Long-Term Follow-Up Guidelines

for Survivors of Childhood, Adolescent, and Young Adult Cancers

Version 3.0 – October 2008

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COG Long-Term Follow-Up Guidelines
Content Outline

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 3.0.* Arcadia, CA: Children's Oncology Group; October 2008; Available on-line: 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.

Content Outline

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Abstract – Version 3.0
The Children's Oncology Group Long-Term Follow-Up Guidelines for Survivors of Childhood, Adolescent, and Young Adult Cancers

Release date: October 2008

Status: Updated from Version 2.0 incorporating modifications based on recommendations from the Children's Oncology Group's Long-Term Follow-Up Guideline Core Committee and its eighteen 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 3.0 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.

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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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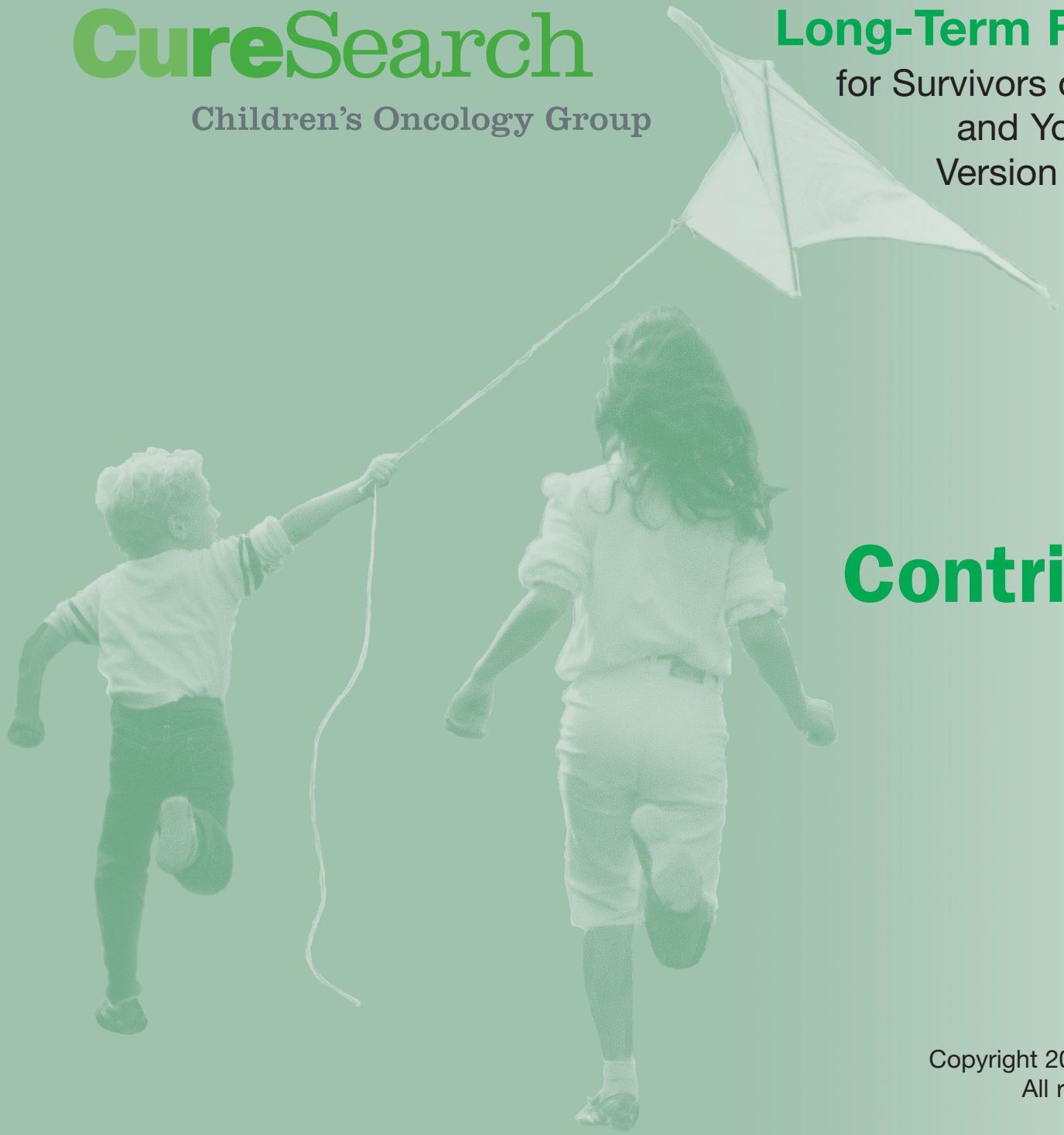
Version 3.0 – October 2008



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Long-Term Follow-Up Guidelines

Guideline Development Task Force – Initial Versions

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

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The following individuals participated in the review process during development of the initial versions (1.0, 1.1, and 1.2) of the *Children's Oncology Group Long-Term Follow-Up Guidelines for Survivors of Childhood, Adolescent, and Young Adult Cancers:*

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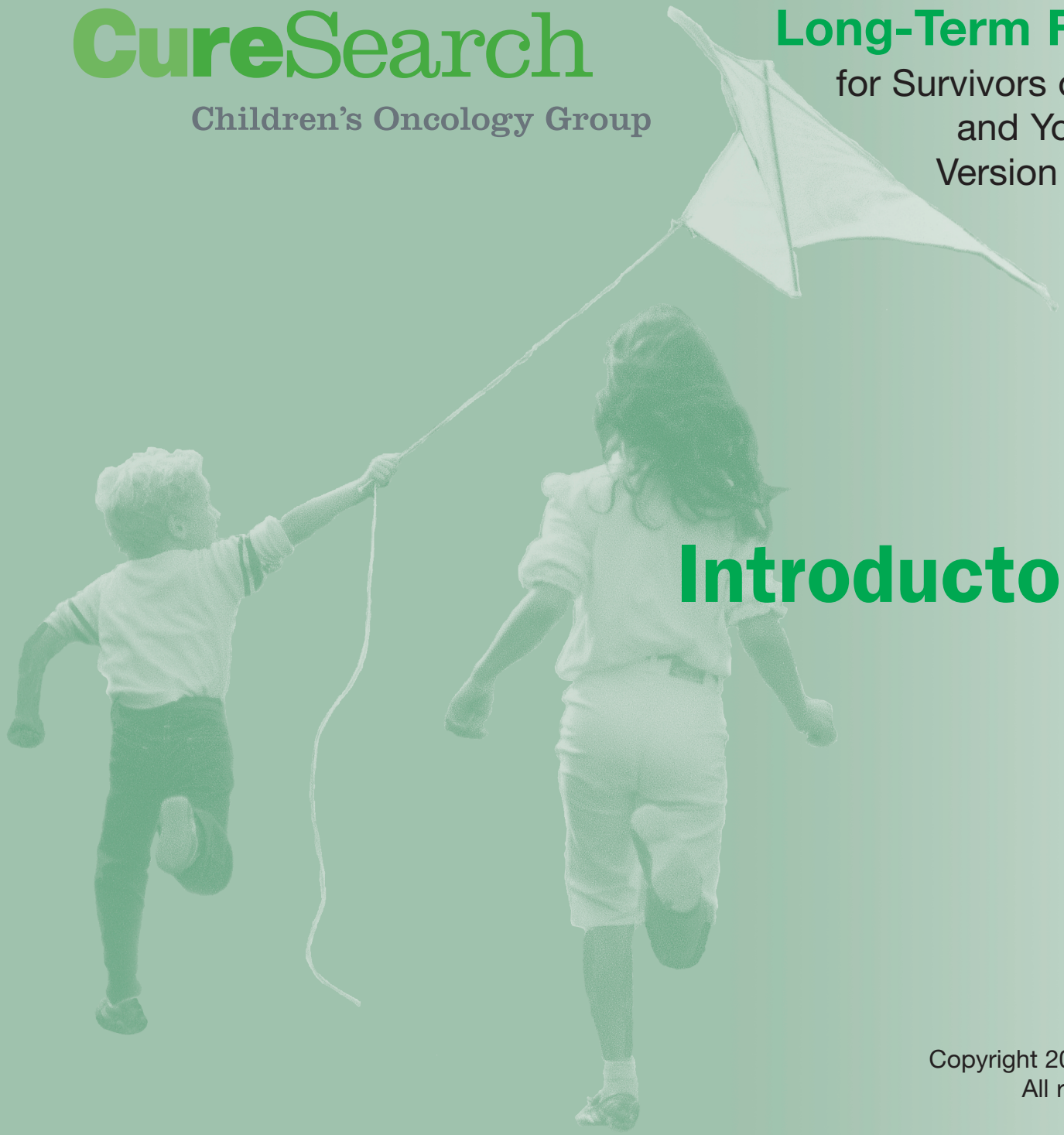
Long-Term Follow-Up Guidelines

for Survivors of Childhood, Adolescent, and Young Adult Cancers

Version 3.0 – October 2008



Introductory Material

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Introduction – Version 3.0
The Children's Oncology Group Long-Term Follow-Up Guidelines for Survivors of Childhood, Adolescent, and Young Adult Cancers

Overview:

The Children's Oncology Group Long-Term Follow-Up Guidelines for Survivors of Childhood, Adolescent, and Young Adult Cancers (COG-LTFU Guidelines) are risk-based, exposure-related clinical practice guidelines for screening and management of late effects resulting from therapeutic exposures used during treatment for pediatric malignancies. These guidelines represent a statement of consensus from a panel of experts in the late effects of pediatric cancer treatment. The guidelines are both evidence-based (utilizing established associations between therapeutic exposures and late effects to identify high-risk categories) and grounded in the collective clinical experience of experts (matching the magnitude of the risk with the intensity of the screening recommendations). Since therapeutic interventions for a specific pediatric malignancy may vary considerably based on the patient's age, presenting features, and treatment era, a therapy-based design was chosen to permit modular formatting of the guidelines by therapeutic exposure. Importantly, the recommended periodic screening underscores the use of a thorough history and physical examination (H&P) as the primary assessment for cancer-related treatment effects. In this regard, 101 (74%) of the screening recommendations outlined for the 136 therapeutic exposures in the COG-LTFU Guidelines comprise assessments derived primarily from the H&P, with 68 (50%) relying solely on the H&P and 33 (24%) relying on the H&P plus a baseline diagnostic study (e.g., lab, imaging), whereas 32 (23%) 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 42 topics, enhancing patient follow-up visits and broadening application of the guidelines. Additional accompanying materials include detailed instructions, templates for cancer treatment summary forms, a radiation reference guide, and a tool to assist in identifying guideline applicability for individual patients based on therapeutic exposures.

Goal:

Implementation of these guidelines is intended to increase quality of life and decrease complication-related healthcare costs for pediatric cancer survivors by providing standardized and enhanced follow-up care throughout the lifespan that (a) promotes healthy lifestyles, (b) provides for ongoing monitoring of health status, (c) facilitates early identification of late effects, and (d) provides timely intervention for late effects.

Introduction – Version 3.0 (cont)

Target Population:

The recommendations for periodic screening evaluations provided in the *Children's Oncology Group Long-Term Follow-Up Guidelines for Survivors of Childhood, Adolescent, and Young Adult Cancers* are appropriate for asymptomatic survivors of childhood, adolescent, or young adult cancers who present for routine exposure-related medical follow-up. More extensive evaluations are presumed, as clinically indicated, for survivors presenting with signs and symptoms suggesting illness or organ dysfunction.

Focus:

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

Intended Users:

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

Although the information within the guidelines will certainly prove valuable to the survivors themselves, at this time the only version available is targeted to healthcare professionals. Therefore, survivors who choose to review these guidelines are strongly encouraged to do so with the assistance of a healthcare professional knowledgeable about long-term follow-up care for survivors of childhood, adolescent, and young adult cancers. This is important in order to put the recommendations in perspective, avoid over-testing, address potential anxieties, and provide a comprehensive evaluation of the survivor's health status. The Children's Oncology Group itself does not provide individualized treatment advice to patients or their families, and strongly recommends discussing this information with a qualified medical professional.

Introduction – Version 3.0 (cont)

Developer:

The *COG-LTFU Guidelines* were developed as a collaborative effort of the Children's Oncology Group Nursing Discipline and Late Effects Committee and are maintained and updated by the Children's Oncology Group's Long-Term Follow-Up Guidelines Core Commitee and its associated Task Forces. All Children's Oncology Group members have complied with the COG conflict of interest policy, which requires disclosure of any potential financial or other conflicting interests.

Funding Source:

This work was supported by the Children's Oncology Group grant U10 CA098543 from the National Cancer Institute.

Evidence Collection:

Pertinent information from the published medical literature over the past 20 years (updated as of October 2008) was retrieved and reviewed during the development and updating of these guidelines. For each therapeutic exposure, a complete search was performed via MEDLINE (National Library of Medicine, Bethesda, MD). Keywords included "childhood cancer therapy," "complications," and "late effects," combined with keywords for each therapeutic exposure. References from the bibliographies of selected articles were used to broaden the search.

Methods:

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

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

Introduction – Version 3.0 (cont)

Methods (cont):

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

Grading Criteria:

The guidelines were scored by the multidisciplinary panel of experts using a modified version of the National Comprehensive Cancer Network "Categories of Consensus" system. Each score reflects the expert panel's assessment of the strength of data from the literature linking a specific late effect with a therapeutic exposure, coupled with an assessment of the appropriateness of the screening recommendation based on the expert panel's collective clinical experience. "High-level evidence" (category 1) was defined as evidence derived from high quality case control or cohort studies. "Lower-level evidence" (category 2A and 2B) was defined as evidence derived from non-analytic studies, case reports, case series and clinical experience. Rather than submitting recommendations representing major disagreements, items scored as "Category 3" were either deleted or revised by the panel of experts to provide at least a "Category 2B" score for all recommendations included in the guidelines.

Pre-Release Review:

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

Revisions:

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

Introduction – Version 3.0 (cont)

Revisions: (cont)

In order to keep the guidelines current and clinically meaningful, the COG Late Effects Committee organized 18 multi disciplinary 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. 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. The revisions incorporated into the previous (*Version 2.0 – March 2006)* and current (*Version 3.0 – October 2008*) release of these guidelines reflect the contributions and recommendations of these task forces.

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. A total of 34 sections and 9 Health Links were added to Version 2.0 of these guidelines.

Plan for Updates:

The 18 task forces described above will continue to monitor the literature and report to the COG Long-Term Follow-Up Guideline Core Committee on a bi-annual basis. Periodic revisions to these guidelines are planned as new information becomes available. Clinicians are advised to check the Children's Oncology Group website periodically for the latest updates and revisions to the guidelines, which will be posted at www.survivorshipguidelines.org.

Definitions:

"Late effects" are defined as therapy-related complications or adverse effects that persist or arise after completion of treatment for a pediatric malignancy. "Pediatric malignancies" are defined as those malignancies commonly associated with the pediatric population that may arise during childhood, adolescence or young adulthood. "Consensus" is defined as general agreement among the panel of experts.

Introduction – Version 3.0 (cont)

Recommendations and Rationale:

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

Potential Benefits and Harms:

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

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

Patient Preferences:

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

Introduction – Version 3.0 (cont)

Implementation Considerations:

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

In addition, the clinical utility of this lengthy document has also been a top concern of the COG Long-Term Follow-Up Guideline Core Committee. While recognizing that the length and depth of these guidelines is important in order to provide clinically-relevant, evidence-based recommendations and supporting health education materials, clinician time limitations and the effort required to identify the specific recommendations relevant to individual patients have been identified as barriers to their clinical application. Therefore, the COG Long-Term Follow-Up Guideline Core Committee is currently partnering with the Baylor School of Medicine in order to develop a web-based interface, known as "Passport for Care," that will generate 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. As additional information regarding implementation of the Passport for Care web-based interface becomes available, updates will be posted at www.survivorshipguidelines.org.

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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

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Explanation of Scoring for the Long-Term Follow-Up Guidelines (cont)

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.

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Instructions for Use – Version 3.0
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-Guidelines for Survivors of Childhood, Adolescent, and Young Adult Cancers* are organized according to therapeutic exposures, arranged by column as follows:

Section Number	Unique identifier for each guideline section.
Therapeutic Agent	Therapeutic intervention for malignancy, including chemotherapy, radiation, surgery, blood/serum products, hematopoietic cell transplant, and other therapeutic modalities.
Potential Late Effects	Most common late treatment complications associated with specified therapeutic intervention.
Risk Factors	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.
Highest Risk Factors	Conditions (host factors, treatment factors, medical conditions and/or health behaviors) associated with the highest risk for developing the complication.
Periodic Evaluations	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.

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Instructions for Use – Version 3.0 (cont)

Health Counseling/ Further Considerations

Health Links: Health education materials developed specifically to accompany these guidelines. Title(s) of Health Link(s) relevant to each guideline section are referenced in this column. Health Link documents are included in Appendix II, and are also available on the COG website at www.survivorshipguidelines.org.
Counseling: Suggested patient counseling regarding measures to prevent/reduce risk or promote early detection of the potential treatment complication.
Resources: Books and websites that may provide the clinician with additional relevant information.
Considerations for Further Testing and Intervention: 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.

System

Body system (e.g., auditory, musculoskeletal) most relevant to each guideline section.

Score

Score assigned by expert panel representing the strength of data from the literature linking a specific late effect with a therapeutic exposure coupled with an assessment of the appropriateness of the screening recommendation based on collective clinical experience.

Cancer Screening Recommendations

Sections 137 – 145 contain preventive screening recommendations for common adult-onset cancers, organized by column as follows:

Organ: The organ at risk for developing malignancy.

At Risk Population: Populations generally considered at increased risk for the specified malignancy based on risk factors such as age, gender, genetic susceptibility, personal or family history, health-related behaviors or co-morbidities.

Highest Risk: 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).

Instructions for Use – Version 3.0 (cont)

Cancer Screening Recommendations (cont)

Periodic Evaluations:
Standard Risk: Guidelines provided under the "Standard Risk" category are per the American Cancer Society recommendations for standard-risk populations and are included here for reference. In addition, clinicians are encouraged to consult recommendations from other organizations, such as the U. S. Preventive Services Task Force (http://www.ahrq.gov/clinic/serfiles.htm).
Highest Risk: Recommendations for high-risk populations, when applicable, are specified and may differ from recommendations for the standard risk groups due to the significantly increased risk of the specified malignancy within the high-risk group.

References

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

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

Explanation of Scoring

Elucidation of the process used by the panel of experts to assign scores to each guideline section.

Patient-Specific Guideline Identification Tool

Due to significant overlap of toxicities between therapeutic agents, and in order to avoid an enormously lengthy document, duplicate entries have been avoided as much as possible. Therefore, ***use of the Patient-Specific Guideline Identification Tool is imperative*** in order to determine each potential late effect associated with each therapeutic agent within this document (see Appendix I).

USING THE COG LTFU GUIDELINES TO DEVELOP INDIVIDUALIZED SCREENING RECOMMENDATIONS:

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

Instructions for Use – Version 3.0 (cont)

1. **Obtain the survivor's Summary of Cancer Treatment** (see templates and instructions for comprehensive and abbreviated treatment summaries in Appendix I). Note: In order to generate accurate exposure-based follow-up recommendations from these guidelines, the following information regarding the survivor's diagnosis and treatment is required, at minimum:
   - 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 6-37), 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 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^2) versus "standard dose" (all single doses $<$1000 mg/m^2)
   - All radiation field(s) and total radiation dose (in Gy) to each field (for chest radiation, include age at first dose). For list of radiation fields addressed by these guidelines (Sections 38-91), see "Radiation" portion of the *Patient-Specific Guideline Identification Tool* in Appendix I. For clarification of anatomical areas included in common radiation fields, see the *Radiation Reference Guide* 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 48 of these guidelines and in the *Radiation Reference Guide* in Appendix I.
   - 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 107-132), 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 133-36), see "Other Therapeutic Modalities" portion of the *Patient-Specific Guideline Identification Tool* in Appendix I.

Instructions for Use – Version 3.0 (cont)

2. **Develop a list of guideline sections relevant to the survivor:**
   - Sections 1 and 2 ("Any Cancer Experience") and 146 ("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 3
     - If survivor was diagnosed prior to 1993, include Section 4
     - If survivor was diagnosed between 1977 and 1985, include Section 5
   - For survivors who received chemotherapy, include relevant sections:
     - If survivor received any chemotherapy, include Section 6.
     - Review "Chemotherapy" portion of the *Patient-Specific Guideline Identification Tool* in Appendix I and include Sections 7-37 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 38 – 41. Exception: If the survivor's **only** radiation exposure was TBI, do NOT include sections 40 or 41.
     - Review "Radiation" portion of the *Patient-Specific Guideline Identification Tool* in Appendix I and include Sections 42-91 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 92-97. If the survivor has a history of chronic GVHD (cGVHD), also include sections 98-106 (Note: Section 103 is applicable only to survivors with currently active cGVHD; Section 105 is applicable only to females).
   - For survivors who underwent surgery, review "Surgery" portion of the *Patient-Specific Guideline Identification Tool* in Appendix I and include Sections 107-132 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 133-136 as applicable.
   - Include cancer screening guidelines (sections 137-145) as applicable based on survivor's sex and current age.

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.

4. **Identify Health Links appropriate for individual survivors** by guideline section number using the *Health Link Index* in Appendix I. Individual Health Link files are available in Appendix II.

Instructions for Use – Version 3.0 (cont)

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 recognize 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 is currently partnering with the Baylor School of Medicine in order to develop a web-based interface, known as "Passport for Care," that will generate individualized exposure-based recommendations from these guidelines in a clinician-focused format for ease of patient-specific application in the clinical setting. As additional information regarding implementation of the "Passport for Care" web-based interface becomes available, updates will be posted at www.survivorshipguidelines.org. In the meantime, use of the *Patient-Specific Guideline Identification Tool* and *Health Links Index by Guideline Section Number* (see Appendix I) should serve to reduce the time required for patient-specific application of these guidelines.

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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CureSearch
Children's Oncology Group

New to Version 3.0 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.

- Breast MRI is now recommended as an adjunct to annual mammography in females who received chest radiation placing them at increased risk for breast cancer (see Section 68).
- Clarification has been added to indicate the potential need to screen for breast and colorectal cancers in patients who received TBI alone (see Sections 68 and 78).
- Anthracycline isotoxic dose equivalent formulas have been updated (see Section 28).
- Detailed instructions have been added for determining applicability of radiation sections with minimum dose specifications for individual patients (see Page 48 of Guidelines and Radiation Reference Guide in Appendix I).
- The definition of metabolic syndrome has been clarified and serum insulin is no longer recommended as a screening measure in those at risk for overweight/obesity and metabolic syndrome (see Sections 48 and 49).
- The recommendation for obtaining fasting blood glucose and lipid profiles in patients at risk for overweight/obesity, metabolic syndrome, and coronary artery disease has changed from a frequency of every 2-5 years, to every 2 years for patients at risk (see Sections 48, 49, and 71).
- Screening for pulmonary complications is now recommended for patients who received radiation to the axillary and mini-mantle fields (see Section 70).
- Screening for cardiac complications is no longer recommended for patients who received radiation to axillary and mini-mantle fields (see Section 71).
- New endocarditis prophylaxis recommendations from the American Heart Association are addressed in Section 71.
- Clarification has been added regarding the definition of "complete audiological evaluation" (see Sections 14 and 58).
- Routine screening for precocious puberty with FSH, LH, and testosterone/estradiol levels is no longer routinely recommended and is now offered for further consideration in patients with an abnormal history or physical exam (see Section 51).
- Routine screening for hypogonadism following unilateral orchiectomy is no longer recommended and is now offered for further consideration in those with an abnormal history or physical exam, and endocrinology referral at age 11 is recommended for boys who have undergone bilateral orchiectomy (see Section 125).
- The reference to new post-transplantation follow-up guidelines from the Center for International Blood and Marrow Transplant Research (CIBMTR) and the American Society for Blood and Marrow Transplant (ASBMT) is provided (see Section 92).
- The risk for post-transplantion functional asplenia has been clarified as applicable to patients with currently active chronic graft-vs-host disease (see Section 103).

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Children's Oncology Group

New to Version 3.0 of the COG Long-Term Follow-Up Guidelines (cont)

- Terminology regarding complications related to reduced bone mineral density has been revised (see Sections 22, 31, and 97).
- Screening for Vitamin B12 deficiency has been added for patients who have undergone ileal enterocystoplasty (see Section 109).
- An Info Link discussing the role of post-splenectomy prophylactic antibiotic therapy and monitoring of pneumococcal titers post-vaccination in splenectomized patients has been added (see Section 131).
- Information regarding the role of the human papillomavirus (HPV) vaccine in prevention of cervical cancer has been added (see Section 138)
- Radiation fields and guideline section numbers have been clarified according to anatomic area (see pages 48-49 of guidelines).
- Sections have been divided into "Male" and "Female" throughout the guidelines as appropriate to content.
- Updated references have been added and outdated reference removed throughout the guidelines.

In addition, the following modifications have been made to Version 3.0 of these guidelines:

- A new "Radiation Reference Guide" has been added to provide radiation field definitions, detailed diagrams of radiation sections by anatomic region, and instructions for determining applicability of guideline sections that have minimum dose specifications (see Appendix 1).
- The "Patient-Specific Guideline Identification Tool" has been updated to incorporate all guideline changes and serves as a useful tool for determining applicable guideline sections for individual patients based on therapeutic exposures.
- Health Links have been updated to reflect changes in guideline Version 3.0.
- Health Links are now available in Spanish for five commonly used topics (Introduction to Long-Term Follow-Up, Diet and Physical Activity, Finding Healthcare, Emotional Issues, and Reducing the Risk of Second Cancers).
- TBI sections have been removed and their content incorporated into the relevant radiation sections of the guidelines.
- The Index has been replaced by the Patient-Specific Guideline Identification Tool (see Appendix I).

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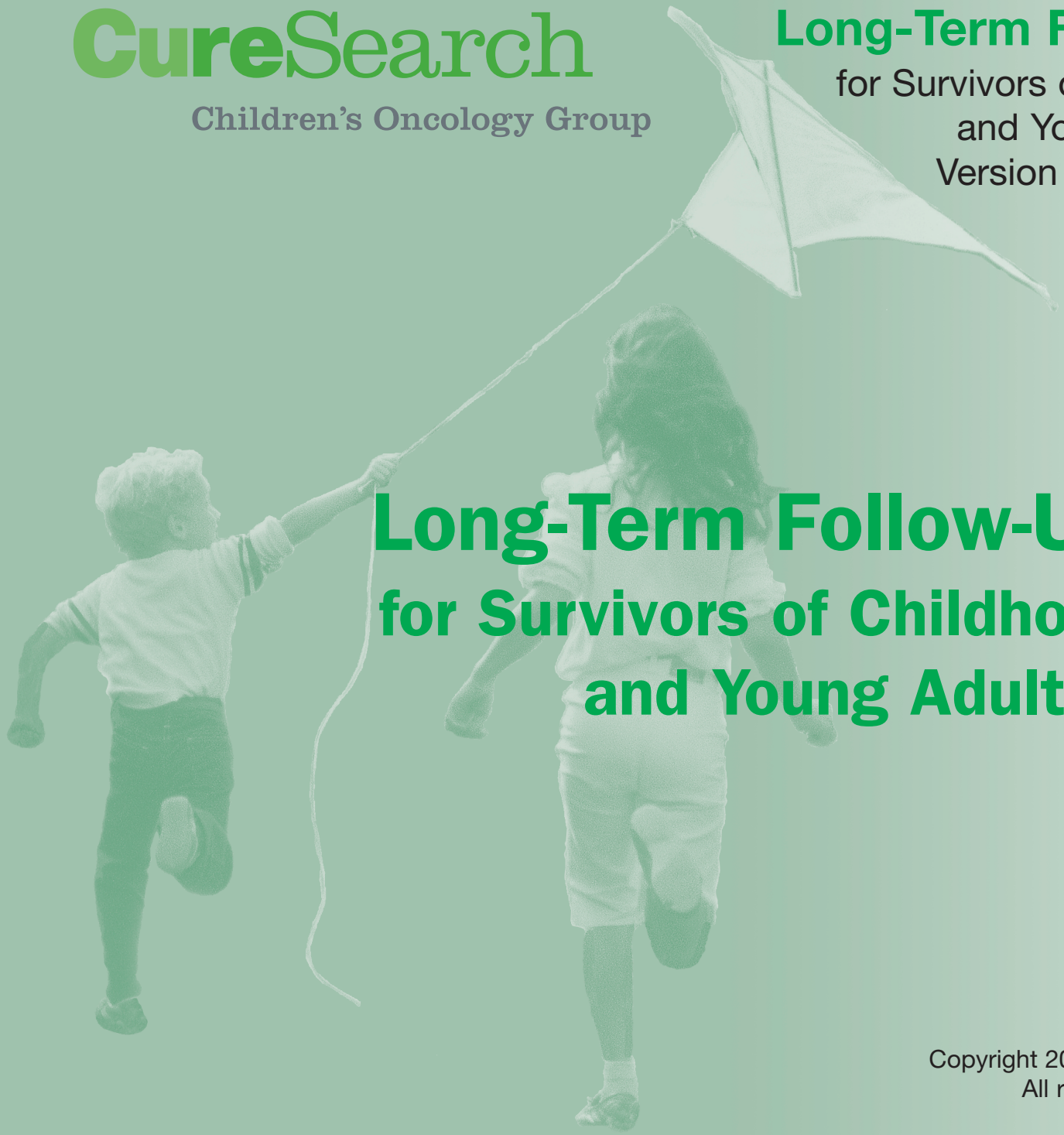

Long-Term Follow-Up Guidelines
for Survivors of Childhood, Adolescent, and Young Adult Cancers

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ANY CANCER EXPERIENCE

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
1	**Any Cancer Experience** **Info Link:** The Children's Oncology Group Long-Term Follow-Up Guidelines apply to patients who have been off therapy for a minimum of 2 years.	**Psychosocial Disorders** Social withdrawal Educational problems	**Host Factors** Female sex Family history of depression, anxiety, or mental illness **Social Factors** Lower household income Lower educational achievement **Treatment Factors** HCT	**Host Factors** CNS tumor CNS-directed therapy Hearing loss Premorbid learning or emotional difficulties **Social Factors** Failure to graduate from high school	**HISTORY** **Psychosocial assessment, with attention to:** - Educational and/or vocational progress - Depression - Anxiety - Post-traumatic stress - Social withdrawal Yearly	**Health Links** **Introduction to Long-Term Follow-Up** **Emotional Issues** **Educational Issues** **Chronic Pain after Childhood Cancer** **Resources** 'Childhood Cancer Survivors' by Nancy Keene, Wendy Hobbie & Kathy Ruccione, Sebastopol, CA: O'Reilly & Associates, 2000 'Educating the Child with Cancer' edited by Nancy Keene, Candlelighters Childhood Cancer Foundation, Bethesda, MD, 2003. See also: www.cancer.gov ('Facing Forward' series for survivors) www.cancer.org (smoking cessation) www.nccn.org (chronic pain) **Considerations for Further Testing and Intervention** 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. 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. Screen for physical sources of fatigue, such as anemia, sleep disturbances, nutritional deficiencies, cardiomyopathy, pulmonary fibrosis, hypothyroidism, or other endocrinopathy. **SYSTEM = Psychosocial** **SCORE = 2A**
		Mental health disorders Depression Anxiety Post-traumatic stress	**Host Factors** Female sex Family history of depression, anxiety, or mental illness **Social Factors** Lower household income Lower educational achievement **Treatment Factors** HCT	**Host Factors** CNS tumor CNS-directed therapy Premorbid learning or emotional difficulties **Social Factors** Failure to graduate from high school		
		Risky behaviors Behaviors known to increase the likelihood of subsequent illness or injury	**Social Factors** Lower household income	**Host Factors** Older age at diagnosis **Social Factors** Lower educational achievement		
		Psychosocial disability due to pain	**Treatment Factors** Amputation Radiation to bone/joint Limb-sparing surgery Vincristine exposure **Medical Conditions** Osteonecrosis	**Host Factors** CNS tumor Hodgkin lymphoma		
		Fatigue	**Host Factors** Female sex Depression Obesity **Social Factors** Unemployment	**Treatment Factors** Pulmonary radiation		

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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**	**Limitations in healthcare and insurance access**	**Social Factors** Lower household income Lower educational achievement Unemployment		**HISTORY** **Psychosocial assessment, with attention to healthcare insurance and access** (Yearly)	**Health Links** **Finding Healthcare** **Considerations for Further Testing and Intervention** Social work consultation **SYSTEM = Psychosocial** **SCORE = 2A**

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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
3	**Diagnosed prior to 1972**: Potential 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) **Info Link:** Since the vast majority of patients received some type of blood product during childhood cancer treatment, screening based on date of diagnosis/treatment is recommended unless there is absolute certainty that the patient did not receive any blood or blood products. Relevant exposures include packed red cells, whole blood, granulocytes, platelets, fresh frozen plasma, cryoprecipitate, IVIG, VZIG, factor concentrates, and allogeneic marrow, cord blood, or stem cells.	**Chronic Hepatitis B**	**Host Factors** Living in hyperendemic area **Treatment Factors** Blood products before 1972 **Health Behaviors** IV drug use Unprotected sex Multiple partners High-risk sexual behavior Sexually transmitted diseases Tattoos Body piercing	**Host Factors** Chronic immunosuppression	**SCREENING** **Hepatitis B surface antigen (HBsAg)** **Hepatitis B core antibody (anti HBc or HBcAb)** Once in patients who received treatment for cancer prior to 1972. *Note: Date may vary for international patients.*	**Health Links** **Hepatitis** **Considerations for Further Testing and Intervention** Gastroenterology or hepatology consultation for patients with chronic hepatitis. Hepatitis A immunization in patients lacking immunity. **SYSTEM = Immune** **SCORE = 1**

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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
4	**Diagnosed prior to 1993:** Potential exposure to blood/serum products prior to initiation of Hepatitis C screening of blood supply (1993 in the United States – dates may differ in other countries) **Info Link:** Since the vast majority of patients received some type of blood product during childhood cancer treatment, screening based on date of diagnosis/treatment is recommended unless there is absolute certainty that the patient did not receive any blood or blood products. Relevant exposures include packed red cells, whole blood, granulocytes, platelets, fresh frozen plasma, cryoprecipitate, IVIG, VZIG, factor concentrates, and allogeneic marrow, cord blood, or stem cells.	**Chronic Hepatitis C**	**Host Factors** Living in hyperendemic area **Treatment Factors** Blood products before 1993 **Health Behaviors** IV drug use Unprotected sex Multiple partners High-risk sexual behavior Sexually transmitted diseases Tattoos Body piercing	**Host Factors** Chronic immunosuppression **Treatment Factors** 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)	**SCREENING** **Hepatitis C antibody** Once in patients who received treatment for cancer prior to 1993. Note: Date may vary for international patients. **Hepatitis C PCR (to establish chronic infection)** Once in patients with positive Hepatitis C antibody.	**Health Links** **Hepatitis** **Considerations for Further Testing and Intervention** 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. **SYSTEM = Immune** **SCORE = 1**

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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
5	**Diagnosed between 1977 and 1985:** Potential 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) **Info Link:** Since the vast majority of patients received some type of blood product during childhood cancer treatment, screening based on date of diagnosis/treatment is recommended unless there is absolute certainty that the patient did not receive any blood or blood products. Relevant exposures include packed red cells, whole blood, granulocytes, platelets, fresh frozen plasma, cryoprecipitate, IVIG, VZIG, factor concentrates, and allogeneic marrow, cord blood, or stem cells.	**HIV infection**	**Treatment Factors** Blood products between 1977 and 1985 **Medical Conditions** HPV infection **Health Behaviors** IV drug use Unprotected sex Multiple partners High-risk sexual behavior Sexually transmitted diseases Tattoos Body piercing		**SCREENING** **HIV testing** Once in patients who received treatment for cancer between 1977 and 1985. Note: Dates may vary for international patients.	**Counseling** Standard counseling regarding safe sex, universal precautions, and high-risk behaviors that exacerbate risk **Considerations for Further Testing and Intervention** HIV/infectious diseases specialist consultation for patients with chronic infection. **SYSTEM = Immune** **SCORE = 1**

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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
6	**Any Chemotherapy**	**Dental abnormalities** Tooth/root agenesis Root thinning/shortening Enamel dysplasia	**Host Factors** Any patient who had not developed permanent dentition at time of cancer therapy **Treatment Factors** Any radiation treatment involving the oral cavity or salivary glands	**Host Factors** Younger age at treatment, especially < 5 years old	**PHYSICAL** **Oral exam** Yearly **SCREENING** **Dental exam and cleaning** Every 6 months	**Health Links** **Dental Health** **Considerations for Further Testing and Intervention** Regular dental care including fluoride applications. Baseline panorex prior to dental procedures to evaluate root development. **SYSTEM = Dental** **SCORE = 1**

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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
7 (Male)	**ALKYLATING AGENTS** Busulfan Carmustine (BCNU) Chlorambucil Cyclophosphamide Ifosfamide Lomustine (CCNU) Mechlorethamine Melphalan Procarbazine Thiotepa **HEAVY METALS** Carboplatin Cisplatin **NON-CLASSICAL ALKYLATORS** Dacarbazine (DTIC) Temozolomide	**Gonadal dysfunction (testicular)** Delayed/arrested puberty Hypogonadism Oligospermia Azoospermia Infertility	**Treatment Factors** Higher cumulative doses of alkylators or combinations of alkylators Combined with radiation to: - Abdomen/pelvis - Testes - Brain, cranium (neuroendocrine axis) **Health Behaviors** Smoking **Info Link** Doses that cause gonadal dysfunction show individual variation. Germ cell function (spermatogenesis) is impaired at lower doses compared to Leydig cell (testosterone production) function. Prepubertal status does not protect from gonadal injury in males.	**Host Factors** Male gender **Treatment Factors** MOPP ≥ 3 cycles Busulfan ≥ 600 mg/m² Cyclophosphamide cumulative dose ≥ 7.5 gm/m² or as conditioning for HCT Ifosfamide ≥ 60 gm/m² Any alkylators combined with: - Testicular radiation - Pelvic radiation - TBI	**HISTORY** **Pubertal (onset, tempo)** **Sexual function (erections, nocturnal emissions, libido)** **Medication use impacting sexual function** Yearly **PHYSICAL** **Tanner staging** **Testicular volume by Prader orchidometry** Yearly until sexually mature **SCREENING** **FSH** **LH** **Testosterone** Baseline at age 14 **and** as clinically indicated in patients with delayed puberty and/or clinical signs and symptoms of testosterone deficiency. **Semen analysis** As requested by patient and for evaluation of infertility. Periodic evaluation over time is recommended as resumption of spermatogenesis can occur up to 10 years post therapy.	**Health Links** **Male Health Issues** **Resources** Extensive information regarding infertility for patients and healthcare professionals is available on the following websites: American Society for Reproductive Medicine (www.asrm.org) Fertile Hope (www.fertilehope.org) **Counseling** 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. **Considerations for Further Testing and Intervention** Bone density evaluation in hypogonadal patients. Refer to endocrinology/urology for delayed puberty, persistently abnormal hormone levels or hormonal replacement for hypogonadal patients. Reproductive endocrinology/urology referral for infertility evaluation and consultation regarding assisted reproductive technologies. **SYSTEM = Reproductive (male)** **SCORE =** **Alkylating Agents: 1** **Heavy Metals: 2A** **Non-Classical Alkylators: 2A**

SECTION 7 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
7 (Female)	**ALKYLATING AGENTS** Busulfan Carmustine (BCNU) Chlorambucil Cyclophosphamide Ifosfamide Lomustine (CCNU) Mechlorethamine Melphalan Procarbazine Thiotepa **HEAVY METALS** Carboplatin Cisplatin **NON-CLASSICAL ALKYLATORS** Dacarbazine (DTIC) Temozolomide	**Gonadal dysfunction (ovarian)** Delayed/arrested puberty Premature menopause Infertility	**Treatment Factors** Higher cumulative doses of alkylators or combinations of alkylators Combined with radiation to: - Abdomen/pelvis - Lumbar or sacral spine (from ovarian scatter) - Brain, cranium (neuroendocrine axis) **Health Behaviors** Smoking **Info Link** Doses that cause gonadal dysfunction show individual variation. Females can typically maintain gonadal function at higher cumulative doses than males.	**Treatment Factors** MOPP > 3 cycles Busulfan > 600 mg/m^2 Cyclophosphamide cumulative dose > 7.5 gm/m^2 or as conditioning for HCT Any alkylators combined with: - Pelvic radiation - TBI	**HISTORY** **Pubertal (onset, tempo)** **Menstrual/pregnancy history** **Sexual function (vaginal dryness, libido)** **Medication use impacting sexual function** Yearly **PHYSICAL** **Tanner staging** Yearly until sexually mature **SCREENING** **FSH** **LH** **Estradiol** Baseline at age 13 **and** as clinically indicated in patients with delayed puberty, irregular menses, primary or secondary amenorrhea, and/or clinical signs and symptoms of estrogen deficiency.	**Health Links** **Female Health Issues** **Resources** Extensive information regarding infertility for patients and healthcare professionals is available on the following websites: American Society for Reproductive Medicine (www.asrm.org) Fertile Hope (www.fertilehope.org) **Counseling** 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. **Considerations for Further Testing and Intervention** Bone density evaluation in hypogonadal patients. Refer to endocrinology/gynecology for delayed puberty, persistently abnormal hormone levels or hormonal replacement for hypogonadal patients. Reproductive endocrinology referral for infertility evaluation and consultation regarding assisted reproductive technologies. **SYSTEM = Reproductive (female)** **SCORE =** **Alkylating Agents: 1** **Heavy Metals: 2A** **Non-Classical Alkylators: 2A**

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

SECTION 8 REFERENCES

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Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
9	**ALKYLATING AGENTS** Busulfan Carmustine (BCNU) Lomustine (CCNU)	**Pulmonary fibrosis**	**Treatment Factors** Higher cumulative doses Combined with bleomycin **Medical Conditions** Atopic history **Health Behaviors** Smoking	**Treatment Factors** BCNU ≥ 600 mg/m² Busulfan ≥ 500 mg (transplant doses) Combined with: - Chest radiation - TBI	**HISTORY** **Cough** **SOB** **DOE** **Wheezing** Yearly **PHYSICAL** **Pulmonary exam** Yearly **SCREENING** **Chest x-ray** **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.	**Health Links** **Pulmonary Health** **Resources** Extensive information regarding smoking cessation is available for patients on the NCI's website: www.smokefree.gov **Counseling** Counsel regarding tobacco avoidance/smoking cessation. Due to the potential pulmonary toxicity of this therapy, patients who desire to SCUBA dive should be advised to obtain medical clearance from a pulmonologist. **Considerations for Further Testing and Intervention** In patients with abnormal PFTs and/or CXR, consider repeat evaluation prior to general anesthesia. Pulmonary consultation for symptomatic pulmonary dysfunction. Influenza and pneumococcal vaccines. **SYSTEM = Pulmonary** **SCORE = 1**

SECTION 9 REFERENCES

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Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
10	**ALKYLATING AGENTS** Busulfan	**Cataracts**	**Treatment Factors** Combined with corticosteroids	**Treatment Factors** Combined with cranial, orbital, or eye radiation TBI Longer interval since treatment	**HISTORY** **Visual changes (decreased acuity, halos, diplopia)** Yearly **PHYSICAL** **Eye exam (visual acuity, funduscopic exam for lens opacity)** Yearly	**Health Links** **Cataracts** **Considerations for Further Testing and Intervention** Ophthalmology consultation if problem identified. Refer patients with visual deficits to school liaison in community or cancer center (psychologist, social worker, school counselor) to facilitate acquisition of educational resources. **SYSTEM = Ocular** **SCORE = 2B**

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

SECTION 11 REFERENCES

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Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
12	**ALKYLATING AGENTS** Cyclophosphamide	**Bladder malignancy**	**Treatment Factors** Combined with pelvic radiation **Health Behaviors** Alcohol use Smoking		**HISTORY** **Hematuria** **Urinary urgency/frequency** **Urinary incontinence/retention** **Dysuria** **Nocturia** **Abnormal urinary stream** Yearly **SCREENING** **Urinalysis** Yearly	**Health Links** **Bladder Health** **Counseling** Counsel to promptly report dysuria or gross hematuria. **Considerations for Further Testing and Intervention** Urine culture, spot urine calcium/creatinine ratio, and ultrasound of kidneys and bladder for patients with microscopic hematuria (defined as > 5 RBC/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. **SYSTEM = SMN** **SCORE = 2A**

SECTION 12 REFERENCES

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Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
13	**ALKYLATING AGENTS** Ifosfamide	**Renal toxicity** Glomerular injury Tubular injury (renal tubular acidosis, Fanconi's syndrome, hypophosphatemic rickets)	**Host Factors** Younger age at treatment Mononephric **Treatment Factors** Higher cumulative dose Combined with other nephrotoxic agents, such as: - Cisplatin - Carboplatin - Aminoglycosides - Amphotericin - Immunosuppressants - Methotrexate - Radiation impacting the kidney **Medical Conditions** Tumor infiltration of kidney(s) Pre-existing renal impairment Nephrectomy	**Host Factors** Age < 4 years at time of treatment **Treatment Factors** Ifosfamide dose ≥60 grams/m^2 Renal radiation dose ≥ 15 Gy	**PHYSICAL** **Blood pressure** Yearly **SCREENING** **BUN** **Creatinine** **Na, K, Cl, CO_2** **Ca, Mg, PO_4** Baseline at entry into long-term follow-up. Repeat as clinically indicated. **Urinalysis** Yearly	**Health Links** **Kidney Health** See also: **Single Kidney Health** **Considerations for Further Testing and Intervention** Electrolyte supplements for patients with persistent electrolyte wasting. Nephrology consultation for patients with hypertension, proteinuria, or progressive renal insufficiency **SYSTEM = Urinary** **SCORE = 1**

SECTION 13 REFERENCES

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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
14	**HEAVY METALS** Carboplatin (in myeloablative doses only) Cisplatin **Info Link:** Patients who received carboplatin in non-myeloablative doses do not appear to be at risk for clinically significant ototoxicity based on results of currently available studies.	**Ototoxicity** Sensorineural hearing loss Tinnitus Vertigo	**Host Factors** Age < 4 years at treatment **Treatment Factors** Combined with: - Cranial/ear radiation - Ototoxic drugs (e.g., aminoglycosides, loop diuretics) **Medical Conditions** Chronic otitis Cerumen impaction Renal dysfunction	**Host Factors** CNS neoplasm **Treatment Factors** Cumulative cisplatin dose ≥ 360 mg/m^2 High dose cisplatin (i.e., 40 mg/m^2 per day x 5 days per course) Cisplatin administered after cranial/ear radiation Carboplatin conditioning for HCT Radiation involving ear ≥ 30 Gy	**HISTORY** **Hearing difficulties (with/without background noise)** **Tinnitus** **Vertigo** Yearly **PHYSICAL** **Otoscopic exam** Yearly **SCREENING** **Complete audiological evaluation** Baseline at entry into long-term follow-up. 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]. **Info Link:** 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.	**Health Links** **Hearing Loss** **Educational Issues** **Considerations for Further Testing and Intervention** Audiology consultation for amplification in patients with progressive hearing loss. Speech and language therapy for children with hearing loss. Otolaryngology consultation in patients with chronic infection, cerumen impaction, or other anatomical problems exacerbating or contributing to hearing loss. Refer patients with auditory deficits to school liaison in community or cancer center (psychologist, social worker, school counselor) to facilitate provision of educational resources. Consider specific needs and/or preferential classroom seating, FM amplification system, and other educational assistance as indicated. **SYSTEM = Auditory** **SCORE = 1**

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Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
15	**HEAVY METALS** Carboplatin Cisplatin	**Peripheral sensory neuropathy** **Info Link:** Neuropathy presents as persistent effect after therapy and is typically not late in onset	**Treatment Factors** Combined with: - Vincristine - Taxanes - Gemcitabine	**Treatment Factors** Cumulative cisplatin dose $\geq$ 300 mg/m^2	**HISTORY** **Peripheral neuropathy** Yearly until 2 to 3 years after therapy. Monitor yearly if symptoms persist. **PHYSICAL** **Neurologic exam** Yearly until 2 to 3 years after therapy. Monitor yearly if symptoms persist.	**Health Links** **Peripheral Neuropathy** **Considerations for Further Testing and Intervention** Physical therapy referral for patients with symptomatic neuropathy. Physical and occupational therapy assessment of hand function. Consider treatment with agent effective for neuropathic pain (e.g., gabapentin or amitriptyline). **SYSTEM = PNS** **SCORE = 2A**

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Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
16	**HEAVY METALS** Carboplatin Cisplatin	**Renal toxicity** Glomerular injury Tubular injury Renal insufficiency	**Host Factors** Mononephric **Treatment Factors** Combined with other nephrotoxic agents such as: - Ifosfamide - Aminoglycosides - Amphotericin - Immunosuppressants - Methotrexate - Radiation impacting the kidney **Medical Conditions** Diabetes mellitus Hypertension Nephrectomy	**Treatment Factors** Cisplatin dose ≥ 200 mg/m^2 Renal radiation dose ≥ 15 Gy	**PHYSICAL** **Blood pressure** Yearly **SCREENING** **BUN** **Creatinine** **Na, K, Cl, CO_2** **Ca, Mg, PO_4** Baseline at entry into long-term follow-up. Repeat as clinically indicated. **Urinalysis** Yearly	**Health Links** **Kidney Health** See also: **Single Kidney Health** **Counseling** In patients with salt-wasting tubular dysfunction, educate that low magnesium levels potentiate coronary atherosclerosis **Considerations for Further Testing and Intervention** Electrolyte supplements for patients with persistent electrolyte wasting. Nephrology consultation for patients with hypertension, proteinuria, or progressive renal insufficiency. **SYSTEM = Urinary** **SCORE = 1**

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Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
17	**HEAVY METALS** Carboplatin Cisplatin	**Dyslipidemia**	**Host Factors** Family history of dyslipidemia **Medical Conditions** Overweight/Obesity		**SCREENING** **Fasting lipid profile** Baseline at entry into long-term follow-up, then as per United States Preventive Task Force Recommendations: www.ahrq.gov/clinic/prevenix.htm	**Health Links** **Diet and Physical Activity** **Considerations for Further Testing and Intervention** Counsel regarding lipid lowering strategies including diet, exercise, and weight loss in patients with dyslipidemia. Consider pharmacologic therapy (e.g., statins) in patients with dyslipidemia. **SYSTEM = Cardiovascular** **SCORE = 2B**

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CHEMOTHERAPY

ANTIMETABOLITES

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
18	**ANTIMETABOLITES** Cytarabine (high dose IV) **Info Link**: High-dose IV is defined as any single dose ≥ 1000 mg/m^2.	**Neurocognitive deficits** Functional deficits in: - Executive function (planning and organization) - Sustained attention - Memory (particularly visual, sequencing, temporal memory) - Processing speed - Visual-motor integration Learning deficits in math and reading (particularly reading comprehension) Diminished IQ Behavioral change **Info Link**: Neurocognitive deficits in survivors of leukemia and lymphoma are more frequently related to information processing (e.g., learning disability). Neurocognitive deficits in brain tumor survivors treated with higher doses of cranial radiation are more global (significant decline in IQ). Extent of deficit depends on age at treatment, intensity of treatment, and time since treatment. New deficits may emerge over time.	**Host Factors** Younger age at treatment CNS leukemia/lymphoma Relapsed leukemia/lymphoma treated with CNS-directed therapy **Treatment Factors** In combination with: - Dexamethasone - TBI - Cranial radiation - Methotrexate (IT, IO, high-dose IV) - Longer elapsed time since therapy **Info Link** Acute toxicity predominates if administered systemically as a single agent. May contribute to late neurotoxicity if combined with high dose or intrathecal methotrexate and/or cranial radiation.	**Host Factors** Age < 3 years old at time of treatment Female sex Premorbid or family history of learning or attention problems **Treatment Factors** Radiation dose ≥ 24 Gy Single fraction TBI (10 Gy)	**HISTORY** **Educational and/or vocational progress** Yearly **SCREENING** **Referral for formal neuropsychological evaluation** Baseline at entry into long-term follow-up, then periodically as clinically indicated for patients with evidence of impaired educational or vocational progress.	**Health Links** **Educational Issues** **Considerations for Further Testing and Intervention** Formal neuropsychological evaluation to include tests of processing speed, computer-based attention, visual motor integration, memory, comprehension of verbal instructions, verbal fluency, executive function and planning. Refer patients with neurocognitive deficits to school liaison in community or cancer center (psychologist, social worker, school counselor) to facilitate acquisition of educational resources and/or social skills training. Consider use of psychotropic medication (e.g., stimulants) or evidence-based rehabilitation training. Caution - lower starting dose and assessment of increased sensitivity when initiating therapy is recommended. Refer to community services for vocational rehabilitation or for services for developmentally disabled. **SYSTEM = CNS** **SCORE = 2A**

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Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
19	**ANTIMETABOLITES** Cytarabine (high dose IV) **Info Link**: High-dose IV is defined as any single dose ≥ 1000 mg/m^2.	**Clinical leukoencephalopathy** Spasticity Ataxia Dysarthria Dysphagia Hemiparesis Seizures **Info Link**: Clinical leukoencephalopathy may present with or without imaging abnormalities (e.g., leukoencephalopathy, cerebral lacunes, cerebral atrophy, dystrophic calcifications, mineralizing microangiopathy). Transient white matter anomalies may follow radiotherapy and high-dose chemotherapy for medulloblastoma/PNET, may mimic tumor recurrence, and signify risk of persistent neurologic sequelae. Neuroimaging changes do not always correlate with degree of cognitive dysfunction. Prospective studies are needed to define the dose/effect relationship of neurotoxic agents. *Note: new deficits may emerge over time.*	**Host Factors** Younger age at treatment CNS leukemia/lymphoma Relapsed leukemia/lymphoma treated with CNS-directed therapy **Treatment Factors** Combined with: - Methotrexate (IT, IO, high-dose IV) - Dexamethasone - Cranial radiation	**Treatment Factors** Radiation dose ≥ 24 Gy	**HISTORY** **Cognitive, motor, and/or sensory deficits** **Seizures** **Other neurologic symptoms** Yearly **PHYSICAL** **Neurologic exam** Yearly	**Considerations for Further Testing and Intervention** Brain MRI, Brain CT with MR angiography as clinically indicated; preferred study based on intracranial lesion to be evaluated: - White matter: MRI with diffusion-tensor imaging (DTI) - Microvascular injury: Gadolinium-enhanced MRI with diffusion-weighted imaging (DWI) - Calcifications: CT Neurology consultation and follow-up as clinically indicated. **SYSTEM = CNS** **SCORE = 2A**

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Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
20	**ANTIMETABOLITES** Cytarabine (low dose IV) Cytarabine IO Cytarabine IT Cytarabine SQ **Info Link**: Low-dose IV is defined as any single dose < 1000 mg/m^2	**No known late effects** **Info Link**: Acute toxicities predominate, from which the majority of patients recover without sequelae.				**SYSTEM = N/A** **SCORE = 1**

SECTION 20 REFERENCES

No known late effects

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
21	**ANTIMETABOLITES** Mercaptopurine (6MP) Thioguanine (6TG) **Info Link**: 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.	**Hepatic dysfunction** **Veno-occlusive disease (VOD)** **Info Link**: 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.	**Medical Conditions** Viral hepatitis Previous VOD Siderosis	**Medical Conditions** Chronic viral hepatitis	**PHYSICAL** **Scleral icterus** **Jaundice** **Ascites** **Hepatomegaly** **Splenomegaly** Yearly **SCREENING** **ALT** **AST** **Bilirubin** Baseline at entry into long-term follow-up. Repeat as clinically indicated.	**Health Links** **Liver Health** **Considerations for Further Testing and Intervention** 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. **SYSTEM = GI/Hepatic** **SCORE = 2A**

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ANTIMETABOLITES (cont)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
22	**ANTIMETABOLITES** Methotrexate (high dose IV) Methotrexate (low dose IV) Methotrexate IM Methotrexate PO **Info Link:** High-dose IV is defined as any single dose ≥ 1000 mg/m^2	**Reduced Bone Mineral Density (BMD)** Defined as Z-score > 2.0 SD below the mean in survivors < 20 years old or T-score >1.0 SD below the mean in survivors ≥ 20 years old **Info Link**: The World Health Organization definition of osteoporosis in adults is based on comparison of a measured bone mineral density (BMD) of young adults at peak bone age and defined as a T-score. A T-score is the number of standard deviations the BMD measurement is above or below the mean. Note: Current definitions of osteopenia (T-scores between 1.0 and 2.5 SD below the mean) and osteoporosis (T-scores > 2.5 SD below the mean) were developed primarily in the context of postmenopausal women. In this population, T-scores have a well-validated correlation with fracture risk that increases with age. The fracture risk associated with T-scores in younger populations, including cancer survivors with treatment-related hypogonadism, has not been established. T-scores are not appropriate to assess skeletal health in pediatric patients who have not achieved peak adult bone mass. Instead, 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. Again, 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.	**Host Factors** Both genders are at risk Younger age at diagnosis Caucasian Lower weight and BMI **Treatment Factors** Corticosteroids Cyclosporine Tacrolimus Cranial radiation Craniospinal radiation HCT/TBI **Medical Conditions** Growth hormone deficiency Hypogonadism/delayed puberty Hyperthyroidism **Health Behaviors** Inadequate intake of calcium and vitamin D Lack of weight bearing exercise Smoking Alcohol use Carbonated beverages	**Host Factors** Older age at time of treatment **Treatment Factors** Methotrexate cumulative dose ≥ 40 gm/m^2 Prolonged corticosteroid therapy (e.g., for chronic GVHD)	**SCREENING** **Bone density evaluation (DEXA or quantitative CT)** (Baseline at entry into long-term follow-up. Repeat as clinically indicated.) **Info Link:** The optimal method of measuring bone health in children is controversial. Existing technologies have limitations. Dual energy x-ray absorptiometry (DEXA) provides an estimate of total bone mass at a given site. Quantitative CT provides distinct measures of trabecular and cortical bone dimension and density.	**Health Links** **Bone Health** **Resources** National Osteoporosis Foundation Website: www.nof.org **Considerations for Further Testing and Intervention** Ensure recommended daily allowance of Vitamin D intake (200 IU/day) and 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**

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Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
23	**ANTIMETABOLITES** Methotrexate (high dose IV) Methotrexate (low dose IV) Methotrexate IM Methotrexate PO **Info Link:** High-dose IV is defined as any single dose ≥ 1000 mg/m^2.	**Renal toxicity** **Info Link:** Acute toxicities predominate, from which the majority of patients recover without sequelae.	**Host Factors** Mononephric **Treatment Factors** Combined with other nephrotoxic agents such as: - Cisplatin/carboplatin - Ifosfamide - Aminoglycosides - Amphotericin - Immunosuppressants - Radiation impacting the kidney **Medical Conditions** Diabetes mellitus Hypertension Nephrectomy	**Treatment Factors** Treatment before 1970	**PHYSICAL** **Blood pressure** Yearly **SCREENING** **BUN** **Creatinine** **Na, K, Cl, CO_2** **Ca, Mg, PO_4** Baseline at entry into long-term follow-up. Repeat as clinically indicated. **Urinalysis** Yearly	**Health Links** **Kidney Health** See also: **Single Kidney Health** **Considerations for Further Testing and Intervention** Nephrology consultation for patients with hypertension, proteinuria, or progressive renal insufficiency. **SYSTEM = Urinary** **SCORE = 2A**

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Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
24	**ANTIMETABOLITES** Methotrexate (high dose IV) Methotrexate (low dose IV) Methotrexate IM Methotrexate PO **Info Link:** High-dose IV is defined as any single dose ≥ 1000 mg/m^2.	**Hepatic dysfunction** **Info Link:** Acute toxicities predominate from which the majority of patients recover without sequelae	**Treatment Factors** Abdominal radiation **Medical Conditions** Viral hepatitis	**Treatment Factors** Treatment before 1970 **Medical Conditions** Chronic viral hepatitis	**PHYSICAL** **Scleral icterus** **Jaundice** **Ascites** **Hepatomegaly** **Splenomegaly** Yearly **SCREENING** **ALT** **AST** **Bilirubin** Baseline at entry into long-term follow-up. Repeat as clinically indicated.	**Health Links** **Liver Health** **Considerations for Further Testing and Intervention** 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. **SYSTEM = GI/Hepatic** **SCORE = 2A**

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ANTIMETABOLITES (cont)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
25	**ANTIMETABOLITES** Methotrexate (high dose IV) Methotrexate IO Methotrexate IT **Info Link:** High-dose IV is defined as any single dose ≥ 1000 mg/m^2.	**Neurocognitive deficits** Functional deficits in: - Executive function (planning and organization) - Sustained attention - Memory (particularly visual, sequencing, temporal memory) - Processing speed - Visual-motor integration Learning deficits in math and reading (particularly reading comprehension) Diminished IQ Behavioral change **Info Link:** Neurocognitive deficits in survivors of leukemia and lymphoma are more frequently related to information processing (e.g., learning disability). Neurocognitive deficits in brain tumor survivors treated with higher doses of cranial radiation are more global (significant decline in IQ). Extent of deficit depends on age at treatment, intensity of treatment, and time since treatment. New deficits may emerge over time.	**Host Factors** Younger age at treatment CNS leukemia/lymphoma Relapsed leukemia/lymphoma treated with CNS-directed therapy **Treatment Factors** In combination with: - Dexamethasone - TBI - Cranial radiation - Cytarabine (high-dose IV) - Longer elapsed time since therapy	**Host Factors** Age < 3 years old at time of treatment Female sex Premorbid or family history of learning or attention problems **Treatment Factors** Radiation dose ≥ 24 Gy Single fraction TBI (10 Gy)	**HISTORY** **Educational and/or vocational progress** Yearly **SCREENING** **Referral for formal neuropsychological evaluation** Baseline at entry into long-term follow-up, then periodically as clinically indicated for patients with evidence of impaired educational or vocational progress.	**Health Links** **Educational Issues** **Considerations for Further Testing and Intervention** Formal neuropsychological evaluation to include tests of processing speed, computer-based attention, visual motor integration, memory, comprehension of verbal instructions, verbal fluency, executive function and planning. Refer patients with neurocognitive deficits to school liaison in community or cancer center (psychologist, social worker, school counselor) to facilitate acquisition of educational resources and/or social skills training; Consider use of psychotropic medication (e.g., stimulants) or evidence-based rehabilitation training. Caution - lower starting dose and assessment of increased sensitivity when initiating therapy is recommended. Refer to community services for vocational rehabilitation or for services for developmentally disabled. **SYSTEM = CNS** **SCORE = 1**

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Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
26	**ANTIMETABOLITES** Methotrexate (high dose IV) Methotrexate IO Methotrexate IT Info Link: High-dose IV is defined as any single dose ≥ 1000 mg/m^2.	**Clinical leukoencephalopathy** Spasticity Ataxia Dysarthria Dysphagia Hemiparesis Seizures **Info Link:** Clinical leukoencephalopathy may present with or without imaging abnormalities (e.g., leukoencephalopathy, cerebral lacunes, cerebral atrophy, dystrophic calcifications, mineralizing microangiopathy). Transient white matter anomalies may follow radiotherapy and high-dose chemotherapy for medulloblastoma/PNET, may mimic tumor recurrence, and signify risk of persistent neurologic sequelae. Neuroimaging changes do not always correlate with degree of cognitive dysfunction. Prospective studies are needed to define the dose/effect relationship of neurotoxic agents. *Note: new deficits may emerge over time.*	**Host Factors** Younger age at treatment CNS leukemia/lymphoma Relapsed leukemia/lymphoma treated with CNS-directed therapy **Treatment Factors** Combined with: - Cytarabine (high-dose IV) - Dexamethasone - Cranial radiation	**Treatment Factors** Radiation dose ≥ 24 Gy	**HISTORY** **Cognitive, motor, and/or sensory deficits** **Seizures** **Other neurologic symptoms** Yearly **PHYSICAL** **Neurological exam** Yearly	**Considerations for Further Testing and Intervention** Brain MRI, Brain CT with MR angiography as clinically indicated; preferred study based on intracranial lesion to be evaluated: - White matter: MRI with diffusion-tensor imaging (DTI) - Microvascular injury: Gadolinium-enhanced MRI with diffusion-weighted imaging (DWI) - Calcifications: CT Neurology consultation and follow-up as clinically indicated. **SYSTEM = CNS** **SCORE = 1**

SECTION 26 REFERENCES

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Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
27	**ANTHRACYCLINE ANTIBIOTICS** Daunorubicin Doxorubicin Epirubicin Idarubicin Mitoxantrone* ***Info link (Mitoxantrone)**: Although Mitoxantrone technically belongs to the anthracenedione class of anti-tumor antibiotics, it is related to the anthracycline family.	**Acute myeloid leukemia**	**Treatment Factors** Less than 5 years since exposure to agent		**HISTORY** **Fatigue** **Bleeding** **Easy bruising** Yearly up to 10 years after exposure to agent. **PHYSICAL** **Dermatologic exam (pallor, petechiae, purpura)** Yearly up to 10 years after exposure to agent. **SCREENING** **CBC/differential** Yearly up to 10 years after exposure to agent.	**Health Links** **Reducing the Risk of Second Cancers** **Counseling** Counsel to promptly report fatigue, pallor, petechiae, or bone pain. **Considerations for Further Testing and Intervention** Bone marrow exam as clinically indicated. **SYSTEM = SMN** **SCORE = 1**

SECTION 27 REFERENCES

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Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
28 (Male)	**ANTHRACYCLINE ANTIBIOTICS** Daunorubicin Doxorubicin Epirubicin Idarubicin Mitoxantrone* ***Info Link (Mitoxantrone):** Although Mitoxantrone technically belongs to the anthracenedione class of anti-tumor antibiotics, it is related to the anthracycline family and is included here because of its cardiotoxic potential. **Info Link (Dose Conversion):** Pediatric studies of anthracycline cardiotoxicity typically describe risks based on combined cumulative doses of doxorubicin. There is a paucity of literature to support isotoxic dose conversion; however, the following conversion factors may be used for convenience in order to gauge screening frequency. Clinical judgment should ultimately be used to determine indicated screening for individual patients. Use the following formulas to convert to doxorubicin isotoxic equivalents prior to calculating total cumulative anthracycline dose. Doxorubicin: Multiply total dose x 1 Daunorubicin: Multiply total dose x 0.833 Epirubicin: Multiply total dose x 0.67 Idarubicin: Multiply total dose x 5 Mitoxantrone: Multiply total dose x 4	**Cardiac toxicity** Cardiomyopathy Arrhythmias Subclinical left ventricular dysfunction (systolic dysfunction as assessed by ECHO or MUGA) **Info Link:** Dose levels correlating with cardiotoxicity are derived from adult studies. Childhood cancer patients exhibit clinical and subclinical toxicity at lower levels. Certain conditions (such as isometric exercise, pregnancy, and viral infections) have been anecdotally reported to precipitate cardiac decompensation. Prospective studies are needed to define risk factors.	**Treatment Factors** Combined with radiation involving the heart Combined with other cardiotoxic chemotherapy: - Cyclophosphamide conditioning for HCT - Amsacrine **Medical Conditions** Obesity Congenital heart disease Febrile illness **Health Behaviors** Isometric exercise Smoking Drug use (e.g., cocaine, diet pills, ephedra, mahuang)	**Host Factors** Black/of African descent Younger than age 5 years at time of treatment **Treatment Factors** Higher cumulative anthracycline doses: - ≥ 550 mg/m² in patients 18 years or older at time of treatment - ≥ 300 mg/m² in patients younger than 18 years at time of treatment - Any dose in infant Chest radiation ≥ 30 Gy Longer time elapsed since treatment	**HISTORY** **SOB** **DOE** **Orthopnea** **Chest pain** **Palpitations** **If under 25 years:** **Abdominal symptoms (nausea, vomiting)** Yearly **Info Link:** Exertional intolerance is uncommon in patients younger than 25 years old. Abdominal symptoms (nausea, emesis) may be observed more frequently than exertional dyspnea or chest pain in younger patients. **PHYSICAL** **Cardiac murmur** **S3, S4** **Increased P2 sound** **Pericardial rub** **Rales** **Wheezes** **Jugular venous distension** **Peripheral edema** Yearly **SCREENING** **ECHO or MUGA for evaluation of systolic function** Baseline at entry to long-term follow-up, then periodically, based on age at treatment, radiation dose, and cumulative anthracycline dose - *see table* **EKG (include evaluation of QTc interval)** Baseline at entry into long-term follow-up. Repeat as clinically indicated.	**Health Links** **Heart Health** **Counseling** Counsel patients with prolonged QTc interval about use of medications that may further prolong the QTc interval (e.g., tricyclic anti-depressants, antifungals, macrolide antibiotics, 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. **Considerations for Further Testing and Intervention** Cardiology consultation in patients with subclinical abnormalities on screening evaluations, left ventricular dysfunction, dysrhythmia, or prolonged QTc interval. Consider excess risk of isometric exercise program in any high risk patient (defined as needing screening every 1 or 2 years). **SYSTEM = Cardiovascular** **SCORE = 1**

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
28 (Female)	**ANTHRACYCLINE ANTIBIOTICS** Daunorubicin Doxorubicin Epirubicin Idarubicin Mitoxantrone* ***Info Link (Mitoxantrone):** Although Mitoxantrone technically belongs to the anthracenedione class of anti-tumor antibiotics, it is related to the anthracyclinefamily and is included here because of its cardiotoxic potential. **Info Link (Dose Conversion):** Pediatric studies of anthracycline cardiotoxicity typically describe risks based on combined cumulative doses of doxorubicin. There is a paucity of literature to support isotoxic dose conversion; however, the following conversion factors may be used for convenience in order to gauge screening frequency. Clinical judgment should ultimately be used to determine indicated screening for individual patients. Use the following formulas to convert to doxorubicin isotoxic equivalents prior to calculating total cumulative anthracycline dose. Doxorubicin: Multiply total dose x 1 Daunorubicin: Multiply total dose x 0.833 Epirubicin: Multiply total dose x 0.67 Idarubicin: Multiply total dose x 5 Mitoxantrone: Multiply total dose x 4	**Cardiac toxicity** Cardiomyopathy Arrhythmias Subclinical left ventricular dysfunction (systolic dysfunction as assessed by ECHO or MUGA) **Info Link:** Dose levels correlating with cardiotoxicity are derived from adult studies. Childhood cancer patients exhibit clinical and subclinical toxicity at lower levels. Certain conditions (such as isometric exercise, pregnancy, and viral infections) have been anecdotally reported to precipitate cardiac decompensation. Prospective studies are needed to define risk factors.	**Treatment Factors** Combined with radiation involving the heart Combined with other cardiotoxic chemotherapy: - Cyclophosphamide conditioning for HCT - Amsacrine **Medical Conditions** Obesity Congenital heart disease Febrile illness Pregnancy **Health Behaviors** Isometric exercise Smoking Drug use (e.g., cocaine, diet pills, ephedra, mahuang)	**Host Factors** Female sex Black/of African descent Younger than age 5 years at time of treatment **Treatment Factors** Higher cumulative anthracycline doses: - ≥ 550 mg/m² in patients 18 years or older at time of treatment - ≥ 300 mg/m² in patients younger than 18 years at time of treatment - Any dose in infant Chest radiation ≥ 30 Gy Longer time elapsed since treatment	**HISTORY** **SOB** **DOE** **Orthopnea** **Chest pain** **Palpitations** **If under 25 years:** **Abdominal symptoms (nausea, vomiting)** Yearly **Info Link:** Exertional intolerance is uncommon in patients younger than 25 years old. Abdominal symptoms (nausea, emesis) may be observed more frequently than exertional dyspnea or chest pain in younger patients. **PHYSICAL** **Cardiac murmur** **S3, S4** **Increased P2 sound** **Pericardial rub** **Rales** **Wheezes** **Jugular venous distension** **Peripheral edema** Yearly **SCREENING** **ECHO or MUGA for evaluation of systolic function** Baseline at entry to long-term follow-up, then periodically, based on age at treatment, radiation dose, and cumulative anthracycline dose - *see table* **EKG (include evaluation of QTc interval)** Baseline at entry into long-term follow-up. Repeat as clinically indicated.	**Health Links** **Heart Health** **Counseling** Counsel patients with prolonged QTc interval about use of medications that may further prolong the QTc interval (e.g., tricyclic anti-depressants, antifungals, macrolide antibiotics, 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. **Considerations for Further Testing and Intervention** Cardiology consultation in patients with subclinical abnormalities on screening evaluations, left ventricular dysfunction, dysrhythmia, or prolonged QTc interval. Consider excess risk of isometric exercise program in any high risk patient (defined as needing screening every 1 or 2 years). Additional cardiology evaluation in patients who received ≥ 300 mg/m² or < 300 mg/m² 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. **SYSTEM = Cardiovascular** **SCORE = 1**

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

28

RECOMMENDED FREQUENCY OF ECHOCARDIOGRAM OR MUGA SCAN

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

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

§See Section 71

†Based on doxorubicin isotoxic equivalent dose [see conversion factors in Section 28 "Info Link (Dose Conversion)"]

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Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
29	**ANTI-TUMOR ANTIBIOTICS** Bleomycin	**Pulmonary toxicity** Interstitial pneumonitis Pulmonary fibrosis Acute respiratory distress syndrome (very rare)	**Host Factors** Younger age at treatment **Treatment Factors** Higher cumulative dose Combined with: - Busulfan - Carmustine (BCNU) - Lomustine (CCNU) **Medical Conditions** Renal dysfunction High dose oxygen support such as during general anesthesia **Health Behaviors** Smoking	**Treatment Factors** Bleomycin dose ≥ 400 U/m² (injury observed in doses 60-100 U/m² in children) Combined with: - Chest radiation - TBI	**HISTORY** **Cough** **SOB** **DOE** **Wheezing** Yearly **PHYSICAL** **Pulmonary exam** Yearly **SCREENING** **Chest x-ray** **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.	**Health Links** **Pulmonary Health** **Bleomycin Alert** **Resources** Extensive information regarding smoking cessation is available for patients on the NCI's website: www.smokefree.gov **Counseling** Notify healthcare providers of history of bleomycin therapy and risk of worsening fibrosis with high oxygen exposure such as during general anesthesia. Administration of high concentrations of oxygen may result in chronic progressive pulmonary fibrosis. Counsel regarding tobacco avoidance/ smoking cessation. Due to the potential pulmonary toxicity of this therapy, patients who desire to SCUBA dive should be advised to obtain medical clearance from a pulmonologist. **Considerations for Further Testing and Intervention** In patients with abnormal PFTs and/or CXR, consider repeat evaluation prior to general anesthesia. Pulmonary consultation in patients with symptomatic or progressive pulmonary dysfunction. Influenza and pneumococcal vaccines. **SYSTEM = Pulmonary** **SCORE =** **Interstitial pneumonitis: 1** **Pulmonary fibrosis: 1** **ARDS: 2B**

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

SECTION 30 REFERENCES

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CORTICOSTEROIDS

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
31	**CORTICOSTEROIDS** Dexamethasone Prednisone	**Reduced Bone Mineral Density (BMD)** Defined as Z-score > 2.0 SD below the mean in survivors < 20 years old or T-score >1.0 SD below the mean in survivors ≥ 20 years old **Info Link**: The World Health Organization definition of osteoporosis in adults is based on comparison of a measured bone mineral density (BMD) of young adults at peak bone age and defined as a T-score. A T-score is the number of standard deviations the BMD measurement is above or below the mean. Note: Current definitions of osteopenia (T-scores between 1.0 and 2.5 SD below the mean) and osteoporosis (T-scores > 2.5 SD below the mean) were developed primarily in the context of post-menopausal women. In this population, T-scores have a well-validated correlation with fracture risk that increases with age. The fracture risk associated with T-scores in younger populations, including cancer survivors with treatment-related hypogonadism, has not been established. T-scores are not appropriate to assess skeletal health in pediatric patients who have not achieved peak adult bone mass. Instead, 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. Again, 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.	**Host Factors** Both genders are at risk Younger age at diagnosis Caucasian Lower weight and BMI **Treatment Factors** Corticosteroids Cyclosporine Tacrolimus Cranial radiation Craniospinal radiation HCT/TBI **Medical Conditions** Growth hormone deficiency Hypogonadism/delayed puberty Hyperthyroidism **Health Behaviors** Inadequate intake of calcium and vitamin D Lack of weight bearing exercise Smoking Alcohol use Carbonated beverages	**Host Factors** Older age at time of treatment **Treatment Factors** Glucocorticoid cumulative dose ≥ 9 gm/m^2 prednisone equivalent Dexamethasone effect is more potent than prednisone	**SCREENING** **Bone density evaluation (DEXA or quantitative CT)** Baseline at entry into long-term follow-up. Repeat as clinically indicated. **Info Link:** The optimal method of measuring bone health in children is controversial. Existing technologies have limitations. Dual energy x-ray absorptiometry (DEXA) provides an estimate of total bone mass at a given site. Quantitative CT provides distinct measures of trabecular and cortical bone dimension and density.	**Health Links** **Bone Health** **Resources** National Osteoporosis Foundation Website: www.nof.org **Considerations for Further Testing and Intervention** Ensure recommended daily allowance of Vitamin D intake (200 IU/day) and 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**

SECTION 31 REFERENCES

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Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
32	**CORTICOSTEROIDS** Dexamethasone Prednisone	**Osteonecrosis** (Avascular Necrosis) **Info Link:** Osteonecrosis typically occurs during the acute treatment phase, may progress over time or resolve. Multifocal osteonecrosis is significantly more common (3:1) than unifocal.	**Host Factors** Both genders are at risk Host polymorphisms may confer increased risk **Treatment Factors** Combined with high-dose radiation to any bone Dexamethasone effect is more potent than prednisone **Medical Conditions** Sickle cell disease	**Host Factors** Age ≥ 10 years at time of treatment **Treatment Factors** Orthovoltage radiation (commonly used before 1970) due to delivery of greater dose to skin and bones	**HISTORY** **Joint pain** **Swelling** **Immobility** **Limited range of motion** Yearly **PHYSICAL** **Musculoskeletal exam** Yearly	**Health Links** **Osteonecrosis** **Considerations for Further Testing and Intervention** MRI as clinically indicated in patients with history suggestive of osteonecrosis (should be done soon after symptom onset). Orthopedic consultation in patients with positive imaging and/or symptoms of osteonecrosis. Physical therapy evaluation (for non-pharmacologic pain management, range of motion, strengthening, stretching, functional mobility). **SYSTEM = Musculoskeletal** **SCORE = 1**

SECTION 32 REFERENCES

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Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
33	**CORTICOSTEROIDS** Dexamethasone Prednisone	**Cataracts**	**Treatment Factors** Combined with: - TBI - Busulfan	**Treatment Factors** TBI Cranial, orbital, or eye radiation Longer interval since treatment	**HISTORY** **Visual changes (decreased acuity, halos, diplopia)** Yearly **PHYSICAL** **Eye exam (visual acuity, funduscopic exam for lens opacity)** Yearly	**Health Links** **Cataracts** **Considerations for Further Testing and Intervention** Ophthalmology consultation if problem identified. Refer patients with visual deficits to school liaison in community or cancer center (psychologist, social worker, school counselor) to facilitate acquisition of educational resources. **SYSTEM = Ocular** **SCORE = 1**

SECTION 33 REFERENCES

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CHEMOTHERAPY

ENZYMES

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
34	**ENZYMES** Asparaginase	**No known late effects** **Info Link:** Acute toxicities predominate, from which the majority of patients recover without sequelae				**SYSTEM = N/A** **SCORE = 1**

SECTION 34 REFERENCES

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Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
35	**PLANT ALKALOIDS** Vinblastine Vincristine	**Peripheral sensory or motor neuropathy** Areflexia Weakness Foot drop Paresthesias **Info Link:** Acute toxicities most commonly occur and usually resolve prior to patients entering long-term follow-up. Neuropathy can persist after treatment and is typically not late in onset.	**Treatment Factors** Combined with platinum chemotherapy, gemcitabine or taxanes **Medical Conditions** Anorexia Severe weight loss	**Medical Conditions** Charcot-Marie-Tooth disease	**HISTORY** **Peripheral neuropathy** Yearly, until 2 to 3 years after therapy. Monitor yearly if symptoms persist. **PHYSICAL** **Neurologic exam** Yearly, until 2 to 3 years after therapy; monitor yearly if symptoms persist.	**Health Links** **Peripheral Neuropathy** **Considerations for Further Testing and Intervention** 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). **SYSTEM = PNS** **SCORE = 2A**

SECTION 35 REFERENCES

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Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
36	**PLANT ALKALOIDS** Vinblastine Vincristine	**Vasospastic attacks** (Raynaud's phenomenon)	**Health Behaviors** Smoking Illicit drug use		**HISTORY** **Vasospasms of hands, feet, nose, lips, cheeks, or earlobes related to stress or cold temperatures** Yearly **PHYSICAL** **Physical exam of affected area** As indicated	**Health Links** **Raynaud's Phenomenon** **Counseling** Counsel to wear appropriate protective clothing in cold environments and not to use tobacco or illicit drugs (vasoconstrictors such as cocaine). **Considerations for Further Testing and Intervention** Consider vasodilating medications (calcium- channel blockers, alpha blockers) for patients with frequent, severe vasospastic attacks unresponsive to behavioral management. **SYSTEM = Cardiovascular** **SCORE = 2A**

SECTION 36 REFERENCES

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Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
37	**EPIPODOPHYLLOTOXINS** Etoposide (VP16) Teniposide (VM26) **Info Link:** Administration schedules since approximately 1990 have been modified to reduce the risk of this complication.	**Acute myeloid leukemia**	**Medical Conditions** Splenectomy (conflicting evidence)	**Treatment Factors** Weekly or twice weekly administration Less than 5 years since exposure to agent	**HISTORY** **Fatigue** **Bleeding** **Easy bruising** Yearly, up to 10 years after exposure to agent. **PHYSICAL** **Dermatologic exam (pallor, petechiae, purpura)** Yearly, up to 10 years after exposure to agent. **SCREENING** **CBC/differential** Yearly, up to 10 years after exposure to agent.	**Health Links** **Reducing the Risk of Second Cancers** **Counseling** Counsel to promptly report fatigue, pallor, petechiae, or bone pain. **Considerations for Further Testing and Intervention** Bone marrow exam as clinically indicated. **SYSTEM = SMN** **SCORE = 1**

SECTION 37 REFERENCES

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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 38 – 91) are organized by anatomic region from the head downward. For specifics regarding relevant exposures to each anatomic region and radiation field, refer to the applicable pages of the "Radiation Reference Guide" in Appendix I and to the Figures in this section.
- To determine specific screening guidelines by section number for an individual patient, use the "Patient-Specific Guideline Identification Tool" in Appendix I together with the "Radiation Reference Guide."

RADIATION DOSE CALCULATIONS:

Some sections of the *COG Long-Term Follow-Up Guidelines* relevant to radiation exposure include dose specifications. These specifications indicate the minimum dose of radiation that is believed (based on available evidence and the recommendations of the expert panel) to place patients sufficiently at risk of the referenced late effect to recommend screening. For guideline sections that have a minimum specified dose, the following considerations apply in determining the applicability of the section for a patient based on his/her radiation exposure (see Appendix I – "Radiation Reference Guide" – for examples).

Sections with minimum dose specifications are applicable to a patient only if:

1. Patient received radiation to any field(s) relevant to the particular guideline section at ≥ the specified minimum dose[†]

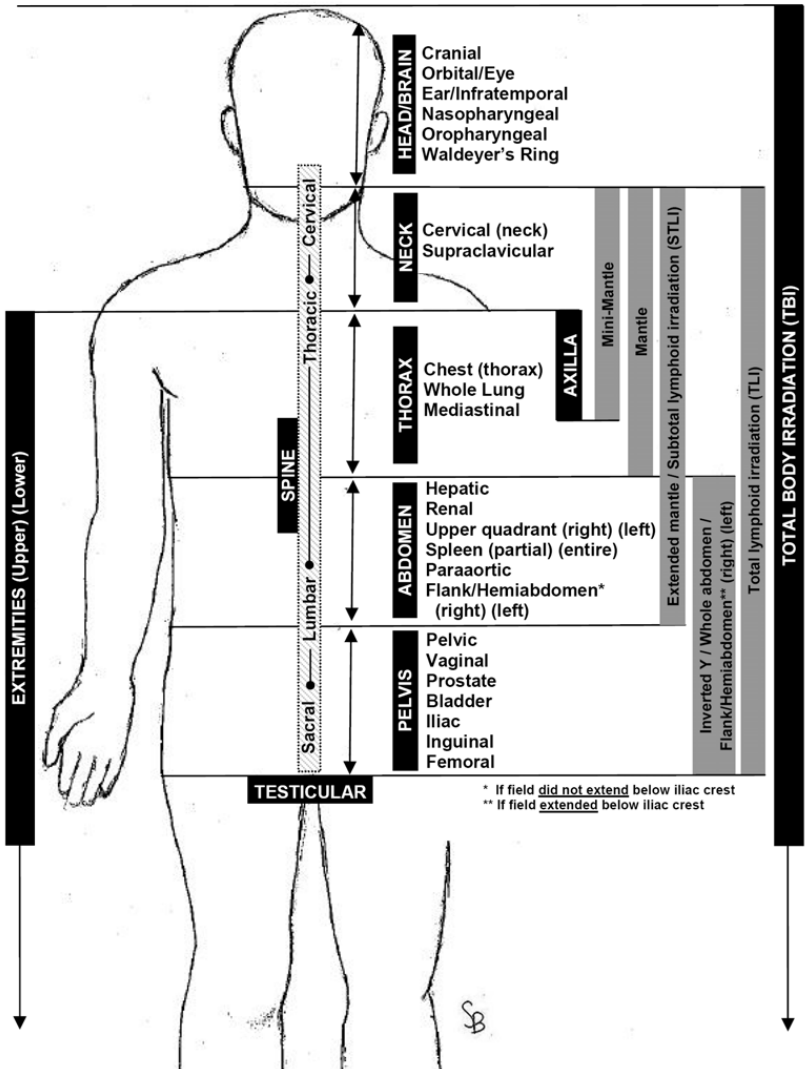
   OR

2. Patient received a combination of radiation to any relevant field(s)[†] **plus** relevant spinal radiation[‡] **and/or** TBI, the sum of which is ≥ the specified minimum dose[§]

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

[‡]Use the largest dose of radiation delivered to the spinal field(s) specified in the guideline section

[§]Whole lung radiation, if given, should be included in minimum dose calculations for Sections 65, 66, 67, 68, 73, and 91.

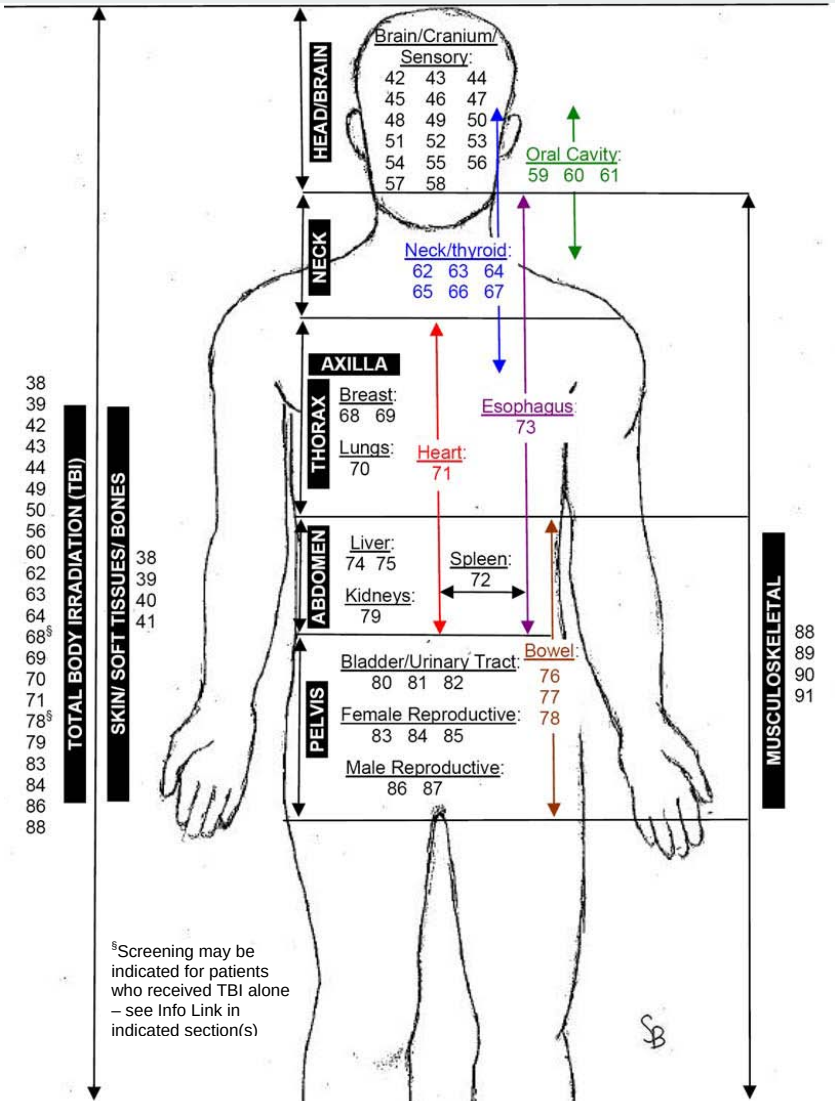


Radiation Fields by Anatomic Region

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.
- See page 48 of these guidelines for information regarding minimum radiation dose specifications included in some guideline sections.
- 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 Section Numbers by Anatomic Region

RADIATION

ALL FIELDS (INCLUDING TBI)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
38	**All Radiation Fields (Including TBI)** **Info Link:** 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.	**Secondary benign or malignant neoplasm** Occurring in or near radiation field **Info Link:** Patients with bilateral or familial retinoblastoma (implying a germline mutation) are at increased risk for developing second malignant neoplasms	**Host Factors** Cancer predisposing mutation (e.g., p53, RB1, NF1) Younger age at treatment **Treatment Factors** High cumulative radiation dose Large radiation treatment volumes Alkylating agent exposure	**Treatment Factors** Orthovoltage radiation (commonly used before 1970) due to delivery of greater dose to skin and bones	**PHYSICAL** **Inspection and palpation of skin and soft tissues in irradiated field(s)** Yearly **SCREENING** **Other evaluations based on treatment volumes** See recommendations for specific fields	**Health Links** **Reducing the Risk of Second Cancers** **Considerations for Further Testing and Intervention** Surgical and/or oncology consultation as clinically indicated. **SYSTEM = SMN** **SCORE = 1**

- 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 38 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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RADIATION

ALL FIELDS (INCLUDING TBI) (cont)

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

- 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 39 REFERENCES

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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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RADIATION

ALL FIELDS (EXCEPT TBI)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
40	**All Radiation Fields (Except TBI)**	**Dermatologic changes** Fibrosis Telangiectasias Permanent alopecia Altered skin pigmentation	**Host Factors** Younger age at treatment **Treatment Factors** Total radiation dose ≥ 40 Gy Large dose fractions (e.g. ≥ 2 Gy per fraction)	**Treatment Factors** Radiation dose ≥ 50 Gy Orthovoltage radiation (commonly used before 1970) due to delivery of greater dose to skin and bones	**PHYSICAL** **Dermatologic exam of irradiated fields** Yearly	**Health Links** **Skin Health** **SYSTEM = Dermatologic** **SCORE = 1**

- 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 40 REFERENCES

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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
41	**All Radiation Fields (Except TBI)**	**Bone malignancies**	**Host Factors** Adolescent at treatment Cancer-predisposing mutation (e.g., p53, RB1, NF1) **Treatment Factors** Higher radiation dose Combined with alkylating agents	**Treatment Factors** Radiation dose ≥ 30 Gy Orthovoltage radiation (commonly used before 1970) due to delivery of greater dose to skin and bones	**HISTORY** **Bone pain (especially in irradiated field)** Yearly **PHYSICAL** **Palpation of bones in irradiated field** Yearly	**Counseling** Counsel patient to report symptoms promptly (e.g., bone pain, bone mass, persistent fevers). **Considerations for Further Testing and Intervention** X-ray or other diagnostic imaging in patients with clinical symptoms. Oncology consultation as clinically indicated. **SYSTEM = SMN** **SCORE = 1**

- 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 41 REFERENCES

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Lindor NM, Greene MH. The concise handbook of family cancer syndromes. Mayo Familial Cancer Program. *J Natl Cancer Inst*. Jul 15 1998;90(14):1039-1071.

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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
42	**Cranial** **Orbital/Eye** **Ear/Infratemporal** **Nasopharyngeal** **Waldeyer's Ring** **TBI**	**Brain tumor (benign or malignant)**	**Host Factors** Younger age at treatment Neurofibromatosis **Treatment Factors** Higher radiation dose (Risk of subsequent CNS tumor after cranial radiation increases in a dose-response relationship)	**Host Factors** Age < 6 years at time of treatment Ataxia telangiectasia	**HISTORY** **Headaches** **Vomiting** **Cognitive, motor or sensory deficits** **Seizures and other neurologic symptoms** Yearly **PHYSICAL** **Neurologic exam** Yearly	**Considerations for Further Testing and Intervention** 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. **SYSTEM = SMN** **SCORE = 1**

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

SECTION 42 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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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.

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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
43	**Cranial** **Ear/Infratemporal** **TBI**	**Neurocognitive deficits** **Neurocognitive deficits** Functional deficits in: - Executive function (planning and organization) - Sustained attention - Memory (particularly visual, sequencing, temporal memory) - Processing speed - Visual-motor integration Learning deficits in math and reading (particularly reading comprehension) Diminished IQ Behavioral change **Info Link:** Neurocognitive deficits in survivors of leukemia and lymphoma are more frequently related to information processing (e.g., learning disability). Neurocognitive deficits in brain tumor survivors treated with higher doses of cranial radiation are more global (significant decline in IQ). Extent of deficit depends on age at treatment, intensity of treatment, and time since treatment. *Note: New deficits may emerge over time.*	**Host Factors** Younger age at treatment Primary CNS tumor CNS leukemia/lymphoma Relapsed leukemia/lymphoma treated with CNS-directed therapy Head/neck tumors with brain in radiation field **Treatment Factors** Radiation in combination with: - Dexamethasone - Methotrexate (IT, IO, high-dose IV) - Cytarabine (high-dose IV) Higher radiation dose Larger radiation field Greater cortical volumes Cranial radiation in combination with TBI Longer elapsed time since therapy	**Host Factors** Age < 3 years at time of treatment Female sex Supratentorial tumor Premorbid or family history of learning or attention problems	**HISTORY** **Educational and/or vocational progress** Yearly **SCREENING** **Referral for formal neuropsychological evaluation** Baseline at entry into long-term follow-up, then periodically as clinically indicated for patients with evidence of impaired educational or vocational progress.	**Health Links** **Educational Issues** **Considerations for Further Testing and Intervention** Formal neuropsychological evaluation to include tests of processing speed, computer-based attention, visual motor integration, memory, comprehension of verbal instructions, verbal fluency, executive function and planning. Refer patients with neurocognitive deficits to school liaison in community or cancer center (psychologist, social worker, school counselor) to facilitate acquisition of educational resources and/or social skills training. Consider use of psychotropic medication (e.g., stimulants) or evidence-based rehabilitation training. Caution - lower starting dose and assessment of increased sensitivity when initiating therapy is recommended. Refer to community services for vocational rehabilitation or for services for developmentally disabled. **SYSTEM = CNS** **SCORE = 1**

- 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
44	**Cranial** **Ear/Infratemporal** **TBI**	**Clinical leukoencephalopathy** Spasticity Ataxia Dysarthria Dysphagia Hemiparesis Seizures **Info Link:** Clinical leukoencephalopathy may present with or without imaging abnormalities (e.g., leukoencephalopathy, cerebral lacunes, cerebral atrophy, dystrophic calcifications, mineralizing microangiopathy). Transient white matter anomalies may follow radiotherapy and high-dose chemotherapy for medulloblastoma/PNET, may mimic tumor recurrence, and signify risk of persistent neurologic sequelae. Neuroimaging changes do not always correlate with degree of cognitive dysfunction. Prospective studies are needed to define the dose/effect relationship of neurotoxic agents. *Note: New deficits may emerge over time.*	**Host Factors** Younger age at treatment CNS leukemia/lymphoma Relapsed leukemia/lymphoma treated with CNS-directed therapy **Treatment Factors** In combination with: - Dexamethasone - Methotrexate (IT, IO, high-dose IV) - Cytarabine (high-dose IV) - Higher radiation dose Larger radiation field Greater cortical volumes Longer elapsed time since therapy	**Host Factors** Radiation dose ≥ 24 Gy **Treatment Factors** Fraction dose ≥ 3 Gy	**HISTORY** **Cognitive, motor, and/or sensory deficits** **Seizures** **Other neurologic symptoms** Yearly **PHYSICAL** **Neurologic exam** Yearly	**Considerations for Further Testing and Intervention** Brain MRI, Brain CT with MR angiography as clinically indicated; preferred study based on intracranial lesion to be evaluated: -White matter: MRI with diffusion-tensor imaging (DTI) -Microvascular injury: Gadolinium-enhanced MRI with diffusion-weighted imaging (DWI) -Calcifications: CT Neurology consultation and follow-up as clinically indicated. **SYSTEM = CNS** **SCORE = 1**

• 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
45	**≥ 18 Gy to:** **Cranial** **Orbital/Eye** **Ear/Infratemporal** **Nasopharyngeal** **Waldeyer's Ring** **TBI*** *TBI included for dose calculation purposes only; this section not applicable to patients who received TBI alone.	**Cerebrovascular complications** Stroke Moyamoya Occlusive cerebral vasculopathy **Info Link:** Moyamoya syndrome is the complete occlusion of one or more of the three major cerebral vessels with the development of small, immature collateral vessels, which reflect an attempt to revascularize the ischemic portion of the brain.	**Host Factors** Down syndrome **Treatment Factors** Suprasellar radiation **Medical Conditions** Sickle cell disease Neurofibromatosis	**Host Factors** Parasellar tumor **Treatment Factors** Radiation dose ≥ 50 Gy	**HISTORY** **Hemiparesis** **Hemiplegia** **Weakness** **Aphasia** Yearly **PHYSICAL** **Neurologic exam** Yearly	**Considerations for Further Testing and Intervention** Brain MRI with diffusion-weighted imaging with MR angiography as clinically indicated. Neurology/neurosurgery consultation and follow-up. Physical and occupational therapy as clinically indicated. Note: Revascularization procedures are likely helpful for moyamoya. Aspirin prophylaxis has not yet been shown to be beneficial for moyamoya or occlusive cerebral vasculopathy. **SYSTEM = CNS** **SCORE = 1**

- This section is only applicable to patients who:
  1) Received radiation to any of the specified fields at ≥ 18 Gy
  OR
  2) Received a combination of radiation to any of the specified fields **and** TBI, the sum of which is ≥ 18 Gy
- See dose calculation rules on page 48 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 BRAIN/CRANIUM (cont)

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

- 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
47	**Cranial** **Orbital/Eye** **Ear/Infratemporal** **Nasopharyngeal** **Waldeyer's Ring**	**Chronic sinusitis**	**Treatment Factors** Radiation dose to sinuses ≥ 30 Gy Radiomimetic chemotherapy (e.g., doxorubicin, dactinomycin) **Medical Conditions** Atopic history Hypogammaglobulinemia		**HISTORY** **Rhinorrhea** **Postnasal discharge** Yearly **PHYSICAL** **Nasal exam** **Sinuses** Yearly	**Considerations for Further Testing and Intervention** CT scan of sinuses as clinically indicated. Otolaryngology consultation as clinically indicated. **SYSTEM = Immune** **SCORE = 1**

- 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
48	**Cranial** **Orbital/Eye** **Ear/Infratemporal** **Nasopharyngeal** **Waldeyer's Ring**	**Overweight** Age 2-20 years: BMI for age ≥ 85th - < 95th percentile Age ≥ 21 years: BMI ≥ 25 - 29.9 **Obesity** Age 2-20 years: BMI for age ≥ 95th percentile Age ≥ 21 years: BMI ≥ 30 **Info Link:** BMI=wt(kg)/ht(M^2) BMI calculator available on-line at: http://nhlbisupport.com/bmi/ Growth charts for patients < 21 years of age available on-line at: www.cdc.gov/growthcharts	**Host Factors** Younger at treatment **Treatment Factors** Higher cranial radiation dose Combined with corticosteroids **Medical Conditions** Familial dyslipidemia Growth hormone deficiency Hypothyroidism	**Host Factors** Age < 4 years old at time of treatment Female sex **Treatment Factors** Hypothalamic radiation dose ≥ 20 Gy **Medical Conditions** Inability to exercise	**PHYSICAL** **Height** **Weight** **BMI** **Blood pressure** Yearly **SCREENING** **Fasting blood glucose** **Fasting lipid profile** Every 2 years. More frequently if indicated based on patient evaluation.	**Health Links** **Diet and Physical Activity** **Counseling** Counsel regarding obesity-related health risks. **Considerations for Further Testing and Intervention** Consider evaluation for other co-morbid conditions including dyslipidemia, hypertension, glucose intolerance, diabetes mellitus, hyperinsulinism, and insulin resistance. Nutritional counseling. Endocrine consultation for patients with dyslipidemia or hyperglycemia. **SYSTEM = Endocrine/Metabolic** **SCORE = 1**

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

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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	**Cranial** **Orbital/Eye** **Ear/Infratemporal** **Nasopharyngeal** **Waldeyer's Ring** **TBI**	**Metabolic syndrome** **Info Link:** 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: hypertension, atherogenic dyslipidemia (elevated triglycerides, reduced HDL cholesterol), and abnormal glucose metabolism (fasting hyperglycemia, hyperinsulinism, insulin resistance, diabetes mellitus type II). *Note: Patients who received TBI may develop features of metabolic syndrome without associated obesity.*	**Treatment Factors** Surgery in suprasellar region Prolonged corticosteroid therapy (e.g., for chronic GVHD) TBI **Medical Conditions** Growth hormone deficiency Hypogonadism	**Host Factors** Obesity **Treatment Factors** Cranial radiation dose ≥ 18 Gy	**PHYSICAL** **Height** **Weight** **BMI** **Blood pressure** Yearly **SCREENING** **Fasting blood glucose** **Fasting lipid profile** Every 2 years. More frequently if indicated based on patient evaluation.	**Health Links** **Diet and Physical Activity** **Counseling** Counsel regarding obesity-related health risks. **Considerations for Further Testing and Intervention** Consider waist:hip ratio screening (>0.5=higher risk). Consider endocrine consult if insulin resistance/metabolic syndrome is suspected. Nutritional counseling. Cardiology consultation as clinically indicated. **SYSTEM = Endocrine/Metabolic** **SCORE = 2A**

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

SECTION 49 REFERENCES

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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
50	**Cranial** **Orbital/Eye** **Ear/Infratemporal** **Nasopharyngeal** **Waldeyer's Ring** **TBI**	**Growth hormone deficiency** **Info Link:** Growth charts available on-line at www.cdc.gov/growthcharts	**Host Factors** Younger age at treatment **Treatment Factors** Higher radiation doses Surgery in suprasellar region Pretransplant radiation TBI ≥ 10 Gy in single fraction TBI ≥ 12 Gy fractionated	**Treatment Factors** Radiation dose ≥ 18 Gy Pretransplant cranial radiation TBI given in single fraction	**HISTORY** **Assessment of nutritional status** Every 6 months until growth is completed, then yearly. **PHYSICAL** **Tanner staging** Every 6 months until sexually mature **Height** **Weight** **BMI** Every 6 months until growth is completed, then yearly.	**Health Links** **Growth Hormone Deficiency** See also: **Hypopituitarism** **Resources** www.magicfoundation.org **Considerations for Further Testing and Intervention** Obtain x-ray for bone age in poorly growing children. Endocrine consultation for: Height below 3rd percentile on growth chart; Drop ≥ 2 percentile rankings on growth chart; Growth velocity < 4-5 cm/year during childhood; Lack of pubertal growth spurt. 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. **SYSTEM = Endocrine/Metabolic** **SCORE = 1**

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

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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
51 (Male)	**Cranial** **Orbital/Eye** **Ear/Infratemporal** **Nasopharyngeal** **Waldeyer's Ring** • See "Patient-Specific Guideline Identification Tool" in Appendix I to determine specific screening guidelines by section number for individual patients.	**Precocious puberty**	**Host Factors** Younger age at treatment **Treatment Factors** Radiation doses ≥ 18 Gy		**PHYSICAL** **Height** **Weight** **Tanner staging** **Testicular volume by Prader orchidometry** Yearly until sexually mature	**Health Links** **Precocious Puberty** **Resources** www.magicfoundation.org **Considerations for Further Testing and Intervention** 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). **SYSTEM = Endocrine/Metabolic** **SCORE = 1**
51 (Female)	**Cranial** **Orbital/Eye** **Ear/Infratemporal** **Nasopharyngeal** **Waldeyer's Ring** • See "Patient-Specific Guideline Identification Tool" in Appendix I to determine specific screening guidelines by section number for individual patients.	**Precocious puberty**	**Host Factors** Female sex Younger age at treatment **Treatment Factors** Radiation doses ≥ 18 Gy		**PHYSICAL** **Height** **Weight** **Tanner staging** Yearly until sexually mature	**Health Links** **Precocious Puberty** **Resources** www.magicfoundation.org **Considerations for Further Testing and Intervention** Obtain FSH, LH, estradiol as clinically indicated in patients with signs of accelerated pubertal progression and growth. Obtain x-ray for bone age in rapidly growing children. Endocrine consultation for accelerated puberty (puberty in girl < 8 years old). Consider pelvic ultrasound in females to evaluate for ovarian tumor. **SYSTEM = Endocrine/Metabolic** **SCORE = 1**

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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
52 (Male)	**≥ 40 Gy to:** **Cranial** **Orbital/Eye** **Ear/Infratemporal** **Nasopharyngeal** **Waldeyer's Ring** **TBI*** *TBI included for dose calculation purposes only; this section not applicable to patients who received TBI alone.	**Hyperprolactinemia**	**Treatment Factors** Higher radiation dose Surgery or tumor in hypothalamic area	**Treatment Factors** Radiation dose ≥ 50 Gy	**HISTORY** **Decreased libido** **Galactorrhea** Yearly **SCREENING** **Prolactin level** In patients with galactorrhea or decreased libido	**Health Links** **Hyperprolactinemia** **Resources** www.magicfoundation.org **Considerations for Further Testing and Intervention** CT evaluation of sella turcica for pituitary adenoma in patients with hyperprolactinemia. Endocrine consultation for patients with hyperprolactinemia or galactorrhea. **SYSTEM = Endocrine/Metabolic** **SCORE = 1**
		• This section is only applicable to patients who: 1) Received radiation to any of the specified fields at ≥ 40 Gy OR 2) Received a combination of radiation to any of the specified fields **and** TBI, the sum of which is ≥ 40 Gy • See dose calculation rules on page 48 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.				
52 (Female)	**≥ 40 Gy to:** **Cranial** **Orbital/Eye** **Ear/Infratemporal** **Nasopharyngeal** **Waldeyer's Ring** **TBI*** *TBI included for dose calculation purposes only; this section not applicable to patients who received TBI alone.	**Hyperprolactinemia**	**Treatment Factors** Higher radiation dose Surgery or tumor in hypothalamic area	**Treatment Factors** Radiation dose ≥ 50 Gy	**HISTORY** **Galactorrhea** **Menstrual history** Yearly **SCREENING** **Prolactin level** In patients with galactorrhea or amenorrhea	**Health Links** **Hyperprolactinemia** **Resources** www.magicfoundation.org **Considerations for Further Testing and Intervention** CT evaluation of sella turcica for pituitary adenoma in patients with hyperprolactinemia. Endocrine consultation for patients with hyperprolactinemia, amenorrhea, or galactorrhea. **SYSTEM = Endocrine/Metabolic** **SCORE = 1**
		• This section is only applicable to patients who: 1) Received radiation to any of the specified fields at ≥ 40 Gy OR 2) Received a combination of radiation to any of the specified fields **and** TBI, the sum of which is ≥ 40 Gy • See dose calculation rules on page 48 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 NEUROENDOCRINE AXIS (cont)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
53	**≥ 40 Gy to:** **Cranial** **Orbital/Eye** **Ear/Infratemporal** **Nasopharyngeal** **Waldeyer's Ring** **TBI*** *TBI included for dose calculation purposes only; this section not applicable to patients who received TBI alone.	**Central hypothyroidism** **Info Link:** Central hypothyroidism includes thyroid-releasing and thyroid-stimulating hormone deficiency	**Treatment Factors** Higher radiation dose		**HISTORY** **Fatigue** **Weight gain** **Cold intolerance** **Constipation** **Dry skin** **Brittle hair** **Depressed mood** Yearly; Consider more frequent screening during periods of rapid growth. **PHYSICAL** **Height** **Weight** **Hair** **Skin** **Thyroid exam** Yearly; Consider more frequent screening during periods of rapid growth. **SCREENING** **TSH** **Free T4** Yearly; Consider more frequent screening during periods of rapid growth.	**Health Links** **Thyroid Problems** See also: **Hypopituitarism** **Counseling** Counsel at-risk females of childbearing potential to have their thyroid levels checked prior to attempting pregnancy and periodically throughout pregnancy. **Considerations for Further Testing and Intervention** Consider TSH surge testing. Endocrine consultation for thyroid hormone replacement. **SYSTEM = Endocrine/Metabolic** **SCORE = 1**

- This section is only applicable to patients who:
  1) Received radiation to any of the specified fields at ≥ 40 Gy
  OR
  2) Received a combination of radiation to any of the specified fields **and** TBI, the sum of which is ≥ 40 Gy
- See dose calculation rules on page 48 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 53 REFERENCES

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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
54 (Male)	**≥ 40 Gy to:** **Cranial** **Orbital/Eye** **Ear/Infratemporal** **Nasopharyngeal** **Waldeyer's Ring** **TBI*** *TBI included for dose calculation purposes only; this section not applicable to patients who received TBI alone.	**Gonadotropin deficiency** **Info Link:** Gonadotropin deficiency includes LH and FSH deficiency.	**Treatment Factors** Higher radiation dose		**HISTORY** **Pubertal (onset, tempo)** **Sexual function (erections, nocturnal emissions, libido)** **Medication use impacting sexual function** Yearly **PHYSICAL** **Tanner staging** **Testicular volume by Prader orchdiometry** Yearly until sexually mature **SCREENING** **FSH** **LH** **Testosterone** Baseline at age 14 **and** as clinically indicated in patients with delayed puberty and/or clinical signs and symptoms of testosterone deficiency. **Semen analysis** As requested by patient and for evaluation of infertility.	**Health Links** **Male Health Issues** See also: **Hypopituitarism** **Resources** American Society for Reproductive Medicine: www.asrm.org Fertile Hope: www.fertilehope.org **Considerations for Further Testing and Intervention** Refer to endocrinologist for delayed puberty or persistently abnormal hormone levels. Hormonal replacement therapy for hypogonadal patients. Reproductive endocrinology referral for infertility evaluation and consultation regarding assisted reproductive technologies. Consider bone density testing in patients who are gonadotropin deficient. **SYSTEM = Reproductive (male)** **SCORE = 1**

- This section is only applicable to patients who:
  1) Received radiation to any of the specified fields at ≥ 40 Gy
  OR
  2) Received a combination of radiation to any of the specified fields **and** TBI, the sum of which is ≥ 40 Gy
- See dose calculation rules on page 48 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

POTENTIAL IMPACT TO NEUROENDOCRINE AXIS (cont)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
54 (Female)	**≥ 40 Gy to:** **Cranial** **Orbital/Eye** **Ear/Infratemporal** **Nasopharyngeal** **Waldeyer's Ring** **TBI*** *TBI included for dose calculation purposes only; this section not applicable to patients who received TBI alone.	**Gonadotropin deficiency** **Info Link:** Gonadotropin deficiency includes LH and FSH deficiency.	**Treatment Factors** Higher radiation dose		**HISTORY** **Pubertal (onset, tempo)** **Menstrual/pregnancy history** **Sexual function (vaginal dryness, libido)** **Medication use impacting sexual function** Yearly **PHYSICAL** **Tanner staging** Yearly until sexually mature **SCREENING** **FSH** **LH** **Estradiol** Baseline at age 13, **and** as clinically indicated in patients with delayed puberty, irregular menses, primary or secondary amenorrhea, or clinical signs and symptoms of estrogen deficiency.	**Health Links** **Female Health Issues** See also: **Hypopituitarism** **Resources** American Society for Reproductive Medicine: www.asrm.org Fertile Hope: www.fertilehope.org **Considerations for Further Testing and Intervention** Refer to endocrinologist for delayed puberty or persistently abnormal hormone levels. Hormonal replacement therapy for hypogonadal patients. Reproductive endocrinology referral for infertility evaluation and consultation regarding assisted reproductive technologies. Consider bone density testing in patients who are gonadotropin deficient. **SYSTEM = Reproductive (female)** **SCORE = 1**

- This section is only applicable to patients who:
  1) Received radiation to any of the specified fields at ≥ 40 Gy
     OR
  2) Received a combination of radiation to any of the specified fields **and** TBI, the sum of which is ≥ 40 Gy
- See dose calculation rules on page 48 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 54 REFERENCES

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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
55	**≥ 40 Gy to:** **Cranial** **Orbital/Eye** **Ear/Infratemporal** **Nasopharyngeal** **Waldeyer's Ring** **TBI*** *TBI included for dose calculation purposes only; this section not applicable to patients who received TBI alone.	**Central adrenal insufficiency**	**Treatment Factors** Higher radiation dose Surgery or tumor in the suprasellar region	**Treatment Factors** Prior development of another hypothalamic-pituitary endocrinopathy	**HISTORY** **Failure to thrive** **Anorexia** **Dehydration** **Hypoglycemia** **Lethargy** **Unexplained hypotension** Yearly **SCREENING** **8:00 a.m. serum cortisol** Yearly for at least 15 years after treatment and as clinically indicated.	**Health Links** **Central Adrenal Insufficiency** See also: **Hypopituitarism** **Resources** www.magicfoundation.org **Counseling** Counsel regarding corticosteroid replacement therapy and stress dosing. Counsel regarding Medical Alert bracelet. **Considerations for Further Testing and Intervention** Endocrine consultation for further evaluation and replacement steroids. **SYSTEM = Endocrine/Metabolic** **SCORE = 1**

- This section is only applicable to patients who:
  1) Received radiation to any of the specified fields at ≥ 40 Gy
  OR
  2) Received a combination of radiation to any of the specified fields **and** TBI, the sum of which is ≥ 40 Gy
- See dose calculation rules on page 48 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 55 REFERENCES

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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
56	**Cranial** **Orbital/Eye** **TBI** **Info Link:** Radiation-related ocular complications other than cataracts are generally associated only with orbital/eye radiation or higher dose cranial radiation. However, 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.	**Cataracts**	**Treatment Factors** Radiation dose ≥ 10 Gy TBI ≥ 2 Gy in single fraction TBI ≥ 5 Gy fractionated Radiation combined with - Corticosteroids - Busulfan - Longer interval since treatment	**Treatment Factors** Radiation dose ≥ 15 Gy Fraction dose ≥ 2 Gy TBI ≥ 5 Gy in single fraction TBI ≥ 10 Gy fractionated Cranial/orbital/eye radiation combined with TBI	**HISTORY** **Visual changes (decreased acuity, halos, diplopia)** Yearly **PHYSICAL** **Eye exam (visual acuity, funduscopic exam to evaluate for lens opacity)** Yearly **SCREENING** **Evaluation by ophthalmologist** Yearly for patients with ocular tumors [regardless of radiation dose] and for those who received TBI or ≥ 30 Gy cranial/orbital/eye radiation; Every 3 years for patients without ocular tumors who received <30 Gy.	**Health Links** **Cataracts** **Considerations for Further Testing and Intervention** 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. **SYSTEM = Ocular** **SCORE = 1**

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

SECTION 56 REFERENCES

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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
57	**≥ 30 Gy to:** **Cranial** **Orbital/Eye** **TBI*** *TBI included for dose calculation purposes only; this section not applicable to patients who received TBI alone. **Info Link:** Radiation-related ocular complications other than cataracts are generally associated only with orbital/eye radiation or higher dose cranial radiation. However, 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.	**Ocular toxicity** Orbital hypoplasia Lacrimal duct atrophy Xerophthalmia (keratoconjunctivitis sicca) Keratitis Telangiectasias Retinopathy Optic chiasm neuropathy Enophthalmos Chronic painful eye Maculopathy Papillopathy Glaucoma **Info Link:** Reduced visual acuity may be associated with cataracts, retinal damage, and optic nerve damage.	**Treatment Factors** Higher radiation dose Higher daily fraction dose Radiomimetic chemotherapy (e.g., doxorubicin, dactinomycin) [problems related to tearing]	**Host Factors** Chronic GVHD (xerophthalmia only) **Treatment Factors** Fraction dose ≥ 2 Gy	**HISTORY** **Visual changes (decreased acuity, halos, diplopia)** **Dry eye** **Persistent eye irritation** **Excessive tearing** **Light sensitivity** **Poor night vision** **Painful eye** Yearly **PHYSICAL** **Visual acuity** **Funduscopic exam** Yearly **SCREENING** **Evaluation by ophthalmologist** Yearly	**Health Links** **Eye Health** **Resources** FACES - The National Craniofacial Association website: www.faces-cranio.org **Considerations for Further Testing and Intervention** Consider every six month ophthalmology evaluation for patients with corneal damage (usually associated with xerophthalmia) or complex ocular 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. **SYSTEM = Ocular** **SCORE = 1**

- This section is only applicable to patients who:
  1) Received radiation to any of the specified fields at ≥ 30 Gy
  OR
  2) Received a combination of radiation to any of the specified fields **and** TBI, the sum of which is ≥ 30 Gy
- See dose calculation rules on page 48 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 57 REFERENCES

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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
58	**≥ 30 Gy to:** **Cranial** **Ear/Infratemporal** **Nasopharyngeal** **Waldeyer's Ring** **TBI*** *TBI included for dose calculation purposes only; this section not applicable to patients who received TBI alone.	**Ototoxicity** Tympanosclerosis Otosclerosis Eustachian tube dysfunction Conductive hearing loss	**Host Factors** Younger age at treatment **Treatment Factors** Higher radiation dose **Medical Conditions** Chronic otitis Chronic cerumen impaction	**Treatment Factors** Dose ≥ 50 Gy	**HISTORY** **Hearing difficulties (with/without background noise)** **Tinnitus** **Vertigo** Yearly **PHYSICAL** **Otoscopic exam** Yearly **SCREENING** **Complete audiological evaluation** Yearly after completion of therapy for 5 years [for patients <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]. **Info Link:** 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.	**Health Links** **Hearing Loss** **Educational Issues** **Considerations for Further Testing and Intervention** Audiology consultation for patients with progressive 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. **SYSTEM = Auditory** **SCORE = 1**
		Sensorineural hearing loss Tinnitus	**Host Factors** Younger age at treatment CNS tumor CSF shunting **Treatment Factors** Higher radiation dose; Conventional (non-conformal) radiation	**Treatment Factors** Radiation administered prior to platinum chemotherapy Combined with other ototoxic agents such as: - Cisplatin - Carboplatin in myeloablative doses - Aminoglycosides		

- 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 48 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 ORAL CAVITY

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
59	**Cranial** **Nasopharyngeal** **Oropharyngeal** **Waldeyer's Ring** **Spine (cervical, whole)** **Cervical (neck)** **Supraclavicular** **Mini-Mantle** **Mantle** **Extended Mantle** **TLI** **STLI**	**Xerostomia** **Salivary gland dysfunction**	**Treatment Factors** Head and neck radiation involving the parotid gland Higher radiation doses Radiomimetic chemotherapy (e.g., doxorubicin, dactinomycin)	**Treatment Factors** Salivary gland dose ≥ 30 Gy **Medical Conditions** Chronic GVHD	**HISTORY** **Xerostomia** Yearly **PHYSICAL** **Oral exam** Yearly **SCREENING** **Dental exam and cleaning** Every 6 months	**Health Links** **Dental Health** **Considerations for Further Testing and Intervention** Supportive care with saliva substitutes, moistening agents, and sialogogues (pilocarpine); Regular dental care including fluoride applications. **SYSTEM = Dental** **SCORE = 1**

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

SECTION 59 REFERENCES

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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
60	**Cranial** **Nasopharyngeal** **Oropharyngeal** **Waldeyer's Ring** **Spine (cervical, whole)** **Cervical (neck)** **Supraclavicular** **Mini-Mantle** **Mantle** **Extended Mantle** **TLI** **STLI** **TBI**	**Dental abnormalities** Tooth/root agenesis Microdontia Root thinning/shortening Enamel dysplasia Periodontal disease Dental caries Malocclusion Temporomandibular joint dysfunction	**Host Factors** Younger age at treatment Gorlin's syndrome (nevoid basal cell carcinoma syndrome) **Treatment Factors** Higher radiation dose	**Host Factors** Age < 5 years at time of treatment **Treatment Factors** Dose ≥ 10 Gy	**PHYSICAL** **Oral exam** Yearly **SCREENING** **Dental exam and cleaning** Every 6 months	**Health Links** **Dental Health** **Considerations for Further Testing and Intervention** 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. **SYSTEM = Dental** **SCORE = 1**

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

SECTION 60 REFERENCES

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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
61	**≥ 40 Gy to:** **Cranial** **Nasopharyngeal** **Oropharyngeal** **Waldeyer's Ring** **Spine (cervical, whole)** **Cervical (neck)** **Supraclavicular** **Mini-Mantle** **Mantle** **Extended Mantle** **TLI** **STLI** **TBI*** *TBI included for dose calculation purposes only; this section not applicable to patients who received TBI alone.	**Osteoradionecrosis**	**Treatment Factors** Radiation dose to bone ≥ 45 Gy	**Treatment Factors** Radiation dose to bone ≥ 50 Gy	**HISTORY** **Impaired or delayed healing following dental work** **Persistent jaw pain or swelling** **Trismus** As clinically indicated **PHYSICAL** **Impaired wound healing** **Jaw swelling** **Trismus** As clinically indicated	**Health Links** **Osteoradionecrosis** **Considerations for Further Testing and Intervention** Imaging studies (x-ray, CT scan and/or MRI) may assist in making diagnosis. Surgical biopsy may be needed to confirm diagnosis. Consider hyperbaric oxygen treatments. **SYSTEM = Dental** **SCORE = 1**

- 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 48 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 61 REFERENCES

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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
62	**Cranial** **Nasopharyngeal** **Oropharyngeal** **Waldeyer's Ring** **Spine (cervical, whole)** **Cervical (neck)** **Supraclavicular** **Chest (thorax)** **Whole lung** **Mediastinal** **Mini-mantle** **Mantle** **Extended Mantle** **TLI** **STLI** **TBI**	**Thyroid nodules**	**Host Factors** Younger age at treatment Female sex **Treatment Factors** Higher radiation dose Thyroid gland directly in radiation field TBI	**Treatment Factors** Radiation dose ≥ 25 Gy	**PHYSICAL** **Thyroid exam** Yearly	**Health Links** **Thyroid Problems** **Considerations for Further Testing and Intervention** Ultrasound and FNA for evaluation of palpable nodule(s). Endocrine and/or surgical consultation for diagnostic biopsy or thyroidectomy. **SYSTEM = SMN** **SCORE = 1**

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

SECTION 62 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
63	**Cranial** **Nasopharyngeal** **Oropharyngeal** **Waldeyer's Ring** **Spine (cervical, whole)** **Cervical (neck)** **Supraclavicular** **Chest (thorax)** **Whole lung** **Mediastinal** **Mini-Mantle** **Mantle** **Extended Mantle** **TLI** **STLI** **TBI**	**Thyroid cancer**	**Host Factors** Younger age at treatment Female sex **Treatment Factors** ≥ 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		**PHYSICAL** **Thyroid exam** Yearly	**Health Links** **Thyroid Problems** **Considerations for Further Testing and Intervention** 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. **SYSTEM = SMN** **SCORE = 1**

• 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
64	**Cranial** **Nasopharyngeal** **Oropharyngeal** **Waldeyer's Ring** **Spine (cervical, whole)** **Cervical (neck)** **Supraclavicular** **Chest (thorax)** **Whole lung** **Mediastinal** **Mini-Mantle** **Mantle** **Extended Mantle** **TLI** **STLI** **TBI** • See "Patient-Specific Guideline Identification Tool" in Appendix I to determine specific screening guidelines by section number for individual patients.	**Hypothyroidism**	**Host Factors** Female sex **Treatment Factors** Radiation dose ≥ 10 Gy Thyroid gland directly in radiation field TBI	**Treatment Factors** Radiation dose ≥ 20 Gy	**HISTORY** **Fatigue** **Weight gain** **Cold intolerance** **Constipation** **Dry skin** **Brittle hair** **Depressed mood** Yearly; Consider more frequent screening during periods of rapid growth. **PHYSICAL** **Height** **Weight** **Hair and skin** **Thyroid exam** Yearly; Consider more frequent screening during periods of rapid growth. **SCREENING** **TSH** **Free T4** Yearly; Consider more frequent screening during periods of rapid growth.	**Health Links** **Thyroid Problems** **Counseling** Counsel at-risk females of childbearing potential to have their thyroid levels checked prior to attempting pregnancy and periodically throughout pregnancy. **Considerations for Further Testing and Intervention** Endocrine consultation for medical management. **SYSTEM = Endocrine/Metabolic** **SCORE = 1**

SECTION 64 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
65	**≥ 40 Gy to:** **Cranial** **Nasopharyngeal** **Oropharyngeal** **Waldeyer's Ring** **Spine (cervical, whole)** **Cervical (neck)** **Supraclavicular** **Chest (thorax)** **Whole lung** **Mediastinal** **Mini-Mantle** **Mantle** **Extended Mantle** **TLI** **STLI** **TBI*** *TBI included for dose calculation purposes only; this section not applicable to patients who received TBI alone.	**Hyperthyroidism**	**Treatment Factors** Higher radiation dose		**HISTORY** **Heat intolerance** **Tachycardia** **Palpitations** **Weight loss** **Emotional lability** **Muscular weakness** **Hyperphagia** Yearly **PHYSICAL** **Eyes** **Skin** **Thyroid** **Cardiac** **Neurologic** Yearly **SCREENING** **TSH** **Free T4** Yearly	**Health Links** **Thyroid Problems** **Considerations for Further Testing and Intervention** Endocrine consultation for medical management. **SYSTEM = Endocrine/Metabolic** **SCORE = 1**

- This section is only applicable to patients who:
  1) Received radiation to any of the specified fields at ≥ 40 Gy
  OR
  2) Received a combination of radiation to any of the specified fields **plus** relevant spinal radiation **and/or** TBI, the sum of which is ≥ 40 Gy
- See dose calculation rules on page 48 for patients who received: (a) radiation to more than one of the specified fields, or (b) more than one planned course of treatment to the same field.
- See "Patient-Specific Guideline Identification Tool" in Appendix I to determine specific screening guidelines by section number for individual patients.

SECTION 65 REFERENCES

Chin D, Sklar C, Donahue B, et al. Thyroid dysfunction as a late effect in survivors of pediatric medulloblastoma/primitive neuroectodermal tumors: a comparison of hyperfractionated versus conventional radiotherapy. *Cancer*. Aug 15 1997;80(4):798-804.

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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
66	**≥ 40 Gy to:** **Cranial** **Nasopharyngeal** **Oropharyngeal** **Waldeyer's Ring** **Spine (cervical, whole)** **Cervical (neck)** **Supraclavicular** **Chest (thorax)** **Whole lung** **Mediastinal** **Mini-Mantle** **Mantle** **Extended Mantle** **TLI** **STLI** **TBI*** *TBI included for dose calculation purposes only; this section not applicable to patients who received TBI alone.	**Carotid artery disease**			**HISTORY** **Memory impairment** Yearly **PHYSICAL** **Diminished carotid pulses** **Carotid bruits** **Abnormal neurologic exam (compromise of blood flow to brain)** Yearly	**Considerations for Further Testing and Intervention** 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. **SYSTEM = Cardiovascular** **SCORE = 2A**

- 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 48 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

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 NECK/THYROID (cont)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
67	**≥ 40 Gy to:** **Spine (cervical, whole)** **Cervical (neck)** **Supraclavicular** **Chest (thorax)** **Whole lung** **Mediastinal** **Mini-Mantle** **Mantle** **Extended Mantle** **TLI** **STLI** **TBI*** *TBI included for dose calculation purposes only; this section not applicable to patients who received TBI alone.	**Subclavian artery disease** • 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 48 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.			**PHYSICAL** **Diminished brachial and radial pulses** **Pallor of upper extremities** **Coolness of skin** **Unequal blood pressure** Yearly	**Considerations for Further Testing and Intervention** 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. **SYSTEM = Cardiovascular** **SCORE = 2A**

SECTION 67 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.

Hull MC, Morris CG, Pepine CJ, Mendenhall NP. Valvular dysfunction and carotid, subclavian, and coronary artery disease in survivors of hodgkin lymphoma treated with radiation therapy. *JAMA.* Dec 3 2003;290(21):2831-2837.

RADIATION

POTENTIAL IMPACT TO BREAST

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
68 (Female)	**≥ 20 Gy to:** **Chest (thorax)** **Whole lung** **Mediastinal** **Axilla** **Mini-Mantle** **Mantle** **Extended Mantle** **TLI** **STLI** **TBI*** **Info Link:** *Important: The risk of breast cancer in patients 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); therefore, monitoring of patients who received TBI without additional radiation potentially impacting the breast should be determined on an individual basis.	**Breast cancer**	**Host Factors** Family history of breast cancer **Treatment Factors** Higher radiation dose Longer time since radiation (≥ 5 years) Decreased risk in women treated with alkylating agents	**Host Factors** Female gender	**PHYSICAL** **Breast exam** Yearly, beginning at puberty until age 25, then every 6 months. **SCREENING** **Mammogram** Yearly, beginning 8 years after radiation or at age 25, whichever occurs last. **Breast MRI** Yearly as an adjunct to mammography beginning 8 years after radiation or at age 25, whichever occurs last. **Info Link:** 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.	**Health Links** **Breast Cancer** **Counseling** Teach breast self-exam and counsel to perform monthly beginning at puberty. **Considerations for Further Testing and Intervention** 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. **SYSTEM = SMN** **SCORE = 1**

- This section is only applicable to patients who:
  1) Received radiation to any of the specified fields at ≥ 20 Gy
     OR
  2) Received a combination of radiation to any of the specified fields **and** TBI, the sum of which is ≥ 20 Gy
- See dose calculation rules on page 48 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 68 REFERENCES

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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
69 (Female)	**Chest (thorax)** **Whole lung** **Mediastinal** **Axilla** **Mini-Mantle** **Mantle** **Extended Mantle** **TLI** **STLI** **TBI**	**Breast tissue hypoplasia**	**Host Factors** Prepubertal at time of breast irradiation **Treatment Factors** Radiation dose ≥ 10 Gy to prepubertal breast bud may cause failure of development (hypoplasia)	**Treatment Factors** ≥ 20 Gy to prepubertal breast bud may ablate development	**PHYSICAL** **Breast exam** Yearly	**Considerations for Further Testing and Intervention** Surgical consultation for breast reconstruction after completion of growth. **SYSTEM = Reproductive (female)** **SCORE = 1**

- 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 LUNGS

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
70	**Chest (thorax)** **Whole lung** **Mediastinal** **Axilla** **Mini-Mantle** **Mantle** **Extended Mantle** **TLI** **STLI** **TBI**	**Pulmonary toxicity** Pulmonary fibrosis Interstitial pneumonitis Restrictive lung disease Obstructive lung disease	**Host Factors** Younger age at irradiation **Treatment Factors** Radiation dose ≥ 10 Gy Chest radiation combined with TBI Radiation combined with: - Bleomycin - Busulfan - Carmustine (BCNU) - Lomustine (CCNU) - Radiomimetic chemotherapy (e.g., doxorubicin, dactinomycin) **Medical Conditions** Atopic history **Health Behaviors** Smoking	**Treatment Factors** Radiation dose ≥ 15 Gy TBI ≥ 6 Gy in single fraction TBI ≥ 12 Gy fractionated	**HISTORY** **Cough** **SOB** **DOE** **Wheezing** Yearly **PHYSICAL** **Pulmonary exam** Yearly **SCREENING** **Chest x-ray** **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	**Health Links** **Pulmonary Health** **Resources** Extensive information regarding smoking cessation is available for patients on the NCI's website: www.smokefree.gov **Counseling** Counsel regarding tobacco avoidance/smoking cessation. Due to the potential pulmonary toxicity of this therapy, patients who desire to SCUBA dive should be advised to obtain medical clearance from a pulmonologist. **Considerations for Further Testing and Intervention** In patients with abnormal PFTs and/or CXR, consider repeat evaluation prior to general anesthesia. Pulmonary consultation for patients with symptomatic pulmonary dysfunction. Influenza and Pneumococcal vaccinations. **SYSTEM = Pulmonary** **SCORE = 1**

- 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 HEART

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
71 (Male)	**Spine (thoracic, whole)** **Chest (thorax)** **Whole lung** **Mediastinal** **Mantle** **Extended Mantle** **Hepatic** **Renal** **Upper quadrant (right, left)** **Spleen (partial, entire)** **Paraaortic** **Flank/Hemiabdomen (right, left)** **Whole abdomen** **Inverted Y** **TLI** **STLI** **TBI**	**Cardiac toxicity** Congestive heart failure Cardiomyopathy Pericarditis Pericardial fibrosis Valvular disease Myocardial infarction Arrhythmia Atherosclerotic heart disease	**Host Factors** Younger age at irradiation Family history of dyslipidemia Coronary artery disease **Treatment Factors** Radiation dose ≥ 20 Gy to chest TBI Combined with radiomimetic chemotherapy (e.g., doxorubicin, dactinomycin) Combined with other cardiotoxic chemotherapy - Anthracyclines - Cyclophosphamide conditioning for HCT - Amsacrine **Medical Conditions** Hypertension Obesity Dyslipidemia Diabetes mellitus Congenital heart disease Febrile illness **Health Behaviors** Smoking Isometric exercise Drug use (e.g., cocaine, diet pills, ephedra)	**Host Factors** Black/ of African descent Younger than age 5 years at time of treatment **Treatment Factors** Anteriorly-weighted radiation fields Lack of subcarinal shielding Doses ≥ 30 Gy in patients who have received anthracyclines Doses ≥ 40 Gy in patients who have not received anthracyclines Longer time since treatment	**HISTORY** **SOB** **DOE** **Orthopnea** **Chest pain** **Palpitations** **If under 25 years: Abdominal symptoms (nausea, vomiting)** Yearly **Info Link:** Exertional intolerance is uncommon in patients younger than 25 years old. Abdominal symptoms (nausea, emesis) may be observed more frequently than exertional dyspnea or chest pain in younger patients. **PHYSICAL** **Cardiac murmur** **S3, S4** **Increased P2 sound** **Pericardial rub** **Rales** **Wheezes** **Jugular venous distension** **Peripheral edema** Yearly **SCREENING** **Fasting glucose and lipid profile** Every 2 years; If abnormal, refer for ongoing management. **EKG (include evaluation of QTc interval)** Baseline at entry into long-term follow-up, repeat as clinically indicated. **ECHO** Baseline at entry into long-term follow-up, then periodically based on age at treatment, radiation dose, and cumulative anthracycline dose [see table]	**Health Links** **Heart Health** **Diet and Physical Activity** **Dental Health** **Counseling** Counsel patients with prolonged QTc interval about use of medications that may further prolong the QTc interval (e.g., tricyclic anti-depressants, antifungals, macrolide antibiotics, 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. **Considerations for Further Testing and Intervention** Cardiology consultation for patients with subclinical abnormalities on screening evaluations or with left ventricular dysfunction, dysrhythmia or prolonged QTc interval. Consider cardiology consultation (5 to 10 years after radiation) to evaluate risk for coronary artery disease in patients who received ≥ 40 Gy chest radiation alone or ≥ 30 Gy chest radiation plus anthracycline. Consider excess risk of isometric exercise program in any high-risk patient defined as needing screening every 1 or 2 years. **SYSTEM = Cardiovascular** **SCORE = 1**

RECOMMENDED FREQUENCY OF ECHOCARDIOGRAM

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

*Age at time of first cardiotoxic therapy (anthracycline or radiation with potential impact to heart, whichever was given first)
†Based on doxorubicin isotoxic equivalent dose [see conversion factors in Section 28 "Info Link (Dose Conversion)"]
‡If patient received radiation to more than one specified field, see dose calculation rules on page 48.

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

RADIATION

POTENTIAL IMPACT TO HEART (cont)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
71 (Female)	**Spine (thoracic, whole)** **Chest (thorax)** **Whole lung** **Mediastinal** **Mantle** **Extended Mantle** **Hepatic** **Renal** **Upper quadrant (right, left)** **Spleen (partial, entire)** **Paraaortic** **Flank/Hemiabdomen (right, left)** **Whole abdomen** **Inverted Y** **TLI** **STLI** **TBI**	**Cardiac toxicity** Congestive heart failure Cardiomyopathy Pericarditis Pericardial fibrosis Valvular disease Myocardial infarction Arrhythmia Atherosclerotic heart disease	**Host Factors** Younger age at irradiation Family history of dyslipidemia Coronary artery disease **Treatment Factors** Radiation dose ≥ 20 Gy to chest TBI Combined with radiomimetic chemotherapy (e.g., doxorubicin, dactinomycin) Combined with other cardiotoxic chemotherapy - Anthracyclines - Cyclophosphamide conditioning for HCT - Amsacrine **Medical Conditions** Hypertension Obesity Dyslipidemia Diabetes mellitus Congenital heart disease Febrile illness Pregnancy Premature ovarian failure (untreated) **Health Behaviors** Smoking Isometric exercise Drug use (e.g., cocaine, diet pills, ephedra)	**Host Factors** Female sex Black/ of African descent Younger than age 5 years at time of treatment **Treatment Factors** Anteriorly-weighted radiation fields Lack of subcarinal shielding Doses ≥ 30 Gy in patients who have received anthracyclines Doses ≥ 40 Gy in patients who have not received anthracyclines Longer time since treatment	**HISTORY** **SOB** **DOE** **Orthopnea** **Chest pain** **Palpitations** **If under 25 years: Abdominal symptoms (nausea, vomiting)** Yearly **Info Link:** Exertional intolerance is uncommon in patients younger than 25 years old. Abdominal symptoms (nausea, emesis) may be observed more frequently than exertional dyspnea or chest pain in younger patients. **PHYSICAL** **Cardiac murmur** **S3, S4** **Increased P2 sound** **Pericardial rub** **Rales** **Wheezes** **Jugular venous distension** **Peripheral edema** Yearly **SCREENING** **Fasting glucose and lipid profile** Every 2 years; If abnormal, refer for ongoing management. **EKG (include evaluation of QTc interval)** Baseline at entry into long-term follow-up, repeat as clinically indicated. **ECHO** Baseline at entry into long-term follow-up, then periodically based on age at treatment, radiation dose, and cumulative anthracycline dose [see table]	**Health Links** **Heart Health** **Diet and Physical Activity** **Dental Health** **Counseling** Counsel patients with prolonged QTc interval about use of medications that may further prolong the QTc interval (e.g., tricyclic anti-depressants, antifungals, macrolide antibiotics, 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. **Considerations for Further Testing and Intervention** Cardiology consultation for patients with subclinical abnormalities on screening evaluations or with left ventricular dysfunction, dysrhythmia or prolonged QTc interval. Additional cardiology evaluation for patients who are pregnant or planning pregnancy who: (1) received ≥ 30 Gy chest radiation, or (2) received chest radiation in combination with cardiotoxic chemotherapy (anthracyclines or high-dose cyclophosphamide). Evaluation to include echocardiogram before and periodically during pregnancy (especially during third trimester) and monitoring during labor and delivery due to risk of cardiac failure. Consider cardiology consultation (5 to 10 years after radiation) to evaluate risk for coronary artery disease in patients who received ≥ 40 Gy chest radiation alone or ≥ 30 Gy chest radiation plus anthracycline. Consider excess risk of isometric exercise program in any high-risk patient defined as needing screening every 1 or 2 years. **SYSTEM = Cardiovascular** **SCORE = 1**

RECOMMENDED FREQUENCY OF ECHOCARDIOGRAM

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

*Age at time of first cardiotoxic therapy (anthracycline or radiation with potential impact to heart, whichever was given first)
†Based on doxorubicin isotoxic equivalent dose [see conversion factors in Section 28 "Info Link (Dose Conversion)"]
‡If patient received radiation to more than one specified field, see dose calculation rules on page 48.

- 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 SPLEEN

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
72	**≥ 40 Gy to:** **Left upper quadrant** **Spleen (entire)** **Paraaortic*** **Left flank/hemiabdomen** **Whole abdomen** **Inverted Y*** **TLI** **STLI** **TBI**** *If spleen in field **TBI included for dose calculation purposes only; this section not applicable to patients who received TBI alone.	**Functional asplenia** At risk for life-threatening infection with encapsulated organisms (e.g., Haemophilus influenzae, streptococcus pneumoniae, meningococcus)	**Treatment Factors** Higher radiation dose to entire spleen		**PHYSICAL** **Physical exam at time of febrile illness to evaluate degree of illness and potential source of infection** When febrile T ≥ 101ºF **SCREENING** **Blood culture** When febrile T ≥ 101ºF	**Health Links** **Splenic Precautions** **Counseling** Medical alert bracelet/card noting functional asplenia; Counsel to avoid malaria and tick bites if living in or visiting endemic areas. **Considerations for Further Testing and Intervention** In patients with T ≥ 101°F (38.3° C) or other signs of serious illness, administer a long-acting, broad-spectrum parenteral antibiotic (e.g., ceftriaxone), and continue close medical monitoring while awaiting blood culture results. Hospitalization and broadening of antimicrobial coverage (e.g., addition of vancomycin) may be necessary under certain circumstances, such as the presence of marked leukocytosis, neutropenia, or significant change from baseline CBC; toxic clinical appearance; fever ≥ 104°F; meningitis, pneumonia, or other serious focus of infection; signs of septic shock; or previous history of serious infection. Immunize with Pneumococcal, Meningococcal, and HIB vaccines. Pneumovax booster in patients ≥10 years old at ≥ 5 years after previous dose. (AAP-CIDP Recommendations, 2003). Discuss with dental provider potential need for antibiotic prophylaxis based on planned procedure. **SYSTEM = Immune** **SCORE = 1**

- This section is only applicable to patients who:
  1) Received radiation to any of the specified fields at ≥ 40 Gy
  OR
  2) Received a combination of radiation to any of the specified fields **and** TBI, the sum of which is ≥ 40 Gy
- See dose calculation rules on page 48 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

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
73	**≥ 30 Gy to:** **Spine (cervical, thoracic, whole)** **Cervical (neck)** **Supraclavicular** **Chest (thorax)** **Whole lung** **Mediastinal** **Mini-Mantle** **Mantle** **Extended mantle** **Hepatic** **Renal** **Upper quadrant (right, left)** **Spleen (partial, entire)** **Paraaortic** **Flank/Hemiabdomen (right, left)** **Whole abdomen** **Inverted Y** **TLI** **STLI** **TBI*** *TBI included for dose calculation purposes only; this section not applicable to patients who received TBI alone.	**Esophageal stricture**	**Treatment Factors** Higher radiation dose Radiomimetic chemotherapy (e.g., doxorubicin, actinomycin) **Medical Conditions** Gastroesophageal reflux History of Candida esophagitis	**Treatment Factors** Radiation dose ≥ 40 Gy **Medical Conditions** Gut GVHD	**HISTORY** **Dysphagia** **Heartburn** Yearly	**Health Links** **Gastrointestinal Health** **Considerations for Further Testing and Intervention** Surgical and/or gastroenterology consultation for symptomatic patients. **SYSTEM = GI/Hepatic** **SCORE = 1**

- This section is only applicable to patients who:
  1) Received radiation to any of the specified fields at ≥ 30 Gy
     OR
  2) Received a combination of radiation to any of the specified fields **plus** relevant spinal radiation **and/or** TBI, the sum of which is ≥ 30 Gy
- See dose calculation rules on page 48 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
74	**≥ 30 Gy to:** **Extended mantle** **Hepatic** **Renal** **Upper quadrant (right, left)** **Spleen (partial, entire)** **Paraaortic** **Flank/Hemiabdomen (right, left)** **Whole abdomen** **Inverted Y** **TLI** **STLI** **TBI*** *TBI included for dose calculation purposes only; this section not applicable to patients who received TBI alone.	**Hepatic fibrosis** **Cirrhosis**	**Treatment Factors** Higher radiation dose **Medical Conditions** Chronic hepatitis History of VOD **Health Behaviors** Alcohol use	**Treatment Factors** Dose ≥ 40 Gy to at least 1/3 of liver volume Dose 20-30 Gy to entire liver	**PHYSICAL** **Jaundice** **Spider angiomas** **Palmar erythema** **Xanthomata** **Hepatomegaly** **Splenomegaly** Yearly **SCREENING** **ALT** **AST** **Bilirubin** Baseline at entry into long-term follow-up, repeat as clinically indicated.	**Health Links** **Liver Health** **Considerations for Further Testing and Intervention** 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. **SYSTEM = GI/Hepatic** **SCORE = 1**

- This section is only applicable to patients who:
  1) Received radiation to any of the specified fields at ≥ 30 Gy
     OR
  2) Received a combination of radiation to any of the specified fields **and** TBI, the sum of which is ≥ 30 Gy
- See dose calculation rules on page 48 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
75	**≥ 30 Gy to:** **Extended mantle** **Hepatic** **Renal** **Upper quadrant (right, left)** **Spleen (partial, entire)** **Paraaortic** **Flank/Hemiabdomen (right, left)** **Whole abdomen** **Inverted Y** **TLI** **STLI** **TBI*** *TBI included for dose calculation purposes only; this section not applicable to patients who received TBI alone.	**Cholelithiasis**	**Host Factors** Ileal conduit Obesity Pregnancy Family history of cholelithiasis **Treatment Factors** Abdominal surgery Abdominal radiation TPN		**HISTORY** **Colicky abdominal pain related to fatty food intake** **Excessive flatulence** Yearly and as clinically indicated **PHYSICAL** **RUQ or epigastric tenderness** **Positive Murphy's sign** Yearly and as clinically indicated	**Health Links** **Gastrointestinal Health** **Considerations for Further Testing and Intervention** Consider gallbladder ultrasound in patients with chronic abdominal pain. **SYSTEM = GI/Hepatic** **SCORE = 2B**

- 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 48 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
76	**≥ 30 Gy to:** **Spine (thoracic, lumbar, sacral, whole)** **Extended Mantle** **Hepatic** **Renal** **Upper quadrant (right, left)** **Spleen (partial, entire)** **Paraaortic** **Flank/Hemiabdomen (right, left)** **Whole abdomen** **Inverted Y** **Pelvic** **Vaginal** **Prostate** **Bladder** **Iliac** **Inguinal** **Femoral** **TLI** **STLI** **TBI*** *TBI included for dose calculation purposes only; this section not applicable to patients who received TBI alone.	**Bowel obstruction**	**Treatment Factors** Higher radiation dose to bowel Abdominal surgery **Info Link** Bowel obstruction is rarely seen in individuals treated with abdominal radiation who have not had abdominal surgery.	**Treatment Factors** Radiation dose ≥ 45 Gy (Obstruction may occur in people who received lower doses of abdominal radiation during childhood)	**HISTORY** **Abdominal pain** **Distention** **Vomiting** **Constipation** With clinical symptoms of obstruction **PHYSICAL** **Tenderness** **Abdominal guarding** **Distension** With clinical symptoms of obstruction	**Health Links** **Gastrointestinal Health** **Considerations for Further Testing and Intervention** Obtain KUB in patients with clinical symptoms of obstruction. Surgical consultation in patients unresponsive to medical management. **SYSTEM = GI/Hepatic** **SCORE = 1**

- This section is only applicable to patients who:
  1) Received radiation to any of the specified fields at ≥ 30 Gy
     OR
  2) Received a combination of radiation to any of the specified fields **plus** relevant spinal radiation **and/or** TBI, the sum of which is ≥ 30 Gy
- See dose calculation rules on page 48 for patients who received: (a) radiation to more than one of the specified fields, or (b) more than one planned course of treatment to the same field.
- See "Patient-Specific Guideline Identification Tool" in Appendix I to determine specific screening guidelines by section number for individual patients.

SECTION 76 REFERENCES

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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
77	**≥ 30 Gy to:** **Spine (thoracic, lumbar, sacral, whole)** **Extended Mantle** **Hepatic** **Renal** **Upper quadrant (right, left)** **Spleen (partial, entire)** **Paraaortic** **Flank/Hemiabdomen (right, left)** **Whole abdomen** **Inverted Y** **Pelvic** **Vaginal** **Prostate** **Bladder** **Iliac** **Inguinal** **Femoral** **TLI** **STLI** **TBI*** *TBI included for dose calculation purposes only; this section not applicable to patients who received TBI alone.	**Chronic enterocolitis** **Fistula** **Strictures**	**Treatment Factors** Higher radiation dose to bowel Abdominal surgery	**Treatment Factors** Radiation dose ≥ 45 Gy	**HISTORY** **Nausea** **Vomiting** **Abdominal pain** **Diarrhea** Yearly	**Health Links** **Gastrointestinal Health** **Considerations for Further Testing and Intervention** Serum protein and albumin yearly in patients with chronic diarrhea or fistula. Surgical and/or gastroenterology consultation for symptomatic patients. **SYSTEM = GI/Hepatic** **SCORE = 1**

- This section is only applicable to patients who:
  1) Received radiation to any of the specified fields at ≥ 30 Gy
     OR
  2) Received a combination of radiation to any of the specified fields **plus** relevant spinal radiation **and/or** TBI, the sum of which is ≥ 30 Gy
- See dose calculation rules on page 48 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
78	**≥ 30 Gy to:** **Spine (thoracic, lumbar, sacral, whole)** **Extended Mantle** **Hepatic** **Renal** **Upper quadrant (right, left)** **Spleen (partial, entire)** **Paraaortic** **Flank/Hemiabdomen (right, left)** **Whole abdomen** **Inverted Y** **Pelvic** **Vaginal** **Prostate** **Bladder** **Iliac** **Inguinal** **Femoral** **TLI** **STLI** **TBI*** **Info Link:** ***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. Therefore, monitoring of patients who received TBI without additional radiation potentially impacting the colon/rectum should be determined on an individual basis. (See Info Link in next column)	**Colorectal cancer** **Info Link:** Reports of colorectal cancer in cohorts of long-term survivors suggest that radiation likely increases risk, but the median age of onset is not as well established as that of secondary breast cancer following chest radiation. The expert panel agreed that early onset of screening is likely beneficial, and that a prudent course would be to initiate screening for colorectal cancer for those at highest risk (abdominal, pelvic, and/or spinal radiation ≥ 30 Gy) at age 35, or 10 years post radiation, whichever occurs last. Surveillance should be done via colonoscopy as per recommendations for populations at highest risk, with information from the first colonoscopy informing the frequency of follow-up testing.	**Host Factors** Current age ≥ 50 years **Treatment Factors** Higher radiation dose to bowel Higher daily dose fraction Combined with chemotherapy (especially alkylators) **Medical Conditions** Obesity **Health Behaviors** High fat/low fiber diet	**Host Factors** Personal history of ulcerative colitis, gastrointestinal malignancy, adenomatous polyps, or hepatoblastoma Familial polyposis Family history of colorectal cancer or polyps in first degree relative	**SCREENING** **Colonoscopy** Every 5 years [minimum] beginning at 10 years after radiation or at age 35 years [whichever occurs last]; more frequently if indicated based on colonoscopy results; Per the ACS, begin screening earlier for the following high-risk groups - HNPCC: at puberty; FAP: at age 21 years; IBD: 8 years after diagnosis of IBD; Information from the first colonoscopy will inform frequency of follow-up testing.	**Health Links** **Colorectal Cancer** **Considerations for Further Testing and Intervention** Surgical and/or oncology consultation as needed. **SYSTEM = SMN** **SCORE = 2A**

- This section is only applicable to patients who:
  1) Received radiation to any of the specified fields at ≥ 30 Gy
  OR
  2) Received a combination of radiation to any of the specified fields **plus** relevant spinal radiation **and/or** TBI, the sum of which is ≥ 30 Gy
- See dose calculation rules on page 48 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

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
79	**Extended Mantle** **Hepatic** **Renal** **Upper quadrant (right, left)** **Spleen (partial, entire)** **Paraaortic** **Flank/Hemiabdomen (right, left)** **Whole abdomen** **Inverted Y** **TLI** **STLI** **TBI**	**Renal toxicity** Renal insufficiency Hypertension	**Host Factors** Bilateral Wilms tumor Mononephric **Treatment Factors** Radiomimetic chemotherapy (e.g., doxorubicin, dactinomycin) Radiation dose ≥ 10 Gy TBI combined with radiation to the kidney Combined with other nephrotoxic agents such as: - Cisplatin - Carboplatin - Ifosfamide - Aminoglycosides - Amphotericin - Immunosuppressants **Medical Conditions** Diabetes mellitus Hypertension Nephrectomy	**Treatment Factors** Radiation dose ≥ 15 Gy TBI ≥ 6 Gy in single fraction TBI ≥ 12 Gy fractionated	**PHYSICAL** **Blood pressure** Yearly **SCREENING** **BUN, Creatinine, Na, K, Cl, CO_2, Ca, Mg, PO_4** Baseline at entry into long-term follow-up, repeat as clinically indicated. **Urinalysis** Yearly	**Health Links** **Kidney Health** See also: **Single Kidney Health** **Considerations for Further Testing and Intervention** Nephrology consultation for patients with hypertension, proteinuria, or progressive renal insufficiency **SYSTEM = Urinary** **SCORE = 1**

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

SECTION 79 REFERENCES

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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
80	**≥ 30 Gy to:** **Spine (sacral, whole)** **Flank/Hemiabdomen (right, left)*** **Whole abdomen** **Inverted Y** **Pelvic** **Vaginal** **Prostate** **Bladder** **Iliac** **Inguinal** **TLI** **TBI**** *Only if field extended below iliac crest **TBI included for dose calculation purposes only; this section not applicable to patients who received TBI alone.	**Hemorrhagic cystitis**	**Treatment Factors** Higher radiation dose (≥ 30 Gy to entire bladder; ≥ 60 Gy to portion of bladder)	**Treatment Factors** Combined with cyclophosphamide and/or ifosfamide	**HISTORY** **Hematuria** **Urinary urgency/frequency** **Urinary incontinence/retention** **Dysuria** **Nocturia** **Abnormal urinary stream** Yearly **SCREENING** **Urinalysis** Yearly	**Health Links** **Bladder Health** **Counseling** Counsel to promptly report dysuria or gross hematuria **Considerations for Further Testing and Intervention** Urine culture, spot urine calcium/creatinine ratio, and ultrasound of kidneys and bladder for patients with microscopic hematuria (defined as ≥ 5 RBC/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. **SYSTEM = Urinary** **SCORE = 2A**

- This section is only applicable to patients who:
  1) Received radiation to any of the specified fields at ≥ 30 Gy
     OR
  2) Received a combination of radiation to any of the specified fields **plus** relevant spinal radiation **and/or** TBI, the sum of which is ≥ 30 Gy
- See dose calculation rules on page 48 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 80 REFERENCES

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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
81	**≥ 30 Gy to:** **Spine (sacral, whole)** **Flank/Hemiabdomen (right, left)*** **Whole abdomen** **Inverted Y** **Pelvic** **Vaginal** **Prostate** **Bladder** **Iliac** **Inguinal** **TLI** **TBI**** *Only if field extended below iliac crest **TBI included for dose calculation purposes only; this section not applicable to patients who received TBI alone.	**Urinary tract toxicity** Bladder fibrosis Dysfunctional voiding Vesicoureteral reflux Hydronephrosis	**Treatment Factors** Higher cumulative radiation dose (≥ 45 Gy) Radiation to entire bladder Combined with: - Cyclophosphamide - Ifosfamide - Vincristine		**HISTORY** **Hematuria** **Urinary urgency/frequency** **Urinary incontinence/retention** **Dysuria** **Nocturia** **Abnormal urinary stream** Yearly **SCREENING** **Urinalysis** Yearly	**Health Links** **Bladder Health** **Considerations for Further Testing and Intervention** Urologic consultation for patients with incontinence or dysfunctional voiding. **SYSTEM = Urinary** **SCORE = 1**

- This section is only applicable to patients who:
  1) Received radiation to any of the specified fields at ≥ 30 Gy
  OR
  2) Received a combination of radiation to any of the specified fields **plus** relevant spinal radiation **and/or** TBI, the sum of which is ≥ 30 Gy
- See dose calculation rules on page 48 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 81 REFERENCES

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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
82	**Spine (sacral, whole)** **Flank/Hemiabdomen (right, left)*** **Whole abdomen** **Inverted Y** **Pelvic** **Vaginal** **Prostate** **Bladder** **Iliac** **Inguinal** **TLI** ***Only if field extended below iliac crest**	**Bladder malignancy**	**Treatment Factors** Radiation to pelvis Combined with: - Cyclophosphamide - Ifosfamide **Health Behaviors** Alcohol use Smoking		**HISTORY** **Hematuria** **Urinary urgency/frequency** **Urinary incontinence/retention** **Dysuria** **Nocturia** **Abnormal urinary stream** Yearly **SCREENING** **Urinalysis** Yearly	**Health Links** **Bladder Health** **Counseling** Counsel to promptly report dysuria or gross hematuria **Considerations for Further Testing and Intervention** Urine culture, spot urine calcium/creatinine ratio, and ultrasound of kidneys and bladder for patients with microscopic hematuria (defined as ≥ 5 RBC/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. **SYSTEM = SMN** **SCORE = 2A**

- 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 FEMALE REPRODUCTIVE SYSTEM

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
83 (Female)	**Spine (lumbar, sacral, whole)** **Flank/Hemiabdomen (right, left)*** **Whole abdomen** **Inverted Y** **Pelvic** **Vaginal** **Bladder** **TLI** **TBI** *Only if field extended below iliac crest	**Uterine vascular insufficiency** Resulting in adverse pregnancy outcomes, such as spontaneous abortion, neonatal death, low-birth weight infant, fetal malposition, and premature labor **Info Link:** 10% of girls with Wilms tumor have congenital uterine anomalies.	**Host Factors** Females with Wilms tumor and associated müllerian anomalies **Treatment Factors** Higher radiation dose to pelvis	**Host Factors** Prepubertal at treatment **Treatment Factors** Radiation dose ≥ 30 Gy TBI	**HISTORY** **Pregnancy** **Childbirth history** Yearly and as clinically indicated	**Health Links** **Female Health Issues** **Resources** American Society for Reproductive Medicine: www.asrm.org Fertile Hope: www.fertilehope.org **Considerations for Further Testing and Intervention** Consider high-level ultrasound evaluation of genitourinary tract after pubertal development as clinically indicated in patients contemplating pregnancy. High-risk obstetrical care during pregnancy. **SYSTEM = Reproductive (female)** **SCORE = 2B**

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

SECTION 83 REFERENCES

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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
84 (Female)	**Spine (lumbar, sacral, whole)** **Flank/Hemiabdomen (right, left)*** **Whole abdomen** **Inverted Y** **Pelvic** **Vaginal** **Bladder** **Iliac** **TLI** **TBI** *Only if field extended below iliac crest	**Gonadal dysfunction (ovarian)** Delayed/arrested puberty Premature menopause Infertility	**Host Factors** Older age at irradiation **Treatment Factors** Prepubertal female: Radiation dose ≥10 Gy Pubertal female: Radiation dose ≥ 5 Gy Combined with alkylating agent chemotherapy Longer time since treatment	**Treatment Factors** Prepubertal female: Radiation dose ≥15 Gy Pubertal female: Radiation dose ≥10 Gy Combined with cyclophosphamide conditioning for HCT	**HISTORY** **Pubertal (onset, tempo)** **Menstrual/pregnancy history** **Sexual function (vaginal dryness, libido)** **Medication use impacting sexual function** Yearly **PHYSICAL** **Tanner staging** Yearly until sexually mature **SCREENING** **FSH** **LH** **Estradiol** Baseline at age 13, **and** as clinically indicated in patients with delayed puberty, irregular menses or primary or secondary amenorrhea, and/or clinical signs and symptoms of estrogen deficiency.	**Health Links** **Female Health Issues** **Resources** American Society for Reproductive Medicine: www.asrm.org Fertile Hope: www.fertilehope.org **Counseling** Counsel regarding the need for contraception, since there is tremendous individual variability in gonadal toxicity after exposure to radiation. Recovery of fertility may occur years after therapy. Counsel regarding risks and benefits of HRT. **Considerations for Further Testing and Intervention** Bone density evaluation in hypogonadal patients. Refer to endocrinology/gynecology for delayed puberty, persistently abnormal hormone levels or hormonal replacement for hypogonadal patients. Reproductive endocrinology referral for infertility evaluation and consultation regarding assisted reproductive technologies. **SYSTEM = Reproductive (female)** **SCORE = 1**

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

SECTION 84 REFERENCES

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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
85 (Female)	**Flank/Hemiabdomen (right, left)*** **Whole abdomen** **Inverted Y** **Pelvic** **Vaginal** **Bladder** **Iliac** **TLI** *Only if field extended below iliac crest	**Vaginal fibrosis/stenosis**	**Host Factors** Vaginal tumor or pelvic tumor adjacent to vagina **Treatment Factors** Prepubertal female: Radiation dose ≥ 25 Gy Postpubertal female: Radiation dose ≥ 50 Gy **Medical Conditions** Chronic GVHD	**Treatment Factors** Prepubertal female: Radiation dose ≥ 35 Gy Postpubertal female: Radiation dose ≥ 55 Gy	**HISTORY** **Psychosocial assessment** **Dyspareunia** **Vulvar pain** **Post-coital bleeding** **Difficulty with tampon insertion** Yearly	**Considerations for Further Testing and Intervention** Gynecologic consultation for management. Psychological consultation in patients with emotional difficulties. **SYSTEM = Reproductive (female)** **SCORE = 2A**

- 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 MALE REPRODUCTIVE SYSTEM

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
86 (Male)	**Flank/Hemiabdomen (right, left)*** **Whole abdomen** **Inverted Y** **Pelvic** **Prostate** **Bladder** **Iliac** **Inguinal** **Femoral** **Testicular** **TLI** **TBI** *Only if field extended below iliac crest	**Gonadal dysfunction (testicular):** **Germ cell failure** Oligospermia Azoospermia Infertility	**Treatment Factors** Radiation dose to testes: - 1 to 3 Gy: Azoospermia may be reversible - 3 to 6 Gy: Azoospermia possibly reversible (but unlikely) **Medical Conditions** Chronic GVHD	**Treatment Factors** Radiation dose to testes ≥ 6 Gy - Azoospermia likely permanent	**SCREENING** **Semen analysis** As requested by patient and for evaluation of infertility; Periodic evaluation over time is recommended as resumption of spermatogenesis can occur up to 10 years post therapy.	**Health Links** **Male Health Issues** **Resources** American Society for Reproductive Medicine: www.asrm.org Fertile Hope: www.fertilehope.org **Counseling** Counsel regarding the need for contraception, since there is tremendous individual variability in gonadal toxicity after exposure to radiation. Recovery of fertility may occur years after therapy. **Considerations for Further Testing and Intervention** Reproductive endocrinology consultation for infertile couples interested in assisted reproductive technologies. **SYSTEM = Reproductive (male)** **SCORE = 1**

- 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 MALE REPRODUCTIVE SYSTEM (cont)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
87 (Male)	**≥ 20 Gy to:** **Flank/Hemiabdomen (right, left)*** **Whole abdomen** **Inverted Y** **Pelvic** **Prostate** **Bladder** **Iliac** **Inguinal** **Femoral** **Testicular** **TLI** **TBI**** *Only if field extended below iliac crest **TBI included for dose calculation purposes only; this section not applicable to patients who received TBI alone.	**Gonadal dysfunction (testicular):** **Leydig cell dysfunction** Delayed/arrested puberty Hypogonadism	**Treatment Factors** Testicular irradiation combined with head/brain irradiation	**Treatment Factors** Combined with alkylating agents Combined with cyclophosphamide conditioning for HCT	**HISTORY** **Pubertal (onset, tempo)** **Sexual function (erections, nocturnal emissions, libido)** **Medication use impacting sexual function** Yearly **PHYSICAL** **Tanner staging** **Testicular volume by Prader orchdiometry** Yearly until sexually mature **SCREENING** **FSH** **LH** **Testosterone** Baseline at age 14, **and** as clinically indicated in patients with delayed puberty or clinical signs and symptoms of testosterone deficiency.	**Health Links** **Male Health Issues** **Resources** American Society for Reproductive Medicine: www.asrm.org Fertile Hope: www.fertilehope.org **Considerations for Further Testing and Intervention** Bone density evaluation in hypogonadal patients. Refer to endocrinology/urology for delayed puberty, persistently abnormal hormone levels or hormonal replacement for hypogonadal patients. **SYSTEM = Reproductive (male)** **SCORE = 1**

- This section is only applicable to patients who:
  1) Received radiation to any of the specified fields at ≥ 20 Gy
  OR
  2) Received a combination of radiation to any of the specified fields **and** TBI, the sum of which is ≥ 20 Gy
- See dose calculation rules on page 48 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
88	**Spine (cervical, thoracic, lumbar, sacral, whole)** **Cervical (neck)** **Supraclavicular** **Chest (thorax)** **Whole lung** **Mediastinal** **Axilla** **Mini-Mantle** **Mantle** **Extended Mantle** **Hepatic** **Renal** **Upper quadrant (right, left)** **Spleen (partial, entire)** **Paraaortic** **Flank/Hemiabdomen (right, left)** **Whole abdomen** **Inverted Y** **Pelvic** **Vaginal** **Prostate** **Bladder** **Iliac** **Inguinal** **Femoral** **Extremity (upper, lower)** **TLI** **STLI** **TBI**	**Musculoskeletal growth problems** Hypoplasia Fibrosis Reduced or uneven growth Shortened trunk height (trunk radiation) Limb length discrepancy (extremity radiation)	**Host Factors** Younger age at treatment **Treatment Factors** Higher cumulative radiation dose Larger radiation treatment field Higher radiation dose per fraction	**Host Factors** Prepubertal at treatment **Treatment Factors** Orthovoltage radiation (commonly used before 1970) due to delivery of greater dose to skin and bones Epiphysis in treatment field Dose ≥ 20 Gy	**PHYSICAL** **Height** **Weight** Yearly **Sitting height** Yearly for patients who had trunk radiation **Limb lengths** Yearly for patients who had extremity radiation	**Counseling** Counsel regarding increased risk of fractures in weight-bearing irradiated bones. **Considerations for Further Testing and Intervention** Orthopedic consultation for any deficit noted in growing child. Consider plastic surgery consult for reconstruction. **SYSTEM = Musculoskeletal** **SCORE = 1**

- 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 (cont)

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

- 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 MUSCULOSKELETAL SYSTEM (cont)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
90	**Spine (thoracic, whole)** **Chest (thorax)** **Whole lung** **Mediastinal** **Mantle** **Extended Mantle** **Hepatic** **Renal** **Upper quadrant (right, left)** **Spleen (partial, entire)** **Paraaortic** **Flank/Hemiabdomen (right, left)** **Whole abdomen** **Inverted Y** **TLI** **STLI**	**Kyphosis**	**Host Factors** Younger age at irradiation Paraspinal malignancies Neurofibromatosis	**Treatment Factors** Radiation doses ≥ 20 Gy (lower doses for infants) Orthovoltage radiation (commonly used before 1970) due to delivery of greater dose to skin and bones	**PHYSICAL** **Spine exam for kyphosis** Yearly until growth completed, may need more frequent assessment during puberty.	**Health Links** **Scoliosis and Kyphosis** **Considerations for Further Testing and Intervention** Spine films in patients with clinically apparent curve. Orthopedic consultation as indicated based on radiographic exam. **SYSTEM = Musculoskeletal** **SCORE = 1**

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

SECTION 90 REFERENCES

de Jonge T, Slullitel H, Dubousset J, Miladi L, Wicart P, Illes T. Late-onset spinal deformities in children treated by laminectomy and radiation therapy for malignant tumours. *Eur Spine J*. Oct 2005;14(8):765-771.

Marcus RB, DiCaprio MR, Lindskog DM, McGrath BE, Gamble K, Scarborough M. Musculoskeletal, Integument, Breast. In: Schwartz CL, Hobbie WL, Constine LS, Ruccione KS, eds. *Survivors of Childhood and Adolescent Cancer: A Multidisciplinary Approach, Second Edition*. Heidelberg, Germany: Springer-Verlag; 2005:262-269.

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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
91	**≥ 40 Gy to:** **Spine (cervical, thoracic, lumbar, sacral, whole)** **Cervical (neck)** **Supraclavicular** **Chest (thorax)** **Whole lung** **Mediastinal** **Axilla** **Mini-Mantle** **Mantle** **Extended Mantle** **Hepatic** **Renal** **Upper quadrant (right, left)** **Spleen (partial, entire)** **Paraaortic** **Flank/Hemiabdomen (right, left)** **Whole abdomen** **Inverted Y** **Pelvic** **Vaginal** **Prostate** **Bladder** **Iliac** **Inguinal** **Femoral** **Extremity (upper, lower)** **TLI** **STLI** **TBI*** *TBI included for dose calculation purposes only; this section not applicable to patients who received TBI alone.	**Radiation-induced fracture**	**Treatment Factors** History of surgery to cortex of bone	**Treatment Factors** Radiation dose ≥ 50 Gy to bone	**PHYSICAL** **Pain, swelling, deformity of bone** As indicated	**Considerations for Further Testing and Intervention** Radiograph of affected bone as clinically indicated. Orthopedic evaluation as clinically indicated. **SYSTEM = Musculoskeletal** **SCORE = 1**

- This section is only applicable to patients who:
  1) Received radiation to any of the specified fields at ≥ 40 Gy
  OR
  2) Received a combination of radiation to any of the specified fields **plus** relevant spinal radiation **and/or** TBI, the sum of which is ≥ 40 Gy
- See dose calculation rules on page 48 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 91 REFERENCES

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HEMATOPOIETIC CELL TRANSPLANT

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
92	**Hematopoietic Cell Transplant (HCT)** **Info Link:** 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. See also Rizzo et al. (2006) 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).	**Acute myeloid leukemia** **Myelodysplasia**	**Treatment Factors** Radiation therapy Stem cell mobilization with etoposide Alkylating agent chemotherapy Epipodophyllotoxins Anthracyclines Autologous transplant	**Host Factors** Older age **Treatment Factors** Autologous transplant for non-Hodgkin's and Hodgkin's lymphoma	**HISTORY** **Fatigue** **Bleeding** **Easy bruising** Yearly up to 10 years after transplant **PHYSICAL** **Dermatologic exam (pallor, petechiae, purpura)** Yearly up to 10 years after transplant **SCREENING** **CBC/differential** Yearly up to 10 years after transplant	**Health Links** **Reducing the Risk of Second Cancers** **Counseling** Counsel to promptly report fatigue, pallor, petechiae, or bone pain. **Considerations for Further Testing and Intervention** Bone marrow exam as clinically indicated. **SYSTEM = SMN** **SCORE = 1**

SECTION 92 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
93 (Male)	**Hematopoietic Cell Transplant (HCT)**	**Solid tumors**	**Host Factors** Younger age at transplant Fanconi's anemia **Treatment Factors** Radiation therapy **Medical Conditions** Hepatitis C infection Chronic GVHD	**Treatment Factors** TBI	**PHYSICAL** **Evaluation for benign or malignant neoplasms** Yearly	**Health Links** **Reducing the Risk of Second Cancers** **Counseling** Avoid excessive sun exposure and tanning booths. **Considerations for Further Testing and Intervention** Oncology consultation as clinically indicated. **SYSTEM = SMN** **SCORE = 1**
93 (Female)	**Hematopoietic Cell Transplant (HCT)**	**Solid tumors**	**Host Factors** Younger age at transplant Fanconi's anemia **Treatment Factors** Radiation therapy **Medical Conditions** Hepatitis C infection Chronic GVHD Human papilloma virus infection	**Treatment Factors** TBI	**PHYSICAL** **Evaluation for benign or malignant neoplasms** Yearly	**Health Links** **Reducing the Risk of Second Cancers** **Counseling** Avoid excessive sun exposure and tanning booths. **Considerations for Further Testing and Intervention** 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 138) with more aggressive monitoring as clinically indicated. Oncology consultation as clinically indicated. **SYSTEM = SMN** **SCORE = 1**

SECTION 93 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
94	**Hematopoietic Cell Transplant (HCT)**	**Lymphoma**	**Medical Conditions** Chronic GVHD	**Medical Conditions** Chronic hepatitis C with siderosis and steatosis	**PHYSICAL** **Lymphadenopathy** **Splenomegaly** Yearly	**Considerations for Further Testing and Intervention** Oncology consultation as clinically indicated. **SYSTEM = SMN** **SCORE = 1**

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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
95	**Hematopoietic Cell Transplant (HCT)**	**Hepatic toxicity** Chronic hepatitis Cirrhosis Iron overload	**Treatment Factors** History of multiple transfusions Radiation to the liver Antimetabolite therapy **Medical Conditions** Chronic GVHD Viral hepatitis History of VOD **Health Behaviors** Alcohol use	**Medical Conditions** Chronic hepatitis C with siderosis and steatosis	**SCREENING** **ALT** **AST** **Bilirubin** **Ferritin** Baseline at entry into long-term follow-up. Repeat as clinically indicated.	**Health Links** **Liver Health** **Gastrointestinal Health** **Considerations for Further Testing and Intervention** 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. Note: *PCR testing for HCV may be required in immunosuppressed patients who are negative for antibody*. Gastroenterology/hepatology consultation in patients with persistent liver dysfunction or known hepatitis. Hepatitis A and B immunizations in patients lacking immunity. Consider liver biopsy in patients with persistent elevation of ferritin (based on clinical context and magnitude of elevation). Consider phlebotomy or chelation therapy for treatment of iron overload. **SYSTEM = GI/Hepatic** **SCORE = 1**

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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
96	**Hematopoietic Cell Transplant (HCT)**	**Osteonecrosis** (Avascular Necrosis) **Info Link:** Osteonecrosis typically occurs during the acute treatment phase, may progress over time or resolve. Multifocal osteonecrosis is significantly more common (3:1) than unifocal.	**Host Factors** Age ≥ 10 years at time of transplant **Treatment Factors** Corticosteroids (dexamethasone effect is more potent than prednisone) TBI High-dose radiation to any bone Allogeneic HCT > autologous	**Treatment Factors** Prolonged corticosteroid therapy (e.g., for chronic GVHD) **Medical Conditions** Chronic GVHD	**HISTORY** **Joint pain** **Swelling** **Immobility** **Limited range of motion** Yearly **PHYSICAL** **Musculoskeletal exam** Yearly	**Health Links** **Osteonecrosis** **Considerations for Further Testing and Intervention** MRI as clinically indicated in patients with history suggestive of osteonecrosis (should be done soon after symptom onset). Orthopedic consultation in patients with positive imaging and/or symptoms of osteonecrosis. Physical therapy evaluation (for non-pharmacologic pain management, range of motion, strengthening, stretching, functional mobility). **SYSTEM = Musculoskeletal** **SCORE = 1**

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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
97	**Hematopoietic Cell Transplant (HCT)**	**Reduced Bone Mineral Density (BMD)** Defined as Z-score > 2.0 SD below the mean in survivors < 20 years old or T-score >1.0 SD below the mean in survivors ≥ 20 years old **Info Link**: The World Health Organization definition of osteoporosis in adults is based on comparison of a measured bone mineral density (BMD) of young adults at peak bone age and defined as a T-score. A T-score is the number of standard deviations the BMD measurement is above or below the mean. Note: Current definitions of osteopenia (T-scores between 1.0 and 2.5 SD below the mean) and osteoporosis (T-scores > 2.5 SD below the mean) were developed primarily in the context of post-menopausal women. In this population, T-scores have a well-validated correlation with fracture risk that increases with age. The fracture risk associated with T-scores in younger populations, including cancer survivors with treatment-related hypogonadism, has not been established. T-scores are not appropriate to assess skeletal health in pediatric patients who have not achieved peak adult bone mass. Instead, 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. Again, 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.	**Host Factors** Both genders are at risk Younger age at diagnosis Caucasian Lower weight and BMI **Treatment Factors** Corticosteroids Cyclosporine Tacrolimus Cranial radiation Craniospinal radiation HCT/TBI **Medical Conditions** Growth hormone deficiency Hypogonadism/delayed puberty Hyperthyroidism **Health Behaviors** Inadequate intake of calcium and vitamin D Lack of weight bearing exercise Smoking Alcohol use Carbonated beverages	**Host Factors** Older age at time of treatment **Treatment Factors** Prolonged corticosteroid therapy (e.g., for chronic GVHD)	**SCREENING** **Bone density evaluation (DEXA or quantitative CT)** Baseline at entry into long-term follow-up. Repeat as clinically indicated. **Info Link:** The optimal method of measuring bone health in children is controversial. Existing technologies have limitations. Dual energy x-ray absorptiometry (DEXA) provides an estimate of total bone mass at a given site. Quantitative CT provides distinct measures of trabecular and cortical bone dimension and density.	**Health Links** **Bone Health** **Resources** National Osteoporosis Foundation Website: www.nof.org **Considerations for Further Testing and Intervention** Ensure recommended daily allowance of Vitamin D intake (200 IU/day) and 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**

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

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Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
99	**HCT with <u>any history of</u> Chronic GVHD**	**Xerophthalmia (keratoconjunctivitis sicca)** **Info Link:** More common with active cGVHD; effects may persist after cGVHD resolves.	**Treatment Factors** Cranial radiation Eye radiation Radiomimetic chemotherapy (e.g., doxorubicin, dactinomycin)	**Treatment Factors** Radiation dose to eye ≥ 30 Gy Radiation fraction ≥ 2 Gy	**HISTORY** **Dry eyes (burning, itching, foreign body sensation, inflammation)** Yearly **PHYSICAL** **Eye exam** Yearly	**Health Links** **Eye Health** **Considerations for Further Testing and Intervention** Supportive care with artificial tears. Schirmer's testing as clinically indicated. Ongoing ophthalmology follow-up for identified problems. Consider every six month ophthalmology evaluation for patients with corneal damage. **SYSTEM = Ocular** **SCORE = 1**

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

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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
101	**HCT with <u>any history of</u> Chronic GVHD**	**Pulmonary toxicity** Bronchiolitis obliterans Chronic bronchitis Bronchiectasis **Info Link:** More common with active cGVHD; effects may persist after cGVHD resolves.	**Treatment Factors** Chest radiation TBI Pulmonary toxic chemotherapy: - Bleomycin - Busulfan - Carmustine (BCNU) - Lomustine (CCNU)	**Medical Conditions** Prolonged immunosuppression related to cGVHD and its treatment	**HISTORY** **Cough** **SOB** **DOE** **Wheezing** Yearly **PHYSICAL** **Pulmonary exam** Yearly **SCREENING** **Chest x-ray** **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.	**Health Links** **Pulmonary Health** **Resources** Extensive information regarding smoking cessation is available for patients on the NCI's website: <u>www.smokefree.gov</u> **Counseling** Counsel regarding tobacco avoidance/smoking cessation. Patients who desire to SCUBA dive should be advised to obtain medical clearance from a pulmonologist. **Considerations for Further Testing and Intervention** In patients with abnormal PFTs and/or CXR, consider repeat evaluation prior to general anesthesia. Pulmonary consultation for patients with symptomatic pulmonary dysfunction. Influenza and Pneumococcal vaccinations. **SYSTEM = Pulmonary** **SCORE = 1**

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Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
102	**HCT with <u>any history of</u> Chronic GVHD**	**Immunologic complications** Secretory IgA deficiency Hypogammaglobulinemia Decreased B cells T cell dysfunction Chronic infections (e.g., conjunctivitis, sinusitis, and bronchitis associated with chronic GVHD) **Info Link:** Related to cGVHD; effects may persist or resolve over time.		**Host Factors** Active cGVHD **Medical Conditions** Prolonged immunosuppression related to cGVHD and its treatment	**HISTORY** **Chronic conjunctivitis** **Chronic sinusitis** **Chronic bronchitis** **Recurrent or unusual infections** **Sepsis** Yearly **PHYSICAL** **Eye exam** **Nasal exam** **Pulmonary exam** Yearly	**Considerations for Further Testing and Intervention** 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. **SYSTEM = Immune** **SCORE = 1**

SECTION 102 REFERENCES

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Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
103	**HCT with currently active Chronic GVHD**	**Functional asplenia** At risk for life-threatening infection with encapsulated organisms (e.g., Haemophilus influenzae, streptococcus pneumoniae, meningococcus) **Info Link:** This section applies only to patients who have active cGVHD.	**Treatment Factors** Splenic radiation Ongoing immunosuppression	**Host Factors** Hypogammaglobulinemia	**PHYSICAL** **Physical exam at time of febrile illness to evaluate degree of illness and potential source of infection** When febrile T ≥ 101ºF as indicated for patients with active chronic GVHD **SCREENING** **Blood culture** When febrile T ≥ 101ºF as indicated for patients with active chronic GVHD	**Health Links** **Splenic precautions** **Considerations for Further Testing and Intervention** Consider antibiotic prophylaxis for encapsulated organisms and bacteremia/endocarditis prophylaxis for duration of immunosuppressive therapy for chronic GVHD (see: American Academy of Pediatric Dentistry, Guideline on Antibiotic Prophylaxis for Dental Patients at Risk for Infection). In patients with T ≥ 101°F (38.3° C) or other signs of serious illness, administer a long-acting, broad-spectrum parenteral antibiotic (e.g., ceftriaxone), and continue close medical monitoring while awaiting blood culture results. Hospitalization and broadening of antimicrobial coverage (e.g., addition of vancomycin) may be necessary under certain circumstances, such as the presence of marked leukocytosis, neutropenia, or significant change from baseline CBC; toxic clinical appearance; fever ≥ 104°F; meningitis, pneumonia, or other serious focus of infection; signs of septic shock; or previous history of serious infection. Immunize with Pneumococcal, Meningococcal, and HIB vaccines. Pneumovax booster in patients ≥10 years old at ≥ 5 years after previous dose (AAP-CIDP Recommendations, 2003). **SYSTEM = Immune** **SCORE = 1**

SECTION 103 REFERENCES

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Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
104	**HCT with <u>any history of</u> Chronic GVHD**	**Esophageal stricture** **Info Link:** Related to cGVHD; generally not reversible over time.	**Treatment Factors** Radiation involving the esophagus Radiomimetic chemotherapy (e.g., doxorubicin, dactinomycin) **Medical Conditions** Gastroesophageal reflux History of Candida esophagitis	**Treatment Factors** Radiation dose ≥ 40 Gy **Medical Conditions** Gut GVHD	**HISTORY** **Dysphagia** **Heartburn** Yearly	**Health Links** **Gastrointestinal Health** **Considerations for Further Testing and Intervention** Surgery and/or gastroenterology consultation for symptomatic patients. **SYSTEM = GI/Hepatic** **SCORE = 1**

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Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
105 (Female)	**HCT with <u>any history of</u> Chronic GVHD**	**Vaginal fibrosis/stenosis** **Info Link:** Related to cGVHD; generally not reversible over time.	**Treatment Factors** Pelvic radiation		**HISTORY** **Psychosocial assessment** **Dyspareunia** **Vulvar pain** **Post-coital bleeding** **Difficulty with tampon insertion** Yearly	**Considerations for Further Testing and Intervention** Gynecologic consultation for management. Psychological consultation in patients with emotional difficulties. **SYSTEM = Reproductive (female)** **SCORE = 1**

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Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
106	**HCT with <u>any history of</u> Chronic GVHD**	**Joint contractures** **Info Link:** Related to cGVHD; generally not reversible over time.			**PHYSICAL** **Musculoskeletal exam** Yearly	**Considerations for Further Testing and Intervention** Consultation with physical therapy, rehabilitation medicine/physiatrist. **SYSTEM = Musculoskeletal** **SCORE = 1**

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AMPUTATION

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
107	**Amputation**	**Amputation-related complications** 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	**Host Factors** Skeletally immature/ growing children **Treatment Factors** Site of amputation: Hemipelvectomy > Trans-femur amputation > Trans-tibia amputation **Medical Conditions** Obesity Diabetes Poor residual limb healing		**HISTORY** **Phantom pain** **Functional and activity limitations** Yearly **PHYSICAL** **Residual limb integrity** Yearly **SCREENING** **Prosthetic evaluation** Every 6 months until skeletally mature, then yearly.	**Health Links** **Amputation** **Counseling** 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. **Considerations for Further Testing and Intervention** 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. **SYSTEM = Musculoskeletal** **SCORE = 1**

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Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
108	**Central venous catheter**	**Thrombosis** **Vascular insufficiency** **Infection of retained cuff or line tract**			**HISTORY** **Tenderness or swelling at previous catheter site** Yearly and as clinically indicated. **PHYSICAL** **Venous stasis** **Swelling** **Tenderness at previous catheter site** Yearly and as clinically indicated.	**SYSTEM = Cardiovascular** **SCORE = 1**

SECTION 108 REFERENCES

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Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
109	**Cystectomy** **Info Link:** All potential late effects for pelvic surgery apply to Cystectomy (see also sections 126-129).	**Cystectomy-related complications** Chronic urinary tract infection Renal dysfunction Vesicoureteral reflux Hydronephrosis Reservoir calculi Spontaneous neobladder perforation Vitamin B12/folate/carotene deficiency (patients with ileal entercystoplasty only) **Info Link:** Reservoir calculi are stones in the neobladder (a reservoir for urine usually constructed of ileum/colon).			**SCREENING** **Urology evaluation** Yearly **Vitamin B12 level** Yearly starting 5 years after cystectomy (patients with ileal enterocystoplasty only)	**Health Links** **Cystectomy** **Kidney Health** **SYSTEM = Urinary** **SCORE =** **Chronic urinary tract infection: 1** **Renal dysfunction: 1** **Vesicoureteral reflux: 1** **Hydronephrosis: 1** **Spontaneous neobladder perforation: 1** **Reservoir calculi: 2A** **Vitamin B12/folate/carotene deficiency: 2B**

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SURGERY

ENUCLEATION

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

SECTION 110 REFERENCES

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HYSTERECTOMY

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
111 (Female)	**Hysterectomy** **Info Link:** For patients who also underwent oophorectomy, see also: Section 123 (unilateral oophorectomy) or Section 124 (bilateral oophorectomy).	**Pelvic floor dysfunction** **Urinary incontinence** **Sexual dysfunction**			**HISTORY** **Psychosocial assessment** **Abdominal pain** **Urinary leakage** **Dyspareunia** Yearly	**Health Links** **Female Health Issues** **Counseling** Counsel patients with ovaries regarding potential for biologic parenthood using gestational surrogate. **Considerations for Further Testing and Intervention** Reproductive endocrinology consultation for patients wishing to pursue pregnancy via gestational surrogate. **SYSTEM = Reproductive (female)** **SCORE = 2A**

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LAPAROTOMY

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

SECTION 112 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
113	**Limb sparing procedure**	**Complications related to limb sparing procedure** Functional and activity limitations Contractures Chronic infection Chronic pain Limb length discrepancy Musculoskeletal pain Increased energy expenditure Fibrosis Prosthetic malfunction (loosening, non-union, fracture) requiring revision, replacement or amputation Prosthetic revision required due to growth Impaired quality of life Complications with pregnancy/delivery (in female patients with internal hemipelvectomy)	**Host Factors** Younger age at surgery Rapid growth spurt Skeletally immature **Treatment Factors** Tibial endoprosthesis Use of biologic material (allograft or autograft) for reconstruction **Medical Conditions** Endoprosthetic infection Obesity **Health Behaviors** High level of physical activity (associated with higher risk loosening) Low level of physical activity (associated with higher risk of contractures or functional limitations)	**Treatment Factors** Radiation to extremity **Medical Conditions** Poor healing Infection of reconstruction	**HISTORY** **Functional and activity limitations** Yearly and as clinically indicated **PHYSICAL** **Residual limb integrity** Yearly and as clinically indicated **SCREENING** **Radiograph of affected limb** Yearly **Evaluation by orthopedic surgeon** Every 6 months until skeletally mature, then yearly.	**Health Links** **Limb Sparing Procedures** **Counseling** Counsel regarding need for antibiotic prophylaxis prior to dental and invasive procedures if applicable. **Considerations for Further Testing and Intervention** Antibiotics may be indicated prior to dental or invasive procedures depending on length of time since surgery, current immune status, history of previous infections, and other factors (see *J Am Dent Assoc.*, 2003,134: 895-899). 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. **SYSTEM = Musculoskeletal** **SCORE = 1**

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SURGERY

NEPHRECTOMY

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
114 (Male)	**Nephrectomy**	**Renal toxicity** Proteinuria Hyperfiltration Renal insufficiency **Hydrocele** **Info Link:** Surgery-induced renal atrophy (vanishing kidney) is a rare complication reported in survivors who have undergone retroperitoneal tumor resections. Once this diagnosis is established, annual screening should include evaluations recommended for children treated with nephrectomy.	**Host Factors** Denys-Drash syndrome WAGR syndrome Hypospadias Cryptorchidism Bilateral Wilms tumor **Treatment Factors** Combined with other nephrotoxic therapy, such as: - Cisplatin - Carboplatin - Ifosfamide - Aminoglycosides - Amphotericin - Immunosuppressants - Methotrexate - Radiation impacting the kidneys		**PHYSICAL** **Blood pressure** **Testicular exam to evaluate for hydrocele** Yearly **SCREENING** **BUN** **Creatinine** **Na, K, Cl, CO_2** **Ca, Mg, PO_4** Baseline at entry into long-term follow-up. Repeat as clinically indicated. **Urinalysis** Yearly	**Health Links** **Single Kidney Health** See also: **Kidney Health** **Counseling** Discuss contact sports, bicycle safety (e.g., avoiding handlebar injuries), and proper use of seatbelts (i.e., wearing lapbelts around hips, not waist). Counsel to use NSAIDS with caution. **Considerations for Further Testing and Intervention** Nephrology consultation for patients with hypertension, proteinuria, or progressive renal insufficiency. **SYSTEM = Urinary** **SCORE = 1**
114 (Female)	**Nephrectomy**	**Renal toxicity** Proteinuria Hyperfiltration Renal insufficiency **Info Link:** Surgery-induced renal atrophy (vanishing kidney) is a rare complication reported in survivors who have undergone retroperitoneal tumor resections. Once this diagnosis is established, annual screening should include evaluations recommended for children treated with nephrectomy.	**Host Factors** Denys-Drash syndrome WAGR syndrome Bilateral Wilms tumor **Treatment Factors** Combined with other nephrotoxic therapy, such as: - Cisplatin - Carboplatin - Ifosfamide - Aminoglycosides - Amphotericin - Immunosuppressants - Methotrexate - Radiation impacting the kidneys		**PHYSICAL** **Blood pressure** Yearly **SCREENING** **BUN** **Creatinine** **Na, K, Cl, CO_2** **Ca, Mg, PO_4** Baseline at entry into long-term follow-up. Repeat as clinically indicated. **Urinalysis** Yearly	**Health Links** **Single Kidney Health** See also: **Kidney Health** **Counseling** Discuss contact sports, bicycle safety (e.g., avoiding handlebar injuries), and proper use of seatbelts (i.e., wearing lapbelts around hips, not waist). Counsel to use NSAIDS with caution. **Considerations for Further Testing and Intervention** Nephrology consultation for patients with hypertension, proteinuria, or progressive renal insufficiency. **SYSTEM = Urinary** **SCORE = 1**

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Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
115	**Neurosurgery - Brain**	**Neurocognitive deficits** Functional deficits in: - Executive function (planning and organization) - Sustained attention - Memory (particularly visual, sequencing, temporal memory) - Processing speed - Visual-motor integration Learning deficits in math and reading (particularly reading comprehension) Diminished IQ Behavioral change **Info Link:** Neurocognitive deficits vary with extent of surgery and postoperative complications. In general, mild delays occur in most areas of neuropsychological function compared to healthy children. Extent of deficit depends on age at treatment, intensity of treatment, and time since treatment. New deficits may emerge over time. Neurosensory deficits (i.e., vision, hearing) due to tumor or its therapy may complicate neurocognitive outcomes.	**Host Factors** Younger age at treatment Primary CNS tumor **Treatment Factors** Extent and location of resection Longer elapsed time since therapy In combination with: - TBI - Cranial radiation - Methotrexate (IT, IO, high-dose IV) - Cytarabine (high-dose IV)	**Host Factors** Age < 3 years at time of treatment Supratentorial tumor Predisposing family history of learning or attention problems **Treatment Factors** Radiation dose ≥ 24 Gy to whole brain Radiation dose ≥ 40 Gy to local fields **Medical Conditions** Posterior fossa syndrome CNS infection	**HISTORY** **Educational and/or vocational progress** Yearly **SCREENING** **Referral for formal neuropsychological evaluation** Baseline at entry into long-term follow-up. Periodically as clinically indicated for patients with evidence of impaired educational or vocational progress.	**Health Links** **Educational Issues** **Considerations for Further Testing and Intervention** Formal neuropsychological evaluation to include tests of processing speed, computer-based attention, visual motor integration, memory, comprehension of verbal instructions, verbal fluency, executive function and planning. Refer patients with neurocognitive deficits to school liaison in community or cancer center (psychologist, social worker, school counselor) to facilitate acquisition of educational resources and/or social skills training. Consider use of psychotropic medication (e.g., stimulants) or evidence-based rehabilitation training. Caution - lower starting dose and assessment of increased sensitivity when initiating therapy is recommended. Refer to community services for vocational rehabilitation or for services for developmentally disabled. **SYSTEM = CNS** **SCORE = 1**

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Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
116	**Neurosurgery - Brain**	**Motor and/or sensory deficits** Paralysis Movement disorders Ataxia Eye problems (ocular nerve palsy, gaze paresis, nystagmus, papilledema, optic atrophy)	**Host Factors** Primary CNS tumor **Medical Conditions** Hydrocephalus	**Host Factors** Optic pathway tumor Hypothalamic tumor Suprasellar tumor (eye problems)	**SCREENING** **Evaluation by neurologist** Yearly, until 2 to 3 years after surgery or stable; continue to monitor if symptoms persist. **Evaluation by physiatrist/rehabilitation medicine specialist** Yearly, or more frequently as clinically indicated in patients with motor dysfunction.	**Considerations for Further Testing and Intervention** 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. **SYSTEM = CNS** **SCORE = 1**

SECTION 116 REFERENCES

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Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
117	**Neurosurgery - Brain**	**Seizures**	**Host Factors** Primary CNS tumor **Treatment Factors** Methotrexate (IV, IT, IO)		**SCREENING** **Evaluation by neurologist** Every 6 months for patients with seizure disorder.	**SYSTEM = CNS** **SCORE = 1**

SECTION 117 REFERENCES

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Mulhern RK, Palmer SL. Neurocognitive late effects in pediatric cancer. *Curr Probl Cancer*. Jul-Aug 2003;27(4):177-197.

Sonderkaer S, Schmiegelow M, Carstensen H, Nielsen LB, Muller J, Schmiegelow K. Long-term neurological outcome of childhood brain tumors treated by surgery only. *J Clin Oncol*. Apr 1 2003;21(7):1347-1351.

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
118	**Neurosurgery - Brain**	**Hydrocephalus** **Shunt malfunction**	**Host Factors** Primary CNS tumor		**SCREENING** **Abdominal x-ray** After pubertal growth spurt for patients with shunts to assure distal shunt tubing in peritoneum. **Evaluation by neurosurgeon** Yearly for patients with shunts.	**Counseling** Education patient/family regarding potential symptoms of shunt malfunction. **Considerations for Further Testing and Intervention** 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). **SYSTEM = CNS** **SCORE = 1**

SECTION 118 REFERENCES

American Academy of Pediatric Dentistry, Guideline on Antibiotic Prophylaxis for Dental Patients at Risk for Infection. *American Academy of Pediatric Dentistry Reference Manual.* Vol 29, No. 7. Chicago: American Academy of Pediatric Dentistry; 2007:pp. 202-204, available: http://www.aapd.org/media/policies.asp (accessed 2-24-08).

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Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
119	**Neurosurgery - Spinal cord**	**Neurogenic bladder** **Urinary incontinence**	**Host Factors** Tumor adjacent to or compressing spinal cord or cauda equina **Treatment Factors** Radiation dose ≥ 45 Gy to lumbar and/or sacral spine and/or cauda equina	**Host Factors** Injury above the level of the sacrum **Treatment Factors** Radiation dose ≥ 50 Gy to lumbar and/or sacral spine and/or cauda equina	**HISTORY** **Hematuria** **Urinary urgency/frequency** **Urinary incontinence/retention** **Dysuria** **Nocturia** **Abnormal urinary stream** Yearly	**Health Links** **Neurogenic Bladder** **Counseling** Counsel regarding adequate fluid intake, regular voiding, seeking medical attention for symptoms of voiding dysfunction or urinary tract infection, and compliance with recommended bladder catheterization regimen. **Considerations for Further Testing and Intervention** Urologic consultation for patients with dysfunctional voiding or recurrent urinary tract infections. **SYSTEM = CNS** **SCORE = 1**

SECTION 119 REFERENCES

Fowler C. *Neurology of Bowel, Bladder, and Sexual Dysfunction* Vol 23: Elsevier; 1999.

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Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
120	**Neurosurgery - Spinal cord**	**Neurogenic bowel** **Fecal incontinence**	**Host Factors** Tumor adjacent to or compressing spinal cord or cauda equina **Treatment Factors** Radiation dose ≥ 50 Gy to bladder, pelvis, or spine	**Host Factors** Injury above the level of the sacrum	**HISTORY** **Chronic constipation** **Fecal soiling** Yearly **PHYSICAL** **Rectal exam** As clinically indicated	**Counseling** Counsel regarding benefits of adherence to bowel regimen, including adequate hydration, fiber, laxatives/enemas as clinically indicated. **Considerations for Further Testing and Intervention** GI consultation to establish bowel regimen for patients with chronic impaction or fecal soiling. **SYSTEM = CNS** **SCORE = 1**

SECTION 120 REFERENCES

Fowler C. *Neurology of Bowel, Bladder, and Sexual Dysfunction* Vol 23: Elsevier; 1999.

Hoover M, Bowman LC, Crawford SE, et al. Long-term outcome of patients with intraspinal neuroblastoma. *Med Pediatr Oncol.* May 1999;32(5):353-359.

Moore SW, Kaschula ROC, Albertyn R, Rode H, Millar AJW, Karabus C. The outcome of solid tumors occurrring during the neonatal period. *Pediatr Surg Int.* 1996;10(5-6):366-370.

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
121 (Male)	**Neurosurgery - Spinal cord**	**Sexual dysfunction (Male)** Erectile dysfunction	**Host Factors** Tumor adjacent to or compressing spinal cord or cauda equina **Treatment Factors** Radiation to bladder, pelvis, or spine **Medical Conditions** Hypogonadism	**Host Factors** Injury above the level of the sacrum **Treatment Factors** Radiation dose ≥ 55 Gy to penile bulb in adult Radiation dose ≥ 45 Gy in prepubertal child	**HISTORY** **Sexual function (erections, nocturnal emissions, libido)** **Medication use impacting sexual function** Yearly	**Health Links** **Male Health Issues** **Resources** www.urologychannel.com **Considerations for Further Testing and Intervention** Urologic consultation in patients with positive history. **SYSTEM = CNS** **SCORE = 2A**
121 (Female)	**Neurosurgery - Spinal cord**	**Sexual dysfunction (Female)**	**Host Factors** Tumor adjacent to or compressing spinal cord or cauda equina **Treatment Factors** Radiation to bladder, pelvis, or spine **Medical Conditions** Hypogonadism Vaginal fibrosis/stenosis Chronic GVHD	**Host Factors** Injury above the level of the sacrum	**HISTORY** **Dyspareunia** **Altered or diminished sensation, loss of sensation** **Medication use impacting sexual function** Yearly	**SYSTEM = CNS** **SCORE = 2A**

SECTION 121 REFERENCES

Fowler C. *Neurology of Bowel, Bladder, and Sexual Dysfunction* Vol 23: Elsevier; 1999.

Hoover M, Bowman LC, Crawford SE, et al. Long-term outcome of patients with intraspinal neuroblastoma. *Med Pediatr Oncol.* May 1999;32(5):353-359.

Moore SW, Kaschula ROC, Albertyn R, Rode H, Millar AJW, Karabus C. The outcome of solid tumors occurrring during the neonatal period. *Pediatr Surg Int.* 1996;10(5-6):366-370.

SURGERY

OOPHOROPEXY

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
122 (Female)	**Oophoropexy** **Info Link:** If shielding from radiation was incomplete: See also Section 84	**Oophoropexy-related complications** Inability to conceive despite normal ovarian function Dyspareunia Symptomatic ovarian cysts Bowel obstruction Pelvic adhesions	**Treatment Factors** Ovarian radiation Tubo-ovarian dislocation, especially with lateral ovarian transposition		**HISTORY** **Abdominal pain** **Pelvic pain** **Dyspareunia** **Inability to conceive despite normal ovarian function** Yearly	**Considerations for Further Testing and Intervention** Gynecologic consultation for patients with positive history and/or physical findings. **SYSTEM = Reproductive (female)** **SCORE = 2A**

SECTION 122 REFERENCES

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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
123 (Female)	**Oophorectomy (unilateral)**	**Premature menopause** **Info Link:** Evidence for premature menopause following unilateral oophorectomy is limited and has been extrapolated from the adult literature.	**Health Behaviors** Smoking	**Treatment Factors** Combined with: - Pelvic radiation - Alkylating agents - TBI	**HISTORY** **Pubertal (onset, tempo)** **Menstrual/pregnancy history** **Sexual function (vaginal dryness, libido)** **Medication use impacting sexual function** Yearly **PHYSICAL** **Tanner staging** Yearly until sexually mature **SCREENING** **FSH** **LH** **Estradiol** Baseline at age 13 **and** as clinically indicated in patients with delayed puberty, irregular menses, primary or secondary amenorrhea, and/or clinical signs and symptoms of estrogen deficiency.	**Health Links** **Female Health Issues** **Resources** American Society for Reproductive Medicine (www.asrm.org) Fertile Hope (www.fertilehope.org) **Counseling** Counsel currently menstruating women to be cautious about delaying childbearing. Counsel regarding need for contraception. **Considerations for Further Testing and Intervention** Refer to reproductive endocrinology for counseling regarding oocyte cryopreservation in patients wishing to preserve options for future fertility. **SYSTEM = Reproductive (female)** **SCORE = 2A**

SECTION 123 REFERENCES

Hale GA, Marina NM, Jones-Wallace D, et al. Late effects of treatment for germ cell tumors during childhood and adolescence. *J Pediatr Hematol Oncol*. Mar-Apr 1999;21(2):115-122.

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Tangir J, Zelterman D, Ma W, Schwartz PE. Reproductive function after conservative surgery and chemotherapy for malignant germ cell tumors of the ovary. *Obstet Gynecol*. Feb 2003;101(2):251-257.

SURGERY

OOPHORECTOMY (BILATERAL)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
124 (Female)	**Oophorectomy (bilateral)**	**Hypogonadism** **Infertility**			**SCREENING** **Gynecologic or endocrinologic consultation for initiation of hormonal replacement therapy** At age 11	**Health Links** **Female Health Issues** **Resources** American Society for Reproductive Medicine (www.asrm.org) Fertile Hope (www.fertilehope.org) **Counseling** 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). **Considerations for Further Testing and Intervention** Bone density evaluation in hypogonadal patients. Reproductive endocrinology referral regarding assisted reproductive technologies. **SYSTEM = Reproductive (female)** **SCORE = 1**

SECTION 124 REFERENCES

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SURGERY

ORCHIECTOMY

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
125 (Male)	**Orchiectomy**	**Hypogonadism** **Infertility**	**Treatment Factors** Unilateral orchiectomy combined with pelvic or testicular radiation and/or alkylating agents	**Treatment Factors** Bilateral orchiectomy	**HISTORY** **Pubertal (onset, tempo)** **Sexual function (erections, nocturnal emissions, libido)** **Medication use impacting sexual function** Yearly **PHYSICAL** **Tanner staging** **Testicular volume by Prader orchdiometry** Yearly until sexually mature **SCREENING** **Semen analysis** As requested by patient and for evaluation of infertility.	**Health Links** **Male Health Issues** **Counseling** For patients with single testis - counsel to wear athletic supporter with protective cup during athletic activities. **Considerations for Further Testing and Intervention** Consider surgical placement of testicular prosthesis. **For patients with unilateral orchiectomy:** Obtain FSH, LH and testosterone as clinically indicated for signs and symptoms of testosterone deficiency (e.g. those with delayed puberty, persistently abnormal hormone levels). **For patients with bilateral orchiectomy:** Refer boys with post-surgical hypogonadism after bilateral orchiectomy to endocrinology at age 11 for initiation of hormonal replacement therapy to initiate puberty. **SYSTEM = Reproductive (male)** **SCORE = 1**

SECTION 125 REFERENCES

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Lee PA, Coughlin MT. The single testis: paternity after presentation as unilateral cryptorchidism. *J Urol.* Oct 2002;168(4 Pt 2):1680-1682; discussion 1682-1683.

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
126	**Pelvic surgery** **Cystectomy** **Info Link:** For patients with cystectomy: See also Section 109	**Urinary incontinence** **Urinary tract obstruction** **Info Link:** Urinary tract obstruction related to retroperitoneal fibrosis	**Host Factors** Tumor adjacent to or compressing spinal cord or cauda equina **Treatment Factors** 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		**HISTORY** **Hematuria** **Urinary urgency/frequency** **Urinary incontinence/retention** **Dysuria** **Nocturia** **Abnormal urinary stream** Yearly	**Counseling** Counsel regarding adequate fluid intake, regular voiding, seeking medical attention for symptoms of voiding dysfunction or urinary tract infection, compliance with recommended bladder catheterization regimen. **Considerations for Further Testing and Intervention** Urologic consultation for patients with dysfunctional voiding or recurrent urinary tract infections. **SYSTEM = Urinary** **SCORE = 1**

SECTION 126 REFERENCES

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

SECTION 127 REFERENCES

Hale GA, Marina NM, Jones-Wallace D, et al. Late effects of treatment for germ cell tumors during childhood and adolescence. *J Pediatr Hematol Oncol*. Mar-Apr 1999;21(2):115-122.
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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
128 (Male)	**Pelvic surgery** **Cystectomy**	**Sexual dysfunction (Male)** Retrograde ejaculation Anejaculation Erectile dysfunction	**Treatment Factors** Retroperitoneal node dissection Retroperitoneal tumor resection Cystectomy Radical prostatectomy Tumor adjacent to spine Radiation to bladder, pelvis, or spine **Medical Conditions** Hypogonadism	**Host Factors** Extensive presacral tumor resection or dissection Radiation dose ≥ 55 Gy to penile bulb in adult and ≥ 45 Gy in prepubertal child	**HISTORY** **Sexual function (erections, nocturnal emissions, libido)** **Medication use impacting sexual function** **Quality of ejaculate (frothy white urine with first void after intercourse suggests retrograde ejaculation)** Yearly	**Health Links** **Male Health Issues** **Resources** www.urologychannel.com **Considerations for Further Testing and Intervention** Urologic consultation in patients with positive history and/or physical exam findings. **SYSTEM = Reproductive (male)** **SCORE = 2A**
128 (Female)	**Pelvic surgery** **Cystectomy**	**Sexual dysfunction (Female)**	**Host Factors** Chronic GVHD Hypogonadism Tumor adjacent to spine **Medical Conditions** Radiation to bladder, pelvis, or spine		**HISTORY** **Dyspareunia** **Altered or diminished sensation, loss of sensation** **Medication use impacting sexual function** Yearly	**SYSTEM = Reproductive (female)** **SCORE = 2A**

SECTION 128 REFERENCES

(Male)

Brydoy M, Fossa SD, Klepp O, et al. Paternity following treatment for testicular cancer. *J Natl Cancer Inst*. Nov 2 2005;97(21):1580-1588.

Fossa SD. Long-term sequelae after cancer therapy--survivorship after treatment for testicular cancer. *Acta Oncol*. 2004;43(2):134-141.

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Hartmann JT, Albrecht C, Schmoll HJ, Kuczyk MA, Kollmannsberger C, Bokemeyer C. Long-term effects on sexual function and fertility after treatment of testicular cancer. *Br J Cancer*. May 1999;80(5-6):801-807.

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(Female)

Burton KA, Wallace WH, Critchley HO. Female reproductive potential post-treatment for childhood cancer. *Hosp Med*. Sep 2002;63(9):522-527.

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Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
129 (Male)	**Pelvic surgery** **Cystectomy**	**Hydrocele**	**Treatment Factors** Retroperitoneal node dissection		**PHYSICAL** **Testicular exam to evaluate for hydrocele** Yearly	**Considerations for Further Testing and Intervention** Urologic consultation for patients with hydrocele. **SYSTEM = Urinary** **SCORE = 1**

SECTION 129 REFERENCES

Ginsberg JP, Hobbie WL, Ogle SK, Canning DA, Meadows AT. Prevalence of and risk factors for hydrocele in survivors of Wilms tumor. *Pediatr Blood Cancer*. Apr 2004;42(4):361-363.

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
130	**Pulmonary lobectomy** **Pulmonary metastasectomy** **Pulmonary wedge resection**	**Pulmonary dysfunction**	**Treatment Factors** Combined with pulmonary toxic therapy - Bleomycin - Busulfan - Carmustine (BCNU) - Lomustine (CCNU) **Medical Conditions** Atopic history **Health Behaviors** Smoking	**Treatment Factors** Combined with: - Chest radiation - TBI	**HISTORY** **Cough** **SOB** **DOE** **Wheezing** Yearly **PHYSICAL** **Pulmonary exam** Yearly **SCREENING** **Chest x-ray** **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.	**Health Links** **Pulmonary Health** **Resources** Extensive information regarding smoking cessation is available for patients on the NCI's website: www.smokefree.gov **Counseling** Counsel regarding tobacco avoidance/smoking cessation. Patients who desire to SCUBA dive should be advised to obtain medical clearance from a pulmonologist. **Considerations for Further Testing and Intervention** In patients with abnormal PFTs and/or CXR, consider repeat evaluation prior to general anesthesia. Pulmonary consultation for patients with symptomatic pulmonary dysfunction; Influenza and pneumococcal vaccinations **SYSTEM = Pulmonary** **SCORE = 2A**

SECTION 130 REFERENCES

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Bolliger CT, Jordan P, Soler M, et al. Pulmonary function and exercise capacity after lung resection. *Eur Respir J*. Mar 1996;9(3):415-421.

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SURGERY

SPLENECTOMY

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
131	**Splenectomy**	**Asplenia** At risk for life-threatening infection with encapsulated organisms (e.g., Haemophilus influenzae, streptococcus pneumoniae, meningococcus)			**PHYSICAL** **Physical exam at time of febrile illness to evaluate degree of illness and potential source of infection** When febrile T ≥ 101ºF **SCREENING** **Blood culture** When febrile T ≥ 101ºF	**Health Links** **Splenic Precautions** **Counseling** Medical alert bracelet/card noting asplenia. Counsel to avoid malaria and tick bites if living in or visiting endemic areas. **Considerations for Further Testing and Intervention** In patients with T ≥101°F (38.3° C) or other signs of serious illness, administer a long-acting, broad-spectrum parenteral antibiotic (e.g., ceftriaxone), and continue close medical monitoring while awaiting blood culture results. Hospitalization and broadening of antimicrobial coverage (e.g., addition of vancomycin) may be necessary under certain circumstances, such as the presence of marked leukocytosis, neutropenia, or significant change from baseline CBC; toxic clinical appearance; fever ≥ 104°F; meningitis, pneumonia, or other serious focus of infection; signs of septic shock; or previous history of serious infection. Immunize with Pneumococcal, Meningococcal, and HIB vaccines. Pneumovax booster in patients ≥10 years old at ≥ 5 years after previous dose (AAP-CIDP Recommendations, 2003). Discuss with dental provider potential need for antibiotic prophylaxis based on planned procedure. **Info Link:** Prophylactic antibiotic therapy may be indicated in a subset of patients. Consider prophylactic PCN for at least 2-3 years post-splenectomy and until at least 5 years of age for young children; some make a strong argument for 5 years post-splenectomy in adults and until age 18 in children. UK investigators recommend lifelong use. Monitor antibody titers to PPV23 annually for first 2-3 years after initial vaccine; re-immunize if sub-protective levels, as opposed to just one booster at 5 years. Check antibody titers to PPV23 after booster at least once at 5 year mark to verify protective titer. **SYSTEM = Immune** **SCORE = 1**

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SURGERY

THYROIDECTOMY

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
132	**Thyroidectomy** **Info Link:** Total thyroidectomy is uncommon, but if done is associated with the risk of hypoparathyroidism. This complication generally occurs in the early postoperative period and may persist. Patients with a history of total thyroidectomy should be monitored for signs and symptoms of hypoparathyroidism (e.g., parasthesias, muscle cramping, altered mental status, hyperreflexia, tetany, hypocalcemia, and hyperphosphatemia).	**Hypothyroidism**			**HISTORY** **Fatigue** **Weight gain** **Cold intolerance** **Constipation** **Dry skin** **Brittle hair** **Depressed mood** Yearly; Consider more frequent screening during periods of rapid growth. **PHYSICAL** **Height** **Weight** **Hair and skin** **Thyroid exam** Yearly; Consider more frequent screening during periods of rapid growth. **SCREENING** **TSH** **Free T4** Yearly; Consider more frequent screening during periods of rapid growth.	**Health Links** **Thyroid Problems** **Counseling** Counsel at-risk females of childbearing potential to have their thyroid levels checked prior to attempting pregnancy and periodically throughout pregnancy. **Considerations for Further Testing and Intervention** Endocrine consultation for medical management. **SYSTEM = Endocrine/Metabolic** **SCORE = 1**

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Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
133	**Radioiodine therapy (I-131 thyroid ablation)**	**Lacrimal duct atrophy**			**HISTORY** **Excessive tearing** Yearly	**Considerations for Further Testing and Intervention** Ophthalmology consultation as clinically indicated. **SYSTEM = Ocular** **SCORE = 2A**

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Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
134	**Radioiodine therapy (I-131 thyroid ablation)**	**Hypothyroidism**			**HISTORY** **Fatigue** **Weight gain** **Cold intolerance** **Constipation** **Dry skin** **Brittle hair** **Depressed mood** Yearly; Consider more frequent screening during periods of rapid growth. **PHYSICAL** **Height** **Weight** **Hair and skin** **Thyroid exam** Yearly; Consider more frequent screening during periods of rapid growth. **SCREENING** **TSH** **Free T4** Yearly; Consider more frequent screening during periods of rapid growth.	**Health Links** **Thyroid Problems** **Counseling** Counsel at-risk females of childbearing potential to have their thyroid levels checked prior to attempting pregnancy and periodically throughout pregnancy. **Considerations for Further Testing and Intervention** Endocrine consultation for medical management. **SYSTEM = Endocrine/Metabolic** **SCORE = 2A**

SECTION 134 REFERENCES

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Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
135	**Systemic MIBG (in therapeutic doses)** **Info Link:** MIBG used for diagnostic purposes (i.e., MIBG scanning) does NOT put patients at risk for hypothyroidism.	**Hypothyroidism**			**HISTORY** **Fatigue** **Weight gain** **Cold intolerance** **Constipation** **Dry skin** **Brittle hair** **Depressed mood** Yearly; Consider more frequent screening during periods of rapid growth. **PHYSICAL** **Height** **Weight** **Hair and skin** **Thyroid exam** Yearly; Consider more frequent screening during periods of rapid growth. **SCREENING** **TSH** **Free T4** Yearly; Consider more frequent screening during periods of rapid growth.	**Health Links** **Thyroid Problems** **Counseling** Counsel at-risk females of childbearing potential to have their thyroid levels checked prior to attempting pregnancy and periodically throughout pregnancy. **Considerations for Further Testing and Intervention** Endocrine consultation for medical management. **SYSTEM = Endocrine/Metabolic** **SCORE = 1**

SECTION 135 REFERENCES

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BIOIMMUNOTHERAPY

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
136	**Bioimmunotherapy** (e.g., G-CSF, IL-2, erythropoietin)	**Insufficient information currently available regarding late effects of biological agents**				SYSTEM = N/A SCORE = N/A

SECTION 136 REFERENCES

No information currently available regarding late effects.

CANCER SCREENING GUIDELINES

BREAST CANCER

Sec #	Organ	At Risk Population	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
137 (Female)	**Breast**	Over age 40 Family history of breast cancer in first degree relative Early onset of menstruation Late onset of menopause (age 55 or older) Older than 30 at birth of first child Never pregnant Obesity Previous breast biopsy with atypical hyperplasia Hormone replacement therapy	Chest radiation with potential impact to the breast (see Section 68), including ≥ 20 Gy to the following fields: - Chest (thorax) - Whole lung - Mediastinal - Axilla - Mini-Mantle - Mantle - Extended Mantle - TLI - STLI - TBI* BRACA1, BRACA2, ATM mutation **Info Link:** *Important: The risk of breast cancer in patients 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); therefore, monitoring of patients who received TBI without additional radiation potentially impacting the breast should be determined on an individual basis.	**PATIENTS AT STANDARD RISK (ACS Recommendation)** **PHYSICAL** **Clinical breast exam** Every 3 years between ages 20-39, then yearly beginning at age 40 **SCREENING** **Mammogram** Yearly, beginning at age 40 **PATIENTS AT HIGHEST RISK** **PHYSICAL** **Breast self exam** Monthly, beginning at puberty **Clinical breast exam** Yearly, beginning at puberty until age 25, then every 6 months **SCREENING** **Mammogram** Yearly, beginning 8 years after radiation or at age 25, whichever occurs last. **Breast MRI** Yearly, as an adjunct to mammography beginning 8 years after radiation or at age 25, whichever occurs last. **Info Link:** The risk of breast cancer in patients 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); therefore, monitoring of patients who received TBI should be determined on an individual basis. 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.	**Health Links** **Breast Cancer** (for patients at highest risk only) **Counseling** For patients at highest risk, counsel to perform breast self-examination monthly, beginning at puberty. For standard risk patients, provide general guidance regarding routine screening beginning at age 40 per current ACS guidelines. **Considerations for Further Testing and Intervention** Surgery and/or oncology consultation as clinically indicated.

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CERVICAL CANCER

Sec #	Organ	At Risk Population	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
138 (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	**PATIENTS AT STANDARD RISK (ACS Recommendation)** **PHYSICAL** **Pelvic exam** Every 1 to 2 years **SCREENING** **Cervical PAP smear** Yearly for regular PAP test. Every 2 years for liquid-based PAP test. After age 30, if patient has had 3 consecutive normal annual PAP tests, may screen every 2-3 years (with conventional or liquid-based cervical cytology) or every 3 years (with HPV DNA test plus cervical cytology). **Info Link:** Begin screening (in patients with a cervix) 3 years after first vaginal intercourse, or at age 21, whichever occurs first.	**Health Links** **Reducing the Risk of Second Cancers** **Counseling** Counsel regarding risk/benefits of HPV vaccination. **Info Link:** Human papillomavirus virus (HPV) is the leading cause of cervical cancer in women. HPV vaccination protects against 70% of cervical cancers and reduces the incidence of genital warts. 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. 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 years of age up to 18 (ACS) or 26 (CDC/ACIP) years to catch up missed vaccines or to complete the series. 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. 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 Saslow D et al. (2007), for further information. **Considerations for Further Testing and Intervention** Gynecology and/or oncology consultation as clinically indicated.

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Sec #	Organ	At Risk Population	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
139	**Colorectal**	High fat/low fiber diet Age ≥ 50 years Obesity	Radiation with potential impact to the colon/rectum (see Section 78), including ≥ 30 Gy to the following fields: - Spine (thoracic, lumbar, sacral, whole) - Extended Mantle - Hepatic - Renal - Upper quadrant (right, left) - Spleen (partial, entire) - Paraaortic - Flank/Hemiabdomen (right, left) - Whole abdomen - Inverted Y - Pelvic - Vaginal - Prostate - Bladder - Iliac - Inguinal - Femoral - TLI - STLI - TBI* Personal history of ulcerative colitis, gastrointestinal malignancy, adenomatous polyps or hepatoblastoma Familial polyposis Family history of colorectal cancer or polyps in first degree relative **Info Link:** *__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. Therefore, monitoring of patients who received TBI without additional radiation potentially impacting the colon/rectum should be determined on an individual basis. (See Info Link in next column)	__PATIENTS AT STANDARD RISK__ **(ACS Recommendation)** **SCREENING** __Option 1:__ **Fecal occult blood (minimum of 3 cards)** Yearly, beginning at age 50 AND/OR **Flexible sigmoidoscopy** Every 5 years, beginning at age 50 *Note: The combination of yearly fecal occult blood testing and every 5 year flexible sigmoidoscopy is preferable to either test done alone.* __Option 2:__ **Double contrast barium enema** Every 5 years, beginning at age 50 __Option 3:__ **Colonoscopy** Every 10 years, beginning at age 50 __PATIENTS AT HIGHEST RISK__ **SCREENING** **Colonoscopy** Every 5 years (minimum); more frequently if indicated based on colonoscopy results. Begin monitoring 10 years after radiation or at age 35, whichever occurs last. Monitor more frequently if clinically indicated. Per the ACS, begin screening earlier for the following high-risk groups: HNPCC (at puberty), FAP (at age 21 years), IBD (8 years after diagnosis of IBD). Information from the first colonoscopy will inform frequency of follow-up testing. **Info Link:** 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. 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. 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. 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. Colonoscopy remains the preferred screening modality for survivors at highest risk of colorectal cancer.	**Health Links** **Colorectal Cancer** **Considerations for Further Testing and Intervention** Gastroenterology, surgery and/or oncology consultation as clinically indicated.

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ENDOMETRIAL CANCER

Sec #	Organ	At Risk Population	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
140 (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)	**PATIENTS AT HIGHEST RISK (ACS Recommendation)** **SCREENING** **Endometrial biopsy** Yearly, beginning at age 35 for patients at highest risk **Info Link:** Women at highest risk should be informed that screening recommendation of endometrial biopsy beginning at age 35 is based on expert opinion in the absence of definitive scientific evidence and the potential benefits, risks, and limitations of testing for early endometrial cancer detection should be discussed.	**Health Links** **Reducing the Risk of Second Cancers**

SECTION 140 REFERENCES

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Sec #	Organ	At Risk Population	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
141	**Lung**	Smoking Workplace exposures to asbestos, arsenic, radiation Second hand smoke (in non-smokers)	Chest radiation with potential impact to the lung	**PATIENTS AT HIGHEST RISK** **HISTORY** **Cough** **Wheezing** **SOB** **DOE** Yearly, and as clinically indicated **PHYSICAL** **Pulmonary Exam** Yearly, and as clinically indicated	**Health Links** **Reducing the Risk of Second Cancers** **Considerations for Further Testing and Intervention** Imaging and surgery and/or oncology consultation as clinically indicated.

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ORAL CANCER

Sec #	Organ	At Risk Population	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
142	**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)	Head/brain radiation Neck radiation TBI Acute/chronic GVHD	**PATIENTS AT HIGHEST RISK** **PHYSICAL** **Oral cavity exam** Yearly	**Health Links** **Reducing Risk of Second Cancers** **Dental Health** **Considerations for Further Testing and Intervention** Head and neck/otolaryngology consultation as indicated.

SECTION 142 REFERENCES

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Sec #	Organ	At Risk Population	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
143 (Male)	**Prostate**	Older age, with steadily increasing risk after age 40 years.	African-American race Family history of prostate cancer in first degree relative	**ALL PATIENTS** **Clinicians should be prepared to discuss prostate cancer testing with patients** **Info Link:** The USPSTF found good evidence that PSA screening can detect early-stage prostate cancer but mixed and inconclusive evidence that early detection improves health outcomes. Screening is associated with important harms, including frequent false-positive results and unnecessary anxiety, biopsies, and potential complications of treatment of some cancers that may never have affected a patient's health. The USPSTF concludes that evidence is insufficient to determine whether the benefits outweigh the harms for a screened population. ACS concurs with this conclusion.	**Health Links** **Reducing the Risk of Second Cancers** **Considerations for Further Testing and Intervention** Urology and/or oncology consultation as clinically indicated.

SECTION 143 REFERENCES

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SKIN CANCER

Sec #	Organ	At Risk Population	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
144	**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	**PATIENTS AT STANDARD RISK** **Info Link:** The U.S. Preventive Services Task Force (USPSTF) concludes that the evidence is insufficient to recommend for or against routine screening for skin cancer using a total-body skin examination for the early detection of cutaneous melanoma, basal cell cancer, or squamous cell skin cancer. There are no randomized trials or case-control studies that directly examine whether screening by clinicians is associated with improved clinical outcomes such as reduced morbidity or mortality from skin cancer. No studies were found that evaluated whether screening improves the outcomes of these cancers. The American Cancer Society recommends skin examination as part of a cancer-related checkup, which should occur on the occasion of the patient's periodic health examination. Self-examination of skin is recommended once a month. **PATIENTS AT HIGHEST RISK** **PHYSICAL** **Skin self exam** Monthly **Dermatologic exam with attention to skin lesions and pigmented nevi in radiation field** Yearly	**Health Links** **Reducing the Risk of Second Cancers** **Skin Health** **Considerations for Further Testing and Intervention** Surgery, dermatology, and/or oncology consultation as clinically indicated.

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TESTICULAR CANCER

Sec #	Organ	At Risk Population	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
145 (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	**Info Link:** For standard and high risk populations, the USPSTF recommends against routine screening for testicular cancer in asymptomatic adolescent and adult males. 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. 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. ACS also no longer recommends clinical testicular cancer screening or testicular self-examination.	

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GENERAL HEALTH SCREENING

ANY CANCER EXPERIENCE

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
146	**General Health Screening**				**SCREENING** **Refer to United States Preventive Services Task Force recommendations at** www.ahrq.gov/clinic/uspstfix.htm Yearly	**Considerations for Further Testing and Intervention** 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 www.ahrq.gov/clinic/uspstfix.htm for specific recommendations. Assess immunization status on all patients; reimmunize as indicated. See http://www.cdc.gov/nip/default.htm#schedules for current immunization schedules. For all HCT patients, reimmunization per CDC Guidelines (http://www.cdc.gov/mmwr/preview/mmwrhtml/rr4910a1.htm - see table 4) or EBMT Guidelines (http://www.nature.com/bmt/journal/v23/n7/pdf/1701641a.pdf).

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