow rescue. *Med Pediatr Oncol*. Feb 1996;26(2):95-100.

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Huang E, Teh BS, Strother DR, et al. Intensity-modulated radiation therapy for pediatric medulloblastoma: early report on the reduction of ototoxicity. *Int J Radiat Oncol Biol Phys*. Mar 1 2002;52(3):599-605.

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Schell MJ, McHaney VA, Green AA, et al. Hearing loss in children and young adults receiving cisplatin with or without prior cranial irradiation. *J Clin Oncol*. Jun 19897(6):754-760.



# RADIATION

# POTENTIAL IMPACT TO ORAL CAVITY

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
68	<b>Cranial</b> <b>Nasopharyngeal</b> <b>Oropharyngeal</b> <b>Waldeyer's Ring</b> <b>Cervical (neck)</b> <b>Supraclavicular</b> <b>Spine (cervical)</b> <b>Spine (whole)</b> <b>Subtotal Lymphoid Irradiation (STLI)</b> <b>Extended Mantle</b> <b>Mantle</b> <b>Mini-Mantle</b> <b>Total Lymphoid Irradiation (TLI)</b>	<b>Xerostomia</b> <b>Salivary gland dysfunction</b>	<b>Treatment Factors</b> Head and neck radiation involving the parotid gland Higher radiation doses Radiomimetic chemotherapy (e.g., doxorubicin, dactinomycin)	<b>Treatment Factors</b> Salivary gland dose $\geq 30$ Gy  <b>Medical Conditions</b> Chronic GVHD	<b>HISTORY</b> <b>Xerostomia</b> Yearly  <b>PHYSICAL</b> <b>Oral exam</b> Yearly  <b>SCREENING</b> <b>Dental exam and cleaning</b> Every 6 months	<b>Health Links</b> <b>Dental Health</b>  <b>Considerations for Further Testing and Intervention</b> Supportive care with saliva substitutes, moistening agents, and sialogogues (pilocarpine) Regular dental care including fluoride applications  <div style="border: 1px solid black; padding: 5px; text-align: center;"> <b>SYSTEM = Dental</b>  <b>SCORE = 1</b> </div>
<div style="border: 1px solid black; padding: 5px; width: fit-content; margin: 0 auto;">                     • See "Patient-Specific Guideline Identification Tool" in Appendix I to determine specific screening guidelines by section number for individual patients.                 </div>						

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# RADIATION

# POTENTIAL IMPACT TO ORAL CAVITY (cont)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
69	<b>Cranial</b> <b>Nasopharyngeal</b> <b>Oropharyngeal</b> <b>Waldeyer's Ring</b> <b>Cervical (neck)</b> <b>Supraclavicular</b> <b>Spine (cervical)</b> <b>Spine (whole)</b> <b>Subtotal Lymphoid Irradiation (STLI)</b> <b>Extended Mantle</b> <b>Mantle</b> <b>Mini-Mantle</b> <b>Total Body Irradiation (TBI)</b> <b>Total Lymphoid Irradiation (TLI)</b>	<b>Dental abnormalities</b> Tooth/root agenesis Microdontia Root thinning/shortening Enamel dysplasia Periodontal disease Dental caries Malocclusion Temporomandibular joint dysfunction	<b>Host Factors</b> Younger age at treatment Gorlin's syndrome (nevoid basal cell carcinoma syndrome) <b>Treatment Factors</b> Higher radiation dose	<b>Host Factors</b> Age < 5 years at time of treatment <b>Treatment Factors</b> Dose ≥ 10 Gy	<b>PHYSICAL</b> <b>Oral exam</b> Yearly <b>SCREENING</b> <b>Dental exam and cleaning</b> Every 6 months	<b>Health Links</b> <b>Dental Health</b> <b>Considerations for Further Testing and Intervention</b> Regular dental care including fluoride applications. Consultation with orthodontist experienced in management of irradiated childhood cancer survivors. Baseline panorex prior to dental procedures to evaluate root development. <div style="border: 1px solid black; padding: 5px; text-align: center;">                         SYSTEM = Dental                          SCORE = 1                     </div>
• See "Patient-Specific Guideline Identification Tool" in Appendix I to determine specific screening guidelines by section number for individual patients.						

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# RADIATION

# POTENTIAL IMPACT TO ORAL CAVITY (cont)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
70	<p>≥ 40 Gy to:  <b>Cranial</b>  <b>Nasopharyngeal</b>  <b>Oropharyngeal</b>  <b>Waldeyer's Ring</b>  <b>Cervical (neck)</b>  <b>Supraclavicular</b>  <b>Spine (cervical)</b>  <b>Spine (whole)</b>  <b>Subtotal Lymphoid Irradiation (STLI)</b>  <b>Extended Mantle Mantle</b>  <b>Mini-Mantle</b>  <b>Total Lymphoid Irradiation (TLI)</b>  <b>TBI*</b></p> <p>*TBI is included for dose calculation purposes only; this section is not applicable to patients who received TBI alone.</p>	<p><b>Osteoradionecrosis</b></p>	<p><b>Treatment Factors</b>            Radiation dose to bone ≥ 45 Gy</p>	<p><b>Treatment Factors</b>            Dose ≥ 50 Gy</p>	<p><b>HISTORY</b>  <b>Impaired or delayed healing following dental work</b>  <b>Persistent jaw pain or swelling</b>  <b>Trismus</b>            As clinically indicated</p> <p><b>PHYSICAL</b>  <b>Impaired wound healing</b>  <b>Jaw swelling</b>  <b>Trismus</b>            As clinically indicated</p>	<p><b>Health Links</b>  <b>Osteoradionecrosis</b></p> <p><b>Considerations for Further Testing and Intervention</b>            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.</p> <p><b>SYSTEM = Dental</b>  <b>SCORE = 1</b></p>

• This section is only applicable to patients who:

- Received radiation to any of the specified fields at ≥ 40 Gy  
OR
- 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.

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# RADIATION

## POTENTIAL IMPACT TO NECK/THYROID

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
71	<b>Cranial</b> <b>Nasopharyngeal</b> <b>Oropharyngeal</b> <b>Waldeyer's Ring</b> <b>Cervical (neck)</b> <b>Supraclavicular</b> <b>Spine (cervical)</b> <b>Spine (whole)</b> <b>Subtotal Lymphoid Irradiation (STLI)</b> <b>Extended Mantle</b> <b>Mantle</b> <b>Mediastinal</b> <b>Mini-Mantle</b> <b>Total Body Irradiation (TBI)</b> <b>Total Lymphoid Irradiation (TLI)</b>	<b>Thyroid nodules</b>	<b>Host Factors</b> Younger age at treatment Female sex  <b>Treatment Factors</b> Higher radiation dose Thyroid gland directly in radiation field TBI	<b>Treatment Factors</b> Radiation dose $\geq$ 25 Gy	<b>PHYSICAL</b>  <b>Thyroid exam</b> Yearly	<b>Health Links</b> <b>Thyroid Problems</b>  <b>Considerations for Further Testing and Intervention</b> Ultrasound and FNA for evaluation of palpable nodule(s). Endocrine and/or surgical consultation for diagnostic biopsy or thyroidectomy.
<div style="border: 1px solid black; padding: 5px; width: fit-content; margin: 0 auto;">                     • See "Patient-Specific Guideline Identification Tool" in Appendix I to determine specific screening guidelines by section number for individual patients.                 </div>						
<div style="border: 1px solid black; padding: 10px; width: fit-content; margin: 0 auto;"> <b>SYSTEM = SMN</b>  <b>SCORE = 1</b> </div>						

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# RADIATION

## POTENTIAL IMPACT TO NECK/THYROID (cont)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
72	<b>Cranial</b> <b>Nasopharyngeal</b> <b>Oropharyngeal</b> <b>Waldeyer's Ring</b> <b>Cervical (neck)</b> <b>Supraclavicular</b> <b>Spine (cervical)</b> <b>Spine (whole)</b> <b>Subtotal Lymphoid Irradiation (STLI)</b> <b>Extended Mantle Mantle</b> <b>Mediastinal Mini-Mantle</b> <b>Total Body Irradiation (TBI)</b> <b>Total Lymphoid Irradiation (TLI)</b>	<b>Thyroid cancer</b>	<b>Host Factors</b> Younger age at treatment Female sex  <b>Treatment Factors</b> > 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		<b>PHYSICAL</b>  <b>Thyroid exam</b> Yearly	<b>Health Links</b> <b>Thyroid Problems</b>  <b>Considerations for Further Testing and Intervention</b> 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.
		• See "Patient-Specific Guideline Identification Tool" in Appendix I to determine specific screening guidelines by section number for individual patients.				
<div style="border: 1px solid black; padding: 5px; display: inline-block;"> <b>SYSTEM = SMN</b>   <b>SCORE = 1</b> </div>						

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# RADIATION

## POTENTIAL IMPACT TO NECK/THYROID (cont)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
73	<b>Cranial</b> <b>Nasopharyngeal</b> <b>Oropharyngeal</b> <b>Waldeyer's Ring</b> <b>Cervical (neck)</b> <b>Supraclavicular</b> <b>Spine (cervical)</b> <b>Spine (whole)</b> <b>Subtotal Lymphoid Irradiation (STLI)</b> <b>Extended Mantle</b> <b>Mantle</b> <b>Mediastinal</b> <b>Mini-Mantle</b> <b>Total Body Irradiation (TBI)</b> <b>Total Lymphoid Irradiation (TLI)</b>	<b>Hypothyroidism</b>	<b>Host Factors</b> Female sex  <b>Treatment Factors</b> Radiation dose $\geq$ 10 Gy Thyroid gland directly in radiation field TBI	<b>Treatment Factors</b> Radiation dose $\geq$ 20 Gy	<b>HISTORY</b> <b>Fatigue</b> <b>Weight gain</b> <b>Cold intolerance</b> <b>Constipation</b> <b>Dry skin</b> <b>Brittle hair</b> <b>Depressed mood</b> Yearly Consider more frequent screening during periods of rapid growth  <b>PHYSICAL</b> <b>Height</b> <b>Weight</b> <b>Hair and skin</b> <b>Thyroid exam</b> Yearly Consider more frequent screening during periods of rapid growth  <b>SCREENING</b> <b>TSH</b> <b>Free T4</b> Yearly Consider more frequent screening during periods of rapid growth	<b>Health Links</b> <b>Thyroid Problems</b>  <b>Counseling</b> Counsel at-risk females of childbearing potential to have their thyroid levels checked prior to attempting pregnancy and periodically throughout pregnancy.  <b>Considerations for Further Testing and Intervention</b> Endocrine consultation for medical management.  <div style="border: 1px solid black; padding: 5px; text-align: center;"> <b>SYSTEM = Endocrine/Metabolic</b>  <b>SCORE = 1</b> </div>

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

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# RADIATION

## POTENTIAL IMPACT TO NECK/THYROID (cont)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
74	<p>≥ 40 Gy to: Oropharyngeal Waldeyer's Ring Cervical (neck) Supraclavicular Spine (cervical) Spine (whole) Subtotal Lymphoid Irradiation (STLI) Extended Mantle Mantle Mediastinal Mini-Mantle Total Lymphoid Irradiation (TLI) TBI*</p> <p>*TBI is included for dose calculation purposes only; this section is not applicable to patients who received TBI alone.</p>	Hyperthyroidism	Treatment Factors Higher radiation dose		<p><b>HISTORY</b></p> <p>Heat intolerance Tachycardia Palpitations Weight loss Emotional lability Muscular weakness Hyperphagia Yearly</p> <p><b>PHYSICAL</b></p> <p>Eyes Skin Thyroid Cardiac Neurologic Yearly</p> <p><b>SCREENING</b></p> <p>TSH Free T4 Yearly</p>	<p><b>Health Links</b></p> <p>Thyroid Problems</p> <p><b>Considerations for Further Testing and Intervention</b></p> <p>Endocrine consultation for medical management.</p> <p><b>SYSTEM = Endocrine/Metabolic</b></p> <p><b>SCORE = 1</b></p>
		<p>• This section is only applicable to patients who:</p> <ol style="list-style-type: none"> <li>Received radiation to any of the specified fields at ≥ 40 Gy OR</li> <li>Received a combination of radiation to any of the specified fields <i>plus</i> relevant spinal radiation <i>and/or</i> TBI, the sum of which is ≥ 40 Gy</li> </ol> <p>• 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.</p> <p>• See "Patient-Specific Guideline Identification Tool" in Appendix I to determine specific screening guidelines by section number for individual patients.</p>				

### SECTION 74 REFERENCES

- Constine LS, Donaldson SS, McDougall IR, Cox RS, Link MP, Kaplan HS. Thyroid dysfunction after radiotherapy in children with Hodgkin's disease. *Cancer*. Feb 15 1984;53(4):878-883.
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# RADIATION

## POTENTIAL IMPACT TO NECK/THYROID (cont)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
75	<p>≥ 40 Gy to:  <b>Cranial</b>  <b>Nasopharyngeal</b>  <b>Oropharyngeal</b>  <b>Waldeyer's Ring</b>  <b>Cervical (neck)</b>  <b>Supraclavicular</b>  <b>Spine (cervical)</b>  <b>Spine (whole)</b>  <b>Subtotal Lymphoid Irradiation (STLI)</b>  <b>Chest (thorax)</b>  <b>Extended Mantle</b>  <b>Mantle</b>  <b>Mediastinal</b>  <b>Mini-Mantle</b>  <b>Whole lung</b>  <b>Total Lymphoid Irradiation (TLI)</b>  <b>TBI*</b></p>	<p><b>Carotid artery disease</b></p>	<p><b>Medical Conditions</b>  Hypertension  Diabetes mellitus  Hypercholesterolemia</p>		<p><b>HISTORY</b>  <b>Memory impairment</b>  <b>Yearly</b></p> <p><b>PHYSICAL</b>  <b>Diminished carotid pulses</b>  <b>Carotid bruits</b>  <b>Abnormal neurologic exam (compromise of blood flow to brain)</b>  <b>Yearly</b></p>	<p><b>Considerations for Further Testing and Intervention</b>  Doppler ultrasound of carotid vessels as clinically indicated. MRI with diffusion-weighted imaging with MR angiography and cardiovascular surgery consultation as clinically indicated. Consider color Doppler 10 years after completion of radiation therapy to the neck as a baseline refer to cardiologist if abnormal.</p> <p><b>SYSTEM = Cardiovascular</b>  <b>SCORE = 2A</b></p>
	<p>*TBI is included for dose calculation purposes only; this section is not applicable to patients who received TBI alone.</p>	<p>• This section is only applicable to patients who:</p> <ol style="list-style-type: none"> <li>Received radiation to any of the specified fields at ≥ 40 Gy OR</li> <li>Received a combination of radiation to any of the specified fields <b>plus</b> relevant spinal radiation <b>and/or</b> TBI, the sum of which is ≥ 40 Gy</li> </ol> <p>• 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.</p> <p>• See “Patient-Specific Guideline Identification Tool” in Appendix I to determine specific screening guidelines by section number for individual patients.</p>				

### SECTION 75 REFERENCES

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# RADIATION

## POTENTIAL IMPACT TO NECK/THYROID (cont)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
76	<p>≥ 40 Gy to:  <b>Cervical (neck)</b>  <b>Supraclavicular Spine (cervical)</b>  <b>Spine (whole)</b>  <b>Subtotal Lymphoid Irradiation (STLI)</b>  <b>Chest (thorax)</b>  <b>Extended Mantle Mantle</b>  <b>Mediastinal Mini-Mantle</b>  <b>Whole lung</b>  <b>Total Lymphoid Irradiation (TLI)</b>  <b>TBI*</b></p>	<p>Subclavian artery disease</p>			<p><b>PHYSICAL</b>  <b>Diminished brachial and radial pulses</b>  <b>Pallor of upper extremities</b>  <b>Coolness of skin</b>  <b>Unequal blood pressure</b>                      Yearly</p>	<p><b>Considerations for Further Testing and Intervention</b>                      Doppler ultrasound of subclavian vessels as clinically indicated. MRI with diffusion-weighted imaging with MR angiography and cardiovascular surgery consultation as clinically indicated. Consider color Doppler 10 years after completion of radiation therapy to the neck as a baseline refer to cardiologist if abnormal.</p>
	<p>*TBI is included for dose calculation purposes only; this section is not applicable to patients who received TBI alone.</p>	<div style="border: 1px solid black; padding: 10px;"> <p>• This section is only applicable to patients who:</p> <ol style="list-style-type: none"> <li>Received radiation to any of the specified fields at ≥ 40 Gy OR</li> <li>Received a combination of radiation to any of the specified fields <b>plus</b> relevant spinal radiation <b>and/or</b> TBI, the sum of which is ≥ 40 Gy</li> </ol> <p>• 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.</p> <p>• See “Patient-Specific Guideline Identification Tool” in Appendix I to determine specific screening guidelines by section number for individual patients.</p> </div>				<div style="border: 1px solid black; background-color: #006699; color: white; padding: 5px; text-align: center;"> <p><b>SYSTEM = Cardiovascular</b> <b>SCORE = 2A</b></p> </div>

### SECTION 76 REFERENCES

Bowers DC, McNeil DE, Liu Y, et al. Stroke as a late treatment effect of Hodgkin's disease: a report from the Childhood Cancer Survivor Study. *J Clin Oncol.* Sep 20 2005;23(27):6508-6515.  
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# RADIATION

# POTENTIAL IMPACT TO BREAST

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
77 (female)	<p>≥ 10 Gy to:  <b>Subtotal Lymphoid Irradiation (STLI)</b>  <b>Axilla</b>  <b>Chest (thorax)</b>  <b>Extended Mantle</b>  <b>Mantle</b>  <b>Mediastinal</b>  <b>Mini-Mantle</b>  <b>Whole lung</b>  <b>Total Body Irradiation (TBI)*</b>  <b>Total Lymphoid Irradiation (TLI)</b></p> <p><b>Info Link</b>                      • <i>*Important:</i> 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).                      • <i>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.</i>                      • 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.</p>	Breast cancer	<p><b>Host Factors</b>                      Family history of breast cancer</p> <p><b>Treatment Factors</b>                      Higher radiation dose                      Longer time since radiation (&gt; 5 years)                      Decreased risk in women treated with alkylating agents</p>	<p><b>Host Factors</b>                      BRCA1, BRCA2, ATM mutation</p>	<p><b>PHYSICAL</b>  <b>Breast exam</b>                      Yearly, beginning at puberty until age 25, then every 6 months</p> <p><b>SCREENING</b>                      ≥ 20 Gy                      Mammogram                      Yearly, beginning 8 years after radiation or at age 25, whichever occurs last.</p> <p><b>Breast MRI</b>                      Yearly, as an adjunct to mammography beginning 8 years after radiation or at age 25, whichever occurs last.</p> <p><b>10–19 Gy or TBI alone</b>                      Clinician to discuss benefits and risks/harms of screening with patient. If decision is made to screen, then follow screening recommendations for ≥ 20 Gy.</p> <p><b>Info Link</b>                      • Mammography is currently limited in its ability to evaluate the premenopausal breast.                      • MRI is now recommended as an adjunct to mammography in women treated with chest radiation for childhood cancer similar to screening of other populations at high risk for breast cancer (e.g., premenopausal known or likely carriers of gene mutation of known penetrance).                      • The upper age limit at which both modalities should be used for breast cancer surveillance has not been established.</p>	<p><b>Health Links</b>  <b>Breast Cancer</b></p> <p><b>Counseling</b>                      Teach breast self-exam and counsel to perform monthly beginning at puberty.</p> <p><b>Considerations for Further Testing and Intervention</b>                      Surgical consultation for diagnostic procedure in patients with breast mass or suspicious radiographic finding. Decisions regarding the use of HRT should be based on current literature and should take into consideration the risk/benefit ratio for individual patients.</p> <div style="border: 1px solid black; padding: 5px; text-align: center;"> <p><b>SYSTEM = SMN</b>  <b>SCORE = 1</b></p> </div>

• This section is only applicable to patients who:

- 1) Received radiation to any of the specified fields at ≥ 10 Gy  
OR
- 2) Received a combination of radiation to any of the specified fields, the sum of which is ≥ 10 Gy  
OR
- 3) Received TBI alone

• 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.

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Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
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# RADIATION

## POTENTIAL IMPACT TO BREAST (cont)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
78 (female)	<b>Subtotal Lymphoid Irradiation (STLI)</b> <b>Axilla</b> <b>Chest (thorax)</b> <b>Extended Mantle</b> <b>Mantle</b> <b>Mediastinal</b> <b>Mini-Mantle</b> <b>Whole lung</b> <b>Total Body Irradiation (TBI)</b> <b>Total Lymphoid Irradiation (TLI)</b>	<b>Breast tissue hypoplasia</b>	<b>Host Factors</b> Prepubertal at time of breast irradiation <b>Treatment Factors</b> Radiation dose $\geq 10$ Gy to prepubertal breast bud may cause failure of development (hypoplasia)	<b>Treatment Factors</b> $\geq 20$ Gy to prepubertal breast bud may ablate development	<b>PHYSICAL</b> <b>Breast exam</b> Yearly	<b>Considerations for Further Testing and Intervention</b> Surgical consultation for breast reconstruction after completion of growth.  <div style="border: 1px solid black; padding: 5px; width: fit-content; margin: 0 auto;">                         SYSTEM = Reproductive (female)                          SCORE = 1                     </div>
<div style="border: 1px solid black; padding: 5px; width: fit-content; margin: 0 auto;">                         • See "Patient-Specific Guideline Identification Tool" in Appendix I to determine specific screening guidelines by section number for individual patients.                     </div>						

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# RADIATION

# POTENTIAL IMPACT TO LUNGS

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
79	<b>Subtotal Lymphoid Irradiation (STLI)</b> <b>Axilla</b> <b>Chest (thorax)</b> <b>Extended Mantle</b> <b>Mantle</b> <b>Mediastinal</b> <b>Mini-Mantle</b> <b>Whole lung</b> <b>Total Body Irradiation (TBI)</b> <b>Total Lymphoid Irradiation (TLI)</b>	<b>Pulmonary toxicity</b> Pulmonary fibrosis Interstitial pneumonitis Restrictive lung disease Obstructive lung disease	<b>Host Factors</b> Younger age at irradiation  <b>Treatment Factors</b> Radiation dose > 10 Gy Radiation combined with: - Bleomycin - Busulfan - Carmustine (BCNU) - Lomustine (CCNU) - Radiomimetic chemotherapy (e.g., doxorubicin, dactinomycin)  Chest radiation combined with TBI  <b>Medical Conditions</b> Atopic history  <b>Health Behaviors</b> Smoking Inhaled illicit drug use	<b>Treatment Factors</b> Radiation dose ≥ 15 Gy TBI ≥ 6 Gy in single fraction or ≥ 12 Gy fractionated	<b>HISTORY</b> <b>Cough</b> <b>SOB</b> <b>DOE</b> <b>Wheezing</b> Yearly  <b>PHYSICAL</b> <b>Pulmonary exam</b> Yearly  <b>SCREENING</b> <b>PFTs (including DLCO and spirometry)</b> Baseline at entry into long-term follow-up, repeat as clinically indicated in patients with abnormal results or progressive pulmonary dysfunction	<b>Health Links</b> <b>Pulmonary Health</b>  <b>Resources</b> Extensive information regarding smoking cessation is available for patients on the NCI's website: <a href="http://www.smokefree.gov">www.smokefree.gov</a>  <b>Counseling</b> 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.  <b>Considerations for Further Testing and Intervention</b> In patients with abnormal PFTs, consider repeat evaluation prior to general anesthesia. Pulmonary consultation for patients with symptomatic pulmonary dysfunction. Influenza and Pneumococcal vaccinations.
<div style="border: 1px solid black; padding: 5px; margin: 10px 0;">                     • See "Patient-Specific Guideline Identification Tool" in Appendix I to determine specific screening guidelines by section number for individual patients.                 </div>						
<div style="border: 1px solid black; padding: 5px; display: inline-block;"> <b>SYSTEM = Pulmonary</b>  <b>SCORE = 1</b> </div>						

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# RADIATION

# POTENTIAL IMPACT TO HEART

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations																											
80 (male)	<b>Chest (thorax)</b> <b>Extended Mantle</b> <b>Mantle</b> <b>Mediastinal</b> <b>Whole lung</b> <b>Hepatic</b> <b>Inverted Y</b> <b>Left Flank/Hemiabdomen</b> <b>Left upper quadrant</b> <b>Paraortic</b> <b>Renal</b> <b>Right Flank/Hemiabdomen</b> <b>Right Upper quadrant</b> <b>Spleen (entire)</b> <b>Spleen (partial)</b> <b>Whole abdomen</b> <b>Spine (thoracic)</b> <b>Spine (whole)</b> <b>Subtotal Lymphoid Irradiation (STLI)</b> <b>Total Body Irradiation (TBI)</b> <b>Total Lymphoid Irradiation (TLI)</b>	<b>Cardiac toxicity</b> Congestive heart failure Cardiomyopathy Pericarditis Pericardial fibrosis Valvular disease Myocardial infarction Arrhythmia Atherosclerotic heart disease	<b>Host Factors</b> Younger age at irradiation Family history of dyslipidemia Coronary artery disease  <b>Treatment Factors</b> Radiation dose $\geq 20$ Gy to chest TBI Combined with radiomimetic chemotherapy (e.g., doxorubicin, dactinomycin) Combined with other cardiotoxic chemotherapy: - Anthracyclines - Cyclophosphamide conditioning for HCT - Amsacrine  <b>Medical Conditions</b> Hypertension Obesity Dyslipidemia Diabetes mellitus Congenital heart disease Febrile illness  <b>Health Behaviors</b> Smoking Isometric exercise Drug use (e.g., cocaine, diet pills, ephedra)	<b>Host Factors</b> Black/of African descent Younger than age 5 years at treatment  <b>Treatment Factors</b> Anteriorly-weighted radiation fields Lack of subcarinal shielding Doses $\geq 30$ Gy in patients who have received anthracyclines Doses $\geq 40$ Gy in patients who have not received anthracyclines Longer time since treatment	<b>HISTORY</b> <b>SOB</b> <b>DOE</b> <b>Orthopnea</b> <b>Chest pain</b> <b>Palpitations</b> <b>If under 25 yrs: abdominal symptoms (nausea, vomiting)</b> Yearly  <b>Info Link</b> • 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.  <b>PHYSICAL</b> <b>Cardiac murmur</b> <b>S3, S4</b> <b>Increased P2 sound</b> <b>Pericardial rub</b> <b>Rales</b> <b>Wheezes</b> <b>Jugular venous distension</b> <b>Peripheral edema</b> Yearly  <b>SCREENING</b> <b>Fasting blood glucose OR HbA1c and lipid profile</b> Every 2 years If abnormal, refer for ongoing management <b>EKG (include evaluation of QTc interval)</b> Baseline at entry into long-term follow-up, repeat as clinically indicated <b>ECHO (or comparable imaging to evaluate cardiac anatomy and function)</b> Baseline at entry into long-term follow-up, then periodically based on age at treatment, radiation dose, and cumulative anthracycline dose.	<b>Health Links</b> <b>Heart Health</b> <b>Cardiovascular Risk Factors</b> <b>Diet and Physical Activity</b> <b>Dental Health</b>  <b>Counseling</b> 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) 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.  <b>Considerations for Further Testing and Intervention</b> 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 $\geq 40$ Gy chest radiation alone or $\geq 30$ 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.																											
		<b>RECOMMENDED FREQUENCY OF ECHOCARDIOGRAM</b> <table border="1"> <thead> <tr> <th>Age at Treatment†</th> <th>Radiation Dose</th> <th>Anthracycline Dose†</th> <th>Recommended Frequency</th> </tr> </thead> <tbody> <tr> <td rowspan="2">&lt; 5 years old</td> <td rowspan="2">Any</td> <td>None</td> <td>Every 2 years</td> </tr> <tr> <td>Any</td> <td>Every year</td> </tr> <tr> <td rowspan="3"><math>\geq 5</math> years old</td> <td rowspan="2">&lt; 30 Gy‡</td> <td>None</td> <td>Every 5 years</td> </tr> <tr> <td><math>\geq 30</math> Gy‡</td> <td>Every 2 years</td> </tr> <tr> <td>Any</td> <td>&lt; 300 mg/m<sup>2</sup></td> <td>Every 2 years</td> </tr> <tr> <td></td> <td></td> <td><math>\geq 300</math> mg/m<sup>2</sup></td> <td>Every year</td> </tr> <tr> <td colspan="3">Any age with decrease in serial function</td> <td>Every year</td> </tr> </tbody> </table>		Age at Treatment†	Radiation Dose	Anthracycline Dose†	Recommended Frequency	< 5 years old	Any	None	Every 2 years	Any	Every year	$\geq 5$ years old	< 30 Gy‡	None	Every 5 years	$\geq 30$ Gy‡	Every 2 years	Any	< 300 mg/m <sup>2</sup>	Every 2 years			$\geq 300$ mg/m <sup>2</sup>	Every year	Any age with decrease in serial function			Every year	• See “Patient-Specific Guideline Identification Tool” in Appendix I to determine specific screening guidelines by section number for individual patients.		
Age at Treatment†	Radiation Dose	Anthracycline Dose†	Recommended Frequency																														
< 5 years old	Any	None	Every 2 years																														
		Any	Every year																														
$\geq 5$ years old	< 30 Gy‡	None	Every 5 years																														
		$\geq 30$ Gy‡	Every 2 years																														
	Any	< 300 mg/m <sup>2</sup>	Every 2 years																														
		$\geq 300$ mg/m <sup>2</sup>	Every year																														
Any age with decrease in serial function			Every year																														
		†Age at time of first cardiotoxic therapy (anthracycline or radiation with potential to impact heart, whichever was given first) ‡Based on doxorubicin isotoxic equivalent dose [see conversion factors in Section 33 “Info Link (Dose Conversion)”] †If patient received radiation to more than one specified field, see dose calculation rules on page 56.																															

**SYSTEM = Cardiovascular**  
**SCORE = 1**

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
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# RADIATION

# POTENTIAL IMPACT TO HEART (cont)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations	
81 (female)	<b>Hepatic</b> <b>Inverted Y</b> <b>Left Flank/Hemiabdomen</b> <b>Left upper quadrant</b> <b>Paraaortic</b> <b>Renal</b> <b>Right Flank/Hemiabdomen</b> <b>Right Upper quadrant</b> <b>Spleen (entire)</b> <b>Spleen (partial)</b> <b>Whole abdomen</b> <b>Spine (thoracic)</b> <b>Spine (whole)</b> <b>Subtotal Lymphoid Irradiation (STLI)</b> <b>Chest (thorax)</b> <b>Extended Mantle</b> <b>Mantle</b> <b>Mediastinal</b> <b>Whole lung</b> <b>Total Body Irradiation (TBI)</b> <b>Total Lymphoid Irradiation (TLI)</b>	<b>Cardiac toxicity</b> Congestive heart failure Cardiomyopathy Pericarditis Pericardial fibrosis Valvular disease Myocardial infarction Arrhythmia Atherosclerotic heart disease	<b>Host Factors</b> Younger age at irradiation Family history of dyslipidemia Coronary artery disease  <b>Treatment Factors</b> Radiation dose ≥ 20 Gy to chest TBI Combined with radiomimetic chemotherapy (e.g., doxorubicin, dactinomycin) Combined with other cardiotoxic chemotherapy: - Anthracyclines - Cyclophosphamide conditioning for HCT - Amsacrine  <b>Medical Conditions</b> Hypertension Obesity Dyslipidemia Diabetes mellitus Congenital heart disease Febrile illness Pregnancy Premature ovarian failure (untreated)	<b>Host Factors</b> Female sex Black/of African descent Younger than age 5 years at treatment  <b>Treatment Factors</b> Anteriorly-weighted radiation fields Lack of subcarinal shielding Doses ≥ 30 Gy in patients who have received anthracyclines Doses ≥ 40 Gy in patients who have not received anthracyclines Longer time since treatment	<b>HISTORY</b> <b>SOB</b> <b>DOE</b> <b>Orthopnea</b> <b>Chest pain</b> <b>Palpitations</b> If under 25 yrs: abdominal symptoms (nausea, vomiting) Yearly  <b>Info Link</b> • 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.  <b>PHYSICAL</b> <b>Cardiac murmur</b> <b>S3, S4</b> <b>Increased P2 sound</b> <b>Pericardial rub</b> <b>Rales</b> <b>Wheezes</b> <b>Jugular venous distension</b> <b>Peripheral edema</b> Yearly  <b>SCREENING</b> <b>Fasting blood glucose OR HbA1c and lipid profile</b> Every 2 years If abnormal, refer for ongoing management  <b>EKG (include evaluation of QTc interval)</b> Baseline at entry into long-term follow-up, repeat as clinically indicated  <b>ECHO (or comparable imaging to evaluate cardiac anatomy and function)</b> Baseline at entry into long-term follow-up, then periodically based on age at treatment, radiation dose, and cumulative anthracycline dose.	<b>Health Links</b> <b>Heart Health</b> <b>Cardiovascular Risk Factors</b> <b>Diet and Physical Activity</b> <b>Dental Health</b>  <b>Counseling</b> 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.  <b>Note:</b> 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.  <b>Considerations for Further Testing and Intervention</b> 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.	
		<b>RECOMMENDED FREQUENCY OF ECHOCARDIOGRAM</b>					
		Age at Treatment†	Radiation Dose	Anthracycline Dose†	Recommended Frequency		
		< 5 years old	Any	None	Every 2 years		
				Any	Every year		
		≥5 years old	< 30 Gy‡	None	Every 5 years		
				≥ 30 Gy‡	None	Every 2 years	
				Any	< 300 mg/m²	Every 2 years	
		≥ 300 mg/m²	Every year				
		Any age with decrease in serial function		Every year			
		†Age at time of first cardiotoxic therapy (anthracycline or radiation with potential to impact heart, whichever was given first) ‡Based on doxorubicin isotoxic equivalent dose [see conversion factors in Section 34 "Info Link (Dose Conversion)"] †If patient received radiation to more than one specified field, see dose calculation rules on page 56.					
		• See "Patient-Specific Guideline Identification Tool" in Appendix I to determine specific screening guidelines by section number for individual patients.					
		<b>SYSTEM = Cardiovascular</b> <b>SCORE = 1</b>					



Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
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# RADIATION

# POTENTIAL IMPACT TO SPLEEN

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
82	<p>≥ 40 Gy to:  <b>Inverted Y</b>  <b>Left Flank/Hemiabdomen</b>  <b>Left upper quadrant</b>  <b>Paraaortic</b>  <b>Spleen (entire)</b>  <b>Whole abdomen</b>  <b>Subtotal Lymphoid Irradiation (STLI)</b>  <b>Total Lymphoid Irradiation (TLI)</b>  <b>TBI*</b></p>	<p><b>Functional asplenia</b>                      At risk for life-threatening infection with encapsulated organisms (e.g., <i>Haemophilus influenzae</i>, <i>Streptococcus pneumoniae</i>, meningococcus)</p>	<p><b>Treatment Factors</b>                      Higher radiation dose to entire spleen</p>		<p><b>PHYSICAL</b>                      Physical exam at time of febrile illness to evaluate degree of illness and potential source of infection                      When febrile T ≥ 101°F</p> <p><b>SCREENING</b>                      Blood culture                      When febrile T ≥ 101°F</p>	<p><b>Health Links</b>                      Splenic Precautions</p> <p><b>Counseling</b>                      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.</p> <p><b>Considerations for Further Testing and Intervention</b>                      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.</p> <p><b>Info Link</b>                      See current edition of AAP <i>Red Book</i> for current recommendations regarding antibiotic prophylaxis and immunizations</p>
	<p>*TBI is included for dose calculation purposes only; this section is not applicable to patients who received TBI alone.</p>	<p>• This section is only applicable to patients who:</p> <ol style="list-style-type: none"> <li>Received radiation to any of the specified fields at ≥ 40 Gy OR</li> <li>Received a combination of radiation to any of the specified fields <b>and</b> TBI, the sum of which is ≥ 40 Gy</li> </ol> <p>• 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.</p> <p>• See “Patient-Specific Guideline Identification Tool” in Appendix I to determine specific screening guidelines by section number for individual patients.</p>				
	<p><b>Info Link</b>                      • 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.</p>					<p><b>SYSTEM = Immune</b>  <b>SCORE = 1</b></p>

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Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
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# RADIATION

## POTENTIAL IMPACT TO GI/HEPATIC SYSTEM

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
83	<p>≥ 30 Gy to:</p> <p><b>Hepatic</b>  <b>Inverted Y</b>  <b>Left Flank/Hemiabdomen</b>  <b>Left upper quadrant</b>  <b>Paraaortic</b>  <b>Renal</b>  <b>Right Flank/Hemiabdomen</b>  <b>Right Upper quadrant</b>  <b>Spleen (entire)</b>  <b>Spleen (partial)</b>  <b>Whole abdomen</b>  <b>Cervical (neck)</b>  <b>Supraclavicular</b>  <b>Spine (cervical)</b>  <b>Spine (thoracic)</b>  <b>Spine (whole)</b>  <b>Subtotal Lymphoid Irradiation (STLI)</b>  <b>Chest (thorax)</b>  <b>Extended Mantle</b>  <b>Mantle</b>  <b>Mediastinal</b>  <b>Mini-Mantle</b>  <b>Whole lung</b>  <b>Total Lymphoid Irradiation (TLI)</b>  <b>TBI*</b></p> <p>*TBI is included for dose calculation purposes only; this section is not applicable to patients who received TBI alone.</p>	<p><b>Esophageal stricture</b></p>	<p><b>Treatment Factors</b>            Higher radiation dose            Radiomimetic chemotherapy (e.g., doxorubicin, actinomycin)</p> <p><b>Medical Conditions</b>            Gastroesophageal reflux            History of Candida esophagitis</p>	<p><b>Treatment Factors</b>            Radiation dose ≥ 40 Gy</p> <p><b>Medical Conditions</b>            Gut GVHD</p>	<p><b>HISTORY</b>  <b>Dysphagia</b>  <b>Heartburn</b>            Yearly</p>	<p><b>Health Links</b>  <b>Gastrointestinal Health</b></p> <p><b>Considerations for Further Testing and Intervention</b>            Surgical and/or gastroenterology consultation for symptomatic patients.</p> <div style="border: 1px solid black; padding: 5px; text-align: center; margin: 10px auto; width: fit-content;"> <p><b>SYSTEM = GI/Hepatic</b>  <b>SCORE = 1</b></p> </div>
<p>• This section is only applicable to patients who:</p> <ol style="list-style-type: none"> <li>1) Received radiation to any of the specified fields at ≥ 30 Gy OR</li> <li>2) Received a combination of radiation to any of the specified fields <b>plus</b> relevant spinal radiation <b>and/or</b> TBI, the sum of which is ≥ 30 Gy</li> </ol> <p>• 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.</p> <p>• See “Patient-Specific Guideline Identification Tool” in Appendix I to determine specific screening guidelines by section number for individual patients.</p>						

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# RADIATION

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

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
84	<p>[Abdominal radiation]</p> <p><b>Hepatic</b></p> <p><b>Inverted Y</b></p> <p><b>Left Flank/Hemiabdomen</b></p> <p><b>Left upper quadrant</b></p> <p><b>Paraaortic</b></p> <p><b>Renal</b></p> <p><b>Right Flank/Hemiabdomen</b></p> <p><b>Right Upper quadrant</b></p> <p><b>Spleen (entire)</b></p> <p><b>Spleen (partial)</b></p> <p><b>Whole abdomen</b></p> <p><b>Subtotal Lymphoid Irradiation (STLI)</b></p> <p><b>Extended Mantle</b></p> <p><b>Total Lymphoid Irradiation (TLI)</b></p> <p><b>Total Body Irradiation (TBI)</b></p>	<p><b>Impaired Glucose Metabolism/Diabetes Mellitus</b></p> <p><b>Info Link</b></p> <ul style="list-style-type: none"> <li>Impaired glucose metabolism may occur in a constellation of conditions known as the metabolic syndrome.</li> <li>Definitions of the metabolic syndrome are evolving but generally include a combination of central (abdominal) obesity with at least 2 or more of the following:                             <ul style="list-style-type: none"> <li>- hypertension</li> <li>- atherogenic dyslipidemia (elevated triglycerides reduced HDL cholesterol)</li> <li>- abnormal glucose metabolism (fasting hyperglycemia, hyperinsulinism, insulin resistance, diabetes mellitus type II).</li> </ul> </li> <li><b>Note:</b> Patients who received TBI may develop features of metabolic syndrome without associated obesity</li> </ul>	<p><b>Host Factors</b></p> <p>Family history of diabetes mellitus</p> <p><b>Treatment Factors</b></p> <p>Prolonged corticosteroid therapy (e.g., for chronic GVHD)</p>	<p><b>Medical Conditions</b></p> <p>Obesity (not <i>necessary</i> in HCT survivors who received TBI)</p>	<p><b>SCREENING</b></p> <p><b>Fasting blood glucose OR HbA1c</b></p> <p>Every 2 years. More frequently if indicated based on patient evaluation</p>	<p><b>Health Links</b></p> <p><b>Diet and Physical Activity</b></p> <p><b>Cardiovascular Risk Factors</b></p> <p><b>Counseling</b></p> <p>Counsel regarding obesity-related health risks and nutrition.</p> <p><b>Considerations for Further Testing and Intervention</b></p> <p>Consider endocrine consultation if impaired glucose metabolism is suspected. Consider evaluation for other co-morbid conditions, including overweight/obesity, hypertension, and dyslipidemia.</p> <div style="border: 1px solid black; padding: 5px; text-align: center;"> <p><b>SYSTEM = Endocrine/Metabolic</b></p> <p><b>SCORE = 1</b></p> </div>
<p>• See “Patient-Specific Guideline Identification Tool” in Appendix I to determine specific screening guidelines by section number for individual patients.</p>						

### SECTION 84 REFERENCES

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# RADIATION

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

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
85	<b>Total Body Irradiation (TBI)</b> <b>Note:</b> For all guideline sections relevant to patients who received TBI please see page 129.	Dyslipidemia	<b>Host Factors</b> Family history of dyslipidemia  <b>Treatment Factors</b> Prolonged corticosteroid therapy (e.g., for chronic GVHD)	Medical Conditions	<b>SCREENING</b> <b>Fasting lipid profile</b> Every 2 years and as clinically indicated	<b>Health Links</b> <b>Diet and Physical Activity</b> <b>Cardiovascular Risk Factors</b>  <b>Counseling</b> Counsel regarding nutrition.  <b>Considerations for Further Testing and Intervention</b> Consider evaluation for other co-morbid conditions including hypertension, impaired glucose metabolism, and overweight/obesity.  <div style="border: 1px solid black; padding: 5px; text-align: center;"> <b>SYSTEM = Endocrine/Metabolic</b>  <b>SCORE = 1</b> </div>

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

### SECTION 85 REFERENCES

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# RADIATION

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

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
86	<p>≥ 30 Gy to:  <b>Hepatic</b>  <b>Inverted Y</b>  <b>Left Flank/Hemiabdomen</b>  <b>Left upper quadrant</b>  <b>Paraaortic</b>  <b>Renal</b>  <b>Right Flank/Hemiabdomen</b>  <b>Right Upper quadrant</b>  <b>Spleen (entire)</b>  <b>Spleen (partial)</b>  <b>Whole abdomen</b>  <b>Subtotal Lymphoid Irradiation (STLI)</b>  <b>Extended Mantle</b>  <b>Total Lymphoid Irradiation (TLI)</b>  <b>TBI*</b></p> <p>*TBI is included for dose calculation purposes only; this section is not applicable to patients who received TBI alone.</p>	<p><b>Hepatic fibrosis</b>  <b>Cirrhosis</b>  <b>Focal nodular hyperplasia</b></p> <p><b>Info Link</b></p> <ul style="list-style-type: none"> <li>• Focal nodular hyperplasia (FNH) is a benign change that represents a scar in the liver.</li> <li>• FNH is usually an asymptomatic finding noted on MRI or ultrasound of the liver.</li> <li>• Continued observation or biopsy may be indicated depending on individual patient factors and imaging features.</li> </ul>	<p><b>Treatment Factors</b>  Higher radiation dose</p> <p><b>Medical Conditions</b>  Chronic hepatitis  History of VOD</p> <p><b>Health Behaviors</b>  Alcohol use</p>	<p><b>Treatment Factors</b>  Dose ≥ 40 Gy to at least 1/3 of liver volume  Dose 20-30 Gy to entire liver</p>	<p><b>PHYSICAL</b></p> <p><b>Jaundice</b>  <b>Spider angiomas</b>  <b>Palmar erythema</b>  <b>Xanthomata</b>  <b>Hepatomegaly</b>  <b>Splenomegaly</b>  Yearly</p> <p><b>SCREENING</b></p> <p><b>ALT</b>  <b>AST</b>  <b>Bilirubin</b>  Baseline at entry into long-term follow-up, repeat as clinically indicated</p>	<p><b>Health Links</b>  <b>Liver Health</b></p> <p><b>Considerations for Further Testing and Intervention</b></p> <p>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 immunizations in patients lacking immunity.</p> <div style="border: 1px solid black; padding: 5px; text-align: center;"> <p><b>SYSTEM = GI/Hepatic</b>  <b>SCORE = 1</b></p> </div>

• 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.

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# RADIATION

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

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
87	<p>≥ 30 Gy to:  <b>Hepatic</b>  <b>Inverted Y</b>  <b>Left Flank/Hemiabdomen</b>  <b>Left upper quadrant</b>  <b>Paraaortic</b>  <b>Renal</b>  <b>Right Flank/Hemiabdomen</b>  <b>Right Upper quadrant</b>  <b>Spleen (entire)</b>  <b>Spleen (partial)</b>  <b>Whole abdomen</b>  <b>Subtotal Lymphoid Irradiation (STLI)</b>  <b>Extended Mantle</b>  <b>Total Lymphoid Irradiation (TLI)</b>  <b>TBI*</b></p> <p>*TBI is included for dose calculation purposes only; this section is not applicable to patients who received TBI alone.</p>	<p><b>Cholelithiasis</b></p>	<p><b>Host Factors</b>                      Ileal conduit                      Obesity                      Pregnancy                      Family history of cholelithiasis</p> <p><b>Treatment Factors</b>                      Abdominal surgery                      Abdominal radiation                      TPN</p>		<p><b>HISTORY</b>  <b>Colicky abdominal pain related to fatty food intake</b>  <b>Excessive flatulence</b>                      Yearly and as clinically indicated</p> <p><b>PHYSICAL</b>  <b>RUQ or epigastric tenderness</b>  <b>Positive Murphy's sign</b>                      Yearly and as clinically indicated</p>	<p><b>Health Links</b>                      Gastrointestinal Health</p> <p><b>Considerations for Further Testing and Intervention</b>                      Consider gallbladder ultrasound in patients with chronic abdominal pain</p> <p><b>SYSTEM = GI/Hepatic</b>  <b>SCORE = 2B</b></p>

• This section is only applicable to patients who:

- Received radiation to any of the specified fields at ≥ 30 Gy  
OR
- 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.

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# RADIATION

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

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
88	<p>≥ 30 Gy to:</p> <p><b>Hepatic</b></p> <p><b>Inverted Y</b></p> <p><b>Left Flank/Hemiabdomen</b></p> <p><b>Left upper quadrant</b></p> <p><b>Paraaortic</b></p> <p><b>Renal</b></p> <p><b>Right Flank/Hemiabdomen</b></p> <p><b>Right Upper quadrant</b></p> <p><b>Spleen (entire)</b></p> <p><b>Spleen (partial)</b></p> <p><b>Whole abdomen</b></p> <p><b>Bladder</b></p> <p><b>Femoral</b></p> <p><b>Iliac</b></p> <p><b>Inguinal</b></p> <p><b>Pelvic</b></p> <p><b>Prostate</b></p> <p><b>Vaginal</b></p> <p><b>Spine (lumbar)</b></p> <p><b>Spine (sacral)</b></p> <p><b>Spine (thoracic)</b></p> <p><b>Spine (whole)</b></p> <p><b>Subtotal Lymphoid Irradiation (STLI)</b></p> <p><b>Extended Mantle</b></p> <p><b>Total Lymphoid Irradiation (TLI)</b></p> <p><b>TBI*</b></p>	<p><b>Bowel obstruction</b></p>	<p><b>Treatment Factors</b></p> <p>Higher radiation dose to bowel</p> <p>Abdominal surgery</p>	<p><b>Treatment Factors</b></p> <p>Radiation dose ≥ 45 Gy (Obstruction may occur in people who received lower doses of abdominal radiation during childhood)</p>	<p><b>HISTORY</b></p> <p><b>Abdominal pain</b></p> <p><b>Distention</b></p> <p><b>Vomiting</b></p> <p><b>Constipation</b></p> <p>With clinical symptoms of obstruction</p> <p><b>PHYSICAL</b></p> <p><b>Tenderness</b></p> <p><b>Abdominal guarding</b></p> <p><b>Distension</b></p> <p>With clinical symptoms of obstruction</p>	<p><b>Health Links</b></p> <p><b>Gastrointestinal Health</b></p> <p><b>Considerations for Further Testing and Intervention</b></p> <p>Obtain KUB in patients with clinical symptoms of obstruction. Surgical consultation in patients unresponsive to medical management.</p> <div style="border: 1px solid black; padding: 5px; text-align: center;"> <p><b>SYSTEM = GI/Hepatic</b></p> <p><b>SCORE = 1</b></p> </div>
<p>• This section is only applicable to patients who:</p> <ol style="list-style-type: none"> <li>Received radiation to any of the specified fields at ≥ 30 Gy OR</li> <li>Received a combination of radiation to any of the specified fields <b>plus</b> relevant spinal radiation <b>and/or</b> TBI, the sum of which is ≥ 30 Gy</li> </ol> <p>• 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.</p> <p>• See “Patient-Specific Guideline Identification Tool” in Appendix I to determine specific screening guidelines by section number for individual patients.</p>						
<p>*TBI is included for dose calculation purposes only; this section is not applicable to patients who received TBI alone.</p>						

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# RADIATION

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

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
89	<p>≥ 30 Gy to:</p> <p><b>Hepatic</b></p> <p><b>Inverted Y</b></p> <p><b>Left Flank/Hemiabdomen</b></p> <p><b>Left upper quadrant</b></p> <p><b>Paraaortic</b></p> <p><b>Renal</b></p> <p><b>Right Flank/Hemiabdomen</b></p> <p><b>Right Upper quadrant</b></p> <p><b>Spleen (entire)</b></p> <p><b>Spleen (partial)</b></p> <p><b>Whole abdomen</b></p> <p><b>Bladder</b></p> <p><b>Femoral</b></p> <p><b>Iliac</b></p> <p><b>Inguinal</b></p> <p><b>Pelvic</b></p> <p><b>Prostate</b></p> <p><b>Vaginal</b></p> <p><b>Spine (lumbar)</b></p> <p><b>Spine (sacral)</b></p> <p><b>Spine (thoracic)</b></p> <p><b>Spine (whole)</b></p> <p><b>Subtotal Lymphoid Irradiation (STLI)</b></p> <p><b>Extended Mantle</b></p> <p><b>Total Lymphoid Irradiation (TLI)</b></p> <p><b>TBI*</b></p>	<p><b>Chronic enterocolitis</b></p> <p><b>Fistula</b></p> <p><b>Strictures</b></p>	<p><b>Treatment Factors</b></p> <p>Higher radiation dose to bowel</p> <p>Abdominal surgery</p>	<p><b>Treatment Factors</b></p> <p>Radiation dose ≥ 45 Gy</p>	<p><b>HISTORY</b></p> <p><b>Nausea</b></p> <p><b>Vomiting</b></p> <p><b>Abdominal pain</b></p> <p><b>Diarrhea</b></p> <p>Yearly</p>	<p><b>Health Links</b></p> <p><b>Gastrointestinal Health</b></p> <p><b>Considerations for Further Testing and Intervention</b></p> <p>Serum protein and albumin yearly in patients with chronic diarrhea or fistula. Surgical and/or gastroenterology consultation for symptomatic patients.</p> <div style="border: 1px solid black; padding: 5px; text-align: center;"> <p><b>SYSTEM = GI/Hepatic</b></p> <p><b>SCORE = 1</b></p> </div>
	<p>*TBI is included for dose calculation purposes only; this section is not applicable to patients who received TBI alone.</p>					

• This section is only applicable to patients who:

- Received radiation to any of the specified fields at ≥ 30 Gy  
OR
- 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 89 REFERENCES

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# RADIATION

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

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
90	<p>≥ 30 Gy to:</p> <p><b>Hepatic</b></p> <p><b>Inverted Y</b></p> <p><b>Left Flank/Hemiabdomen</b></p> <p><b>Left upper quadrant</b></p> <p><b>Paraaortic</b></p> <p><b>Renal</b></p> <p><b>Right Flank/Hemiabdomen</b></p> <p><b>Right Upper quadrant</b></p> <p><b>Spleen (entire)</b></p> <p><b>Spleen (partial)</b></p> <p><b>Whole abdomen</b></p> <p><b>Bladder</b></p> <p><b>Femoral</b></p> <p><b>Iliac</b></p> <p><b>Inguinal</b></p> <p><b>Pelvic</b></p> <p><b>Prostate</b></p> <p><b>Vaginal</b></p> <p><b>Spine (lumbar)</b></p> <p><b>Spine (sacral)</b></p> <p><b>Spine (thoracic)</b></p> <p><b>Spine (whole)</b></p> <p><b>Subtotal Lymphoid Irradiation (STLI)</b></p> <p><b>Extended Mantle</b></p> <p><b>Total Body Irradiation (TBI)*</b></p> <p><b>Total Lymphoid Irradiation (TLI)</b></p>	<p><b>Colorectal cancer</b></p> <p><b>Info Link</b></p> <ul style="list-style-type: none"> <li>• 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.</li> <li>• 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.</li> <li>• 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.</li> </ul>	<p><b>Host Factors</b></p> <p>Current age ≥ 50 years</p> <p><b>Treatment Factors</b></p> <p>Higher radiation dose to bowel</p> <p>Higher daily dose fraction</p> <p>Combined with chemotherapy (especially alkylators)</p> <p><b>Medical Conditions</b></p> <p>Obesity</p> <p><b>Health Behaviors</b></p> <p>High fat/low fiber diet</p>	<p><b>Host Factors</b></p> <p>Personal history of ulcerative colitis, gastrointestinal malignancy, adenomatous polyps, or hepatoblastoma</p> <p>Familial polyposis</p> <p>Family history of colorectal cancer or polyps in first degree relative</p>	<p><b>SCREENING</b></p> <p><b>Colonoscopy</b></p> <p>Every 5 years [minimum] beginning at 10 years after radiation or at age 35 years [whichever occurs last]</p> <p>More frequently if indicated based on colonoscopy results</p> <p>Per the ACS, begin screening earlier for the following high-risk groups—HNPCC: at puberty</p> <p>FAP: at age 21 years</p> <p>IBD: 8 years after diagnosis of IBD</p> <p>Information from the first colonoscopy will inform frequency of follow-up testing</p>	<p><b>Health Links</b></p> <p><b>Colorectal Cancer</b></p> <p><b>Considerations for Further Testing and Intervention</b></p> <p>Surgical and/or oncology consultation as needed.</p> <div style="border: 1px solid black; padding: 5px; text-align: center; margin-top: 20px;"> <p><b>SYSTEM = SMN</b></p> <p><b>SCORE = 2A</b></p> </div>
	<p><b>Info Link</b></p> <ul style="list-style-type: none"> <li>• *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.</li> <li>• <i>Monitoring of patients who received TBI without additional radiation potentially impacting the colon/rectum should be determined on an individual basis.</i> (See Info Link in next column.)</li> </ul>					
<p>• This section is only applicable to patients who:</p> <ol style="list-style-type: none"> <li>1) Received radiation to any of the specified fields at ≥ 30 Gy</li> <li>OR</li> <li>2) Received a combination of radiation to any of the specified fields <b>plus</b> relevant spinal radiation <b>and/or</b> TBI, the sum of which is ≥ 30 Gy</li> </ol> <ul style="list-style-type: none"> <li>• 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.</li> <li>• See “Patient-Specific Guideline Identification Tool” in Appendix I to determine specific screening guidelines by section number for individual patients.</li> </ul>						

# RADIATION

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

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
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### SECTION 90 REFERENCES

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# RADIATION

# POTENTIAL IMPACT TO URINARY TRACT

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
91	<b>Hepatic</b> <b>Inverted Y</b> <b>Left Flank/Hemiabdomen</b> <b>Left upper quadrant</b> <b>Paraaortic</b> <b>Renal</b> <b>Right Flank/Hemiabdomen</b> <b>Right Upper quadrant</b> <b>Spleen (entire)</b> <b>Spleen (partial)</b> <b>Whole abdomen</b> <b>Subtotal Lymphoid Irradiation (STLI)</b> <b>Extended Mantle</b> <b>Total Body Irradiation (TBI)</b> <b>Total Lymphoid Irradiation (TLI)</b>	<b>Renal toxicity</b> <b>Renal insufficiency</b> <b>Hypertension</b>	<b>Host Factors</b> Bilateral Wilms tumor Mononephric  <b>Treatment Factors</b> Radiomimetic chemotherapy (e.g., doxorubicin, dactinomycin) Radiation dose $\geq 10$ Gy TBI combined with radiation to the kidney Combined with other nephrotoxic agents, such as: - Cisplatin - Carboplatin - Ifosfamide - Aminoglycosides - Amphotericin - Immunosuppressants  <b>Medical Conditions</b> Diabetes mellitus Hypertension Nephrectomy	<b>Treatment Factors</b> Radiation dose $\geq 15$ Gy TBI $\geq 6$ Gy in single fraction or $\geq 12$ Gy fractionated	<b>PHYSICAL</b> <b>Blood pressure</b> Yearly  <b>SCREENING</b> <b>BUN</b> <b>Creatinine</b> <b>Na, K, Cl, CO<sub>2</sub></b> <b>Ca, Mg, PO<sub>4</sub></b> Baseline at entry into long-term follow-up, repeat as clinically indicated  <b>Urinalysis</b> Yearly	<b>Health Links</b> <b>Kidney Health</b> <b>Cardiovascular Risk Factors</b>  <b>Considerations for Further Testing and Intervention</b> Nephrology consultation for patients with hypertension, proteinuria, or progressive renal insufficiency  <div style="border: 1px solid black; padding: 5px; text-align: center;"> <b>SYSTEM = Urinary</b>  <b>SCORE = 1</b> </div>

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

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# RADIATION

# POTENTIAL IMPACT TO URINARY TRACT (cont)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
92	<p>≥ 30 Gy to:  <b>Inverted Y</b>  <b>Left Flank/Hemiabdomen</b>  <b>Right Flank/Hemiabdomen</b>  <b>Whole abdomen</b>  <b>Bladder</b>  <b>Iliac</b>  <b>Inguinal</b>  <b>Pelvic</b>  <b>Prostate</b>  <b>Vaginal</b>  <b>Spine (sacral)</b>  <b>Spine (whole)</b>  <b>Total Lymphoid Irradiation (TLI)</b>  <b>TBI*</b></p> <p>*TBI is included for dose calculation purposes only; this section is not applicable to patients who received TBI alone.</p> <p><b>Info Link</b>                      The bladder is included in the left and right flank/hemiabdomen treatment fields only if the fields extended below iliac crest.</p>	<p><b>Hemorrhagic cystitis</b></p>	<p><b>Treatment Factors</b>                      Higher radiation dose (≥ 30 Gy to entire bladder, ≥ 60 Gy to portion of bladder)</p>	<p><b>Treatment Factors</b>                      Combined with cyclophosphamide and/or ifosfamide</p>	<p><b>HISTORY</b>  <b>Hematuria</b>  <b>Urinary urgency/frequency</b>  <b>Urinary incontinence/retention</b>  <b>Dysuria</b>  <b>Nocturia</b>  <b>Abnormal urinary stream</b>                      Yearly</p>	<p><b>Health Links</b>  <b>Bladder Health</b></p> <p><b>Counseling</b>                      Counsel to promptly report dysuria or gross hematuria</p> <p><b>Considerations for Further Testing and Intervention</b>                      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.</p> <p style="text-align: center;"><b>SYSTEM = Urinary</b> <b>SCORE = 2A</b></p>

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# RADIATION

# POTENTIAL IMPACT TO URINARY TRACT (cont)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
93	<p>≥ 30 Gy to:  <b>Inverted Y</b>  <b>Left Flank/Hemiabdomen</b>  <b>Right Flank/Hemiabdomen</b>  <b>Whole abdomen</b>  <b>Bladder</b>  <b>Iliac</b>  <b>Inguinal</b>  <b>Pelvic</b>  <b>Prostate</b>  <b>Vaginal</b>  <b>Spine (sacral)</b>  <b>Spine (whole)</b>  <b>Total Lymphoid Irradiation (TLI)</b>  <b>TBI*</b></p> <p>*TBI is included for dose calculation purposes only; this section is not applicable to patients who received TBI alone.</p> <p><b>Info Link</b>                      The bladder is included in the left and right flank/hemiabdomen treatment fields only if the fields extended below iliac crest.</p>	<p><b>Urinary tract toxicity</b>                      Bladder fibrosis                      Dysfunctional voiding                      Vesicoureteral reflux                      Hydronephrosis</p>	<p><b>Treatment Factors</b>                      Higher cumulative radiation dose (≥ 45 Gy)                      Radiation to entire bladder                      Combined with:                      - Cyclophosphamide                      - Ifosfamide                      - Vincristine</p>		<p><b>HISTORY</b>                      Hematuria                      Urinary urgency/frequency                      Urinary incontinence/retention                      Dysuria                      Nocturia                      Abnormal urinary stream                      Yearly</p> <p><b>SCREENING</b>                      Urinalysis                      Yearly</p>	<p><b>Health Links</b>                      Bladder Health</p> <p><b>Considerations for Further Testing and Intervention</b>                      Urologic consultation for patients with incontinence or dysfunctional voiding.</p> <p><b>SYSTEM = Urinary</b>  <b>SCORE = 1</b></p>

• This section is only applicable to patients who:

- Received radiation to any of the specified fields at ≥ 30 Gy  
OR
- 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.

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# RADIATION

## POTENTIAL IMPACT TO URINARY TRACT (cont)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
94	<b>Inverted Y</b> <b>Left Flank/Hemiabdomen</b> <b>Right Flank/Hemiabdomen</b> <b>Whole abdomen</b> <b>Bladder</b> <b>Iliac</b> <b>Inguinal</b> <b>Pelvic</b> <b>Prostate</b> <b>Vaginal</b> <b>Spine (sacral)</b> <b>Spine (whole)</b> <b>Total Lymphoid Irradiation (TLI)</b>	Bladder malignancy	<b>Treatment Factors</b> Radiation to pelvis Combined with: - Cyclophosphamide - Ifosfamide  <b>Health Behaviors</b> Alcohol use Smoking		<b>HISTORY</b> <b>Hematuria</b> <b>Urinary urgency/frequency</b> <b>Urinary incontinence/retention</b> <b>Dysuria</b> <b>Nocturia</b> <b>Abnormal urinary stream</b> Yearly	<b>Health Links</b> <b>Bladder Health</b>  <b>Counseling</b> Counsel to promptly report dysuria or gross hematuria  <b>Considerations for Further Testing and Intervention</b> 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 > 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.
	<b>Info Link</b> The bladder is included in the left and right flank/hemiabdomen treatment fields 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.				<b>SYSTEM = SMN</b>  <b>SCORE = 2A</b>

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# RADIATION

# POTENTIAL IMPACT TO FEMALE REPRODUCTIVE SYSTEM

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
95 (female)	<b>Inverted Y</b> <b>Left Flank/Hemiabdomen</b> <b>Right Flank/Hemiabdomen</b> <b>Whole abdomen</b> <b>Bladder</b> <b>Pelvic</b> <b>Vaginal</b> <b>Spine (lumbar)</b> <b>Spine (sacral)</b> <b>Spine (whole)</b> <b>Total Body Irradiation (TBI)</b> <b>Total Lymphoid Irradiation (TLI)</b>	<b>Uterine vascular insufficiency</b> Resulting in adverse pregnancy outcomes, such as spontaneous abortion, neonatal death, low-birth weight infant, fetal malposition, and premature labor	<b>Host Factors</b> Females with Wilms tumor and associated Müllerian anomalies  <b>Treatment Factors</b> Higher radiation dose to pelvis	<b>Host Factors</b> Prepubertal at treatment  <b>Treatment Factors</b> Radiation dose $\geq$ 30 Gy TBI	<b>HISTORY</b>  <b>Pregnancy</b> Yearly and as clinically indicated  <b>Childbirth history</b> Yearly and as clinically indicated	<b>Health Links</b> <b>Female Health Issues</b>  <b>Resources</b> 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>  <b>Considerations for Further Testing and Intervention</b> Consider high-level ultrasound evaluation of genitourinary tract after pubertal development as clinically indicated in patients contemplating pregnancy. High-risk obstetrical care during pregnancy.
	<b>Info Link</b> The uterus is included in the left and right flank/hemiabdomen fields only if the fields extended below iliac crest.	<b>Info Link</b> 10% of girls with Wilms tumor have congenital uterine anomalies.	• See "Patient-Specific Guideline Identification Tool" in Appendix I to determine specific screening guidelines by section number for individual patients.			<div style="border: 1px solid black; padding: 5px; text-align: center;"> <b>SYSTEM = Reproductive (Female)</b>  <b>SCORE = 2B</b> </div>

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# RADIATION

## POTENTIAL IMPACT TO FEMALE REPRODUCTIVE SYSTEM (cont)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
96 (female)	<b>Inverted Y</b> <b>Left Flank/Hemiabdomen</b> <b>Right Flank/Hemiabdomen</b> <b>Whole abdomen</b> <b>Bladder</b> <b>Pelvic</b> <b>Vaginal</b> <b>Spine (lumbar)</b> <b>Spine (sacral)</b> <b>Spine (whole)</b> <b>Total Body Irradiation (TBI)</b> <b>Total Lymphoid Irradiation (TLI)</b>	<b>Gonadal dysfunction (ovarian)</b> Delayed/arrested puberty Premature menopause Infertility	<b>Host Factors</b> Older age at irradiation  <b>Treatment Factors</b> Radiation dose $\geq 5$ Gy if pubertal, $\geq 10$ Gy if prepubertal Combined with alkylating agent chemotherapy Longer time since treatment	<b>Treatment Factors</b> Radiation dose $\geq 10$ Gy if pubertal, $\geq 15$ Gy if prepubertal Combined with cyclophosphamide conditioning for HCT	<b>HISTORY</b> <b>Pubertal (onset, tempo), menstrual, pregnancy history</b> <b>Sexual function (vaginal dryness, libido)</b> <b>Medication use</b> Yearly  <b>PHYSICAL</b> <b>Tanner staging</b> Yearly until sexually mature  <b>SCREENING</b> <b>FSH</b> <b>LH</b> <b>Estradiol</b> 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	<b>Health Links</b> <b>Female Health Issues</b>  <b>Resources</b> 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>  <b>Counseling</b> 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.  <b>Considerations for Further Testing and Intervention</b> 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.
	<b>Info Link</b> The ovaries are included in the left and right flank/hemiabdomen treatment fields 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.				
						<b>SYSTEM = Reproductive (Female)</b> <b>SCORE = 1</b>

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Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
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## SECTION 96 REFERENCES–CONTINUED

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# RADIATION

## POTENTIAL IMPACT TO FEMALE REPRODUCTIVE SYSTEM (cont)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
97 (female)	<b>Inverted Y</b> <b>Left Flank/Hemiabdomen</b> <b>Right Flank/Hemiabdomen</b> <b>Whole abdomen</b> <b>Bladder</b> <b>Iliac</b> <b>Pelvic</b> <b>Vaginal</b> <b>Total Lymphoid Irradiation (TLI)</b>	Vaginal fibrosis/stenosis	<b>Host Factors</b> Vaginal tumor or pelvic tumor adjacent to vagina  <b>Treatment Factors</b> Radiation dose $\geq$ 50 Gy in postpubertal female Radiation dose $\geq$ 25 Gy in prepubertal female  <b>Medical Conditions</b> Chronic GVHD	<b>Treatment Factors</b> Radiation dose $\geq$ 55 Gy in postpubertal female Radiation dose $\geq$ 35 Gy in prepubertal female	<b>HISTORY</b> <b>Psychosocial assessment</b> <b>Dyspareunia</b> <b>Vulvar pain</b> <b>Post-coital bleeding</b> <b>Difficulty with tampon insertion</b> Yearly	<b>Considerations for Further Testing and Intervention</b> Gynecologic consultation for management. Psychological consultation in patients with emotional difficulties.
	<b>Info Link</b> The vagina is included in the left and right flank/hemiabdomen treatment fields 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.				<b>SYSTEM = Reproductive (Female)</b> <b>SCORE = 2A</b>

### SECTION 97 REFERENCES

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# RADIATION

# POTENTIAL IMPACT TO MALE REPRODUCTIVE SYSTEM

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
98 (male)	<b>Inverted Y</b> <b>Left Flank/Hemiabdomen</b> <b>Right Flank/Hemiabdomen</b> <b>Whole abdomen</b> <b>Bladder</b> <b>Femoral</b> <b>Iliac</b> <b>Inguinal</b> <b>Pelvic</b> <b>Prostate</b> <b>Testicular</b> <b>Total Body Irradiation (TBI)</b> <b>Total Lymphoid Irradiation (TLI)</b>	<b>Gonadal dysfunction (testicular)</b> Reduced fertility Oligospermia Azoospermia Infertility	<b>Host Factors</b> Testicular cancer Obesity Ejaculatory dysfunction Medications Occupational exposures (pesticides, heavy metals, solvents) <b>Treatment Factors</b> 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 Genitourinary surgery <b>Medical Conditions</b> Chronic GVHD <b>Health Behaviors</b> Tobacco/marijuana use History of sexually transmitted diseases	<b>Treatment Factors</b> Radiation dose to testes ≥ 6 Gy—azoospermia likely permanent	<b>HISTORY</b> <b>Pubertal (onset, tempo)</b> <b>Sexual function (erections, nocturnal emissions, libido)</b> <b>Medication use</b> Yearly <b>PHYSICAL</b> <b>Tanner staging until sexually mature</b> <b>Testicular volume by Prader orchimeter</b> Yearly <b>SCREENING</b> <b>Semen analysis</b> At request of sexually mature patient Periodic evaluation over time is recommended as resumption of spermatogenesis can occur up to 10 years post therapy <b>FSH</b> In sexually mature patient if unable to obtain semen analysis	<b>Health Links</b> <b>Male Health Issues</b> <b>Resources</b> 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> <b>Counseling</b> 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. <b>Considerations for Further Testing and Intervention</b> Reproductive endocrinology consultation for infertile couples interested in assisted reproductive technologies. <div style="border: 1px solid black; padding: 5px; text-align: center;"> <b>SYSTEM = Reproductive (Male)</b>  <b>SCORE = 1</b> </div>
	<b>Info Link</b> The testes are included in the left and right flank/hemiabdomen only if the fields extended below iliac crest.					
	<ul style="list-style-type: none"> <li>See “Patient-Specific Guideline Identification Tool” in Appendix I to determine specific screening guidelines by section number for individual patients.</li> </ul>					

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Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
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### SECTION 98 REFERENCES—CONTINUED

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# RADIATION

## POTENTIAL IMPACT TO MALE REPRODUCTIVE SYSTEM (cont)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
99 (male)	<p>≥ 20 Gy to:  <b>Inverted Y</b>  <b>Left Flank/Hemiabdomen</b>  <b>Right Flank/Hemiabdomen</b>  <b>Whole abdomen</b>  <b>Bladder</b>  <b>Femoral</b>  <b>Iliac</b>  <b>Inguinal</b>  <b>Pelvic</b>  <b>Prostate</b>  <b>Testicular</b>  <b>Total Lymphoid Irradiation (TLI)</b>  <b>TBI*</b></p> <p>*TBI is included for dose calculation purposes only; this section is not applicable to patients who received TBI alone.</p> <p><b>Info Link</b>                      The testes are included in the left and right flank/hemiabdomen only if the fields extended below iliac crest.</p>	<p><b>Gonadal dysfunction (testicular): Testosterone deficiency/insufficiency</b>                      Delayed/arrested puberty</p>	<p><b>Host Factors</b>                      Testicular cancer                      Aging</p> <p><b>Treatment Factors</b>                      Testicular irradiation combined with head/brain irradiation                      Combined with unilateral orchiectomy</p>	<p><b>Treatment Factors</b>                      Combined with alkylating agents                      Combined with cyclophosphamide conditioning for HCT</p>	<p><b>HISTORY</b>  <b>Pubertal (onset, tempo)</b>  <b>Sexual function (erections, nocturnal emissions, libido)</b>  <b>Medication use</b>                      Yearly</p> <p><b>PHYSICAL</b>  <b>Tanner staging until sexually mature</b>  <b>Testicular volume by Prader orchimeter</b>                      Yearly</p> <p><b>SCREENING</b>  <b>Testosterone</b> (ideally morning)                      Baseline at age 14 <b>AND</b> as clinically indicated in patients with delayed or arrested puberty and/or clinical signs and symptoms of testosterone deficiency</p>	<p><b>Health Links</b>  <b>Male Health Issues</b></p> <p><b>Considerations for Further Testing and Intervention</b>                      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.</p> <p><b>SYSTEM = Reproductive (Male)</b>  <b>SCORE = 1</b></p>

• This section is only applicable to patients who:

- Received radiation to any of the specified fields at ≥ 20 Gy  
OR
- 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.

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# RADIATION

## POTENTIAL IMPACT TO MUSCULOSKELETAL SYSTEM

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
100	All Radiation Fields (including TBI)	<b>Musculoskeletal growth problems</b> Hypoplasia Fibrosis Reduced or uneven growth Shortened trunk height (trunk radiation) Limb length discrepancy (extremity radiation)	<b>Host Factors</b> Younger age at treatment  <b>Treatment Factors</b> Higher cumulative radiation dose Larger radiation treatment field Higher radiation dose per fraction	<b>Host Factors</b> Prepubertal at treatment  <b>Treatment Factors</b> Orthovoltage radiation (commonly used before 1970) due to delivery of greater dose to skin and bones Epiphysis in treatment field Dose ≥ 20 Gy	<b>PHYSICAL</b>  <b>Limb lengths</b> Yearly for patients who had extremity radiation  <b>Height</b> <b>Weight</b> Yearly  <b>Sitting height</b> Yearly for patients who had trunk radiation	<b>Counseling</b> Counsel regarding increased risk of fractures in weight-bearing irradiated bones  <b>Considerations for Further Testing and Intervention</b> Orthopedic consultation for any deficit noted in growing child. Consider plastic surgery consult for reconstruction.
		• See “Patient-Specific Guideline Identification Tool” in Appendix I to determine specific screening guidelines by section number for individual patients.				

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

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# RADIATION

## POTENTIAL IMPACT TO MUSCULOSKELETAL SYSTEM (cont)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
101	<b>Hepatic</b> <b>Inverted Y</b> <b>Left Flank/Hemiabdomen</b> <b>Left upper quadrant</b> <b>Paraaortic</b> <b>Renal</b> <b>Right Flank/Hemiabdomen</b> <b>Right Upper quadrant</b> <b>Spleen (entire)</b> <b>Spleen (partial)</b> <b>Whole abdomen</b> <b>Spine (thoracic)</b> <b>Spine (whole)</b> <b>Subtotal Lymphoid Irradiation (STLI)</b> <b>Chest (thorax)</b> <b>Extended Mantle</b> <b>Mantle</b> <b>Mediastinal</b> <b>Whole lung</b> <b>Total Lymphoid Irradiation (TLI)</b>	Scoliosis/Kyphosis	<b>Host Factors</b> Younger age at irradiation Paraspinal malignancies Neurofibromatosis  <b>Treatment Factors</b> Hemithoracic or abdominal radiation Hemithoracic, abdominal or spinal surgery Radiation of only a portion of (rather than whole) vertebral body  <b>Info Link</b> With contemporary treatment approaches, scoliosis is infrequently seen as a consequence of radiation unless the patient has also undergone surgery to the hemithorax, abdomen or spine.	<b>Treatment Factors</b> Radiation doses $\geq 20$ Gy (lower doses for infants) Orthovoltage radiation (commonly used before 1970) due to delivery of greater dose to skin and bones	<b>PHYSICAL</b> <b>Spine exam for scoliosis and kyphosis</b> Yearly until growth completed, may need more frequent assessment during puberty or if curve detected	<b>Health Links</b> <b>Scoliosis and Kyphosis</b>  <b>Considerations for Further Testing and Intervention</b> Spine films in patients with clinically apparent curve. Orthopedic consultation as indicated based on radiographic exam.  <div style="border: 1px solid black; padding: 5px; text-align: center;"> <b>SYSTEM = Musculoskeletal</b>  <b>SCORE = 1</b> </div>
<div style="border: 1px solid black; padding: 5px;">                     • See "Patient-Specific Guideline Identification Tool" in Appendix I to determine specific screening guidelines by section number for individual patients.                 </div>						

### SECTION 101 REFERENCES

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# RADIATION

## POTENTIAL IMPACT TO MUSCULOSKELETAL SYSTEM (cont)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
102	<p>≥ 40 Gy to:</p> <p>Hepatic Inverted Y Left Flank/Hemiabdomen Left upper quadrant Paraaortic Renal Right Flank/Hemiabdomen Right Upper quadrant Spleen (entire) Spleen (partial) Whole abdomen Lower extremity Upper extremity Cervical (neck) Supraclavicular Bladder Femoral Iliac Inguinal Pelvic Prostate Vaginal Spine (cervical) Spine (lumbar) Spine (sacral) Spine (thoracic) Spine (whole) Subtotal Lymphoid Irradiation (STLI) Axilla Chest (thorax) Extended Mantle Mantle Mediastinal Mini-Mantle Whole lung Total Lymphoid Irradiation (TLI) TBI*</p>	Radiation-induced fracture	<p><b>Treatment Factors</b> History of surgery to cortex of bone</p>	<p><b>Treatment Factors</b> Radiation dose ≥ 50 Gy to bone</p>	<p><b>PHYSICAL</b> <b>Pain, swelling, deformity of bone</b> As indicated</p>	<p><b>Considerations for Further Testing and Intervention</b> Radiograph of affected bone as clinically indicated. Orthopedic evaluation as clinically indicated.</p> <div style="border: 1px solid black; padding: 5px; text-align: center; margin: 10px auto; width: fit-content;"> <p><b>SYSTEM = Musculoskeletal</b> <b>SCORE = 1</b></p> </div>
	<p>*TBI is included for dose calculation purposes only; this section is not applicable to patients who received TBI alone.</p>					

• 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.



# RADIATION

# MUSCULOSKELETAL SYSTEM (cont)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
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## 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.
- For HCT follow-up recommendations from the European Group for Blood and Marrow Transplantation, Center for International Blood and Marrow Transplant Research, and the American Society for Blood and Marrow Transplantation (EBMT/CIBMTR/ASBMT), see: Majhail NS, Rizzo JD, Lee SJ, et al. Recommended screening and preventive practices for long-term survivors after hematopoietic cell transplantation. *Bone Marrow Transplant*. Mar 2012;47(3):337-341.

### 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.

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

\*Screening may be indicated for patients who received TBI alone – see Info Link in this section

# HEMATOPOIETIC CELL TRANSPLANT

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
103	Autologous Hematopoietic Cell Transplant (HCT)	Myelodysplasia Acute myeloid leukemia	<b>Treatment Factors</b> Radiation therapy Stem cell mobilization with etoposide Alkylating agent chemotherapy Epidodophyllotoxins Anthracyclines Autologous transplant	<b>Host Factors</b> Older age  <b>Treatment Factors</b> Autologous transplant for non-Hodgkin and Hodgkin lymphoma Peripheral blood stem cells	<b>HISTORY</b>  <b>Fatigue</b> <b>Bleeding</b> <b>Easy bruising</b> Yearly, up to 10 years after transplant  <b>PHYSICAL</b>  <b>Dermatologic exam (pallor, petechiae, purpura)</b> Yearly, up to 10 years after transplant	<b>Health Links</b> <b>Reducing the Risk of Second Cancers</b>  <b>Counseling</b> Counsel to promptly report fatigue, pallor, petechiae or bone pain.  <b>Considerations for Further Testing and Intervention</b> CBC and bone marrow exam as clinically indicated.  <b>SYSTEM = SMN</b> <b>SCORE = 1</b>

## SECTION 103 REFERENCES

- Baker KS, DeFor TE, Burns LJ, Ramsay NK, Neglia JP, Robison LL. New malignancies after blood or marrow stem-cell transplantation in children and adults: incidence and risk factors. *J Clin Oncol.* Apr 1 2003;21(7):1352-1358.
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# HEMATOPOIETIC CELL TRANSPLANT

(cont)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
104 (male)	Hematopoietic Cell Transplant (HCT)	Solid tumors	<b>Host Factors</b> Younger age at transplant Fanconi's anemia  <b>Treatment Factors</b> Radiation therapy  <b>Medical Conditions</b> Hepatitis C infection Chronic GVHD Human Papillomavirus (HPV) infection	<b>Treatment Factors</b> TBI	<b>PHYSICAL</b> Evaluation for benign or malignant neoplasms Yearly	<b>Health Links</b> Reducing the Risk of Second Cancers  <b>Counseling</b> Avoid excessive sun exposure and tanning booths. Counsel regarding safer sexual practices.  <b>Considerations for Further Testing and Intervention</b> Oncology consultation as clinically indicated. HPV vaccination per current recommendations.  <div style="border: 1px solid black; padding: 5px; text-align: center;">                         SYSTEM = SMN                          SCORE = 1                     </div>

## SECTION 104 REFERENCES

- Baker KS, DeFor TE, Burns LJ, Ramsay NK, Neglia JP, Robison LL. New malignancies after blood or marrow stem-cell transplantation in children and adults: incidence and risk factors. *J Clin Oncol.* Apr 1 2003;21(7):1352-1358.
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# HEMATOPOIETIC CELL TRANSPLANT

(cont)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
105 (female)	Hematopoietic Cell Transplant (HCT)	Solid tumors	<b>Host Factors</b> Younger age at transplant Fanconi's anemia  <b>Treatment Factors</b> Radiation therapy  <b>Medical Conditions</b> Hepatitis C infection Chronic GVHD Human Papillomavirus (HPV) infection	<b>Treatment Factors</b> TBI	<b>PHYSICAL</b> <b>Evaluation for benign or malignant neoplasms</b> Yearly	<b>Health Links</b> <b>Reducing the Risk of Second Cancers</b>  <b>Counseling</b> Avoid excessive sun exposure and tanning booths. Counsel regarding safer sexual practices.  <b>Considerations for Further Testing and Intervention</b> Females with cGVHD appear to be at increased risk for cervical cancer and should, at minimum, have pelvic exams and PAP testing according to ACS recommendations (see Section 158) with more aggressive monitoring as clinically indicated. Oncology consultation as clinically indicated. HPV vaccination per current recommendations.

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

## SECTION 105 REFERENCES

- Baker KS, DeFor TE, Burns LJ, Ramsay NK, Neglia JP, Robison LL. New malignancies after blood or marrow stem-cell transplantation in children and adults: incidence and risk factors. *J Clin Oncol.* Apr 1 2003;21(7):1352-1358.
- Bhatia S, Louie AD, Bhatia R, et al. Solid cancers after bone marrow transplantation. *J Clin Oncol.* Jan 15 2001;19(2):464-471.
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- Socie G, Curtis RE, Deeg HJ, et al. New malignant diseases after allogeneic marrow transplantation for childhood acute leukemia. *J Clin Oncol.* Jan 2000;18(2):348-357.

# HEMATOPOIETIC CELL TRANSPLANT

(cont)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
106	Hematopoietic Cell Transplant (HCT)	Lymphoma	Medical Conditions Chronic GVHD	<b>Host Factors</b> Diagnosis of primary immune deficiency  <b>Treatment Factors</b> HLA mismatch Unrelated donor transplant T-cell depletion ATG	<b>PHYSICAL</b>  <b>Lymphadenopathy</b> Yearly  <b>Splenomegaly</b> Yearly	<b>Considerations for Further Testing and Intervention</b> Oncology consultation as clinically indicated.  <div style="border: 1px solid black; padding: 5px; text-align: center;">                         SYSTEM = SMN                          SCORE = 1                     </div>

## SECTION 106 REFERENCES

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# HEMATOPOIETIC CELL TRANSPLANT

(cont)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
107	Hematopoietic Cell Transplant (HCT)	<b>Hepatic toxicity</b> Chronic hepatitis Cirrhosis Iron overload	<b>Treatment Factors</b> History of multiple transfusions Radiation to the liver Antimetabolite therapy  <b>Medical Conditions</b> Chronic GVHD Viral hepatitis History of VOD  <b>Health Behaviors</b> Alcohol use	<b>Medical Conditions</b> Chronic hepatitis C with siderosis and steatosis	<b>SCREENING</b>  ALT AST Bilirubin Ferritin Baseline at entry into long-term follow-up, repeat as clinically indicated	<b>Health Links</b> <b>Liver Health</b> <b>Gastrointestinal Health</b>  <b>Considerations for Further Testing and Intervention</b> 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.  <b>Note:</b> 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.  <b>SYSTEM = GI/Hepatic</b> <b>SCORE = 1</b>

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# HEMATOPOIETIC CELL TRANSPLANT

(cont)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
108	Hematopoietic Cell Transplant (HCT)	<p><b>Osteonecrosis (Avascular Necrosis)</b></p> <p><b>Info Link</b></p> <ul style="list-style-type: none"> <li>• Osteonecrosis typically occurs during the acute treatment phase, and may progress over time or resolve.</li> <li>• Multifocal osteonecrosis is significantly more common (3:1) than unifocal.</li> </ul>	<p><b>Treatment Factors</b></p> <p>Corticosteroids (dexamethasone effect is more potent than prednisone)</p> <p>Other immunosuppressants</p> <p>TBI</p> <p>High-dose radiation to any bone</p> <p>Allogeneic HCT &gt; autologous</p>	<p><b>Host Factors</b></p> <p>Pubertal or post-pubertal at time of transplant</p> <p><b>Treatment Factors</b></p> <p>Prolonged immunosuppressive therapy (e.g., for chronic GVHD)</p> <p><b>Medical Conditions</b></p> <p>Chronic GVHD</p>	<p><b>HISTORY</b></p> <p>Joint pain</p> <p>Swelling</p> <p>Immobility</p> <p>Limited range of motion</p> <p>Yearly</p> <p><b>PHYSICAL</b></p> <p>Musculoskeletal exam</p> <p>Yearly</p>	<p><b>Health Links</b></p> <p><b>Osteonecrosis</b></p> <p><b>Considerations for Further Testing and Intervention</b></p> <p>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).</p> <p><b>SYSTEM = Musculoskeletal</b></p> <p><b>SCORE = 1</b></p>

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# HEMATOPOIETIC CELL TRANSPLANT

(cont)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
109	Hematopoietic Cell Transplant (HCT)	<p><b>Reduced bone mineral density (BMD)</b> 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</p> <p><b>Info Link</b></p> <ul style="list-style-type: none"> <li>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.</li> <li>Current definitions of osteopenia (T-scores between 1.0 and 2.5 SD below the mean) and osteoporosis (T-scores &gt; 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.</li> <li>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.</li> <li>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.</li> <li>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.</li> </ul>	<p><b>Host Factors</b> Both genders are at risk Younger age at diagnosis Caucasian Lower weight and BMI</p> <p><b>Treatment Factors</b> Corticosteroids Cyclosporine Tacrolimus Cranial radiation Craniospinal radiation HCT/TBI</p> <p><b>Medical Conditions</b> Growth hormone deficiency Hypogonadism/delayed puberty Hyperthyroidism</p> <p><b>Health Behaviors</b> Inadequate intake of calcium and vitamin D Lack of weight bearing exercise Smoking Alcohol use Carbonated beverages</p>	<p><b>Host Factors</b> Older age at time of treatment</p> <p><b>Treatment Factors</b> Prolonged corticosteroid therapy (e.g., for chronic GVHD)</p>	<p><b>SCREENING</b> <b>Bone density evaluation (DEXA or quantitative CT)</b> Baseline at entry into long-term follow-up, repeat as clinically indicated</p> <p><b>Info Link</b></p> <ul style="list-style-type: none"> <li>The optimal method of measuring bone health in children is controversial. Existing technologies have limitations.</li> <li>Dual energy x-ray absorptiometry (DEXA) provides an estimate of total bone mass at a given site.</li> <li>Quantitative CT provides distinct measures of trabecular and cortical bone dimension and density.</li> </ul>	<p><b>Health Links</b> <b>Bone Health</b></p> <p><b>Resources</b> National Osteoporosis Foundation website: <a href="http://www.nof.org">www.nof.org</a></p> <p><b>Considerations for Further Testing and Intervention</b> 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).</p> <div style="border: 1px solid black; padding: 5px; text-align: center; margin-top: 20px;"> <p><b>SYSTEM = Musculoskeletal</b></p> <p><b>SCORE = 2B</b></p> </div>

# HEMATOPOIETIC CELL TRANSPLANT

(cont)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
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# HEMATOPOIETIC CELL TRANSPLANT

(cont)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
110	Hematopoietic Cell Transplant (HCT)	<b>Renal toxicity</b> Glomerular injury Tubular injury Hypertension	<b>Treatment Factors</b> Chronic cyclosporine use	<b>Host Factors</b> Older age at transplant <b>Treatment Factors</b> TBI <b>Medical Conditions</b> Acute kidney injury within 6 months of HCT History of cGVHD	<b>PHYSICAL</b> <b>Blood pressure</b> Yearly  <b>SCREENING</b> <b>BUN</b> <b>Creatinine</b> <b>Na, K, Cl, CO<sub>2</sub></b> <b>Ca, Mg, PO<sub>4</sub></b> Baseline at entry into long-term follow-up, repeat as clinically indicated <b>Urinalysis</b> Yearly	<b>Health Links</b> <b>Kidney Health</b> <b>Cardiovascular Risk Factors</b>  <b>Considerations for Further Testing and Intervention</b> Nephrology consultation for patients with hypertension, proteinuria, or progressive renal insufficiency  <b>SYSTEM = Renal</b> <b>SCORE = 1</b>

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# HEMATOPOIETIC CELL TRANSPLANT

# WITH CHRONIC GVHD

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
111	HCT with <i>any history of Chronic GVHD</i>	<p><b>Dermatologic toxicity</b>                      Permanent alopecia                      Nail dysplasia                      Vitiligo                      Scleroderma                      Squamous cell carcinoma of the skin</p> <p><b>Info Link</b>                      Dermatologic toxicity is more common in presence of active cGVHD; effects may persist after cGVHD resolves.</p>			<p><b>PHYSICAL</b>                      Hair (alopecia)                      Nails (hypoplasia)                      Skin (vitiligo, scleroderma)                      Yearly</p>	<p><b>Health Links</b>                      Skin Health</p> <p><b>SYSTEM = Dermatologic</b>  <b>SCORE = 1</b></p>

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# HEMATOPOIETIC CELL TRANSPLANT

# WITH CHRONIC GVHD (cont)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
112	HCT with <i>any history of Chronic GVHD</i>	<p><b>Xerophthalmia (keratoconjunctivitis sicca)</b></p> <p><b>Info Link</b> Xerophthalmia is more common in presence of active cGVHD; effects may persist after cGVHD resolves.</p>	<p><b>Treatment Factors</b> Cranial radiation Eye radiation Radiomimetic chemotherapy (e.g., doxorubicin, dactinomycin)</p>	<p><b>Treatment Factors</b> Radiation dose to eye <math>\geq 30</math> Gy Radiation fraction <math>\geq 2</math> Gy</p>	<p><b>HISTORY</b> <b>Dry eyes (burning, itching, foreign body sensation, inflammation)</b> Yearly</p> <p><b>PHYSICAL</b> <b>Eye exam</b> Yearly</p>	<p><b>Health Links</b> <b>Eye Health</b></p> <p><b>Considerations for Further Testing and Intervention</b> 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.</p> <div style="border: 1px solid black; padding: 5px; text-align: center;"> <p><b>SYSTEM = Ocular</b></p> <p><b>SCORE = 1</b></p> </div>

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# HEMATOPOIETIC CELL TRANSPLANT

# WITH CHRONIC GVHD (cont)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
113	HCT with <i>any history of Chronic GVHD</i>	<p><b>Xerostomia</b>  <b>Salivary gland dysfunction</b>  <b>Dental caries</b>  <b>Periodontal disease</b>  <b>Oral cancer (squamous cell carcinoma)</b></p> <p><b>Info Link</b>                      Oral-dental late effects are more common in presence of active cGVHD; effects may persist after cGVHD resolves.</p>	<p><b>Treatment Factors</b>                      Head and neck radiation involving the parotid gland                      Higher radiation doses                      Radiomimetic chemotherapy (e.g., doxorubicin, dactinomycin)</p>	<p><b>Treatment Factors</b>                      Salivary gland radiation dose <math>\geq 30</math> Gy                      Use of azathioprine for cGVHD management</p> <p><b>Medical Conditions</b>                      High grade of cGVHD                      Fanconi anemia</p>	<p><b>HISTORY</b>  <b>Xerostomia</b>                      Yearly</p> <p><b>PHYSICAL</b>  <b>Oral exam</b>                      Yearly</p> <p><b>SCREENING</b>  <b>Dental exam and cleaning</b>                      Every 6 months</p>	<p><b>Health Links</b>  <b>Dental Health</b></p> <p><b>Considerations for Further Testing and Intervention</b>                      Supportive care with saliva substitutes, moistening agents, and sialogogues (pilocarpine). Regular dental care including fluoride applications and regular screening for intraoral malignancy.</p> <p><b>SYSTEM = Dental</b>  <b>SCORE = 1</b></p>

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# HEMATOPOIETIC CELL TRANSPLANT

# WITH CHRONIC GVHD (cont)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
114	HCT with <i>any history of Chronic GVHD</i>	<p><b>Pulmonary toxicity</b>  <b>Bronchiolitis obliterans</b>  <b>Chronic bronchitis</b>  <b>Bronchiectasis</b></p> <p><b>Info Link</b>                      Pulmonary late effects are more common in presence of active cGVHD; effects may persist after cGVHD resolves.</p>	<p><b>Treatment Factors</b>                      Chest radiation                      TBI                      Pulmonary toxic chemotherapy:                      - Busulfan                      - Bleomycin                      - Carmustine (BCNU)                      - Lomustine (CCNU)</p> <p><b>Health Behaviors</b>                      Smoking                      Inhaled illicit drug use</p>	<p><b>Medical Conditions</b>                      Prolonged immunosuppression related to cGVHD and its treatment</p>	<p><b>HISTORY</b>                      Cough                      SOB                      DOE                      Wheezing                      Yearly</p> <p><b>PHYSICAL</b>                      Pulmonary exam                      Yearly</p> <p><b>SCREENING</b>  <b>PFTs (including DLCO and spirometry)</b>                      Baseline at entry into long-term follow-up, repeat as clinically indicated in patients with abnormal results or progressive pulmonary dysfunction</p>	<p><b>Health Links</b>  <b>Pulmonary Health</b></p> <p><b>Resources</b>                      Extensive information regarding smoking cessation is available for patients on the NCI's website: <a href="http://www.smokefree.gov">www.smokefree.gov</a></p> <p><b>Counseling</b>                      Counsel regarding tobacco avoidance/smoking cessation. Patients who desire to SCUBA dive should be advised to obtain medical clearance from a pulmonologist.</p> <p><b>Considerations for Further Testing and Intervention</b>                      In patients with abnormal PFTs, consider repeat evaluation prior to general anesthesia. Pulmonary consultation for patients with symptomatic pulmonary dysfunction. Influenza and Pneumococcal vaccinations.</p> <p style="text-align: center;"><b>SYSTEM = Pulmonary</b> <b>SCORE = 1</b></p>

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# HEMATOPOIETIC CELL TRANSPLANT

# WITH CHRONIC GVHD (cont)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
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# HEMATOPOIETIC CELL TRANSPLANT

# WITH CHRONIC GVHD (cont)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
115	HCT with <i>any history of Chronic GVHD</i>	<p><b>Immunologic complications</b>                      Secretory IgA deficiency                      Hypogammaglobulinemia                      Decreased B cells                      T cell dysfunction                      Chronic infections (e.g., conjunctivitis, sinusitis, and bronchitis associated with chronic GVHD)</p> <p><b>Info Link</b>                      Immunologic complications related to cGVHD may persist or resolve over time.</p>		<p><b>Host Factors</b>                      Active cGVHD</p> <p><b>Medical Conditions</b>                      Prolonged immunosuppression related to cGVHD and its treatment</p>	<p><b>HISTORY</b>                      Chronic conjunctivitis                      Chronic sinusitis                      Chronic bronchitis                      Recurrent or unusual infections                      Sepsis                      Yearly</p> <p><b>PHYSICAL</b>                      Pulmonary exam                      Yearly                      Eye exam                      Yearly                      Nasal exam                      Yearly</p>	<p><b>Considerations for Further Testing and Intervention</b>                      Consider PCP and anti-fungal prophylaxis in patients with active cGVHD for duration of immunosuppressive therapy. Immunology or infectious diseases consultation for assistance with management of infections. Immunologic abnormalities may persist for up to 20 years post transplant.</p> <div style="border: 1px solid black; padding: 5px; text-align: center;"> <p><b>SYSTEM = Immune</b> <b>SCORE = 1</b></p> </div>

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# HEMATOPOIETIC CELL TRANSPLANT

# WITH CHRONIC GVHD (cont)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
116	HCT with <i>currently active</i> chronic GVHD	<p><b>Functional asplenia</b> At risk for life-threatening infection with encapsulated organisms (e.g., <i>Haemophilus influenzae</i>, <i>Streptococcus pneumoniae</i>, meningococcus)</p> <p><b>Info Link</b> This section applies only to patients who have active cGVHD.</p>	<p><b>Treatment Factors</b> Splenic radiation Ongoing immunosuppression</p>	<p><b>Host Factors</b> Hypogammaglobulinemia</p>	<p><b>PHYSICAL</b> <b>Physical exam at time of febrile illness to evaluate degree of illness and potential source of infection</b> When febrile T <math>\geq 101^{\circ}\text{F}</math> as indicated for patients with active chronic GVHD</p> <p><b>SCREENING</b> <b>Blood culture</b> When febrile T <math>\geq 101^{\circ}\text{F}</math> as indicated for patients with active chronic GVHD</p>	<p><b>Health Links</b> <b>Splenic Precautions</b></p> <p><b>Counseling</b> 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</p> <p><b>Considerations for Further Testing and Intervention</b> 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 <math>\geq 101^{\circ}</math> (38.3<math>^{\circ}</math> 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 <math>\geq 104^{\circ}\text{F}</math>; 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.</p> <p><b>Info Link</b> See current edition of AAP <i>Red Book</i> for current recommendations regarding antibiotic prophylaxis and immunizations</p> <p style="text-align: center;"><b>SYSTEM = Immune</b> <b>SCORE = 1</b></p>

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# HEMATOPOIETIC CELL TRANSPLANT

# WITH CHRONIC GVHD (cont)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
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## SECTION 116 REFERENCES—continued

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# HEMATOPOIETIC CELL TRANSPLANT

# WITH CHRONIC GVHD (cont)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
117	HCT with <i>any history of chronic GVHD</i>	<p><b>Esophageal stricture</b></p> <p><b>Info Link</b> Esophageal stricture related to cGVHD is generally not reversible over time.</p>	<p><b>Treatment Factors</b> Radiation involving the esophagus Radiomimetic chemotherapy (e.g., doxorubicin, dactinomycin)</p> <p><b>Medical Conditions</b> Gastroesophageal reflux History of Candida esophagitis</p>	<p><b>Treatment Factors</b> Radiation dose <math>\geq</math> 40 Gy</p> <p><b>Medical Conditions</b> Gut GVHD</p>	<p><b>HISTORY</b> <b>Dysphagia</b> <b>Heartburn</b> Yearly</p>	<p><b>Health Links</b> <b>Gastrointestinal Health</b></p> <p><b>Considerations for Further Testing and Intervention</b> Surgery and/or gastroenterology consultation for symptomatic patients.</p> <div style="border: 1px solid black; padding: 5px; text-align: center;"> <p><b>SYSTEM = GI/Hepatic</b></p> <p><b>SCORE = 1</b></p> </div>

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# HEMATOPOIETIC CELL TRANSPLANT

# WITH CHRONIC GVHD (cont)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
118 (female)	HCT with <i>any history of chronic GVHD</i>	<p><b>Vaginal fibrosis/stenosis</b></p> <p><b>Info Link</b> Vaginal fibrosis/stenosis related to cGVHD is generally not reversible over time.</p>	<p><b>Treatment Factors</b> Pelvic radiation</p>		<p><b>HISTORY</b></p> <p>Psychosocial assessment Dyspareunia Vulvar pain Post-coital bleeding Difficulty with tampon insertion Yearly</p> <p><b>PHYSICAL</b></p> <p>Examine genitalia for lichen planus-like features as well as erosions, fissures, and ulcers Yearly</p> <p><b>SCREENING</b></p> <p>Gynecologic consultation when age appropriate</p>	<p><b>Considerations for Further Testing and Intervention</b> Psychological consultation in patients with emotional difficulties.</p> <p><b>SYSTEM = Reproductive (female)</b> <b>SCORE = 1</b></p>

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# HEMATOPOIETIC CELL TRANSPLANT

# WITH CHRONIC GVHD (cont)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
119	HCT with <i>any history of chronic GVHD</i>	<p>Joint contractures</p> <p><b>Info Link</b> Joint contractures related to cGVHD are generally not reversible over time.</p>			Musculoskeletal exam Yearly	<p><b>Considerations for Further Testing and Intervention</b> Consultation with physical therapy, rehabilitation medicine/physiatrist.</p> <p><b>SYSTEM = Musculoskeletal</b> <b>SCORE = 1</b></p>

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# SURGERY

# AMPUTATION

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
120	<b>Amputation</b>	<b>Amputation-related complications</b> Impaired cosmesis Functional and activity limitations Residual limb integrity problems Phantom pain Neuropathic pain Musculoskeletal pain Increased energy expenditure Impaired quality of life and functional status Psychological maladjustment	<b>Host Factors</b> Skeletally immature/growing children  <b>Treatment Factors</b> Site of amputation: Hemipelvectomy > Trans-femur amputation > Trans-tibia amputation  <b>Medical Conditions</b> Obesity Diabetes Poor residual limb healing		<b>HISTORY</b> <b>Phantom pain</b> <b>Functional and activity limitations</b> Yearly  <b>PHYSICAL</b> <b>Residual limb integrity</b> Yearly  <b>SCREENING</b> <b>Prosthetic evaluation</b> Every 6 months until skeletally mature, then yearly	<b>Health Links</b> <b>Amputation</b>  <b>Counseling</b> Counsel regarding skin checks, signs of poor prosthetic fit, residual limb and prosthetic hygiene, physical fitness and importance of maintaining a healthy weight and lifestyle.  <b>Considerations for Further Testing and Intervention</b> Physical therapy consultation as needed per changing physical status such as weight gain or gait training with a new prosthesis, and for non-pharmacological pain management. Occupational therapy consultation as needed to assist with activities of daily living. Psychological/social work consultation to assist with emotional difficulties related to body image, marriage, pregnancy, parenting, employment, insurance and depression. Vocational counseling/training to identify vocations that will not produce/exacerbate functional limitations.  <b>SYSTEM = Musculoskeletal</b> <b>SCORE = 1</b>

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# SURGERY

# CENTRAL VENOUS CATHETER

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
121	Central venous catheter	Thrombosis Vascular insufficiency Infection of retained cuff or line tract			<b>HISTORY</b> Tenderness or swelling at previous catheter site Yearly  <b>PHYSICAL</b> Venous stasis Swelling Tenderness at previous catheter site Yearly and as clinically indicated	<div style="border: 1px solid black; padding: 5px; text-align: center;">                         SYSTEM = Cardiovascular                          SCORE = 1                     </div>

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# SURGERY

# CYSTECTOMY

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
122	<b>Cystectomy</b>	<b>Cystectomy-related complications</b>			<b>SCREENING</b>	<b>Health Links</b>
	<b>Info Link</b> All potential late effects for pelvic surgery apply to Cystectomy (see also Sections 145–148).	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)			<b>Vitamin B12 level</b> Yearly starting 5 years after cystectomy (patients with ileal enterocystoplasty only)	<b>Cystectomy Kidney Health</b> <div style="border: 1px solid black; padding: 10px; margin-top: 10px;"> <p><b>SYSTEM = Urinary</b></p> <p><b>SCORE =</b></p> <p><b>Asymptomatic bacteriuria: 1</b></p> <p><b>Chronic urinary tract infection: 1</b></p> <p><b>Renal dysfunction: 1</b></p> <p><b>Vesicoureteral reflux: 1</b></p> <p><b>Hydronephrosis: 1</b></p> <p><b>Spontaneous neobladder perforation: 1</b></p> <p><b>Reservoir calculi: 2A</b></p> <p><b>Vitamin B12/folate/carotene deficiency: 2B</b></p> </div>
		<b>Info Link</b> Reservoir calculi are stones in the neobladder (a reservoir for urine usually constructed of ileum/colon)			<b>Urology evaluation</b> Yearly	

## SECTION 122 REFERENCES

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# SURGERY

# ENUCLEATION

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
123	Enucleation	Impaired cosmesis Poor prosthetic fit Orbital hypoplasia	<b>Host Factors</b> Younger age at enucleation <b>Treatment Factors</b> Combined with radiation		<b>SCREENING</b> <b>Evaluation by ophthalmologist</b> Yearly <b>Evaluation by ocularist</b> Yearly	<b>Health Links</b> <b>Eye Health</b> <b>Considerations for Further Testing and Intervention</b> Psychological consultation in patients with emotional difficulties related to cosmetic and visual impairment. Vocational rehabilitation referral as indicated.  <b>SYSTEM = Ocular</b> <b>SCORE = 1</b>

## SECTION 123 REFERENCES

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# SURGERY

# HYSTERECTOMY

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
124 (female)	<b>Hysterectomy</b>  <b>Info Link</b> For patients who also underwent oophorectomy, see also: Section 141 (unilateral oophorectomy) or Section 142 (bilateral oophorectomy)	<b>Pelvic floor dysfunction</b> <b>Urinary incontinence</b> <b>Sexual dysfunction</b>	<b>Treatment Factors</b> Pelvic radiation		<b>HISTORY</b> Urinary leakage Abdominal pain Dyspareunia Psychosocial assessment Yearly	<b>Health Links</b> <b>Female Health Issues</b>  <b>Counseling</b> Counsel patients with ovaries regarding potential for biologic parenthood using gestational surrogate.  <b>Considerations for Further Testing and Intervention</b> Reproductive endocrinology consultation for patients wishing to pursue pregnancy via gestational surrogate.  <div style="border: 1px solid black; padding: 5px; text-align: center;">                         SYSTEM = Reproductive (female)                          SCORE = 2A                     </div>

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# SURGERY

# LAPAROTOMY

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
125	Laparotomy	Adhesions Bowel obstruction	Treatment Factors Combined with radiation		<b>HISTORY</b> Abdominal pain Distention Vomiting <b>Constipation</b> With clinical symptoms of obstruction  <b>PHYSICAL</b> Tenderness Abdominal guarding Distension With clinical symptoms of obstruction	<b>Health Links</b> Gastrointestinal Health  <b>Considerations for Further Testing and Intervention</b> KUB as clinically indicated for suspected obstruction. Surgical consultation for patients unresponsive to medical management.  <div style="border: 1px solid black; padding: 5px; text-align: center;">                         SYSTEM = GI/Hepatic                          SCORE = 1                     </div>

## SECTION 125 REFERENCES

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# SURGERY

# LIMB SPARING PROCEDURE

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
126	Limb sparing procedure	<p><b>Complications related to limb sparing procedure</b></p> <p>Functional and activity limitations</p> <p>Contractures</p> <p>Chronic infection</p> <p>Chronic pain</p> <p>Limb length discrepancy</p> <p>Musculoskeletal pain</p> <p>Increased energy expenditure</p> <p>Fibrosis</p> <p>Prosthetic malfunction (loosening, non-union, fracture) requiring revision, replacement or amputation</p> <p>Prosthetic revision required due to growth</p> <p>Impaired quality of life</p> <p>Complications with pregnancy/delivery (in female patients with internal hemipelvectomy)</p>	<p><b>Host Factors</b></p> <p>Younger age at surgery</p> <p>Rapid growth spurt</p> <p>Skeletally immature</p> <p><b>Treatment Factors</b></p> <p>Tibial endoprosthesis</p> <p>Use of biologic material (allograft or autograft) for reconstruction</p> <p><b>Medical Conditions</b></p> <p>Endoprosthetic infection</p> <p>Obesity</p> <p><b>Health Behaviors</b></p> <p>High level of physical activity (associated with higher risk loosening)</p> <p>Low level of physical activity (associated with higher risk of contractures or functional limitations)</p>	<p><b>Treatment Factors</b></p> <p>Radiation to extremity</p> <p><b>Medical Conditions</b></p> <p>Poor healing; Infection of reconstruction</p>	<p><b>HISTORY</b></p> <p><b>Functional and activity limitations</b></p> <p>Yearly and as clinically indicated</p> <p><b>PHYSICAL</b></p> <p><b>Residual limb integrity</b></p> <p>Yearly and as clinically indicated</p> <p><b>SCREENING</b></p> <p><b>Radiograph of affected limb</b></p> <p>Yearly</p> <p><b>Evaluation by orthopedic surgeon (ideally by an orthopedic oncologist)</b></p> <p>Every 6 months until skeletally mature, then yearly</p>	<p><b>Health Links</b></p> <p><b>Limb Sparing Procedures</b></p> <p><b>Counseling</b></p> <p>Counsel regarding need for antibiotic prophylaxis prior to dental and invasive procedures if applicable.</p> <p><b>Considerations for Further Testing and Intervention</b></p> <p>There is not consensus at the present time regarding antibiotic prophylaxis for patients with orthopedic implants undergoing dental procedures; guidelines are currently under development by the American Dental Association (ADA) and American Academy of Orthopedic Surgery (AAOS). Counsel patients to discuss the potential need for antibiotic prophylaxis prior to dental and invasive procedures with their treating dentist/orthopedic surgeon. Physical therapy consultation as needed per changes in functional status (such as post-lengthening, revisions, life changes such as pregnancy), and for non-pharmacological pain management. Consider psychological consultation as needed to assist with emotional difficulties related to body image, marriage, pregnancy, parenting, employment, insurance and depression. Vocational counseling/training to identify vocations that will not produce/exacerbate functional limitations.</p> <p><b>SYSTEM = Musculoskeletal</b></p> <p><b>SCORE = 1</b></p>

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# LIMB SPARING PROCEDURE (cont)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
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# SURGERY

# NEPHRECTOMY

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
127 (male)	<b>Nephrectomy</b>	<p><b>Hydrocele</b> <b>Renal toxicity</b> Proteinuria Hyperfiltration Renal insufficiency</p> <p><b>Info Link</b>  <ul style="list-style-type: none"> <li>• Surgery-induced renal atrophy (vanishing kidney) is a rare complication reported in survivors who have undergone retroperitoneal tumor resections.</li> <li>• Once this diagnosis is established, annual screening should include evaluations recommended for children treated with nephrectomy.</li> </ul> </p>	<p><b>Host Factors</b> Denys-Drash syndrome WAGR syndrome Hypospadias Cryptorchidism Bilateral Wilms tumor</p> <p><b>Treatment Factors</b> Combined with other nephrotoxic therapy such as:  <ul style="list-style-type: none"> <li>- Cisplatin</li> <li>- Carboplatin</li> <li>- Ifosfamide</li> <li>- Aminoglycosides</li> <li>- Amphotericin</li> <li>- Immunosuppressants</li> <li>- Methotrexate</li> <li>- Radiation impacting the kidneys</li> </ul> </p>		<p><b>PHYSICAL</b></p> <p><b>Blood pressure</b> Yearly</p> <p><b>Testicular exam to evaluate for hydrocele</b> Yearly</p> <p><b>SCREENING</b></p> <p><b>BUN</b> <b>Creatinine</b> <b>Na, K, Cl, CO<sub>2</sub></b> <b>Ca, Mg, PO<sub>4</sub></b> Baseline at entry into long-term follow-up. Repeat as clinically indicated</p> <p><b>Urinalysis</b> Yearly</p>	<p><b>Health Links</b> <b>Single Kidney Health</b> <b>See also: Kidney Health</b> <b>Cardiovascular Risk Factors</b></p> <p><b>Counseling</b> 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.</p> <p><b>Considerations for Further Testing and Intervention</b> Nephrology consultation for patients with hypertension, proteinuria or progressive renal insufficiency.</p> <div style="border: 1px solid black; padding: 5px; text-align: center; margin-top: 10px;"> <p><b>SYSTEM = Urinary</b> <b>SCORE = 1</b></p> </div>

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# SURGERY

# NEPHRECTOMY (cont)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
128 (female)	<b>Nephrectomy</b>	<p><b>Renal toxicity</b> Proteinuria Hyperfiltration Renal insufficiency</p> <p><b>Info Link</b>  <ul style="list-style-type: none"> <li>• Surgery-induced renal atrophy (vanishing kidney) is a rare complication reported in survivors who have undergone retroperitoneal tumor resections.</li> <li>• Once this diagnosis is established, annual screening should include evaluations recommended for children treated with nephrectomy.</li> </ul> </p>	<p><b>Host Factors</b> Denys-Drash syndrome WAGR syndrome Bilateral Wilms tumor</p> <p><b>Treatment Factors</b> Combined with other nephrotoxic therapy such as: Cisplatin Carboplatin Ifosfamide Aminoglycosides Amphotericin Immunosuppressants Methotrexate Radiation impacting the kidneys</p>		<p><b>PHYSICAL</b> <b>Blood pressure</b> Yearly</p> <p><b>SCREENING</b> <b>BUN</b> <b>Creatinine</b> <b>Na, K, Cl, CO<sub>2</sub></b> <b>Ca, Mg, PO<sub>4</sub></b> Baseline at entry into long-term follow-up. Repeat as clinically indicated</p> <p><b>Urinalysis</b> Yearly</p>	<p><b>Health Links</b> <b>Single Kidney Health</b> <b>See also: Kidney Health</b> <b>Cardiovascular Risk Factors</b></p> <p><b>Counseling</b> 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.</p> <p><b>Considerations for Further Testing and Intervention</b> Nephrology consultation for patients with hypertension, proteinuria, or progressive renal insufficiency.</p> <div style="border: 1px solid black; padding: 5px; text-align: center; margin-top: 20px;"> <p><b>SYSTEM = Urinary</b> <b>SCORE = 1</b></p> </div>

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# SURGERY

# NEUROSURGERY—BRAIN

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
129	Neurosurgery—Brain	<p><b>Neurocognitive deficits</b> Functional deficits in:</p> <ul style="list-style-type: none"> <li>- Executive function (planning and organization)</li> <li>- Sustained attention</li> <li>- Memory (particularly visual, sequencing, temporal memory)</li> <li>- Processing speed</li> <li>- Visual-motor integration</li> </ul> <p>Learning deficits in math and reading (particularly reading comprehension) Diminished IQ Behavioral change</p> <hr/> <p><b>Info Link</b></p> <ul style="list-style-type: none"> <li>• Neurocognitive deficits vary with extent of surgery and postoperative complications.</li> <li>• In general, mild delays occur in most areas of neuropsychological function compared to healthy children.</li> <li>• Extent of deficit depends on age at treatment, intensity of treatment, and time since treatment.</li> <li>• New deficits may emerge over time.</li> <li>• Neurosensory deficits (i.e., vision, hearing) due to tumor or its therapy may complicate neurocognitive outcomes.</li> </ul>	<p><b>Host Factors</b> Younger age at treatment Primary CNS tumor</p> <p><b>Treatment Factors</b> In combination with:</p> <ul style="list-style-type: none"> <li>- TBI</li> <li>- Cranial radiation; Methotrexate (IT, IO, high-dose IV)</li> <li>- Cytarabine (high-dose IV)</li> </ul> <p>Longer elapsed time since therapy Extent and location of resection</p> <p><b>Medical Conditions</b> Hydrocephalus/history of shunt placement</p>	<p><b>Host Factors</b> Age &lt; 3 years at time of treatment Predisposing family history of learning or attention problems</p> <p><b>Treatment Factors</b> Radiation dose ≥ 24 Gy to whole brain Radiation dose ≥ 40 Gy to local fields</p> <p><b>Medical Conditions</b> Posterior fossa syndrome CNS infection</p>	<p><b>HISTORY</b> <b>Educational and/or vocational progress</b> Yearly</p> <hr/> <p><b>SCREENING</b> <b>Referral for formal neuropsychological evaluation</b> Baseline at entry into long-term follow-up, then periodically as clinically indicated for patients with evidence of impaired educational or vocational progress</p>	<p><b>Health Links</b> <b>Educational Issues</b></p> <hr/> <p><b>Considerations for Further Testing and Intervention</b> 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.</p> <div style="text-align: center; border: 1px solid black; padding: 5px; margin-top: 20px;"> <p><b>SYSTEM = CNS</b></p> <p><b>SCORE = 1</b></p> </div>

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# SURGERY

# NEUROSURGERY—BRAIN (cont)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
130	Neurosurgery—Brain	<b>Motor and/or sensory deficits</b> Paralysis Movement disorders Ataxia Eye problems (ocular nerve palsy, gaze paresis, nystagmus, papilledema, optic atrophy)	<b>Host Factors</b> Primary CNS tumor  <b>Medical Conditions</b> Hydrocephalus	<b>Host Factors</b> Optic pathway tumor; Hypothalamic tumor; Suprasellar tumor (eye problems)	<b>SCREENING</b>  <b>Evaluation by neurologist</b> Yearly, until 2 to 3 years after surgery or stable; Continue to monitor if symptoms persist  <b>Evaluation by physiatrist/rehabilitation medicine specialist</b> Yearly, or more frequently as clinically indicated in patients with motor dysfunction	<b>Considerations for Further Testing and Intervention</b>  Speech, physical, and occupational therapy in patients with persistent deficits. Consider consultations with nutrition, endocrine, and psychiatry (for obsessive-compulsive behaviors) in patients with hypothalamic-pituitary axis tumors. Ophthalmology evaluation as clinically indicated.  <div style="border: 1px solid black; padding: 5px; text-align: center;"> <b>SYSTEM = CNS</b>  <b>SCORE = 1</b> </div>

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# SURGERY

# NEUROSURGERY—BRAIN (cont)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
131	Neurosurgery—Brain	Seizures	<b>Host Factors</b> Primary CNS tumor  <b>Treatment Factors</b> Methotrexate (IV, IT, IO)		<b>SCREENING</b>  <b>Evaluation by neurologist</b> As clinically indicated	<div style="border: 1px solid black; padding: 5px; text-align: center;">                         SYSTEM = CNS                          SCORE = 1                     </div>

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# SURGERY

# NEUROSURGERY—BRAIN (cont)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
132	Neurosurgery—Brain	Hydrocephalus Shunt malfunction	Host Factors Primary CNS tumor		<b>SCREENING</b> <b>Abdominal x-ray</b> After pubertal growth spurt for patients with shunts to assure distal shunt tubing in peritoneum  <b>Evaluation by neurologist</b> Yearly for patients with shunts	<b>Counseling</b> Education patient/family regarding potential symptoms of shunt malfunction.  <b>Considerations for Further Testing and Intervention</b> 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).  <div style="border: 1px solid black; padding: 5px; text-align: center;"> <b>SYSTEM = CNS</b>  <b>SCORE = 1</b> </div>

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# SURGERY

# NEUROSURGERY—BRAIN (cont)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
133	<b>Neurosurgery—Brain</b> (applies only to neurosurgery with potential to affect the Hypothalamic-Pituitary Axis)	<p><b>Overweight/obesity</b></p> <p><b>Info Link</b> Overweight - Age 2–20 years: BMI for age ≥ 85th–&lt; 95th percentile - Age ≥ 21 years: BMI ≥ 25–29.9; Obesity - Age 2–20 years: BMI for age ≥ 95th percentile - Age ≥ 21 years: BMI ≥ 30</p> <p>BMI = wt(kg)/ht(M<sup>2</sup>) BMI calculator available on-line at: <a href="http://www.nhlbi.nih.gov/guidelines/obesity/BMI/bmicalc.htm">www.nhlbi.nih.gov/guidelines/obesity/BMI/bmicalc.htm</a>// Growth charts for patients &lt; 21 years of age available on-line at: <a href="http://www.cdc.gov/growthcharts">www.cdc.gov/growthcharts</a></p>	<b>Treatment Factors</b> Surgery in suprasellar region	<b>Host Factors</b> Extension of tumor into hypothalamus Pre-treatment obesity Craniopharyngioma	<b>PHYSICAL</b> <b>Height</b> <b>Weight</b> <b>BMI</b> Yearly	<p><b>Health Links</b></p> <p><b>Diet and Physical Activity</b> <b>Cardiovascular Risk Factors</b></p> <p><b>Counseling</b> Nutritional counseling. Counsel regarding obesity-related health risks</p> <p><b>Considerations for Further Testing and Intervention</b> 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.</p> <p><b>SYSTEM = Endocrine/Metabolic</b> <b>SCORE = 2A</b></p>

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# SURGERY

# NEUROSURGERY—BRAIN (cont)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
134	<b>Neurosurgery—Brain</b> (applies only to neurosurgery with potential to affect the Hypothalamic-Pituitary Axis)	<b>Diabetes insipidus</b>	<b>Treatment Factors</b> Surgery in suprasellar region Reoperation for recurrent tumor	<b>Host Factors</b> Extension of tumor into hypothalamus Craniopharyngioma	<b>HISTORY</b> Assessment of excessive thirst/polyuria Yearly  <b>SCREENING</b> <b>Na, K, Cl, CO<sub>2</sub></b> <b>Serum Osmolality</b> <b>Urine Osmolality</b> As clinically indicated if history consistent with excessive thirst and/or polyuria	<b>Health Links</b> <b>Hypopituitarism</b>  <b>Considerations for Further Testing and Intervention</b> Consider evaluation for other central endocrinopathies, including growth hormone deficiency, central hypothyroidism, central adrenal insufficiency, precocious puberty, and gonadotropin deficiency. Refer to endocrine to manage hormonal dysfunction.  <div style="border: 1px solid black; padding: 5px; text-align: center;"> <b>SYSTEM = Endocrine/Metabolic</b>  <b>SCORE = 1</b> </div>

## SECTION 134 REFERENCES

- Elliott RE, Hsieh K, Hochm T, Belitskaya-Levy I, Wisoff J, Wisoff JH. Efficacy and safety of radical resection of primary and recurrent craniopharyngiomas in 86 children. *J Neurosurg Pediatr.* Jan 2010;5(1):30-48.
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# SURGERY

# NEUROSURGERY—SPINAL CORD

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
135	Neurosurgery—Spinal cord	Neurogenic bladder Urinary incontinence	<b>Host Factors</b> Tumor adjacent to or compressing spinal cord or cauda equina  <b>Treatment Factors</b> Radiation dose ≥ 45 Gy to lumbar and/or sacral spine and/or cauda equina	<b>Host Factors</b> Injury above the level of the sacrum  <b>Treatment Factors</b> Radiation dose ≥ 50 Gy to lumbar and/or sacral spine and/or cauda equina	<b>HISTORY</b> Hematuria Urinary urgency/frequency Urinary incontinence/retention Dysuria Nocturia Abnormal urinary stream Yearly	<b>Health Links</b> Neurogenic Bladder  <b>Counseling</b> 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.  <b>Considerations for Further Testing and Intervention</b> Urologic consultation for patients with dysfunctional voiding or recurrent urinary tract infections.  <div style="text-align: center; border: 1px solid black; padding: 5px;">                         SYSTEM = CNS                          SCORE = 1                     </div>

## SECTION 135 REFERENCES

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# SURGERY

# NEUROSURGERY—SPINAL CORD (cont)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
136	Neurosurgery—Spinal cord	Neurogenic bowel Fecal incontinence	<b>Host Factors</b> Tumor adjacent to or compressing spinal cord or cauda equina  <b>Treatment Factors</b> Radiation dose $\geq$ 50 Gy to bladder, pelvis, or spine	<b>Host Factors</b> Injury above the level of the sacrum	<b>HISTORY</b> <b>Chronic constipation</b> <b>Fecal soiling</b> Yearly  <b>PHYSICAL</b> <b>Rectal exam</b> As clinically indicated	<b>Counseling</b> Counsel regarding benefits of adherence to bowel regimen, including adequate hydration, fiber, laxatives/enemas as clinically indicated.  <b>Considerations for Further Testing and Intervention</b> GI consultation to establish bowel regimen for patients with chronic impaction or fecal soiling.  <div style="border: 1px solid black; padding: 5px; text-align: center;">                         SYSTEM = CNS                          SCORE = 1                     </div>

## SECTION 136 REFERENCES

- Fowler C, ed. Neurology of Bladder, Bowel, and Sexual Dysfunction. Vol 23. 2nd ed. Burlington, MA: Butterworth-Heinemann; 1999.
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# SURGERY

# NEUROSURGERY—SPINAL CORD (cont)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
137 (male)	Neurosurgery—Spinal cord	<b>Psychosexual dysfunction</b> Erectile dysfunction Ejaculatory dysfunction	<b>Host Factors</b> Tumor adjacent to or compressing spinal cord or cauda equina  <b>Treatment Factors</b> Radiation to bladder, pelvis, or spine  <b>Medical Conditions</b> Hypogonadism	<b>Host Factors</b> Injury above the level of the sacrum  <b>Treatment Factors</b> Radiation dose $\geq$ 55 Gy to penile bulb in adult and $\geq$ 45 Gy in prepubertal child	<b>HISTORY</b> <b>Sexual function (erections, nocturnal emissions, libido)</b> Yearly  <b>Medication use</b> Yearly	<b>Health Links</b> <b>Male Health Issues</b>  <b>Counseling</b> 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>  <b>Considerations for Further Testing and Intervention</b> Urologic consultation in patients with positive history.  <div style="border: 1px solid black; padding: 5px; text-align: center;">SYSTEM = CNS SCORE = 2A</div>

## SECTION 137 REFERENCES

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# SURGERY

# NEUROSURGERY—SPINAL CORD (cont)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
138 (female)	Neurosurgery—Spinal cord	Psychosexual dysfunction	<b>Host Factors</b> Tumor adjacent to or compressing spinal cord or cauda equina  <b>Treatment Factors</b> Radiation to bladder, pelvis, or spine  <b>Medical Conditions</b> Hypogonadism Vaginal fibrosis/stenosis Chronic GVHD	<b>Host Factors</b> Injury above the level of the sacrum	<b>HISTORY</b> Altered or diminished sensation, loss of sensation ) Dyspareunia Medication use Yearly	<b>Considerations for Further Testing and Intervention</b> Gynecologic consultation in patients with positive history.  <div style="border: 1px solid black; padding: 5px; width: fit-content; margin: auto;">                         SYSTEM = CNS                          SCORE = 2A                     </div>

## SECTION 138 REFERENCES

- Fowler C, ed. Neurology of Bladder, Bowel, and Sexual Dysfunction. Vol 23. 2nd ed. Burlington, MA: Butterworth-Heinemann; 1999.
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# SURGERY

# NEUROSURGERY—SPINAL CORD (cont)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
139	<b>Neurosurgery—Spinal cord</b> Laminectomy Laminoplasty	<b>Scoliosis/Kyphosis</b>	<b>Host Factors</b> Preoperative deformity Young age (deformity can still develop even if skeletally mature at time of surgery)  <b>Treatment Factors</b> Radiation to the spine Increasing number of laminae removed Facetectomy Laminectomy (versus laminotomy) Laminectomy without fusion	<b>Treatment Factors</b> > 3 laminae removed; Increasing number of resections Surgery of thoracolumbar junction	<b>PHYSICAL</b>  <b>Spine exam for scoliosis and kyphosis</b> Yearly until growth completed, may need more frequent assessment during puberty or if curve detected	<b>Health Links</b> <b>Scoliosis and Kyphosis</b>  <b>Considerations for Further Testing and Intervention</b> Spine films in patients with clinically apparent curve. Orthopedic consultation as indicated based on radiographic exam.  <div style="border: 1px solid black; padding: 5px; text-align: center;"> <b>SYSTEM = Musculoskeletal</b>  <b>SCORE = 1</b> </div>

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# SURGERY

# OOPHOROPEXY

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
140 (female)	<b>Oophoropexy</b>	<b>Oophoropexy-related complications</b> Inability to conceive despite normal ovarian function Dyspareunia Symptomatic ovarian cysts Bowel obstruction Pelvic adhesions	<b>Treatment Factors</b> Ovarian radiation Tubo-ovarian dislocation, especially with lateral ovarian transposition		<b>HISTORY</b> <b>Inability to conceive despite normal ovarian function</b> <b>Dyspareunia</b> <b>Abdominal pain</b> <b>Pelvic pain</b> Yearly	<b>Considerations for Further Testing and Intervention</b> Gynecologic consultation for patients with positive history and/or physical findings.
	<b>Info Link</b> Also see Section 96 if shielding from radiation was incomplete.					

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

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# SURGERY

# OOPHORECTOMY (UNILATERAL)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
141 (female)	Oophorectomy (unilateral)	<p>Premature menopause</p> <p><b>Info Link</b> Evidence for premature menopause following unilateral oophorectomy is limited and has been extrapolated from the adult literature.</p>	Health Behaviors Smoking	<p><b>Treatment Factors</b></p> <ul style="list-style-type: none"> <li>- Combined with:</li> <li>- Pelvic radiation</li> <li>- Alkylating agents</li> <li>- TBI</li> </ul>	<p><b>SCREENING</b></p> <p><b>FSH</b></p> <p><b>LH</b></p> <p><b>Estradiol</b></p> <p>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</p>	<p><b>Health Links</b></p> <p><b>Female Health Issues</b></p> <p><b>Resources</b></p> <p>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>)</p> <p><b>Counseling</b></p> <p>Counsel currently menstruating women to be cautious about delaying childbearing. Counsel regarding need for contraception.</p> <p><b>Considerations for Further Testing and Intervention</b></p> <p>Refer to reproductive endocrinology for counseling regarding oocyte cryopreservation in patients wishing to preserve options for future fertility.</p> <p><b>SYSTEM = Reproductive (female)</b></p> <p><b>SCORE = 2A</b></p>

## SECTION 141 REFERENCES

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# SURGERY

# OOPHORECTOMY (BILATERAL)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
142 (female)	Oophorectomy (bilateral)	Hypogonadism Infertility			<b>SCREENING</b> Gynecologic or endocrinologic consultation for initiation of hormonal replacement therapy At age 11 or immediately for post-pubertal patients	<b>Health Links</b> Female Health Issues  <b>Resources</b> 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> )  <b>Counseling</b> 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).  <b>Considerations for Further Testing and Intervention</b> Bone density evaluation in hypogonadal patients. Reproductive endocrinology referral regarding assisted reproductive technologies. Monitor cardiovascular health.  <div style="border: 1px solid black; padding: 5px; text-align: center;"> <b>SYSTEM = Reproductive (female)</b>  <b>SCORE = 1</b> </div>

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# SURGERY

# ORCHIECTOMY (UNILATERAL)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
143 (male)	<b>Orchiectomy</b> unilateral	<b>Gonadal dysfunction (testicular)</b> Reduced fertility Testosterone insufficiency	<p><b>Host Factors</b>                      Testicular cancer                      Obesity                      Ejaculatory dysfunction                      Medications                      Occupational exposures (pesticides, heavy metals, solvents)</p> <p><b>Treatment Factors</b>                      Unilateral orchiectomy combined with pelvic or testicular radiation and/or alkylating agents</p> <p><b>Health Behaviors</b>                      Tobacco/marijuana use                      History of sexually transmitted diseases</p>		<p><b>HISTORY</b>                      Pubertal (onset, tempo)                      Sexual function (erections, nocturnal emissions, libido)                      Medication use                      Yearly</p> <p><b>PHYSICAL</b>                      Tanner staging                      Until sexually mature                      Testicular volume by Prader orchimeter; Testicular examination (including prosthesis)                      Yearly</p> <p><b>SCREENING</b>                      Screening for reduced fertility: Semen analysis                      As requested by sexually mature patient</p> <p><b>FSH</b>                      In sexually mature patient if unable to obtain semen analysis</p> <p><b>Screening for testosterone insufficiency: Testosterone</b> (ideally morning)                      As clinically indicated in patients with delayed or arrested puberty and/or clinical signs and symptoms of testosterone deficiency</p>	<p><b>Health Links</b>                      Male Health Issues</p> <p><b>Counseling</b>                      Counsel to wear athletic supporter with protective cup during athletic activities.</p> <p><b>Considerations for Further Testing and Intervention</b>                      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.</p> <div style="border: 1px solid black; padding: 5px; text-align: center;"> <p><b>SYSTEM = Reproductive (male)</b> <b>SCORE = 1</b></p> </div>

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# SURGERY

# ORCHIECTOMY (BILATERAL)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
144 (male)	<b>Orchiectomy</b> bilateral	<b>Gonadal dysfunction (testicular)</b> Infertility Testosterone Deficiency			<b>PHYSICAL</b> Examination of testicular prostheses Yearly  <b>SCREENING</b> Refer to endocrinology at age 11 for initiation of hormonal replacement therapy to induce puberty (or immediately for post-pubertal patients)	<b>Health Links</b> Male Health Issues  <b>Considerations for Further Testing and Intervention</b> 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.  <div style="border: 1px solid black; padding: 5px; text-align: center;">                         SYSTEM = Reproductive (male)                          SCORE = 1                     </div>

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# SURGERY

# PELVIC SURGERY

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
145	<b>Pelvic surgery Cystectomy</b>	<b>Urinary incontinence Urinary tract obstruction</b>	<b>Host Factors</b> Tumor adjacent to or compressing spinal cord or cauda equina  <b>Treatment Factors</b> Retroperitoneal node dissection Extensive pelvic dissection (e.g., bilateral ureteral re-implantation, retroperitoneal tumor resection) Radiation to the bladder, pelvis, and/or lumbar-sacral spine		<b>HISTORY</b> <b>Hematuria</b> <b>Urinary urgency/frequency</b> <b>Urinary incontinence/retention</b> <b>Dysuria</b> <b>Nocturia</b> <b>Abnormal urinary stream</b> Yearly	<b>Counseling</b> 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.
	<b>Info Link</b> For patients with cystectomy: See also Section 122					<b>Considerations for Further Testing and Intervention</b> Urologic consultation for patients with dysfunctional voiding or recurrent urinary tract infections.

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

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# SURGERY

# PELVIC SURGERY (cont)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
146	Pelvic surgery Cystectomy	Fecal incontinence	<b>Host Factors</b> Tumor adjacent to or compressing spinal cord or cauda equina  <b>Treatment Factors</b> Radiation to the bladder, pelvis, or spine		<b>HISTORY</b> <b>Chronic constipation</b> <b>Fecal soiling</b> Yearly  <b>PHYSICAL</b> <b>Rectal exam</b> As clinically indicated	<b>Counseling</b> Counsel regarding benefits of adherence to bowel regimen, including adequate hydration, fiber, laxatives/enemas as clinically indicated.  <b>Considerations for Further Testing and Intervention</b> GI consultation to establish bowel regimen for patients with chronic impaction or fecal soiling.  <div style="border: 1px solid black; padding: 5px; text-align: center;">                         SYSTEM = GI/Hepatic                          SCORE = 1                     </div>

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# SURGERY

# PELVIC SURGERY (cont)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
147 (male)	<b>Pelvic surgery</b> <b>Cystectomy</b>	<b>Sexual dysfunction (male)</b> Retrograde ejaculation Anejaculation Erectile dysfunction	<b>Treatment Factors</b> Retroperitoneal node dissection Retroperitoneal tumor resection Cystectomy Radical prostatectomy Tumor adjacent to spine; Radiation to bladder, pelvis, or spine  <b>Medical Conditions</b> Hypogonadism	<b>Host Factors</b> Extensive presacral tumor resection or dissection; Radiation dose ≥ 55 Gy to penile bulb in adult and ≥ 45 Gy in prepubertal child	<b>HISTORY</b> <b>Sexual function (erections, nocturnal emissions, libido)</b> <b>Medication use</b> <b>Quality of ejaculate (frothy white urine with first void after intercourse suggests retrograde ejaculation)</b> Yearly	<b>Health Links</b> Male Health Issues  <b>Resources</b> <a href="http://www.urologychannel.com">www.urologychannel.com</a>  <b>Counseling</b> Men with erectile/ejaculatory dysfunction desiring paternity can consider assisted reproductive technology for sperm retrieval.  <b>Considerations for Further Testing and Intervention</b> Urologic consultation in patients with positive history and/or physical exam findings.  <div style="border: 1px solid black; padding: 5px; text-align: center;"> <b>SYSTEM = Reproductive (male)</b> <b>SCORE = 2A</b> </div>

## SECTION 147 REFERENCES

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# SURGERY

# PELVIC SURGERY (cont)

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

## SECTION 148 REFERENCES

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# SURGERY

# SPLENECTOMY

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
149	Splenectomy	<b>Asplenia</b> At risk for life-threatening infection with encapsulated organisms (e.g., <i>Haemophilus influenzae</i> , <i>Streptococcus pneumoniae</i> , <i>meningococcus</i> )			<b>PHYSICAL</b> Physical exam at time of febrile illness to evaluate degree of illness and potential source of infection When febrile T ≥ 101°F  <b>SCREENING</b> <b>Blood culture</b> When febrile T ≥ 101°F	<b>Health Links</b> <b>Splenic Precautions</b>  <b>Counseling</b> 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.  <b>Considerations for Further Testing and Intervention</b> 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.  <b>Info Link</b> See current edition of AAP <i>Red Book</i> for recommendations regarding antibiotic prophylaxis and immunizations
						<b>SYSTEM = Immune</b> <b>SCORE = 2A</b>

## SECTION 149 REFERENCES

- American Academy of Pediatrics. Red Book: 2012 Report of the Committee on Infectious Diseases. Pickering LK, ed. 29th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2012
- American Academy of Pediatric Dentistry, Guideline on Dental Management of Pediatric Patients Receiving Chemotherapy, Hematopoietic Cell Transplantation, and/or Radiation. *Pediatr Dent*. 2013;35(5):185-193.
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# SURGERY

# SPLENECTOMY (cont)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
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## SECTION 149 REFERENCES

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# SURGERY

# THORACIC SURGERY

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
150	Thoracic surgery (includes thoracotomy, chest wall surgery, rib resection, pulmonary lobectomy, pulmonary metastasectomy, pulmonary wedge resection)	Pulmonary dysfunction	<b>Treatment Factors</b> Combined with pulmonary toxic therapy: - Bleomycin - Busulfan - Carmustine (BCNU) - Lomustine (CCNU)  <b>Medical Conditions</b> Atopic history  <b>Health Behaviors</b> Smoking Inhaled illicit drug use	<b>Treatment Factors</b> Combined with: - Chest radiation - TBI	<b>HISTORY</b> Cough SOB DOE Wheezing Yearly  <b>PHYSICAL</b> Pulmonary exam Yearly  <b>SCREENING</b> <b>PFTs (including DLCO and spirometry)</b> Baseline at entry into long-term follow-up, repeat as clinically indicated in patients with abnormal results or progressive pulmonary dysfunction	<b>Health Links</b> Pulmonary Health  <b>Resources</b> Extensive information regarding smoking cessation is available for patients on the NCI's website: <a href="http://www.smokefree.gov">www.smokefree.gov</a>  <b>Counseling</b> Counsel regarding tobacco avoidance/smoking cessation. Patients who desire to SCUBA dive should be advised to obtain medical clearance from a pulmonologist.  <b>Considerations for Further Testing and Intervention</b> In patients with abnormal PFTs, consider repeat evaluation prior to general anesthesia. Pulmonary consultation for patients with symptomatic pulmonary dysfunction; Influenza and pneumococcal vaccinations .  <div style="text-align: center; border: 1px solid black; padding: 5px;">                         SYSTEM = Pulmonary                          SCORE = 2A                     </div>

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# SURGERY

# THORACIC SURGERY (cont)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
151	Thoracic surgery (includes thoracotomy, chest wall surgery, rib resection, pulmonary lobectomy, pulmonary metastasectomy, pulmonary wedge resection)	Scoliosis/Kyphosis	<b>Host Factors</b> Young age (deformity can still develop even if skeletally mature at time of surgery) Preoperative deformity <b>Treatment Factors</b> Radiation to the spine	<b>Treatment Factors</b> Greater number of ribs resected	<b>PHYSICAL</b> <b>Spine exam for scoliosis and kyphosis</b> Yearly until growth completed, may need more frequent assessment during puberty or if curve detected	<b>Health Links</b> Scoliosis and Kyphosis  <b>Considerations for Further Testing and Intervention</b> Spine films in patients with clinically apparent curve. Orthopedic consultation as indicated based on radiographic exam  <div style="border: 1px solid black; padding: 5px; text-align: center;">                         SYSTEM = Musculoskeletal                          SCORE = 2A                     </div>

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# SURGERY

# THYROIDECTOMY

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
152	<b>Thyroidectomy</b>  <b>Info Link</b> <ul style="list-style-type: none"> <li>• 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.</li> <li>• 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).</li> </ul>	Hypothyroidism			<b>HISTORY</b> Fatigue Weight gain Cold intolerance Constipation Dry skin Brittle hair Depressed mood Yearly  <b>PHYSICAL</b> Height Weight Hair and skin Thyroid exam Yearly, consider more frequent screening during periods of rapid growth  <b>SCREENING</b> TSH Free T4 Yearly, consider more frequent screening during periods of rapid growth	<b>Health Links</b> Thyroid Problems  <b>Counseling</b> Counsel at-risk females of childbearing potential to have their thyroid levels checked prior to attempting pregnancy and periodically throughout pregnancy.  <b>Considerations for Further Testing and Intervention</b> Endocrine consultation for medical management.  <div style="border: 1px solid black; padding: 5px; text-align: center;"> <b>SYSTEM = Endocrine/Metabolic</b>   <b>SCORE = 1</b> </div>

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## OTHER THERAPEUTIC MODALITIES

## SYSTEMIC RADIATION

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
153	Radioiodine therapy (I-131 thyroid ablation)	Lacrimal duct atrophy			<b>HISTORY</b> Excessive tearing Yearly	<b>Considerations for Further Testing and Intervention</b> Ophthalmology consultation as clinically indicated.  <div style="border: 1px solid black; padding: 5px; text-align: center;">                         SYSTEM = Ocular                          SCORE = 2A                     </div>

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# OTHER THERAPEUTIC MODALITIES

# SYSTEMIC RADIATION (cont)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
154	Radioiodine therapy (I-131 thyroid ablation)	Hypothyroidism			<p><b>HISTORY</b></p> <p>Fatigue Weight gain Cold intolerance Constipation Dry skin Brittle hair Depressed mood</p> <p>Yearly, consider more frequent screening during periods of rapid growth</p> <p><b>PHYSICAL</b></p> <p>Height Weight Hair and skin Thyroid exam</p> <p>Yearly, consider more frequent screening during periods of rapid growth</p> <p><b>SCREENING</b></p> <p><b>TSH</b></p> <p><b>Free T4</b></p> <p>Yearly, consider more frequent screening during periods of rapid growth</p>	<p><b>Health Links</b></p> <p>Thyroid Problems</p> <p><b>Counseling</b></p> <p>Counsel at-risk females of childbearing potential to have their thyroid levels checked prior to attempting pregnancy and periodically throughout pregnancy.</p> <p><b>Considerations for Further Testing and Intervention</b></p> <p>Endocrine consultation for medical management.</p> <div style="border: 1px solid black; padding: 5px; text-align: center; margin-top: 20px;"> <p><b>SYSTEM = Endocrine/Metabolic</b></p> <p><b>SCORE = 2A</b></p> </div>

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# OTHER THERAPEUTIC MODALITIES

# SYSTEMIC RADIATION (cont)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
155	<b>Systemic MIBG (in therapeutic doses)</b>	Hypothyroidism			<b>HISTORY</b> Fatigue Weight gain Cold intolerance Constipation Dry skin Brittle hair Depressed mood Yearly, consider more frequent screening during periods of rapid growth	<b>Health Links</b> Thyroid Problems  <b>Counseling</b> Counsel at-risk females of childbearing potential to have their thyroid levels checked prior to attempting pregnancy and periodically throughout pregnancy.  <b>Considerations for Further Testing and Intervention</b> Endocrine consultation for medical management.
	<b>Info Link</b> MIBG used for diagnostic purposes (i.e., MIBG scanning) does NOT put patients at risk for hypothyroidism.					

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

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## OTHER THERAPEUTIC MODALITIES

## BIOIMMUNOTHERAPY

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

### SECTION 156 REFERENCES

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# CANCER SCREENING GUIDELINES

## BREAST CANCER

Sec #	Organ	Population Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
157 (female)	Breast	<p>Over age 40</p> <p>Family history of breast cancer in first degree relative</p> <p>Early onset of menstruation</p> <p>Late onset of menopause (age 55 or older)</p> <p>Older than 30 at birth of first child</p> <p>Never pregnant</p> <p>Obesity</p> <p>Previous breast biopsy with atypical hyperplasia</p> <p>Hormone replacement therapy</p>	<p>Chest radiation with potential impact to the breast (see Section 77), including <math>\geq 20</math> Gy to the following fields:</p> <ul style="list-style-type: none"> <li>- Chest (thorax)</li> <li>- Whole lung</li> <li>- Mediastinal</li> <li>- Axilla</li> <li>- Mini-Mantle</li> <li>- Mantle</li> <li>- Extended Mantle</li> <li>- TLI</li> <li>- STLI</li> <li>- TBI*</li> </ul> <p><i>BRCA1, BRCA2, ATM</i> mutation</p>	<p><b>PATIENTS AT STANDARD RISK (ACS Recommendation)</b></p> <p><b>PHYSICAL</b></p> <p><b>Clinical breast exam</b> Every 3 years between ages 20–39, then yearly beginning at age 40</p> <p><b>SCREENING</b></p> <p><b>Mammogram</b> Yearly, beginning at age 40</p> <p><b>PATIENTS AT HIGHEST RISK</b> (<math>\geq 20</math> Gy radiation with potential impact to the breast)</p> <p><b>PHYSICAL</b></p> <p><b>Breast self exam</b> Monthly, beginning at puberty</p> <p><b>Clinical breast exam</b> Yearly, beginning at puberty until age 25, then every 6 months</p> <p><b>SCREENING</b></p> <p><b>Mammogram</b> Yearly, beginning 8 years after radiation or at age 25, whichever occurs last.</p> <p><b>Breast MRI</b> Yearly, as an adjunct to mammography beginning 8 years after radiation or at age 25, whichever occurs last.</p> <p><b>Info Link</b></p> <ul style="list-style-type: none"> <li>• Mammography is currently limited in its ability to evaluate the premenopausal breast.</li> <li>• 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).</li> <li>• The upper age limit at which both modalities should be used for breast cancer surveillance has not been established.</li> </ul>	<p><b>Health Links</b></p> <p><b>Breast Cancer</b> (for patients at highest risk only)</p> <p><b>Counseling</b></p> <p>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.</p> <p><b>Considerations for Further Testing and Interventions</b></p> <p>Surgery and/or oncology consultation as clinically indicated</p>
<p><b>Info Link</b></p> <ul style="list-style-type: none"> <li>• <i>Important:</i> 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 <math>\geq 20</math> Gy of radiation with potential impact to the breast (e.g., thorax, axilla).</li> <li>• <b>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.</b></li> <li>• <b>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 <math>\geq 20</math> Gy.</b></li> </ul>					

### SECTION 157 REFERENCES

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Sec #	Organ	Population Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
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# CANCER SCREENING GUIDELINES

## CERVICAL CANCER

Sec #	Organ	Population Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
158 (female)	Cervical	Early age at first intercourse Multiple lifetime sex partners Smoking Sexually transmitted diseases	Personal history of cervical dysplasia Prenatal DES exposure HPV infection Immunosuppression Chronic steroid use HIV positive Chronic GVHD	<p><b>PATIENTS AT STANDARD RISK (ACS Recommendation)</b></p> <p><b>PHYSICAL</b></p> <p><b>Pelvic exam</b> Every 3–5 years beginning at age 21 (see “Screening” below for specific recommendations)</p> <p><b>SCREENING</b></p> <p><b>Cervical PAP smear</b></p> <ul style="list-style-type: none"> <li>• Cervical cancer screening should begin at age 21 y.</li> <li>• For women aged 21–29 y, screening should be done every 3 y with conventional or liquid-based Pap tests.</li> <li>• For women aged 30–65 y, screening should be done every 5 y with both the HPV test and the Pap test (preferred), or every 3 y with the Pap test alone (acceptable).</li> <li>• 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.</li> <li>• Women at any age should not be screened annually by any screening method.</li> </ul>	<p><b>Health Links</b></p> <p><b>Reducing the Risk of Second Cancers</b></p> <p><b>Counseling</b></p> <p><b>Counsel regarding risk/benefits of HPV vaccination.</b></p> <p><b>Info Link</b></p> <ul style="list-style-type: none"> <li>• 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.</li> <li>• 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.</li> <li>• Females as young as 9 years can the 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.</li> <li>• 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.</li> <li>• 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.</li> </ul> <p><b>Considerations for Further Testing and Interventions</b></p> <p>Gynecology and/or oncology consultation as clinically indicated.</p>

### SECTION 158 REFERENCES

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# CANCER SCREENING GUIDELINES

## COLORECTAL CANCER

Sec #	Organ	Population Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
159	Colorectal	High fat/low fiber diet Age ≥ 50 years Obesity	<p>Radiation with potential impact to the colon/rectum (see Section 90), including ≥ 30 Gy to the following fields:</p> <ul style="list-style-type: none"> <li>- Spine (thoracic, lumbar, sacral, whole)</li> <li>- Extended Mantle</li> <li>- Hepatic</li> <li>- Renal</li> <li>- Upper quadrant (right, left)</li> <li>- Spleen (partial, entire)</li> <li>- Paraaortic</li> <li>- Flank/Hemiabdomen (right, left)</li> <li>- Whole abdomen</li> <li>- Inverted Y</li> <li>- Pelvic</li> <li>- Vaginal</li> <li>- Prostate</li> <li>- Bladder</li> <li>- Iliac</li> <li>- Inguinal</li> <li>- Femoral</li> <li>- TLI</li> <li>- STLI</li> <li>- TBI*</li> </ul> <p>Personal history of ulcerative colitis, gastrointestinal malignancy, adenomatous polyps or hepatoblastoma</p> <p>Familial polyposis</p> <p>Family history of colorectal cancer or polyps in first degree relative</p> <p><b>Info Link</b></p> <ul style="list-style-type: none"> <li>• *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.</li> <li>• <b>Monitoring of patients who received TBI without additional radiation potentially impacting the colon/rectum should be determined on an individual basis.</b> (See Info Link in next column).</li> </ul>	<p><b>PATIENTS AT STANDARD RISK (ACS Recommendation)</b></p> <p><b>SCREENING</b></p> <p><b>Option 1</b> <b>Fecal occult blood (minimum of 3 cards)</b> Yearly, beginning at age 50</p> <p><b>AND/OR</b></p> <p><b>Flexible sigmoidoscopy</b> Every 5 years, beginning at age 50</p> <p><b>Note:</b> The combination of yearly fecal occult blood testing and every 5 year flexible sigmoidoscopy is preferable to either test done alone.</p> <p><b>Option 2</b> <b>Double contrast barium enema</b> Every 5 years, beginning at age 50</p> <p><b>Option 3</b> <b>Colonoscopy</b> Every 10 years, beginning at age 50</p> <hr/> <p><b>PATIENTS AT HIGHEST RISK</b></p> <p><b>SCREENING</b></p> <p><b>Colonoscopy</b> 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.</p> <hr/> <p><b>Info Link</b></p> <ul style="list-style-type: none"> <li>• 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.</li> <li>• 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.</li> <li>• 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.</li> <li>• 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.</li> <li>• Colonoscopy remains the preferred screening modality for survivors at highest risk of colorectal cancer.</li> </ul>	<p><b>Health Links</b></p> <p>Colorectal Cancer</p> <hr/> <p><b>Considerations for Further Testing and Interventions</b></p> <p>Gastroenterology, surgery and/or oncology consultation as clinically indicated.</p>

Sec #	Organ	Population Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
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# CANCER SCREENING GUIDELINES

## ENDOMETRIAL CANCER

Sec #	Organ	Population Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
160 (female)	Endometrial	Obesity Older age Unopposed estrogen therapy Tamoxifen Diabetes Hypertension High fat diet Early menopause Late menopause Nulliparity Infertility Failure to ovulate	History of/at risk for hereditary nonpolyposis colon cancer (HNPCC)	<p><b>PATIENTS AT STANDARD RISK (ACS Recommendation)</b></p> <p><b>SCREENING</b></p> <p><b>Endometrial biopsy</b> Yearly, beginning at age 35 for patients at highest risk</p> <p><b>Info Link</b></p> <ul style="list-style-type: none"> <li>• Women at highest risk should be informed that the screening recommendation for endometrial biopsy beginning at age 35 is based on expert opinion.</li> <li>• In the absence of definitive scientific evidence, the potential benefits and risks/harms of testing for early endometrial cancer detection should be discussed.</li> </ul>	<p><b>Health Links</b></p> <p><b>Reducing the Risk of Second Cancers</b></p>

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# CANCER SCREENING GUIDELINES

## LUNG CANCER

Sec #	Organ	Population Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
161	Lung	Chest radiation with potential impact to the lung Smoking Workplace exposures to asbestos, arsenic, radiation Second hand smoke (in non-smokers)	Chest radiation with potential impact to the lung combined with smoking	<p><b>PATIENTS AT HIGHEST RISK</b></p> <p><b>HISTORY</b></p> <p>Cough Wheezing SOB DOE Yearly, and as clinically indicated</p> <p><b>PHYSICAL</b></p> <p>Pulmonary Exam Yearly, and as clinically indicated</p> <p><b>SCREENING</b></p> <p>Clinicians should discuss the benefits and risks/harms of spiral CT scanning for patients at highest risk</p>	<p><b>Health Links</b></p> <p>Reducing the Risk of Second Cancers</p> <p><b>Considerations for Further Testing and Intervention</b></p> <p>Imaging and surgery and/or oncology consultation as clinically indicated.</p>

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# CANCER SCREENING GUIDELINES

## ORAL CANCER

Sec #	Organ	Population Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
162	Oral	Tobacco use (smoking cigars, cigarettes, or pipes; dipping, chewing) Alcohol abuse Excessive sun exposure (increases risk of cancer of lower lip) HCT (allogeneic > autologous) Human Papillomavirus (HPV) infection	Head/brain radiation Neck radiation TBI Acute/chronic GVHD	<b>PATIENTS AT STANDARD RISK (ACS Recommendation)</b> <b>PHYSICAL</b> <b>Oral cavity exam</b> Yearly	<b>Health Links</b> Reducing the Risk of Second Cancers Dental Health  <b>Considerations for Further Testing and Intervention</b> Head and neck/otolaryngology consultation as indicated.

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# CANCER SCREENING GUIDELINES

## PROSTATE CANCER

Sec #	Organ	Population Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
163 (male)	Prostate	Older age, with steadily increasing risk after age 40 years.	African-American race Family history of prostate cancer in first degree relative	<p><b>ALL PATIENTS</b> Clinicians should be prepared to discuss prostate cancer testing with patients</p> <p><b>Info Link</b></p> <ul style="list-style-type: none"> <li>• 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.</li> <li>• 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.</li> <li>• The USPSTF concludes that evidence is insufficient to determine whether the benefits outweigh the harms for a screened population. ACS concurs with this conclusion.</li> </ul>	<p><b>Health Links</b></p> <p><b>Reducing the Risk of Second Cancers</b></p> <p><b>Considerations for Further Testing and Intervention</b></p> <p>Urology and/or oncology consultation as clinically indicated.</p>

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# CANCER SCREENING GUIDELINES

## SKIN CANCER

Sec #	Organ	Population Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
164	Skin	Light skin color Chronic exposure to sun Atypical moles or ≥ 50 moles	Any history of radiation Personal history of melanoma or skin cancer Dysplastic nevi Family history of melanoma or skin cancer History of severe sunburn at young age	<p><b>PATIENTS AT STANDARD RISK</b></p> <p><b>Info Link</b></p> <ul style="list-style-type: none"> <li>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.</li> <li>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.</li> <li>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.</li> </ul> <p><b>PATIENTS AT HIGHEST RISK</b></p> <p><b>PHYSICAL</b></p> <p><b>Skin self exam</b> Monthly</p> <p><b>Dermatologic exam with attention to skin lesions and pigmented nevi in radiation field</b> Yearly</p>	<p><b>Health Links</b></p> <p><b>Reducing the Risk of Second Cancers</b> <b>Skin Health</b></p> <p><b>Considerations for Further Testing and Intervention</b></p> <p>Surgery, dermatology, and/or oncology consultation as clinically indicated.</p>

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# CANCER SCREENING GUIDELINES

## TESTICULAR CANCER

Sec #	Organ	Population Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
165 (male)	Testicular	Young males	History of cryptorchidism History of testicular cancer or carcinoma in-situ in contralateral testis History of gonadal dysgenesis Klinefelter's syndrome Family history of testicular cancer	<b>Info Link</b> <ul style="list-style-type: none"> <li>• For standard and high risk populations, the USPSTF recommends against routine screening for testicular cancer in asymptomatic adolescent and adult males.</li> <li>• 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.</li> <li>• 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.</li> <li>• ACS also no longer recommends clinical testicular cancer screening or testicular self-examination.</li> </ul>	

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# GENERAL HEALTH SCREENING

# ANY CANCER EXPERIENCE

Sec #	Organ	Population Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
166	General Health Screening			<p><b>SCREENING</b></p> <p>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></p> <p>Yearly</p>	<p><b>Considerations for Further Testing and Intervention</b></p> <p>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.</p> <p>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.</p> <p>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>).</p>

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