COG Long-Term Follow-Up Guidelines

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- Long-Term Follow-Up Guidelines

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Appendix II: Health Links (Patient Education Materials)

Suggested Citations for COG Long-Term Follow-Up Guidelines

Guidelines

Guidelines Methodology:

Health Links Background and Application:
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.
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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# COG Long Term Follow-Up Guidelines

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# COG Long Term Follow-Up Guidelines
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Long-Term Follow-Up Guidelines

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Long-Term Follow-Up Guidelines
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Introductory Material

Long-Term Follow-Up Guidelines
for Survivors of Childhood, Adolescent, and Young Adult Cancers
Version 3.0 – October 2008

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

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

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.

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.
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.
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.

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.

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

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

**Potential Benefits and Harms:**

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

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

**Patient Preferences:**

Ultimately, as with all clinical guidelines, decisions regarding screening and clinical management for any specific patient should be individually tailored, taking into consideration the patient’s treatment history, risk factors, co-morbidities, and lifestyle. These guidelines are therefore not intended to replace clinical judgment or to exclude other reasonable alternative follow-up procedures. The Children’s Oncology Group recognizes that specific patient care decisions are the prerogative of the patient, family, and healthcare provider.
Implementation 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.
These guidelines represent a statement of consensus from a multidisciplinary panel of experts in the late effects of pediatric cancer treatment. The guidelines outline minimum recommendations for specific health screening evaluations in order to detect potential late effects arising as a result of therapeutic exposures received during treatment of childhood, adolescent, and young adult cancers.

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

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

<table>
<thead>
<tr>
<th>Category</th>
<th>Statement of Consensus</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>There is uniform consensus of the panel that: (1) there is high-level evidence linking the late effect with the therapeutic exposure and (2) the screening recommendation is appropriate based on the collective clinical experience of panel members.</td>
</tr>
<tr>
<td>2A</td>
<td>There is uniform consensus of the panel that: (1) there is lower-level evidence linking the late effect with the therapeutic exposure and (2) the screening recommendation is appropriate based on the collective clinical experience of panel members.</td>
</tr>
<tr>
<td>2B</td>
<td>There is non-uniform consensus of the panel that: (1) there is lower-level evidence linking the late effect with the therapeutic exposure and (2) the screening recommendation is appropriate based on the collective clinical experience of panel members.</td>
</tr>
<tr>
<td>3</td>
<td>There is major disagreement that the recommendation is appropriate</td>
</tr>
</tbody>
</table>
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.
**GUIDELINE ORGANIZATION:**
The *Children’s Oncology Group Long-Term Follow-Up Guidelines for Survivors of Childhood, Adolescent, and Young Adult Cancers* are organized according to therapeutic exposures, arranged by column as follows:

<table>
<thead>
<tr>
<th>Section Number</th>
<th>Unique identifier for each guideline section.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Therapeutic Agent</td>
<td>Therapeutic intervention for malignancy, including chemotherapy, radiation, surgery, blood/serum products, hematopoietic cell transplant, and other therapeutic modalities.</td>
</tr>
<tr>
<td>Potential Late Effects</td>
<td>Most common late treatment complications associated with specified therapeutic intervention.</td>
</tr>
<tr>
<td>Risk Factors</td>
<td>Host factors (e.g., age, sex, race, genetic predisposition), treatment factors (e.g., cumulative dose of therapeutic agent, mode of administration, combinations of agents), medical conditions (e.g., pre-morbid or co-morbid conditions), and health behaviors (e.g., diet, smoking, alcohol use) that may increase risk of developing the complication.</td>
</tr>
<tr>
<td>Highest Risk Factors</td>
<td>Conditions (host factors, treatment factors, medical conditions and/or health behaviors) associated with the highest risk for developing the complication.</td>
</tr>
<tr>
<td>Periodic Evaluations</td>
<td>Recommended screening evaluations, including health history, physical examination, laboratory evaluation, imaging, and psychosocial assessment. Recommendation for minimum frequency of periodic evaluations is based on risk factors and magnitude of risk, as supported by the medical literature and/or the combined clinical experience of the reviewers and panel of experts.</td>
</tr>
</tbody>
</table>
Health Counseling/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).
Cancer Screening 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).
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.
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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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-transplantation functional asplenia has been clarified as applicable to patients with currently active chronic graft-vs-host disease (see Section 103).
• 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).
## ANY CANCER EXPERIENCE

<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Any Cancer Experience</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Info Link:</strong> The Children’s Oncology Group Long-Term Follow-Up Guidelines apply to patients who have been off therapy for a minimum of 2 years.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
|       | 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 | |}

|     | 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 | | |}

### Health Links
- Introduction to Long-Term Follow-Up
- Emotional Issues
- Educational Issues
- Chronic Pain after Childhood Cancer

### Resources
- 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**
## SECTION 1 REFERENCES

### Psychosocial Disorders


### Mental health disorders

### SECTION 1 REFERENCES - continued

#### Risky behaviors

#### Psychosocial disability due to pain

#### Fatigue
### ANY CANCER EXPERIENCE

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

### SECTION 2 REFERENCES


## BLOOD/SERUM PRODUCTS

<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>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)</td>
<td>Chronic Hepatitis B</td>
<td>Host Factors</td>
<td>Chronic Hepatitis B</td>
<td>SCREENING</td>
<td>Health Links</td>
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<td></td>
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<td>Living in hyperendemic area</td>
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<td>Hepatitis</td>
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<td></td>
<td>Blood products before 1972</td>
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<td>Considerations for Further Testing and Intervention</td>
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<td></td>
<td></td>
<td>Health Behaviors</td>
<td></td>
<td>Gastroenterology or hepatology consultation for patients with chronic hepatitis. Hepatitis A immunization in patients lacking immunity.</td>
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<td>IV drug use</td>
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<td>Unprotected sex</td>
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<td></td>
<td></td>
<td>Multiple partners</td>
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<td>High-risk sexual behavior</td>
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<td></td>
<td>Tattoos</td>
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<td></td>
<td></td>
<td></td>
<td>Body piercing</td>
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</table>

**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.

**SECTION 3 REFERENCES**


## BLOOD/SERUM PRODUCTS

### SECTION 4 REFERENCES

### BLOOD/SERUM PRODUCTS

<table>
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<tr>
<th>Sec #</th>
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<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling Further Considerations</th>
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<td>5</td>
<td>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)</td>
<td>HIV infection</td>
<td>Treatment Factors</td>
<td>Blood products between 1977 and 1985</td>
<td>SCREENING HIV testing</td>
<td>Counseling</td>
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<td>Medical Conditions</td>
<td>HPV infection</td>
<td>Once in patients who received treatment for cancer between 1977 and 1985. Note: Dates may vary for international patients.</td>
<td>Considerations for Further Testing and Intervention</td>
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<td></td>
<td>Health Behaviors</td>
<td>IV drug use, Unprotected sex, Multiple partners, High-risk sexual behavior, Sexually transmitted diseases, Tattoos, Body piercing</td>
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</tr>
</tbody>
</table>

**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.

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**SECTION 5 REFERENCES**


### CHEMOTHERAPY

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

# Chemotherapy

**Section 7**

### Alkylating Agents

<table>
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<tr>
<th><strong>#</strong></th>
<th><strong>Therapeutic Agent(s)</strong></th>
<th><strong>Potential Late Effects</strong></th>
<th><strong>Risk Factors</strong></th>
<th><strong>Highest Risk Factors</strong></th>
<th><strong>Periodic Evaluation</strong></th>
<th><strong>Health Counseling Further Considerations</strong></th>
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<tr>
<td>7</td>
<td>ALKYLATING AGENTS</td>
<td>Gonadal dysfunction</td>
<td>Treatment Factors</td>
<td>Host Factors</td>
<td>History</td>
<td>Health Links</td>
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<tr>
<td></td>
<td></td>
<td>(testicular)</td>
<td>Higher cumulative doses of alkylators or combinations of alkylators Combined with radiation to:</td>
<td>Male gender</td>
<td>Pubertal (onset, tempo)</td>
<td>Male Health Issues</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>- Abdomen/pelvis</td>
<td>Treatment Factors</td>
<td>Sexual function (erections, nocturnal emissions, libido)</td>
<td>Resources</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>- Testes</td>
<td>MOPP ≥ 3 cycles</td>
<td>Medication use impacting sexual function</td>
<td>Extensive information regarding infertility for patients and healthcare professionals is available on the following websites: American Society for Reproductive Medicine (<a href="http://www.asrm.org">www.asrm.org</a>) Fertile Hope (<a href="http://www.fertilehope.org">www.fertilehope.org</a>)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>- Brain, cranium</td>
<td>Busulfan ≥ 600 mg/m²</td>
<td>Yearly</td>
<td>Counseling</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>(neuroendocrine axis)</td>
<td>Cyclophosphamide cumulative dose ≥ 7.5 gm/m² or as conditioning for HCT Ifosfamide ≥ 60 gm/m² Any alkylators combined with:</td>
<td>PHYSICAL</td>
<td>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.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Abnormal testicular function</td>
<td>Testicular volume by Prader orchidometry</td>
<td>Yearly until sexually mature</td>
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<tr>
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<td></td>
<td></td>
<td>- Testicular radiation</td>
<td>any alkylators combined with:</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- Pelvic radiation</td>
<td>Testicular function</td>
<td></td>
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<td></td>
<td></td>
<td>- TBI</td>
<td>Yearly</td>
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<td></td>
<td></td>
<td>Smoking</td>
<td>Health Behaviors</td>
<td></td>
<td>SCREENING</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Info Link</td>
<td>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.</td>
<td>FSH</td>
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<td></td>
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<td></td>
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<td></td>
<td>Baseline at age 14 and as clinically indicated in patients with delayed puberty and/or clinical signs and symptoms of testosterone deficiency.</td>
<td>LH</td>
</tr>
<tr>
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<td>Semen analysis</td>
<td></td>
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<td></td>
<td></td>
<td>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.</td>
<td>Testosterone</td>
</tr>
</tbody>
</table>

### System = Reproductive (male)

### Score =

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

**Section 7 References**


## CHEMOTHERAPY

### ALKYLATED AGENTS (cont)

<table>
<thead>
<tr>
<th>Section #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling Further Considerations</th>
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<tbody>
<tr>
<td>7 (Female)</td>
<td>ALKYLATED AGENTS</td>
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<tr>
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<td></td>
<td></td>
<td></td>
<td>Health Links</td>
</tr>
<tr>
<td></td>
<td>Busulfan</td>
<td>Gonadal dysfunction</td>
<td>Treatment Factors</td>
<td>Higher cumulative doses of alkylators or combinations of alkylators</td>
<td>MOPP &gt; 3 cycles</td>
<td>Female Health Issues</td>
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<tr>
<td></td>
<td>Carmustine (BCNU)</td>
<td>(ovarian)</td>
<td></td>
<td>Combined with radiation to:</td>
<td>Busulfan &gt; 600 mg/m²</td>
<td>Resources</td>
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<td></td>
<td>Chlorambucil</td>
<td>Delayed/arrested puberty</td>
<td></td>
<td>- Abdomen/pelvis</td>
<td>Cyclophosphamide cumulative dose &gt; 7.5 gm/m² or as conditioning for HCT</td>
<td>Extensive information regarding infertility for patients and healthcare professionals is available on the following websites: American Society for Reproductive Medicine (<a href="http://www.asrm.org">www.asrm.org</a>) Fertile Hope (<a href="http://www.fertilehope.org">www.fertilehope.org</a>)</td>
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<tr>
<td></td>
<td>Cyclophosphamide</td>
<td>Premature menopause</td>
<td></td>
<td>- Lumbar or sacral spine (from ovarian scatter)</td>
<td>Any alkylators combined with:</td>
<td>Counseling</td>
</tr>
<tr>
<td></td>
<td>Ifosfamide</td>
<td>Infertility</td>
<td></td>
<td>- Brain, cranium (neuroendocrine axis)</td>
<td>- Pelvic radiation</td>
<td>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.</td>
</tr>
<tr>
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<td>Lomustine (CCNU)</td>
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<td>Considerations for Further Testing and Intervention</td>
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<td>Mechlorethamine</td>
<td></td>
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<td></td>
<td>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.</td>
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<tr>
<td></td>
<td>Melphalan</td>
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<td>SYSTEM = Reproductive (female)</td>
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<td>Procarbazine</td>
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### SECTION 7 REFERENCES


## CHEMOTHERAPY

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<th>Potential Late Effects</th>
<th>Risk Factors</th>
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<th>Further Considerations</th>
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<td>Busulfan</td>
<td>Acute myeloid leukemia</td>
<td>Treatment Factors</td>
<td>Less than 10 years since exposure to agent</td>
<td>Yearly, up to 10 years after exposure to agent</td>
<td>Health Links</td>
<td>Reducing the Risk of Second Cancers</td>
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<td>Carmustine (BCNU)</td>
<td>Myelodysplasia</td>
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<td>Higher cumulative alkylator dose or combination of alkylators</td>
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<td>Counseling</td>
<td>Counsel to promptly report fatigue, pallor, petechiae, or bone pain.</td>
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<td>Chlorambucil</td>
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<td>Note: Melphalan and mechlorethamine are more potent leukemogens than cyclophosphamide</td>
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<td>Considerations for Further Testing and Intervention</td>
<td>Bone marrow exam as clinically indicated.</td>
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</tbody>
</table>

### 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

### SYSTEM = SMN
- SCORE = Alkylating Agents: 1
- Heavy Metals: 2A
- Non-Classical Alkylators: 2A

## SECTION 8 REFERENCES

### CHEMOTHERAPY

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<th>Health Counseling Further Considerations</th>
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</thead>
<tbody>
<tr>
<td>9</td>
<td>ALKYLATING AGENTS</td>
<td>Pulmonary fibrosis</td>
<td>Treatment Factors: Higher cumulative doses, Combined with bleomycin</td>
<td>Treatment Factors: BCNU ≥ 600 mg/m², Busulfan ≥ 500 mg (transplant doses), Combined with: - Chest radiation, - TBI</td>
<td>HISTORY: Cough, SDB, DOE, Wheezing, Yearly</td>
<td>HEALTH LINKS: Pulmonary Health, Resources: Extensive information regarding smoking cessation is available for patients on the NCI's website: <a href="http://www.smokefree.gov">www.smokefree.gov</a>, Counseling: Counsel regarding tobacco avoidance/smoking cessation. Due to the potential pulmonary toxicity of this therapy, patients who desire to SCUBA dive should be advised to obtain medical clearance from a pulmonologist. Considerations for Further Testing and Intervention: In patients with abnormal PFTs and/or CXR, consider repeat evaluation prior to general anesthesia. Pulmonary consultation for symptomatic pulmonary dysfunction. Influenza and pneumococcal vaccines.</td>
</tr>
</tbody>
</table>

**ALKYLATING AGENTS (cont)**

- **Busulfan**
- **Carmustine (BCNU)**
- **Lomustine (CCNU)**

**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

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**SECTION 9 REFERENCES**


## CHEMOTHERAPY

### ALKYLATING AGENTS (cont)

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<th>Sec #</th>
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<td>HISTORY</td>
<td>Health Links</td>
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<td></td>
<td>Busulfan</td>
<td></td>
<td>Combined with corticosteroids</td>
<td>Combined with cranial, orbital, or eye radiation</td>
<td>Visual changes (decreased acuity, halos, diplopia)</td>
<td>Cataracts</td>
</tr>
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<td>TBI</td>
<td>Yearly</td>
<td>Considerations for Further Testing and Intervention</td>
</tr>
<tr>
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<td></td>
<td></td>
<td>Longer interval since treatment</td>
<td></td>
<td>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.</td>
</tr>
<tr>
<td></td>
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<td>SYSTEM = Ocular</td>
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### SECTION 10 REFERENCES


## CHEMOTHERAPY

### ALKYLATING AGENTS (cont)

<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling Further Considerations</th>
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<td>ALKYLATING AGENTS</td>
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<tr>
<td></td>
<td>Cyclophosphamide</td>
<td>Urinary tract toxicity</td>
<td>Treatment Factors</td>
<td>Treatment Factors</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>Ifosfamide</td>
<td>Hemorrhagic cystitis</td>
<td>Higher cumulative doses (decreased incidence with Mesna)</td>
<td>Cyclophosphamide dose ≥ 3 gm/m²</td>
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<td></td>
<td></td>
<td>Bladder fibrosis</td>
<td>Combined with pelvic radiation</td>
<td>Pelvic radiation dose ≥ 30 Gy</td>
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<td></td>
<td></td>
<td>Dysfunctional voiding</td>
<td>Health Behaviors</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Vesicoureteral reflux</td>
<td>Alcohol use</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>Hydronephrosis</td>
<td>Smoking</td>
<td></td>
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</tbody>
</table>

### HISTORY
- Hematuria
- Urinary urgency/frequency
- Urinary incontinence/retention
- Dysuria
- Nocturia
- Abnormal urinary stream

### SCREENING
- Urinalysis
  - Yearly

### Health Links
- Bladder Health

### 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.

### SECTION 11 REFERENCES

### CHEMOTHERAPY

#### ALKYLATING AGENTS (cont)

<table>
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<th>Health Counseling Further Considerations</th>
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<tr>
<td>12</td>
<td>ALKYLATING AGENTS</td>
<td>Bladder malignancy</td>
<td>Treatment Factors Combined with pelvic radiation</td>
<td>History</td>
<td>Bladder Health</td>
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<tr>
<td></td>
<td>Cyclophosphamide</td>
<td></td>
<td>Health Behaviors Alcohol use Smoking</td>
<td>Hematuria Urinary urgency/frequency Urinary incontinence/retention Dysuria Nocturia Abnormal urinary stream Yearly</td>
<td>Counseling Counsel to promptly report dysuria or gross hematuria.</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Screening Urinalysis Yearly</td>
<td>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 &gt; 5 RBC/HFP on at least 2 occasions). Nephrology or urology referral for patients with culture-negative microscopic hematuria AND abnormal ultrasound and/or abnormal calcium/creatinine ratio. Urology referral for patients with culture negative macroscopic hematuria.</td>
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### SECTION 12 REFERENCES


### CHEMOTHERAPY

<table>
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<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>13 ALKYLATING AGENTS (cont) Ifosfamide</td>
<td>Renal toxicity Glomerular injury Tubular injury (renal tubular acidosis, Fanconi’s syndrome, hypophosphatemic rickets)</td>
<td>Host Factors Younger age at treatment Mononephric</td>
<td>Host Factors Age &lt; 4 years at time of treatment</td>
<td>PHYSICAL Blood pressure Yearly</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Treatment Factors Higher cumulative dose Combined with other nephrotoxic agents, such as: - Cisplatin - Carboplatin - Aminoglycosides - Amphotericin - Immunosuppressants - Methotrexate - Radiation impacting the kidney</td>
<td>Treatment Factors Ifosfamide dose ≥60 grams/m² Renal radiation dose ≥ 15 Gy</td>
<td>SCREENING BUN Creatinine Na, K, Cl, CO₂ Ca, Mg, PO₄ Baseline at entry into long-term follow-up. Repeat as clinically indicated. Urinalysis Yearly</td>
</tr>
<tr>
<td></td>
<td>Medical Conditions Tumor infiltration of kidney(s) Pre-existing renal impairment Nephrectomy</td>
<td></td>
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</table>

**Section 13 References**

## CHEMOTHERAPY

### HEAVY METALS

<table>
<thead>
<tr>
<th>Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carboplatin</td>
<td>Ototoxicity</td>
<td>Host Factors</td>
<td>Host Factors</td>
<td>HISTORY</td>
<td>Health Links</td>
</tr>
<tr>
<td>(in myeloablative doses only)</td>
<td>Sensorineural hearing loss</td>
<td>Age &lt; 4 years at treatment</td>
<td>CNS neoplasm</td>
<td>Hearing difficulties</td>
<td>Hearing Loss</td>
</tr>
<tr>
<td>Cisplatin</td>
<td>Tinnitus</td>
<td>Treatment Factors</td>
<td>Treatment Factors</td>
<td>(with/without background noise)</td>
<td>Educational Issues</td>
</tr>
<tr>
<td></td>
<td>Vertigo</td>
<td>Combined with:</td>
<td>Cumulative cisplatin dose</td>
<td>Tinnitus</td>
<td>Considerations for Further Testing and Intervention</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Cranial/ear radiation</td>
<td>≥ 360 mg/m²</td>
<td>Vertigo</td>
<td>Audiology consultation for amplification in patients with progressive hearing loss.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Ototoxic drugs (e.g., aminoglycosides, loop diuretics)</td>
<td>High dose cisplatin</td>
<td>Yearly</td>
<td>Speech and language therapy for children with hearing loss.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Medical Conditions</td>
<td></td>
<td></td>
<td>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.</td>
</tr>
<tr>
<td></td>
<td>Chronic otitis</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td></td>
<td>Cerumen impaction</td>
<td></td>
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<tr>
<td></td>
<td>Renal dysfunction</td>
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</tbody>
</table>

### 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.

### 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
<table>
<thead>
<tr>
<th>SECTION 14 REFERENCES</th>
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<tr>
<td>Sec #</td>
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**SECTION 15 REFERENCES**


## CHEMOTHERAPY

### Section 16: Heavy Metals

<table>
<thead>
<tr>
<th>#</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>16</td>
<td><strong>HEAVY METALS</strong>&lt;br&gt;Carboplatin&lt;br&gt;Cisplatin</td>
<td>Renal toxicity&lt;br&gt;Glomerular injury&lt;br&gt;Tubular injury&lt;br&gt;Renal insufficiency</td>
<td>Host Factors&lt;br&gt;Mononephric</td>
<td>Treatment Factors&lt;br&gt;Cisplatin dose $\geq$ 200 mg/m²&lt;br&gt;Renal radiation dose $\geq$ 15 Gy</td>
<td>PHYSICAL&lt;br&gt;Blood pressure&lt;br&gt;Yearly</td>
<td>Health Links&lt;br&gt;Kidney Health&lt;br&gt;See also: <a href="#">Single Kidney Health</a></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Treatment Factors&lt;br&gt;Combined with other nephrotoxic agents such as:&lt;br&gt;- Ifosfamide&lt;br&gt;- Aminoglycosides&lt;br&gt;- Amphotericin&lt;br&gt;- Immunosuppressants&lt;br&gt;- Methotrexate&lt;br&gt;- Radiation impacting the kidney</td>
<td></td>
<td>Screening&lt;br&gt;BUN&lt;br&gt;Creatinine&lt;br&gt;Na, K, Cl, CO₂&lt;br&gt;Ca, Mg, PO₄&lt;br&gt;Baseline at entry into long-term follow-up. Repeat as clinically indicated.</td>
<td>Counseling&lt;br&gt;In patients with salt-wasting tubular dysfunction, educate that low magnesium levels potentiate coronary atherosclerosis</td>
</tr>
<tr>
<td></td>
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<td></td>
<td>Medical Conditions&lt;br&gt;Diabetes mellitus&lt;br&gt;Hypertension&lt;br&gt;Nephrectomy</td>
<td></td>
<td>Urinalysis&lt;br&gt;Yearly</td>
<td>Considerations for Further Testing and Intervention&lt;br&gt;Electrolyte supplements for patients with persistent electrolyte wasting. Nephrology consultation for patients with hypertension, proteinuria, or progressive renal insufficiency.</td>
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### Physiological Screening

<table>
<thead>
<tr>
<th>System</th>
<th>Score</th>
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<tbody>
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<td>Urinary</td>
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### Section 16 References


### CHEMOTHERAPY

#### HEAVY METALS

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<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling Further Considerations</th>
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<tbody>
<tr>
<td>17</td>
<td>HEAVY METALS</td>
<td></td>
<td></td>
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</tr>
<tr>
<td></td>
<td>Carboplatin</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Cisplatin</td>
<td></td>
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</tr>
</tbody>
</table>

- **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](http://www.ahrq.gov/clinic/prevenix.htm)

**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**

### SECTION 17 REFERENCES


### CHEMOTHERAPY

<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>18</td>
<td><strong>ANTIMETABOLITES</strong></td>
<td>Cytarabine (high dose IV)</td>
<td>Neurocognitive deficits</td>
<td>Host Factors: Younger age at treatment</td>
<td>History: Educational and/or vocational progress</td>
<td></td>
</tr>
</tbody>
</table>

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

**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

**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**
- Younger age at treatment
- CNS leukemia/lymphoma
- Relapsed leukemia/lymphoma treated with CNS-directed therapy

**Treatment Factors**
- Radiation dose ≥ 24 Gy
- Single fraction TBI (10 Gy)

**Health Links**
- Educational Issues
- Considerations for Further Testing and Intervention

**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.

**SYSTEM = CNS**

**SCORE = 2A**

### SECTION 18 REFERENCES

### CHEMOTHERAPY

<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling Further Considerations</th>
</tr>
</thead>
</table>
| 19    | ANTIMETABOLITES Cytarabine (high dose IV) | Clinical leukoencephalopathy | Younger age at treatment CNS leukemia/lymphoma Relapsed leukemia/lymphoma treated with CNS-directed therapy | 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. |

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

- Cytarabine (high dose IV)
- Clinical leukoencephalopathy
- Spasticity
- Ataxia
- Dysarthria
- Dysphagia
- Hemiparesis
- Seizures

**Note:** New deficits may emerge over time.

### SYSTEM = CNS

**SCORE = 2A**

---

### SECTION 19 REFERENCES

### CHEMOTHERAPY

#### ANTIMETABOLITES (cont)

<table>
<thead>
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<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling Further Considerations</th>
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<td>20</td>
<td>ANTIMETABOLITES</td>
<td>No known late effects</td>
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<td>SYSTEM = N/A</td>
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<tr>
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<td>Cytarabine (low dose IV)</td>
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<td>SCORE = 1</td>
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<tr>
<td></td>
<td>Cytarabine IO</td>
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<td>Cytarabine IT</td>
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<td>Cytarabine SQ</td>
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</table>

Info Link: Low-dose IV is defined as any single dose < 1000 mg/m²

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

### SECTION 20 REFERENCES

No known late effects
### CHEMOTHERAPY

#### ANTIMETABOLITES (cont)

<table>
<thead>
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<th>Therapeutic Agent(s)</th>
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<th>Risk Factors</th>
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<th>Periodic Evaluation</th>
<th>Health Counseling Further Considerations</th>
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<tbody>
<tr>
<td>21</td>
<td><strong>ANTIMETABOLITES</strong></td>
<td>Mercaptopurine (6MP)</td>
<td>Hepatic dysfunction</td>
<td>Medical Conditions</td>
<td>PHYSICAL</td>
<td>Health Links</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Thioguanine (6TG)</td>
<td>Veno-occlusive disease (VOD)</td>
<td>Viral hepatitis</td>
<td>Solera icterus</td>
<td>Liver Health</td>
</tr>
<tr>
<td></td>
<td>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.</td>
<td></td>
<td></td>
<td></td>
<td>Jaundice</td>
<td>Considerations for Further Testing and Intervention</td>
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<tr>
<td></td>
<td>Thioguanine (6TG)</td>
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<td></td>
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<td>Splenomegaly</td>
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<td>Yearly</td>
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<tr>
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<td>Info Link: Acute toxicities predominately 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.</td>
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#### SECTION 21 REFERENCES


## CHEMOTHERAPY

### ANTIMETABOLITES

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<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
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<th>Health Counseling Further Considerations</th>
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<tr>
<td>22</td>
<td>ANTIMETABOLITES</td>
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<td></td>
</tr>
<tr>
<td></td>
<td>Methotrexate (high dose IV)</td>
<td>Reduced Bone Mineral Density (BMD)</td>
<td>Host Factors</td>
<td>Host Factors</td>
<td>SCREENING</td>
<td>Bone density evaluation (DEXA or quantitative CT)</td>
</tr>
<tr>
<td></td>
<td>Methotrexate (low dose IV)</td>
<td>Defined as Z-score &gt; 2.0 SD below the mean in survivors &lt; 20 years old or T-score &gt;1.0 SD below the mean in survivors ≥ 20 years old</td>
<td>Both genders are at risk</td>
<td>Older age at time of treatment</td>
<td>Baseline at entry into long-term follow-up. Repeat as clinically indicated.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Methotrexate IM</td>
<td>Treatment Factors</td>
<td>Caucasian</td>
<td>Methotrexate cumulative dose ≥ 40 gm/m²</td>
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<td></td>
<td>Methotrexate PO</td>
<td>Medical Conditions</td>
<td>Lower weight and BMI</td>
<td>Prolonged corticosteroid therapy (e.g., for chronic GVHD)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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

**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.

**Screening:**
Bone density evaluation (DEXA or quantitative CT) (Baseline at entry into long-term follow-up. Repeat as clinically indicated.)

**Host Factors:**
- Both genders are at risk
- Younger age at diagnosis
- Caucasian
- Lower weight and BMI

**Treatment Factors:**
- Methotrexate cumulative dose ≥ 40 gm/m²
- Prolonged corticosteroid therapy (e.g., for chronic GVHD)

**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

**Health Links:**
Bone Health

**Resources:**
National Osteoporosis Foundation Website: [www.nof.org](http://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**
## CHEMOTHERAPY

### ANTIMETABOLITES (cont)

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

## SECTION 22 REFERENCES


### CHEMOTHERAPY

#### Sec 23

<table>
<thead>
<tr>
<th>#</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Treatment Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling Further Considerations</th>
</tr>
</thead>
</table>
| 23 | ANTIMETABOLITES Methotrexate (high dose IV) Methotrexate (low dose IV) Methotrexate IM Methotrexate PO | Renal toxicity

**Info Link:** Acute toxicities predominate, from which the majority of patients recover without sequelae.

**Treatment Factors**

- 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

<p>| | | | | | | | |</p>
<table>
<thead>
<tr>
<th></th>
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</tr>
</tbody>
</table>

**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**

### SECTION 23 REFERENCES


### ANTIMETABOLITES (cont)

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

- **Renal toxicity**

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

- **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

- **Risk Factors**
  - Host Factors
    - Mononephric

- **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.
### CHEMOTHERAPY

#### ANTIMETABOLITES (cont)

<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>24</td>
<td>ANTIMETABOLITES</td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td></td>
<td>Methotrexate (high dose IV)</td>
<td></td>
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<td></td>
</tr>
<tr>
<td></td>
<td>Methotrexate (low dose IV)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Methotrexate IM</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Methotrexate PO</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Info Link:</strong></td>
<td>High-dose IV is defined as any single dose ≥ 1000 mg/m².</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Hepatic dysfunction</td>
<td></td>
<td>Treatment Factors</td>
<td>Treatment Factors</td>
<td>PHYSICAL</td>
<td>Liver Health</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Abdominal radiation</td>
<td>Treatment before 1970</td>
<td>Solera icterus</td>
<td>Jaundice</td>
</tr>
<tr>
<td></td>
<td>Medical Conditions</td>
<td></td>
<td>Viral hepatitis</td>
<td>Medical Conditions</td>
<td>Ascites</td>
<td>Hepatomegaly</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Chronic viral hepatitis</td>
<td>Splenomegaly</td>
<td>Yearly</td>
</tr>
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<td></td>
<td><strong>Treatment Factors</strong></td>
<td><strong>Medical Conditions</strong></td>
<td></td>
<td></td>
<td><strong>SCREENING</strong></td>
<td><strong>Alt</strong></td>
</tr>
<tr>
<td></td>
<td>Abdominal radiation</td>
<td>Viral hepatitis</td>
<td></td>
<td></td>
<td>ALT</td>
<td>AS</td>
</tr>
<tr>
<td></td>
<td>Medical Conditions</td>
<td>Viral hepatitis</td>
<td></td>
<td></td>
<td>Baseline at entry into long-term follow-up. Repeat as clinically indicated.</td>
<td><strong>SYSTEM = GI/Hepatic</strong></td>
</tr>
</tbody>
</table>

#### SECTION 24 REFERENCES


### Section 25: References


### CHEMOTHERAPY

#### ANTIMETABOLITES (cont)

<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>26</td>
<td>ANTIMETABOLITES</td>
<td>Methotrexate (high dose IV) Methotrexate IO Methotrexate IT</td>
<td>Clinical leukoencephalopathy Spasticity Ataxia Dysarthria Dysphagia Hemiparesis Seizures</td>
<td>Host Factors Younger age at treatment CNS leukemia/lymphoma Relapsed leukemia/lymphoma treated with CNS-directed therapy</td>
<td>Treatment Factors Radiation dose ≥ 24 Gy</td>
<td>HISTORY Cognitive, motor, and/or sensory deficits Seizures Other neurologic symptoms Yearly PHYSICAL Neurological exam Yearly</td>
</tr>
</tbody>
</table>

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

### SECTION 26 REFERENCES


<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>27</td>
<td>ANTHRACYCLINE ANTIBIOTICS</td>
<td>Acute myeloid leukemia</td>
<td>Treatment Factors</td>
<td></td>
<td></td>
<td>HISTORY</td>
</tr>
<tr>
<td></td>
<td>Daunorubicin</td>
<td></td>
<td>Less than 5 years since exposure to agent</td>
<td></td>
<td></td>
<td>Fatigue</td>
</tr>
<tr>
<td></td>
<td>Doxorubicin</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Bleeding</td>
</tr>
<tr>
<td></td>
<td>Epirubicin</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Easy bruising</td>
</tr>
<tr>
<td></td>
<td>Idarubicin</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Yearly up to 10 years after exposure to agent</td>
</tr>
<tr>
<td></td>
<td>Mitoxantrone*</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>PHYSICAL</td>
</tr>
<tr>
<td></td>
<td>*Info link (Mitoxantrone): Although Mitoxantrone technically belongs to the anthracenedione class of anti-tumor antibiotics, it is related to the anthracycline family.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Dermatologic exam (pallor, petechiae, purpura)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Yearly up to 10 years after exposure to agent</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>SCREENING</td>
</tr>
<tr>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>CBC/differential</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Yearly up to 10 years after exposure to agent</td>
</tr>
</tbody>
</table>

**SECTION 27 REFERENCES**


### CHEMOTHERAPY

<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling Further Considerations</th>
</tr>
</thead>
</table>
| 28    | **ANTHRACYCLINE ANTIBIOTICS**  

Daunorubicin  
Doxorubicin  
Epirubicin  
Idarubicin  
Mitoxantrone*  

*Info Link (Mitoxantrone): Although Mitoxantrone technically belongs to the anthracycene 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.  

<table>
<thead>
<tr>
<th>Treatment Factors</th>
<th>Host Factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Combined with radiation involving the heart</td>
<td>Black or of African descent</td>
</tr>
</tbody>
</table>
| Combined with other cardiotoxic chemotherapy:  
- Cyclophosphamide conditioning for HCT  
- Amsacrine | Younger than age 5 years at time of treatment |  
| Medical Conditions | Treatment Factors |  
| Obesity | Higher cumulative anthracycline doses:  
- ≥ 550 mg/m² in patients 18 years or older at time of treatment |  
| Congenital heart disease | ≥ 300 mg/m² in patients younger than 18 years at time of treatment |  
| Febrile illness | Any dose in infant |  
| Isometric exercise | Chest radiation ≥ 30 Gy |  
| Smiling | Longer time elapsed since treatment |  

### ANTHRACYCLINE ANTIBIOTICS (cont)

<table>
<thead>
<tr>
<th>HISTORY</th>
</tr>
</thead>
<tbody>
<tr>
<td>SOB</td>
</tr>
<tr>
<td>DOE</td>
</tr>
<tr>
<td>Orthopnea</td>
</tr>
<tr>
<td>Chest pain</td>
</tr>
</tbody>
</table>
| Palpitations | If under 25 years:  
- Abdominal symptoms (nausea, vomiting) | Yearly |  
| 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. |  
| 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. |  

**SYSTEM = Cardiovascular**  
**SCORE = 1**
<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>28</td>
<td>ANTHRACYCLINE ANTIBIOTICS (cont)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Daunorubicin</td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Doxorubicin</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Epirubicin</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
|      | Idarubicin | | | | | *
|      | Mitoxantrone* | | | | |*
|      | *Info Link (Mitoxantrone): Although Mitoxantrone technically belongs 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 Pregnancy Health Behaviors Isometric exercise Smoking Drug use (e.g., cocaine, diet pills, ephedra, mahuang) | Host Factors Female sex Black/or 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. | | |

**SYSTEM = Cardiovascular**

**SCORE = 1**
### CHEMOTHERAPY

#### ANTHRACYCLINE ANTIBIOTICS (cont)

<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
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<td></td>
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#### RECOMMENDED FREQUENCY OF ECHOCARDIOGRAM OR MUGA SCAN

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

*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)"]
## CHEMOTHERAPY

### ANTHRACYCLINE ANTIBIOTICS (cont)

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

### SECTION 28 REFERENCES


### CHEMOTHERAPY

<table>
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<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>29</td>
<td>ANTI-TUMOR ANTIBIOTICS</td>
<td>Bleomycin</td>
<td>Pulmonary toxicity</td>
<td>Host Factors: Younger age at treatment</td>
<td>Treatment Factors: Bleomycin dose ≥ 400 U/m² (injury observed in doses 60-100 U/m² in children) Combined with: - Chest radiation - TBI</td>
<td>HISTORY: Cough, SOB, DOE, Wheezing Yearly</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Interstitial pneumonitis</td>
<td>Treatment Factors: Higher cumulative dose Combined with: - Busulfan - Carmustine (BCNU) - Lomustine (CCNU)</td>
<td></td>
<td>PHYSICAL: Pulmonary exam Yearly</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Pulmonary fibrosis</td>
<td>Medical Conditions: Renal dysfunction High dose oxygen support such as during general anesthesia</td>
<td></td>
<td>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.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Acute respiratory distress syndrome (very rare)</td>
<td>Health Behaviors: Smoking</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### ANTI-TUMOR ANTIBIOTICS

**SYSTEM = Pulmonary**

**SCORE =**

- Interstitial pneumonitis: 1
- Pulmonary fibrosis: 1
- ARDS: 2B

### SECTION 29 REFERENCES

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

### CHEMOTHERAPY

<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
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<th>Periodic Evaluation</th>
<th>Health Counseling Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>31</td>
<td>CORTICOSTEROIDS&lt;br&gt;Dexamethasone&lt;br&gt;Prednisone</td>
<td>Reduced Bone Mineral Density (BMD) Defined as Z-score &gt; 2.0 SD below the mean in survivors &lt; 20 years old or T-score &gt; 1.0 SD below the mean in survivors ≥ 20 years old</td>
<td>Host Factors&lt;br&gt;Both genders are at risk&lt;br&gt;Younger age at diagnosis&lt;br&gt;Caucasian&lt;br&gt;Lower weight and BMI</td>
<td>Host Factors&lt;br&gt;Older age at time of treatment&lt;br&gt;Treatment Factors&lt;br&gt;Gluocorticoid cumulative dose ≥ 9 gm/m² prednisone equivalent</td>
<td>SCREENING&lt;br&gt;Bone density evaluation (DEXA or quantitative CT) Baseline at entry into long-term follow-up. Repeat as clinically indicated.</td>
<td>Considerations for Further Testing and Intervention&lt;br&gt;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).</td>
</tr>
</tbody>
</table>

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

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.

#### Screening
Bone density evaluation (DEXA or quantitative CT) Baseline at entry into long-term follow-up. Repeat as clinically indicated.

#### 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

#### Treatment Factors
- Corticosteroids
- Cyclosporine
- Tacrolimus
- Cranial radiation
- Craniospinal radiation
- HCT/TBI

#### Health Links
- Bone Health

#### Resources
- National Osteoporosis Foundation Website: www.nof.org

#### SYSTEM = Musculoskeletal
#### SCORE = 2B
SECTION 31 REFERENCES


<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>32</td>
<td>CORTICOSTEROIDS (cont)</td>
<td>Osteonecrosis (Avascular Necrosis)</td>
<td>Host Factors: Both genders are at risk Host polymorphisms may confer increased risk</td>
<td>Host Factors: Age ≥ 10 years at time of treatment</td>
<td>HISTORY:</td>
<td>Health Links: Osteonecrosis</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Treatment Factors: Combined with high-dose radiation to any bone Dexamethasone effect is more potent than prednisone</td>
<td>Treatment Factors: Orthovoltage radiation (commonly used before 1970) due to delivery of greater dose to skin and bones</td>
<td>Joint pain, Swelling, Immobility, Limited range of motion</td>
<td>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).</td>
</tr>
<tr>
<td></td>
<td>Dexamethasone, Prednisone</td>
<td></td>
<td>Medical Conditions: Sickle cell disease</td>
<td></td>
<td>Yearly</td>
<td></td>
</tr>
</tbody>
</table>

**SYSTEM = Musculoskeletal  
SCORE = 1**

### SECTION 32 REFERENCES


### CORTICOSTEROIDS (cont)

<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>33</td>
<td>CORTICOSTEROIDS</td>
<td>Cataracts</td>
<td>Treatment Factors Combined with: - TBI - Busulfan</td>
<td>Treatment Factors TBI Cranial, orbital, or eye radiation Longer interval since treatment</td>
<td>HISTORY Visual changes (decreased acuity, halos, diplopia) Yearly PHYSICAL Eye exam (visual acuity, funduscopic exam for lens opacity) Yearly</td>
<td>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.</td>
</tr>
</tbody>
</table>

### SECTION 33 REFERENCES

<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>34</td>
<td>ENZYMES Asparaginase</td>
<td>No known late effects</td>
<td></td>
<td></td>
<td></td>
<td>SYSTEM = N/A</td>
</tr>
</tbody>
</table>

**Info Link:** Acute toxicities predominate, from which the majority of patients recover without sequelae

---

**SECTION 34 REFERENCES**


### CHEMOTHERAPY

<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>35</td>
<td>PLANT ALKALOIDS</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Vinblastine</td>
<td>Peripheral sensory or motor neuropathy</td>
<td>Treatment Factors Combined with platinum chemotherapy, gemcitabine or taxanes</td>
<td>Medical Conditions Charcot-Marie-Tooth disease</td>
<td>History Peripheral neuropathy Yearly, until 2 to 3 years after therapy. Monitor yearly if symptoms persist.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Vincristine</td>
<td>Areflexia</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Weakness</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Foot drop</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Paresthesias</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>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.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Treatment Factors Combined with platinum chemotherapy, gemcitabine or taxanes</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Medical Conditions Anorexia Severe weight loss</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>PHYSICAL Neurologic exam Yearly, until 2 to 3 years after therapy; monitor yearly if symptoms persist.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>SYSTEM = PNS SCORE = 2A</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### SECTION 35 REFERENCES


<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>36</td>
<td>PLANT ALKALOIDS</td>
<td>Vinblastine Vincristine</td>
<td>Vasospastic attacks (Raynaud’s phenomenon)</td>
<td>Health Behaviors Smoking Illicit drug use</td>
<td>HISTORY Vasospasms of hands, feet, nose, lips, cheeks, or earlobes related to stress or cold temperatures Yearly PHYSICAL Physical exam of affected area As indicated</td>
<td>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.</td>
</tr>
</tbody>
</table>

**SYSTEM = Cardiovascular**

**SCORE = 2A**

**SECTION 36 REFERENCES**


## CHEMOTHERAPY

### EPPODOPHYLLOTOXINS

<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>37</td>
<td>EPPODOPHYLLOTOXINS</td>
<td>Acute myeloid leukemia</td>
<td>Medical Conditions</td>
<td>Treatment Factors</td>
<td>HISTORY</td>
<td>Health Links&lt;br&gt;Reducing the Risk of Second Cancers</td>
</tr>
<tr>
<td></td>
<td>Etoposide (VP16)</td>
<td></td>
<td>Splenectomy (conflicting evidence)</td>
<td>Weekly or twice weekly administration</td>
<td>Fatigue</td>
<td>Counseling</td>
</tr>
<tr>
<td></td>
<td>Teniposide (VM26)</td>
<td></td>
<td></td>
<td>Less than 5 years since exposure to agent</td>
<td>Bleeding</td>
<td>Considerations for Further Testing and Intervention</td>
</tr>
</tbody>
</table>

**Info Link:** Administration schedules since approximately 1990 have been modified to reduce the risk of this complication.

**HISTORY**
- Fatigue
- Bleeding
- Easy bruising

**PHYSICAL**
- Dermatologic exam (pallor, petechiae, purpura)

**SCREENING**
- CBC/differential

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

### SECTION 37 REFERENCES


RADIATION

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.
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

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<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>38</td>
<td>All Radiation Fields (Including TBI)</td>
<td>Secondary benign or malignant neoplasm Occurring in or near radiation field</td>
<td>Host Factors Cancer predisposing mutation (e.g., p53, RB1, NF1) Younger age at treatment</td>
<td>Treatment Factors Orthovoltage radiation (commonly used before 1970) due to delivery of greater dose to skin and bones</td>
<td>PHYSICAL Inspection and palpation of skin and soft tissues in irradiated field(s) Yearly</td>
<td>Health Links Reducing the Risk of Second Cancers</td>
</tr>
</tbody>
</table>

#### 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
- Patients with bilateral or familial retinoblastoma (implying a germline mutation) are at increased risk for developing second malignant neoplasms

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

### SYSTEM = SMN

#### Score = 1

---

### SECTION 38 REFERENCES


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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.
### RADIATION

<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>39</td>
<td>All Radiation Fields (Including TBI)</td>
<td>Dysplastic nevi; Skin cancer Basal cell carcinoma Squamous cell carcinoma Melanoma</td>
<td>Host Factors Gorlin’s syndrome (nevoid basal cell carcinoma syndrome) Health Behaviors Sun exposure Tanning booths</td>
<td>Treatment Factors Orthovoltage radiation (commonly used before 1970) due to delivery of greater dose to skin and bones</td>
<td>HISTORY Skin lesions Changing moles (asymmetry, bleeding, increasing size, indistinct borders) Yearly</td>
<td>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</td>
</tr>
</tbody>
</table>

- 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

### RADIATION

#### Sec 40

<table>
<thead>
<tr>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling</th>
<th>Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Radiation Fields (Except TBI)</td>
<td>Dermatologic changes Fibrosis Telangiectasias Permanent alopecia Altered skin pigmentation</td>
<td>Host Factors Younger age at treatment</td>
<td>Treatment Factors Total radiation dose ≥ 40 Gy Large dose fractions (e.g. ≥ 2 Gy per fraction) Radiation dose ≥ 50 Gy Orthovoltage radiation (commonly used before 1970) due to delivery of greater dose to skin and bones</td>
<td>Physical Dermatologic exam of irradiated fields Yearly</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- 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

### RADIATION

<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling Further Considerations</th>
</tr>
</thead>
</table>
| 41    | All Radiation Fields (Except TBI) | Bone malignancies | Host Factors  
Adolescent at treatment  
Cancer-predisposing mutation  
(e.g., p53, RB1, NF1) | 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 |
|       |                      |                        | Treatment Factors  
Higher radiation dose  
Combined with alkylating agents |                          | PHYSICAL  
Palpation of bones in irradiated field | Yearly |

- 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**

## RADIATION

<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>42</td>
<td>Cranial Orbital/Eye Ear/Infratemporal Nasopharyngeal Waldeyer’s Ring TBI</td>
<td>Brain tumor (benign or malignant)</td>
<td>Host Factors</td>
<td>Host Factors</td>
<td>HISTORY</td>
<td>Considerations for Further Testing and Intervention</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Younger age at treatment Neurofibromatosis</td>
<td>Age &lt; 6 years at time of treatment Ataxia telangiectasia</td>
<td>Headaches Vomiting Cognitive, motor or sensory deficits Seizures and other neurologic symptoms</td>
<td>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.</td>
</tr>
</tbody>
</table>

### POTENTIAL IMPACT TO BRAIN/CRANIUM

<table>
<thead>
<tr>
<th>HISTORY</th>
<th>PHYSICAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Headaches Vomiting Cognitive, motor or sensory deficits Seizures and other neurologic symptoms</td>
<td>Neurologic exam Yearly</td>
</tr>
</tbody>
</table>

### SYSTEM = SMN

| SYSTEM = SMN | SCORE = 1 |

### SECTION 42 REFERENCES


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

#### Sec Therapeutic Potential Risk Highest Periodic Health Counseling

<table>
<thead>
<tr>
<th>#</th>
<th>Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>43</td>
<td>Cranial Ear/Infratemporal TBI</td>
<td>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</td>
<td>Host Factors Younger age at treatment Primary CNS tumor CNS leukemia/lymphoma Relapsed leukemia/lymphoma treated with CNS-directed therapy Head/neck tumors with brain in radiation field</td>
<td>Host Factors Age &lt; 3 years at time of treatment Female sex Supratentorial tumor Premorbid or family history of learning or attention problems</td>
<td>History Educational and/or vocational progress Yearly</td>
<td></td>
</tr>
</tbody>
</table>

#### Info Link: Neurocognitive deficits in survivors of leukemia and lymphoma are more frequently related to information processing (e.g., learning disability). Neurocognitive deficits in brain tumor survivors treated with higher doses of cranial radiation are more global (significant decline in IQ). Extent of deficit depends on age at treatment, intensity of treatment, and time since treatment. Note: New deficits may emerge over time.

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

<table>
<thead>
<tr>
<th>HISTORY</th>
<th>SCREENING</th>
<th>Health Links Educational Issues</th>
</tr>
</thead>
<tbody>
<tr>
<td>Educational and/or vocational progress Yearly</td>
<td>Referral for formal neuropsychological evaluation Baseline at entry into long-term follow-up, then periodically as clinically indicated for patients with evidence of impaired educational or vocational progress.</td>
<td>Considerations for Further Testing and Intervention Formal neuropsychological evaluation to include tests of processing speed, computer-based attention, visual motor integration, memory, comprehension of verbal instructions, verbal fluency, executive function and planning. Refer patients with neurocognitive deficits to school liaison in community or cancer center (psychologist, social worker, school counselor) to facilitate acquisition of educational resources and/or social skills training. Consider use of psychotropic medication (e.g., stimulants) or evidence-based rehabilitation training. Caution - lower starting dose and assessment of increased sensitivity when initiating therapy is recommended. Refer to community services for vocational rehabilitation or for services for developmentally disabled.</td>
</tr>
</tbody>
</table>

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

*See “Patient-Specific Guideline Identification Tool” in Appendix I to determine specific screening guidelines by section number for individual patients.*
<table>
<thead>
<tr>
<th>Section</th>
<th>Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Evaluation</th>
<th>Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>43</td>
<td></td>
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</tr>
</tbody>
</table>

**SECTION 43 REFERENCES**


### RADIATION

**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

<table>
<thead>
<tr>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Evaluation</th>
<th>Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Host Factors</td>
<td>Radiation dose ≥ 24 Gy</td>
<td>Periodic</td>
<td>History</td>
</tr>
<tr>
<td>Treatment Factors</td>
<td>Fraction dose ≥ 3 Gy</td>
<td></td>
<td>Cognitive, motor, and/or sensory deficits</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Seizures</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Other neurologic symptoms</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Yearly</td>
</tr>
</tbody>
</table>

**SYSTEM = CNS**

**SCORE = 1**

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

#### 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.

#### SECTION 44 REFERENCES


### RADIATION

<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>45</td>
<td>≥ 18 Gy to: Cranial Orbital/Eye Ear/Infratemporal Nasopharyngeal Waldeyer’s Ring TBI*</td>
<td>Cerebrovascular complications Stroke Moyamoya Occlusive cerebral vasculopathy</td>
<td>Host Factors Down syndrome</td>
<td>Host Factors Parasellar tumor</td>
<td>HISTORY Hemiparesis</td>
<td>Considerations for Further Testing and Intervention Brain MRI with diffusion-weighted imaging with MR angiography as clinically indicated. Neurology/neurosurgery consultation and follow-up. Physical and occupational therapy as clinically indicated. Note: Revascularization procedures are likely helpful for moyamoya. Aspirin prophylaxis has not yet been shown to be beneficial for moyamoya or occlusive cerebral vasculopathy.</td>
</tr>
</tbody>
</table>

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

**Host Factors**
- Down syndrome

**Treatment Factors**
- Suprasellar radiation

**Medical Conditions**
- Sickle cell disease
- Neurofibromatosis

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

**HISTORY**
- Hemiparesis
- Hemiplegia
- Weakness
- Aphasia

**PHYSICAL**
- Neurologic exam
  - Yearly

**SYSTEM = CNS**

**SCORE = 1**

### SECTION 45 REFERENCES


### RADIATION

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

### SECTION 46 REFERENCES


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

<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
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<th>Periodic Evaluation</th>
<th>Health Counseling Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>47</td>
<td>Cranial Orbital/Eye Ear/Infratemporal Nasopharyngeal Waldeyer’s Ring</td>
<td>Chronic sinusitis</td>
<td>Treatment Factors Radiation dose to sinuses ≥ 30 Gy Radiomimetic chemotherapy (e.g., doxorubicin, dactinomycin)</td>
<td>Medical Conditions Atopic history Hypogammaglobulinemia</td>
<td>HISTORY Rhinorrhea Postnasal discharge Yearly</td>
<td>Considerations for Further Testing and Intervention CT scan of sinuses as clinically indicated. Otolaryngology consultation as clinically indicated.</td>
</tr>
</tbody>
</table>

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

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### SECTION 47 REFERENCES


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

<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Host Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling Further Considerations</th>
</tr>
</thead>
</table>
| 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(M²)  
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  
Now 2006;149(4):518-525.  

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

<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>49</td>
<td>Cranial Orbital/Eye Ear/Infratemporal Nasopharyngeal Waldeyer’s Ring TBI</td>
<td>Metabolic syndrome</td>
<td>Treatment Factors Surgery in suprasellar region Prolonged corticosteroid therapy (e.g., for chronic GVHD) TBI</td>
<td>Host Factors Obesity</td>
<td>PHYSICAL Height Weight BMI Blood pressure Yearly</td>
<td>Health Links Diet and Physical Activity Counseling Considerations for Further Testing and Intervention</td>
</tr>
</tbody>
</table>

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

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

**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.

**Medical Conditions**
- Growth hormone deficiency
- Hypogonadism

**Treatment Factors**
- Cranial radiation dose ≥ 18 Gy

**Screening**
- Fasting blood glucose
- Fasting lipid profile

*Every 2 years. More frequently if indicated based on patient evaluation.*

**Score**: 2A

- **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

## RADIATION

<table>
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<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>50</td>
<td>Cranial Orbital/Eye Ear/Infratemporal Nasopharyngeal Waldeyer’s Ring TBI</td>
<td>Growth hormone deficiency</td>
<td>Host Factors Younger age at treatment</td>
<td>Treatment Factors Radiation dose ≥ 18 Gy Pretransplant cranial radiation TBI given in single fraction</td>
<td>HISTORY Assessment of nutritional status Every 6 months until growth is completed, then yearly.</td>
<td>Health Links Growth Hormone Deficiency See also: Hypopituitarism</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>PHYSICAL Tanner staging Every 6 months until sexually mature</td>
<td>Resources <a href="http://www.magicfoundation.org">www.magicfoundation.org</a></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Height Weight BMI Every 6 months until growth is completed, then yearly.</td>
<td>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 &lt; 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.</td>
</tr>
</tbody>
</table>

### Information Links

- Growth charts available online at [www.cdc.gov/growthcharts](http://www.cdc.gov/growthcharts)

### System Score

**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.
SECTION 50 REFERENCES


<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>51</td>
<td>Cranial</td>
<td>Precocious puberty</td>
<td>Host Factors</td>
<td>PHYSICAL</td>
<td>Health Links</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Orbital/Eye</td>
<td></td>
<td>Younger age at treatment</td>
<td>Height</td>
<td>Precocious Puberty</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Ear/Infratemporal</td>
<td></td>
<td>Treatment Factors</td>
<td>Weight</td>
<td>Resources</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Nasopharyngeal</td>
<td></td>
<td>Radiation doses ≥ 18 Gy</td>
<td>Tanner staging</td>
<td><a href="http://www.magicfoundation.org">www.magicfoundation.org</a></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Waldeyer's Ring</td>
<td></td>
<td></td>
<td>Testicular volume by Prader orchidometry</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Yearly until sexually mature</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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

| 51   | Cranial              | Precocious puberty     | Host Factors | PHYSICAL             | Health Links         |
|      | Orbital/Eye          |                        | Female sex   | Height               | Precocious Puberty   |
|      | Ear/Infratemporal    |                        | Younger age at treatment | Weight               | Resources            |
|      | Nasopharyngeal       |                        | Treatment Factors | Tanner staging       | www.magicfoundation.org |
|      | Waldeyer's Ring      |                        | Radiation doses ≥ 18 Gy | Yearly until sexually mature |                          |

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

**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

**Considerations for Further Testing and Intervention**

**System** = Endocrine/Metabolic  
**Score** = 1
### RADIATION

#### POTENTIAL IMPACT TO NEUROENDOCRINE AXIS (cont)

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

#### SECTION 51 REFERENCES

### RADIATION

<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>52 (Male)</td>
<td>≥ 40 Gy to: Cranial Orbital/Eye Ear/Infratemporal Nasopharyngeal Waldeyer’s Ring TBI*</td>
<td>Hyperprolactinemia</td>
<td>Treatment Factors: Higher radiation dose Surgery or tumor in hypothalamic area</td>
<td>Treatment Factors: Radiation dose ≥ 50 Gy</td>
<td>HISTORY: Decreased libido Galactorrhea Yearly</td>
<td>SCREENING: Prolactin level In patients with galactorrhea or decreased libido</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• 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.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>52 (Female)</td>
<td>≥ 40 Gy to: Cranial Orbital/Eye Ear/Infratemporal Nasopharyngeal Waldeyer’s Ring TBI*</td>
<td>Hyperprolactinemia</td>
<td>Treatment Factors: Higher radiation dose Surgery or tumor in hypothalamic area</td>
<td>Treatment Factors: Radiation dose ≥ 50 Gy</td>
<td>HISTORY: Galactorrhea Menstrual history Yearly</td>
<td>SCREENING: Prolactin level In patients with galactorrhea or amenorrhea</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• 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.</td>
<td></td>
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</table>

### SECTION 52 REFERENCES

### RADIATION

#### Section 53

<table>
<thead>
<tr>
<th>Agent(s)</th>
<th>Late Effects</th>
<th>Risk Factors</th>
<th>Evaluation</th>
<th>Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥ 40 Gy to:</td>
<td>Central hypothyroidism</td>
<td>Treatment Factors: Higher radiation dose</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cranial</td>
<td>Info Link: Central hypothyroidism includes thyroid-releasing and thyroid-stimulating hormone deficiency</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Orbital/Eye</td>
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</tr>
<tr>
<td>Ear/Infratemporal</td>
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</tr>
<tr>
<td>Nasopharyngeal</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Waldeyer’s Ring</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TBI*</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>*TBI included for dose calculation purposes only; this section not applicable to patients who received TBI alone.</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

- **This section is only applicable to patients who:**
  - 1) Received radiation to any of the specified fields at ≥ 40 Gy
  - 2) Received a combination of radiation to any of the specified fields 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.

### POTENTIAL IMPACT TO NEUROENDOCRINE AXIS (cont)

#### History

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

#### Screening

- TSH
- Free T4

Yearly; Consider more frequent screening during periods of rapid growth.

#### Considerations for Further Testing and Intervention

- Consider TSH surge testing.
- Endocrine consultation for thyroid hormone replacement.

#### Health Counseling

- **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.

SECTION 53 REFERENCES


<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>54</td>
<td>≥ 40 Gy to: Cranial Orbital/Eye Ear/Infratemporal Nasopharyngeal Waldeyer's Ring TBI*</td>
<td>Gonadotropin deficiency</td>
<td>Treatment Factors Higher radiation dose</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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

- This section is only applicable to patients who:
  1) Received radiation to any of the specified fields at ≥ 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)**

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

**PHYSICAL**
- Tanner staging
- Testicular volume by Prader orchidiometry
- 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.

**System = Reproductive (male)**

**Score = 1**
<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>54</td>
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<tr>
<td></td>
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<td></td>
<td>Ear/Infratemporal</td>
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<td></td>
<td>Nasopharyngeal</td>
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<td></td>
</tr>
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<td>Waldeyer's Ring</td>
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<td>TBI*</td>
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</tr>
</tbody>
</table>

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.

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

- Health Links
  - Female Health Issues
  - See also: Hypopituitarism

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

- Considerations for Further Testing and Intervention
  - Refer to endocrinologist for delayed puberty or persistently abnormal hormone levels. Hormonal replacement therapy for hypogonadal patients. Reproductive endocrinology referral for infertility evaluation and consultation regarding assisted reproductive technologies. Consider bone density testing in patients who are gonadotropin deficient.
## Section 54 References


### RADIATION

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<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling Further Considerations</th>
</tr>
</thead>
</table>
| 55    | ≥ 40 Gy to: Cranial Orbital/Eye Ear/Infratemporal Nasopharyngeal Waldeyer’s Ring TBI* | 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 | 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.  

SCREENING  
8:00 a.m. serum cortisol  
Yearly for at least 15 years after treatment and as clinically indicated.  

SYSTEM = Endocrine/Metabolic  
SCORE = 1 |

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

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

See dose calculation rules on page 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.

### POTENTIAL IMPACT TO NEUROENDOCRINE AXIS (cont)

**SECTION 55 REFERENCES**


### Potential Impact to Eye

#### Section 56

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<th>Risk Factors</th>
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</thead>
<tbody>
<tr>
<td>56</td>
<td>Cranial Orbital/Eye TBI</td>
<td>Cataracts</td>
<td>Treatment Factors</td>
<td>Treatment Factors</td>
<td>Evaluation</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Radiation dose $\geq 10$ Gy</td>
<td>Radiation dose $\geq 15$ Gy</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>TBI $\geq 2$ Gy in single fraction</td>
<td>Fraction dose $\geq 2$ Gy</td>
<td></td>
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<tr>
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<td></td>
<td></td>
<td>TBI $\geq 5$ Gy fractionated</td>
<td>TBI $\geq 5$ Gy in single fraction</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Radiation combined with</td>
<td>Radiation combined with</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>- Corticosteroids</td>
<td>- Busulfan</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>- Longer interval since treatment</td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

**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.

**Screening**

- Evaluation by ophthalmologist

- Yearly for patients with ocular tumors [regardless of radiation dose] and for those who received TBI or $\geq 30$ Gy cranial/orbital/eye radiation; Every 3 years for patients without ocular tumors who received <30 Gy.

**Physical**

- Eye exam (visual acuity, funduscopic exam to evaluate for lens opacity)

- Yearly

**System** = Ocular

**Score** = 1

---

**SECTION 56 REFERENCES**


---

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

<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>57</td>
<td>≥ 30 Gy to: Cranial Orbital/Eye TBI*</td>
<td>Ocular toxicity Orbital hypoplasia Lacrimal duct atrophy Xerophthalmia (keratoconjunctivitis sicca) Keratitis Telangiectasias Retinopathy Optic chiasm neuropathy Enophthalmos Chronic painful eye Maculopathy Papillopathy Glaucoma</td>
<td>Treatment Factors Higher radiation dose Higher daily fraction dose Radiomimetic chemotherapy (e.g., doxorubicin, dactinomycin) [problems related to tearing]</td>
<td>Host Factors Chronic GVHD (xerophtalmia only)</td>
<td>History Visual changes (decreased acuity, halos, diplopia) Dry eye Persistent eye irritation Excessive tearing Light sensitivity Poor night vision Painful eye Yearly</td>
<td>SYSTEM = Ocular SCORE = 1</td>
</tr>
</tbody>
</table>

- **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

- **Systems**
  - Ocular
  - Score = 1

**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.

### POTENTIAL IMPACT TO EYE (cont)

**SECTION 57 REFERENCES**


### Radiation Therapy Late Effects - Ear

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<tr>
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<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
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<th>Periodic Evaluation</th>
<th>Health Counseling Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>58</td>
<td>≥ 30 Gy to: Cranial Ear/Infratemporal Nasopharyngeal Waldeyer’s Ring TBI*</td>
<td>Otoxicity Tympanosclerosis Otosclerosis Eustachian tube dysfunction Conductive hearing loss</td>
<td>Host Factors Younger age at treatment Treatment Factors Higher radiation dose Medical Conditions Chronic otitis Chronic cerumen impaction</td>
<td>Treatment Factors Dose ≥ 50 Gy</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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

- **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 |

**Host Factors**
- Younger age at treatment
- CNS tumor
- CSF shunting

**Treatment Factors**
- Higher radiation dose;
- Conventional (non-conformal) radiation

**Medical Conditions**
- Chronic otitis
- Chronic cerumen impaction

**Treatment Factors**
- Radiation administered prior to platinum chemotherapy
- Combined with other ototoxic agents such as:
  - Cisplatin
  - Carboplatin in myeloablative doses
  - Aminoglycosides

**Periodic Evaluation**
- 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 uncevaluable, 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.

**System = Auditory**
**Score = 1**

---

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

See dose calculation rules on page 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 EAR (cont)

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<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
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<th>Further Considerations</th>
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<tr>
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</tr>
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</table>

### SECTION 58 REFERENCES


## Radiation

<table>
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<tr>
<th>Section</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>59</td>
<td>Cranial Nasopharyngeal Oropharyngeal Waldeyer's Ring Spine (cervical, whole) Cervical (neck) Supravacularial Mini-Mantle Mantle Extended Mantle TLI STLI</td>
<td>Xerostomia Salivary gland dysfunction</td>
<td>Treatment Factors Head and neck radiation involving the parotid gland Higher radiation doses Radiomimetic chemotherapy (e.g., doxorubicin, dactinomycin)</td>
<td>Treatment Factors Salivary gland dose ≥ 30 Gy Medical Conditions Chronic GVHD</td>
<td>HISTORY Xerostomia Yearly</td>
<td><strong>SYSTEM = Dental</strong> <strong>SCORE = 1</strong></td>
</tr>
</tbody>
</table>

**Screening**
- Dental exam and cleaning Every 6 months

**Considerations for Further Testing and Intervention**
- Supportive care with saliva substitutes, moistening agents, and sialogogues (pilocarpine); Regular dental care including fluoride applications.

---

### Section 59 References


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

<table>
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<th>Potent Late Effects</th>
<th>Risk Factors</th>
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<th>Periodic Evaluation</th>
<th>Health Counseling Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>60</td>
<td>Cranial Nasopharyngeal Oropharyngeal Waldeyer’s Ring Spine (cervical, whole) Supraventricular Mini-Mantle Mantle Extended Mantle TLI STLI TBI</td>
<td>Dental abnormalities Tooth/root agenesis Microdontia Root thinning/shortening Enamel dysplasia Periodontal disease Dental caries Malocclusion Temporomandibular joint dysfunction</td>
<td>Host Factors Younger age at treatment Gorlin’s syndrome (nevoid basal cell carcinoma syndrome)</td>
<td>Host Factors Age &lt; 5 years at time of treatment Treatment Factors Dose ≥ 10 Gy</td>
<td>PHYSICAL Oral exam Yearly</td>
<td>SYSTEM = Dental SCORE = 1</td>
</tr>
</tbody>
</table>

**Host Factors**
- Younger age at treatment
- Gorlin’s syndrome (nevoid basal cell carcinoma syndrome)

**Treatment Factors**
- Dose ≥ 10 Gy

**Host Factors**
- Age < 5 years at time of treatment

**Treatment Factors**
- Dose ≥ 10 Gy

**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.

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**SECTION 60 REFERENCES**


### RADIATION

#### Potential Impact to Oral Cavity (cont)

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<th>Health Counseling Further Considerations</th>
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</thead>
<tbody>
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<td>61</td>
<td>≥ 40 Gy to: Cranial Nasopharyngeal Oropharyngeal Waldeyer’s Ring Spine (cervical, whole) Cervical (neck) Supraclavicular Mini-Mantle Mantle Extended Mantle TLI STL TBI*</td>
<td>Osteoradionecrosis</td>
<td>Treatment Factors Radiation dose to bone ≥ 45 Gy</td>
<td>Treatment Factors Radiation dose to bone ≥ 50 Gy</td>
<td>HISTORY Impaired or delayed healing following dental work Persistent jaw pain or swelling Trismus As clinically indicated</td>
<td></td>
</tr>
</tbody>
</table>

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

- See dose calculation rules on page 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.

**Health Links**

- Osteoradionecrosis

**Considerations for Further Testing and Intervention**

Imaging studies (x-ray, CT scan and/or MRI) may assist in making diagnosis. Surgical biopsy may be needed to confirm diagnosis. Consider hyperbaric oxygen treatments.

**SYSTEM = Dental**

**SCORE = 1**

---

### SECTION 61 REFERENCES

RADIATION

POTENTIAL IMPACT TO NECK/THYROID

| Therapeutic Agent(s) | Late Effects | Risk Factors | Highest Risk Factors | Periodic Evaluation | Health Counseling
<table>
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</thead>
<tbody>
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<td>Cranial</td>
<td>Thyroid nodules</td>
<td>Host Factors</td>
<td>Treatment Factors</td>
<td>PHYSICAL</td>
<td>System = SNM</td>
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<tr>
<td>Nasopharyngeal</td>
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<td>Younger age at treatment</td>
<td>Radiation dose ≥ 25 Gy</td>
<td>Thyroid exam</td>
<td>Score = 1</td>
</tr>
<tr>
<td>Oropharyngeal</td>
<td></td>
<td>Female sex</td>
<td>Yearly</td>
<td>Endocrine and/or surgical consultation for diagnostic biopsy or thyroidectomy.</td>
<td></td>
</tr>
<tr>
<td>Waldeyer's Ring</td>
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<td>Treatment Factors</td>
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<td>Spine (cervical, whole)</td>
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<td>Higher radiation dose</td>
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<tr>
<td>Cervical (neck)</td>
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<td>Thyroid gland directly in radiation field</td>
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<td>Supraclavicular</td>
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<tr>
<td>Chest (thorax)</td>
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<tr>
<td>Whole lung</td>
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<tr>
<td>Mini-mantle</td>
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<td>Mantle</td>
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<td>Extended Mantle</td>
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<tr>
<td>TLI</td>
<td></td>
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<tr>
<td>TBI</td>
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- See “Patient-Specific Guideline Identification Tool” in Appendix I to determine specific screening guidelines by section number for individual patients.

SECTION 62 REFERENCES


### RADIATION

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<tr>
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<td>Cranial&lt;br&gt;Nasopharyngeal&lt;br&gt;Oropharyngeal&lt;br&gt;Waldeyer’s Ring&lt;br&gt;Spine (cervical, whole)&lt;br&gt;Cervical (neck)&lt;br&gt;Supraventricular&lt;br&gt;Chest (thorax)&lt;br&gt;Whole lung&lt;br&gt; Mediastinal&lt;br&gt;Mini-Mantle&lt;br&gt;Mantle&lt;br&gt;Extended Mantle&lt;br&gt;TLI&lt;br&gt;STLI&lt;br&gt;TBI</td>
<td>Thyroid cancer</td>
<td>Host Factors&lt;br&gt;Younger age at treatment&lt;br&gt;Female sex</td>
<td>Treatment Factors&lt;br&gt;≥ 5 years after irradiation&lt;br&gt;Thyroid gland directly in radiation field&lt;br&gt;TBI</td>
<td>Thyroid exam&lt;br&gt;Yearly</td>
<td>Thyroid cancer&lt;br&gt;Considerations for Further Testing and Intervention&lt;br&gt;Ultrasound and FNA for evaluation of palpable nodule(s). Surgical consultation for resection. Nuclear medicine consultation for ablation of residual disease. Endocrine consultation for postoperative medical management.</td>
</tr>
</tbody>
</table>

**System = SMN**

**Score = 1**

---

### SECTION 63 REFERENCES


---

*See “Patient-Specific Guideline Identification Tool” in Appendix I to determine specific screening guidelines by section number for individual patients.*
### Potential Impact to Neck/Thyroid (cont)

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<th>Periodic Evaluation</th>
<th>Health Counseling Further Considerations</th>
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</thead>
<tbody>
<tr>
<td>64</td>
<td>Cranial</td>
<td></td>
<td>Host Factors</td>
<td>Treatment Factors</td>
<td>History</td>
<td>Health Links</td>
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<td>Nasopharyngeal</td>
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<td>Female sex</td>
<td>Radiation dose ≥ 10 Gy</td>
<td>Fatigue</td>
<td>Thyroid Problems</td>
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<tr>
<td></td>
<td>Oropharyngeal</td>
<td></td>
<td></td>
<td>Thyroid gland directly in radiation field</td>
<td>Weight gain</td>
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<tr>
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<td>Waldeyer’s Ring</td>
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<td></td>
<td>TBI</td>
<td>Constipation</td>
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<td></td>
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<td>Dry skin</td>
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<tr>
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<td>Supraventricular</td>
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<td></td>
<td></td>
<td>Brittle hair</td>
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</tr>
<tr>
<td></td>
<td>Chest (thorax)</td>
<td></td>
<td></td>
<td></td>
<td>Depressed mood</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Whole lung</td>
<td></td>
<td></td>
<td></td>
<td>Yearly: Consider more frequent screening during periods of rapid growth.</td>
<td>Counseling</td>
</tr>
<tr>
<td></td>
<td>Mediastinal</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Counsel at-risk females of childbearing potential to have their thyroid levels checked prior to attempting pregnancy and periodically throughout pregnancy.</td>
</tr>
<tr>
<td></td>
<td>Mini-Mantle</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Considerations for Further Testing and Intervention</td>
</tr>
<tr>
<td></td>
<td>Mantle</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Endocrine consultation for medical management.</td>
</tr>
<tr>
<td></td>
<td>Extended Mantle</td>
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<td></td>
<td>TLI</td>
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<td></td>
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<td>SYSTEM = Endocrine/Metabolic</td>
</tr>
<tr>
<td></td>
<td>STLI</td>
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<td></td>
<td>SCORE = 1</td>
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<tr>
<td></td>
<td>TBI</td>
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</table>

**SECTION 64 REFERENCES**


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

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<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling Further Considerations</th>
</tr>
</thead>
</table>

- 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.

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

#### HISTORY
- Heat intolerance
- Tachycardia
- Palpitations
- Weight loss
- Emotional lability
- Muscular weakness
- Hyperphagia
  - Yearly

#### PHYSICAL
- Eyes
- Skin
- Thyroid
- Cardiac
- Neurologic
  - Yearly

#### SCREENING
- TSH
  - Yearly
- Free T4
  - Yearly

### SECTION 65 REFERENCES


RADIATION

### 66

<table>
<thead>
<tr>
<th><strong>Therapeutic Agent(s)</strong></th>
<th><strong>Potential Late Effects</strong></th>
<th><strong>Risk Factors</strong></th>
<th><strong>Highest Risk Factors</strong></th>
<th><strong>Periodic Evaluation</strong></th>
<th><strong>Health Counseling Further Considerations</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>≥ 40 Gy to:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td><strong>CAROTID ARTERY DISEASE</strong></td>
</tr>
<tr>
<td>Cranial</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td><strong>HISTORY</strong></td>
</tr>
<tr>
<td>Nasopharyngeal</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Memory impairment Yearly</td>
</tr>
<tr>
<td>Oropharyngeal</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td><strong>PHYSICAL</strong></td>
</tr>
<tr>
<td>Waldeyer's Ring</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Diminished carotid pulses Yearly</td>
</tr>
<tr>
<td>Spine (cervical, whole)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Carotid bruits Yearly</td>
</tr>
<tr>
<td>Cervical (neck)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Abnormal neurologic exam (compromise of blood flow to brain) Yearly</td>
</tr>
<tr>
<td>Supraclavicular</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td><strong>SYSTEM = Cardiovascular</strong></td>
</tr>
<tr>
<td>Chest (thorax)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td><strong>SCORE = 2A</strong></td>
</tr>
<tr>
<td>Whole lung</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td><strong>Considerations for Further Testing and Intervention</strong></td>
</tr>
<tr>
<td>Mediastinal</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Doppler ultrasound of carotid vessels as clinically indicated.</td>
</tr>
<tr>
<td>Mini-Mantle</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>MRI with diffusion-weighted imaging with MR angiography and vascular 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.</td>
</tr>
<tr>
<td>Mantle</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td><strong>SYSTEM = Cardiovascular</strong></td>
</tr>
<tr>
<td>Extended Mantle</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td><strong>SCORE = 2A</strong></td>
</tr>
<tr>
<td>TLI</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td><strong>Considerations for Further Testing and Intervention</strong></td>
</tr>
<tr>
<td>STLI</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Doppler ultrasound of carotid vessels as clinically indicated.</td>
</tr>
<tr>
<td>TBI*</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>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.</td>
</tr>
</tbody>
</table>

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

See dose calculation rules on page 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**


<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>67</td>
<td>≥ 40 Gy to: Spine (cervical, whole) Cervical (neck) Supraclavicular Chest (thorax) Whole lung Mediastinal Mini-Mantle Mantle Extended Mantle TLI STL TBI*</td>
<td>Subclavian artery disease</td>
<td>- Diminished brachial and radial pulses - Pallor of upper extremities - Coolness of skin - Unequal blood pressure</td>
<td>Yearly</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- This section is only applicable to patients who:
  1) Received radiation to any of the specified fields at ≥ 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.

**SYSTEM = Cardiovascular**

**SCORE = 2A**

---

**SECTION 67 REFERENCES**


RADIATION

<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>68</td>
<td>≥ 20 Gy to: Chest (thorax) Whole lung Mediastinal Axilla Mini-Mantle Mantle Extended Mantle TLI STLI TBI*</td>
<td>Breast cancer</td>
<td>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</td>
<td>Host Factors Female gender</td>
<td>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.</td>
<td>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.</td>
</tr>
</tbody>
</table>

*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.

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

## RADIATION

<table>
<thead>
<tr>
<th>Section #</th>
<th>Therapeutic Agent(s) (Female)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>69</td>
<td>Chest (thorax)</td>
<td>Breast tissue hypoplasia</td>
<td>Host Factors</td>
<td>Treatment Factors ≥ 20 Gy to prepubertal breast bud may ablate development</td>
<td>PHYSICAL Breast exam Yearly</td>
<td>Considerations for Further Testing and Intervention Surgical consultation for breast reconstruction after completion of growth.</td>
</tr>
<tr>
<td></td>
<td>Whole lung</td>
<td></td>
<td>Prepubertal at time of breast irradiation</td>
<td></td>
<td></td>
<td>SYSTEM = Reproductive (female) SCORE = 1</td>
</tr>
<tr>
<td></td>
<td>Mediastinal</td>
<td></td>
<td>Treatment Factors Radiation dose ≥ 10 Gy to prepubertal breast bud may cause failure of development (hypoplasia)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Axilla</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Mini-Mantle</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Mantle</td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Extended Mantle</td>
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<tr>
<td></td>
<td>TLI</td>
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<td></td>
</tr>
<tr>
<td></td>
<td>STLI</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>TBI</td>
<td></td>
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</tr>
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</table>

### SECTION 69 REFERENCES


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

<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>70</td>
<td>Chest (thorax)</td>
<td></td>
<td>Host Factors</td>
<td>Treatment Factors</td>
<td>HISTORY</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Whole lung</td>
<td></td>
<td>Younger age at irradiation</td>
<td>Radiation dose ≥ 15 Gy</td>
<td>Cough</td>
<td>Health Links</td>
</tr>
<tr>
<td></td>
<td>Mediastinal Axilla</td>
<td></td>
<td>Treatment combined with TBI</td>
<td>TBI ≥ 6 Gy in single fraction</td>
<td>SOB</td>
<td>Pulmonary Health</td>
</tr>
<tr>
<td></td>
<td>Mini-Mantle</td>
<td></td>
<td>Radiation combined with:</td>
<td>TBI ≥ 12 Gy fractionated</td>
<td>DOE</td>
<td>Resources</td>
</tr>
<tr>
<td></td>
<td>Mantle</td>
<td></td>
<td>- Bleomycin</td>
<td></td>
<td>Wheezing</td>
<td>Extensive information regarding smoking cessation is available for patients on the NCI’s website: <a href="http://www.smokefree.gov">www.smokefree.gov</a></td>
</tr>
<tr>
<td></td>
<td>Extended Mantle</td>
<td></td>
<td>- Busulfan</td>
<td></td>
<td>Yearly</td>
<td>Counseling</td>
</tr>
<tr>
<td></td>
<td>TLI</td>
<td></td>
<td>- Carmustine (BCNU)</td>
<td></td>
<td></td>
<td>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.</td>
</tr>
<tr>
<td></td>
<td>STLII</td>
<td></td>
<td>- Lomustine (CCNU)</td>
<td></td>
<td></td>
<td>Considerations for Further Testing and Intervention</td>
</tr>
<tr>
<td></td>
<td>TBI</td>
<td></td>
<td>- Radiomimetic chemotherapy</td>
<td></td>
<td></td>
<td>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.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(e.g., doxorubicin, dactinomycin)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Medical Conditions</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Atopic history</td>
<td></td>
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</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Health Behaviors</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Smoking</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

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

### POTENTIAL IMPACT TO LUNGS

<table>
<thead>
<tr>
<th>SYSTEM</th>
<th>SCORE</th>
<th>HISTORY</th>
<th>PHYSICAL</th>
<th>SCREENING</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pulmonary</td>
<td>1</td>
<td>Cough</td>
<td>Pulmonary exam</td>
<td>Chest x-ray</td>
</tr>
<tr>
<td></td>
<td></td>
<td>SOB</td>
<td>Yearly</td>
<td>PFTs (including DLCO and spirometry)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>DOE</td>
<td>Yearly</td>
<td>Baseline at entry into long-term follow-up, repeat as clinically indicated in patients with abnormal results or progressive pulmonary dysfunction</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Wheezing</td>
<td>Yearly</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- **SYSTEM = Pulmonary**
- **SCORE = 1**
<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling Further Considerations</th>
</tr>
</thead>
</table>

### SECTION 70 REFERENCES


### RADIATION

<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling Further Considerations</th>
</tr>
</thead>
</table>
| 71    | Spine (thoracic, whole) | Cardiac toxicity | Host Factors | Black/ of African descent | HISTORY | **SOS**
|       | Chest (thorac)       | Congestive heart failure | Younger age at irradiation | **DOE** | **Orthopnea**
|       | Whole lung           | Cardiomyopathy          | Family history of dyslipidemia | **Orthopnea** | **Chest pain**
|       | Mediastinal          | Pericarditis            | Coronary artery disease | **Pulitations** | If Patient 25 years: Abdominal symptoms (nausea, vomiting) Yearly |
|       | Mantle                | Pericardial fibrosis    | Treatment Factors | Anteriorly-weighted radiation fields | **Info Link:** Exertional intolerance is uncommon in patients younger than 25 years. Abdominal symptoms (nausea, emesis) may be observed more frequently than exertional dyspnea or chest pain in younger patients. |
|       | Renal                 | Valvular disease        | 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 - Armascline | **Meds** | **Cardiac**
|       | Upper quadrant (right, left) Spleen (partial, entire) Flank/Hemiabdomen (right, left) Whole abdomen Inverted Y TLI STL TLI TBI | Myocardial infarction Arhythmia | Medical Conditions | Hypertension | **Physical**
|       |                      | Atherosclerotic heart disease | Health Behaviors | Smoking | **Cardiac murmur** S3, S4 Increased P2 sound Pericardial rub Rules | **Screening**
|       |                      |                          | Drug use (e.g., cocaine, diet pills, ephedra) | Isometric exercise | **Fasting glucose and lipid profile** Every 2 years; If abnormal, refer for ongoing management. |
|       |                      |                          | Febrile illness | Drug use (e.g., cocaine, diet pills, ephedra) | **EKG** (include evaluation of QTc interval) Baseline at entry into long-term follow-up, repeat as clinically indicated. |
|       |                      |                          | Health Behaviors | Smoking | **ECHO** Baseline at entry into long-term follow-up, then periodically based on age at treatment, radiation dose, and cumulative anthracycline dose [see table] |
|       |                      |                          | Drug use (e.g., cocaine, diet pills, ephedra) | Isometric exercise | **SYSTEM** = Cardiovascular **SCORE** = 1 |
|       |                      |                          | Drug use (e.g., cocaine, diet pills, ephedra) | Isometric exercise | **Considerations for Further Testing and Intervention** Cardiology consultation for patients with subclinical abnormalities on screening evaluations or with left ventricular dysfunction, dyssrhythmia 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. |

**RECOMMENDED FREQUENCY OF ECHOCARDIOGRAM**

<table>
<thead>
<tr>
<th>Age at Treatment*</th>
<th>Radiation Dose</th>
<th>Anthracycline Dose†</th>
<th>Recommended Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 5 years old</td>
<td>Any</td>
<td>None</td>
<td>Every 2 years</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Any</td>
<td>Every year</td>
</tr>
<tr>
<td>≥ 5 years old</td>
<td>&lt;30 Gy‡</td>
<td>None</td>
<td>Every 5 years</td>
</tr>
<tr>
<td></td>
<td>≥30 Gy‡</td>
<td>None</td>
<td>Every 2 years</td>
</tr>
<tr>
<td></td>
<td>Any</td>
<td>&lt; 300 mg/m²</td>
<td>Every 2 years</td>
</tr>
<tr>
<td></td>
<td></td>
<td>≥ 300 mg/m²</td>
<td>Every year</td>
</tr>
<tr>
<td>Any age with serial decrease in function</td>
<td>Any</td>
<td>Any</td>
<td>Every year</td>
</tr>
</tbody>
</table>

*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.

- See “Info Link: Exertional intolerance is uncommon in patients younger than 25 years. Abdominal symptoms (nausea, emesis) may be observed more frequently than exertional dyspnea or chest pain in younger patients.”
<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Host Factors</td>
<td>Host Factors</td>
<td></td>
<td>Health Links</td>
</tr>
<tr>
<td>71</td>
<td>Spine (thoracic, whole)</td>
<td>Cardiac toxicity</td>
<td>Younger age at irradiation</td>
<td>Female sex</td>
<td></td>
<td>Heart Health</td>
</tr>
<tr>
<td></td>
<td>Chest (thorax)</td>
<td>Congestive heart failure</td>
<td>Family history of dyslipidemia</td>
<td>Black/ of African descent</td>
<td></td>
<td>Diet and Physical Activity</td>
</tr>
<tr>
<td></td>
<td>Whole lung</td>
<td>Cardiomyopathy</td>
<td>Coronary artery disease</td>
<td></td>
<td></td>
<td>Dental Health</td>
</tr>
<tr>
<td></td>
<td>Mediastinal</td>
<td>Pericarditis</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Manto</td>
<td>Pericardial fibrosis</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Extended Mantle</td>
<td>Valvular disease</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Renal</td>
<td>Myocardial infarction</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Upper quadrant (right, left)</td>
<td>Atherosclerotic heart disease</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Spleen (partial, entire)</td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Paraaortic Flank/Hemiabdomen (right, left)</td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td></td>
<td>Whole abdomen</td>
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<tr>
<td></td>
<td>Inverted Y</td>
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<tr>
<td></td>
<td>TLI</td>
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</tr>
<tr>
<td></td>
<td>STLI</td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>TBI</td>
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</tr>
</tbody>
</table>

### Cardiac Late Effects

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

### Risk Factors

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

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

### 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)

### Periodic Evaluation

- **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.**

### Health Counseling Further Considerations

- **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.

### 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.
### SECTION 71 REFERENCES


<table>
<thead>
<tr>
<th>Radiation</th>
<th>Potential Impact to Spleen</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sec #</strong></td>
<td><strong>Therapeutic Agent(s)</strong></td>
</tr>
<tr>
<td>72</td>
<td>≥ 40 Gy to: Left upper quadrant Spleen (entire) Paraaortic* Left flank/hemiabdomen Whole abdomen Inverted Y* TLI STLI TBI**</td>
</tr>
<tr>
<td></td>
<td>*If spleen in field **TBI included for dose calculation purposes only; this section not applicable to patients who received TBI alone.</td>
</tr>
</tbody>
</table>

- **This section is only applicable to patients who:**
  1. Received radiation to any of the specified fields at ≥ 40 Gy
  2. Received a combination of radiation to any of the specified fields 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.

- **Health Links**
  - Splenic Precautions
  - Counseling

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

### SECTION 72 REFERENCES

### RADIATION

<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>73</td>
<td>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*</td>
<td>Esophageal stricture</td>
<td>Treatment Factors Higher radiation dose Radiomimetic chemotherapy (e.g., doxorubicin, actinomycin) Medical Conditions Gastroesophageal reflux History of Candida esophagitis</td>
<td>Treatment Factors Radiation dose ≥ 40 Gy Medical Conditions Gut GVHD</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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

### POTENTIAL IMPACT TO GI/HEPATIC SYSTEM

**HISTORY**
- Dysphagia
- Heartburn
- Yearly

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


**SECTION 73 REFERENCES**

**SECTION 73 REFERENCES**

**SECTION 73 REFERENCES**

**SECTION 73 REFERENCES**
### RADIATION

#### Potential Late Effects

| Section # | Therapeutic Agent(s) | Potential Late Effects | Risk Factors | Highest Risk Factors | Periodic Evaluation | Health Counseling  
Further Considerations |
<table>
<thead>
<tr>
<th></th>
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</thead>
<tbody>
<tr>
<td>74</td>
<td>≥ 30 Gy to:</td>
<td></td>
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<td></td>
</tr>
<tr>
<td></td>
<td>Extended mantle</td>
<td>Hepatic</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>Renal</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Upper quadrant (right, left)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Spleen (partial, entire)</td>
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<td></td>
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<td></td>
</tr>
<tr>
<td></td>
<td>Paraaoartic</td>
<td></td>
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<td></td>
</tr>
<tr>
<td></td>
<td>Flank/Hemiabdomen</td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>(right, left)</td>
<td>Whole abdomen</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>Inverted Y TLI</td>
<td>STLI</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td></td>
<td>TBLi</td>
<td>TBI*</td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

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

- This section is only applicable to patients who:
  1) Received radiation to any of the specified fields at ≥ 30 Gy OR
  2) Received a combination of radiation to any of the specified fields 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.

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

#### 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

### SCREENING

- ALT
- AST
- Bilirubin

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

### HEALTH LINKS

- Liver Health

- Prothrombin time for evaluation of hepatic synthetic function in patients with abnormal liver function.
- 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**

### SECTION 74 REFERENCES


## RADIATION

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

<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
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<th>Health Counseling Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>75</td>
<td>≥ 30 Gy to: Extended mantle Hepatic Renal Upper quadrant (right, left) Spleen (partial, entire) Para-aortic Flank/Hemiabdomen (right, left) Whole abdomen Inverted Y TLI STLI TBI*</td>
<td>Cholelithiasis</td>
<td>Host Factors ileal conduit Obesity Pregnancy Family history of cholelithiasis</td>
<td>Treatment Factors Abdominal surgery Abdominal radiation TPN</td>
<td>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</td>
<td>Health Links Gastrointestinal Health Considerations for Further Testing and Intervention Consider gallbladder ultrasound in patients with chronic abdominal pain.</td>
</tr>
</tbody>
</table>

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

- See dose calculation rules on page 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 75 REFERENCES

Table: Potential Impact to GI/Hepatic System (cont)

### Section 76

<table>
<thead>
<tr>
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<th>Health Counseling Further Considerations</th>
</tr>
</thead>
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<tr>
<td>76</td>
<td>≥ 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*</td>
<td>Bowel obstruction</td>
<td>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.</td>
<td>Treatment Factors Radiation dose ≥ 45 Gy (Obstruction may occur in people who received lower doses of abdominal radiation during childhood)</td>
<td>History Abdominal pain Distention Vomiting Constipation With clinical symptoms of obstruction Physiological Tenderness Abdominal guarding Distension With clinical symptoms of obstruction</td>
<td>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.</td>
</tr>
</tbody>
</table>

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

### RADIATION

#### Sec 77

<table>
<thead>
<tr>
<th>#</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>77</td>
<td>≥ 30 Gy to:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Spine (thoracic, lumbar, sacral, whole)</td>
<td>Chronic enterocolitis Fistula Strictures</td>
<td>Treatment Factors Higher radiation dose to bowel Abdominal surgery</td>
<td>Treatment Factors Radiation dose ≥ 45 Gy</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Extended Mantle Hepatic Renal</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Upper quadrant (right, left) Spleen (partial, entire) Paaaraoartic Flank/Hemiabdomen (right, left) Whole abdomen Inverted Y Pelvic Vaginal Prostate Bladder Iliac Inguinal Femoral TLI STLI TBI*</td>
<td></td>
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</tr>
</tbody>
</table>

- This section is only applicable to patients who:
  1. Received radiation to any of the specified fields at ≥ 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.

#### 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.

---

### SECTION 77 REFERENCES


### RADIATION

<table>
<thead>
<tr>
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<th>Therapeutic Agent(s)</th>
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<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>78</td>
<td>≥ 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*</td>
<td>Colorectal cancer</td>
<td>Host Factors</td>
<td>Host Factors</td>
<td>SCREENING</td>
<td>Health Links Colorectal Cancer</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Current age ≥ 50 years</td>
<td>Personal history of ulcerative colitis, gastrointestinal malignancy, adenomatous polyps, or hepatoblastoma Familial polyposis</td>
<td>Colonoscopy Every 5 years [minimum] beginning at 10 years after radiation or at age 35 years [whichever occurs last]: more frequently if indicated based on colonoscopy results; Per the ACS, begin screening earlier for the following high-risk groups - HNPCC: at puberty; FAP: at age 21 years; IBD: 8 years after diagnosis of IBD; Information from the first colonoscopy will inform frequency of follow-up testing.</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Treatment Factors Higher radiation dose to bowel Higher daily dose fraction Combined with chemotherapy (especially alkylators)</td>
<td>Medical Conditions Obesity</td>
<td>Health Behaviors High fat/low fiber diet</td>
<td></td>
</tr>
</tbody>
</table>

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

**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

**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**

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**SECTION 78 REFERENCES**


### RADIATION

<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>79</td>
<td>Extended Mantle Hepatic Renal Upper quadrant (right, left) Spleen (partial, entire) Paraaortic Flank/Hemiabdomen (right, left) Whole abdomen Inverted Y TLI STLI TBI</td>
<td>Renal toxicity Renal insufficiency Hypertension</td>
<td>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 - Amphoteracin - Immunosuppressants Medical Conditions Diabetes mellitus Hypertension Nephrectomy</td>
<td>Treatment Factors Radiation dose ≥ 15 Gy TBI ≥ 6 Gy in single fraction TBI ≥ 12 Gy fractionated</td>
<td>PHYSICAL Blood pressure Yearly SCREENING BUN, Creatinine, Na, K, Cl, CO₂, Ca, Mg, PO₄ Baseline at entry into long-term follow-up, repeat as clinically indicated. Urinalysis Yearly</td>
<td>Health Links Kidney Health See also: Single Kidney Health Considerations for Further Testing and Intervention Nephrology consultation for patients with hypertension, proteinuria, or progressive renal insufficiency</td>
</tr>
</tbody>
</table>

**SECTION 79 REFERENCES**


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

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.

- 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

## RADIATION

<table>
<thead>
<tr>
<th>Section #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>81</td>
<td>≥ 30 Gy to: Spine (sacral, whole) Flank/Hemiabdomen (right, left)* Whole abdomen Inverted Y Pelvic Vaginal Prostate Bladder Iliac Inguinal TLI TBI**</td>
<td>Urinary tract toxicity Bladder fibrosis Dysfunctional voiding Vesicoureteral reflux Hydronephrosis</td>
<td>Treatment Factors Higher cumulative radiation dose (≥ 45 Gy) Radiation to entire bladder Combined with: - Cyclophosphamide - Ifosfamide - Vincristine</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- This section is only applicable to patients who:
  1) Received radiation to any of the specified fields at ≥ 30 Gy OR
  2) Received a combination of radiation to any of the specified fields 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.

### POTENTIAL IMPACT TO URINARY TRACT (cont)

#### System
- **Urinary**
- **Score**: 1

#### Screening
- Urinalysis
- Yearly

#### History
- Hematuria
- Urinary urgency/frequency
- Urinary incontinence/retention
- Dysuria
- Nocturia
- Abnormal urinary stream
- Yearly

#### Considerations for Further Testing and Intervention
- Urologic consultation for patients with incontinence or dysfunctional voiding.

### SECTION 81 REFERENCES


## RADIATION

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<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
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<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>82</td>
<td>Spine (sacral, whole) Flank/Hemiabdomen (right, left)* Whole abdomen Inverted Y Pelvic Vaginal Prostate Bladder Iliac Inguinal TLI</td>
<td>Bladder malignancy</td>
<td>Treatment Factors Radiation to pelvis Combined with: - Cyclophosphamide - Ifosfamide Health Behaviors Alcohol use Smoking</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Only if field extended below iliac crest

- **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.

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**SECTION 82 REFERENCES**


**RADIATION**

<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
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<th>Periodic Evaluation</th>
<th>Health Counseling Further Considerations</th>
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</thead>
<tbody>
<tr>
<td>83</td>
<td>Spine (lumbar, sacral, whole)</td>
<td>Uterine vascular insufficiency</td>
<td>Host Factors Females with Wilms tumor and associated müllerian anomalies</td>
<td>Host Factors Prepubertal at treatment</td>
<td>HISTORY</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Flank/Hemiabdomen (right, left)*</td>
<td>Resulting in adverse pregnancy outcomes, such as spontaneous abortion, neonatal death, low-birth weight infant, fetal malposition, and premature labor</td>
<td>Treatment Factors Higher radiation dose to pelvis</td>
<td>Treatment Factors Radiation dose ≥ 30 Gy TBI</td>
<td>Pregnancy</td>
<td>Childbirth history</td>
</tr>
<tr>
<td></td>
<td>Whole abdomen</td>
<td></td>
<td></td>
<td></td>
<td>Yearly and as clinically indicated</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Inverted Y</td>
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<td></td>
<td>Pelvic</td>
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<td></td>
<td>Vaginal</td>
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<td></td>
<td>Bladder</td>
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<td></td>
<td>TLI</td>
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<td></td>
<td>TBI</td>
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<td></td>
<td>*Only if field extended below iliac crest</td>
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<tr>
<td></td>
<td>Uterine vascular insufficiency</td>
<td>Resulting in adverse pregnancy outcomes, such as spontaneous abortion, neonatal death, low-birth weight infant, fetal malposition, and premature labor</td>
<td>Info Link: 10% of girls with Wilms tumor have congenital uterine anomalies.</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**SECTION 83 REFERENCES**


**Health Links**

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

**Resources**


**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.
<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling Further Considerations</th>
</tr>
</thead>
</table>
| 84   | **Spine (lumbar, sacral, whole)**<br>**Flank/Hemiabdomen (right, left)**<br>**Whole abdomen**<br>**Inverted Y**<br>**Pelvic**<br>**Vaginal**<br>**Bladder**<br>**Iliac**<br>**TLI**<br>**TBI**<br>**Only if field extended below iliac crest**<br><br><br><br><br>**Gonadal dysfunction (ovarian)**<br>**Delayed/arrested puberty**<br>**Premature menopause**<br>**Infertility**<br><br><br><br><br>**Host Factors**<br>**Older age at irradiation**<br>**Prepubertal female:**<br>**Radiation dose ≥ 10 Gy**<br><br><br><br><br>**Treatment Factors**<br>**Radiation dose ≥ 15 Gy**<br>**Pubertal female:**<br>**Radiation dose ≥ 10 Gy**<br><br><br><br><br>**Combined with alkylating agent chemotherapy**<br>**Longer time since treatment**|**Treatment Factors**<br>**Prepubertal female:**<br>**Radiation dose ≥ 10 Gy**<br><br><br><br><br>**Pubertal female:**<br>**Radiation dose ≥ 5 Gy**<br>**Combined with cyclophosphamide conditioning for HCT**|**HISTORY**<br>**Pubertal (onset, tempo)**<br>**Menstrual/pregnancy history**<br>**Sexual function (vaginal dryness, libido)**<br>**Medication use impacting sexual function**<br>**Yearly**<br><br><br><br><br>**PHYSICAL:**<br>**Tanner staging**<br>**Yearly until sexually mature**|**SCREENING**<br>**FSH**<br>**LH**<br>**Estradiol**<br>**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.**<br><br><br><br><br>**Health Links**<br>Female Health Issues<br><br><br><br><br>**Resources**<br>American Society for Reproductive Medicine: [www.asrm.org](http://www.asrm.org)<br>Fertile Hope: [www.fertilehope.org](http://www.fertilehope.org)<br><br><br><br><br>**Counseling**<br>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.<br><br><br><br><br>**Considerations for Further Testing and Intervention**<br>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.*
### RADIATION

#### SECTION 84 REFERENCES


<table>
<thead>
<tr>
<th>Sec #</th>
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<th>Periodic Evaluation</th>
<th>Health Counseling Further Considerations</th>
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</thead>
</table>

Considerations for Further Testing and Intervention

**SYSTEM = Reproductive (female)**

**SCORE = 2A**

**SECTION 85 REFERENCES**
# RADIATION

<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
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<th>Periodic Evaluation</th>
<th>Health Counseling Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>86</td>
<td>Flank/Hemiabdomen (right, left)*</td>
<td>Whole abdomen Inverted Y Pelvic Prostate Bladder Iliac Inguinal Femoral Testicular TLI TBI</td>
<td>Gonadal dysfunction (testicular): Germ cell failure Oligospermia Azospermia Infertility</td>
<td>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</td>
<td>Treatment Factors Radiation dose to testes ≥ 6 Gy - Azoospermia likely permanent</td>
<td>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.</td>
</tr>
</tbody>
</table>

*Only if field extended below iliac crest

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

**SYSTEM = Reproductive (male)**

**SCORE = 1**

---

**Potential Impact to Male Reproductive System**

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

**Counseling**
- Counsel regarding the need for contraception, since there is tremendous individual variability in gonadal toxicity after exposure to radiation. Recovery of fertility may occur years after therapy.
- Considerations for Further Testing and Intervention
  - Reproductive endocrinology consultation for infertile couples interested in assisted reproductive technologies.


### RADIATION

<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling Further Considerations</th>
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</thead>
<tbody>
<tr>
<td>87</td>
<td>≥ 20 Gy to: Flank/Hemiabdomen (right, left)* Whole abdomen Inverted Y Pelvic Prostate Bladder Iliac Inguinal Femoral Testicular TLI TBI**</td>
<td>Gonadal dysfunction (testicular): Leydig cell dysfunction Delayed/arrested puberty Hypogonadism</td>
<td>Treatment Factors Testicular irradiation combined with head/brain irradiation</td>
<td>Treatment Factors Combined with alkylating agents Combined with cyclophosphamide conditioning for HCT</td>
<td>HISTORY Pubertal (onset, tempo) Sexual function (erections, nocturnal emissions, libido) Medication use impacting sexual function Yearly</td>
<td>POTENTIAL IMPACT TO MALE REPRODUCTIVE SYSTEM (cont)</td>
</tr>
</tbody>
</table>
*Only if field extended below iliac crest  
**TBI included for dose calculation purposes only; this section not applicable to patients who received TBI alone.

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

- See dose calculation rules on page 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 87 REFERENCES


### RADIATION

<table>
<thead>
<tr>
<th>Sec #</th>
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<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>88</td>
<td>Spine (cervical, thoracic, lumbar, sacral, whole) Cervical (neck) Supravacular Chest (thorax) Whole lung Mediastinal Axilla Mini-Mantle Mantle Extended Mantle Hepatic Renal Upper quadrant (right, left) Spleen (partial, entire) Paraortic Flank/Hemiabdomen (right, left) Whole abdomen Inverted Y Pelvic Vaginal Prostate Bladder Iliac Inguinal Femoral Extremity (upper, lower) TLI STLI TBI</td>
<td>Musculoskeletal growth problems Hypoplasia Fibrosis Reduced or uneven growth Shortened trunk height (trunk radiation) Limb length discrepancy (extremity radiation)</td>
<td>Host Factors Younger age at treatment Treatment Factors Higher cumulative radiation dose Larger radiation treatment field Higher radiation dose per fraction</td>
<td>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</td>
<td>PHYSICAL Height Weight Yearly Sitting height Yearly for patients who had trunk radiation Limb lengths Yearly for patients who had extremity radiation</td>
<td>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.</td>
</tr>
</tbody>
</table>

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

**SYSTEM = Musculoskeletal**

**SCORE = 1**
### RADIATION

#### POTENTIAL IMPACT TO MUSCULOSKELETAL SYSTEM (cont)

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

#### SECTION 88 REFERENCES


## RADIATION

### POTENTIAL IMPACT TO MUSCULOSKELETAL SYSTEM (cont)

<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>89</td>
<td>Spine (thoracic, whole) Chest (thorax) Whole lung Mediastinal Mantle Extended Mantle Mantle Extended Mantle Hepatic Renal Upper quadrant (right, left) Spleen (partial, entire) Paraaortic Flank/Hemiabdomen (right, left) Whole abdomen Inverted Y TLI STLI</td>
<td>Scoliosis</td>
<td>Host Factors Younger age at irradiation Paraspinal malignancies</td>
<td>Treatment Factors Hemithoracic or abdominal radiation Hemithoracic, abdominal or spinal surgery Radiation of only a portion of (rather than whole) vertebral body</td>
<td>Treatment Factors Radiation doses ≥ 20 Gy (lower doses for infants) Orthovoltage radiation (commonly used before 1970) due to delivery of greater dose to skin and bones</td>
<td>PHYSICAL Spine exam for scoliosis Yearly until growth completed, may need more frequent assessment during puberty</td>
</tr>
</tbody>
</table>

### SYSTEM = Musculoskeletal

### SCORE = 1

---

**SELECTION 89 REFERENCES**


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

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**SECTION 90 REFERENCES**


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

### SECTION 91 REFERENCES


### 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).

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

#### System = SMN

**Score = 1**

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

**SECTION 92 REFERENCES**


<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(Male)</td>
<td></td>
<td>Younger age at transplant Fanconi’s anemia Radiation therapy</td>
<td></td>
<td></td>
<td>SYSTEM = SMN SCORE = 1</td>
</tr>
<tr>
<td></td>
<td>(Female)</td>
<td></td>
<td>Host Factors</td>
<td>Treatment Factors TBI</td>
<td>PHYSICAL Evaluation for benign or malignant neoplasms Yearly</td>
<td>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.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Younger age at transplant Fanconi’s anemia Radiation therapy</td>
<td></td>
<td></td>
<td>SYSTEM = SMN SCORE = 1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Medical Conditions</td>
<td></td>
<td></td>
<td>SYSTEM = SMN SCORE = 1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Hepatitis C infection Chronic GVHD</td>
<td></td>
<td></td>
<td>SYSTEM = SMN SCORE = 1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Human papilloma virus infection</td>
<td></td>
<td></td>
<td>SYSTEM = SMN SCORE = 1</td>
</tr>
</tbody>
</table>
**HEMATOPOIETIC CELL TRANSPLANT**

<table>
<thead>
<tr>
<th>Section</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
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<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling Further Considerations</th>
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<tbody>
<tr>
<td>93</td>
<td></td>
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</tr>
</tbody>
</table>

**SECTION 93 REFERENCES**

<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
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<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>94</td>
<td>Hematopoietic Cell Transplant (HCT)</td>
<td>Lymphoma</td>
<td>Medical Conditions Chronic GVHD</td>
<td>Medical Conditions Chronic hepatitis C with siderosis and steatosis</td>
<td>Yearly</td>
<td>Physical</td>
</tr>
</tbody>
</table>

### SECTION 94 REFERENCES


### HEMATOPOIETIC CELL TRANSPLANT

**Section 95**

<table>
<thead>
<tr>
<th>#</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
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<th>Periodic Evaluation</th>
<th>Health Counseling Further Considerations</th>
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</thead>
<tbody>
<tr>
<td>95</td>
<td>Hematopoietic Cell Transplant (HCT)</td>
<td>Hepatic toxicity</td>
<td>Treatment Factors</td>
<td>Medical Conditions</td>
<td>SCREENING</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Chronic hepatitis</td>
<td>History of multiple transfusions</td>
<td>Chronic hepatitis C with siderosis and steatosis</td>
<td>ALT, AST, Bilirubin, Ferritin</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cirrhosis</td>
<td>Radiation to the liver</td>
<td></td>
<td>Baseline at entry into long-term follow-up. Repeat as clinically indicated.</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Iron overload</td>
<td>Antimetabolite therapy</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Heat</td>
<td>Medical Conditions</td>
<td>Chronic GVHD</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Viral hepatitis</td>
<td></td>
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<tr>
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<td></td>
<td></td>
<td>History of VOD</td>
<td></td>
<td></td>
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</tr>
<tr>
<td></td>
<td>Health Behaviors</td>
<td>Alcohol use</td>
<td></td>
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</table>

**SECTION 95 REFERENCES**


## HEMATOPOIETIC CELL TRANSPLANT

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<th>Periodic Evaluation</th>
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</thead>
<tbody>
<tr>
<td>96</td>
<td>Hematopoietic Cell Transplant (HCT)</td>
<td>Osteonecrosis (Avascular Necrosis)</td>
<td>Host Factors</td>
<td>Treatment Factors</td>
<td>HISTORY</td>
<td>Health Links</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Age ≥ 10 years at time of transplant</td>
<td>Prolonged corticosteroid therapy (e.g., for chronic GVHD)</td>
<td>Joint pain</td>
<td>Osteonecrosis</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Treatment Factors</td>
<td>Corticosteroids (dexamethasone effect is more potent than prednisone)</td>
<td>Swelling</td>
<td>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).</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>TBI</td>
<td>High-dose radiation to any bone</td>
<td>Immobility</td>
<td>Yearly</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Allogeneic HCT &gt; autologous</td>
<td>Allogeneic HCT &gt; autologous</td>
<td>Limited range of motion</td>
<td>Yearly</td>
</tr>
</tbody>
</table>

### HISTORY
- Joint pain
- Swelling
- Immobility
- Limited range of motion

### PHYSICAL
- Musculoskeletal exam
  - Yearly

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

## SECTION 96 REFERENCES

### 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 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

**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 Counseling Further Considerations**

**Bone Health**

**Resources**
- National Osteoporosis Foundation Website: [www.noif.org](http://www.noif.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).
### SECTION 97 REFERENCES


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<tr>
<th>Sec #</th>
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<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
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</thead>
</table>
| 98    | HCT with any history of Chronic GVHD | Dermatologic toxicity  
Permanent alopecia  
Nail dysplasia  
Vitiligo  
Scleroderma  
Squamous cell carcinoma of the skin | PHYSICAL  
Hair (alopecia)  
Nails (hypoplasia)  
Skin (vitiligo, scleroderma)  
Yearly | Health Links  
Skin Health |
|       | Info Link: More common with active cGVHD; effects may persist after cGVHD resolves. | | | |

### SECTION 98 REFERENCES


### Section 99: HCT with any history of Chronic GVHD

<table>
<thead>
<tr>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>HCT with any history of Chronic GVHD</td>
<td>Xerophthalmia (keratoconjunctivitis sicca)</td>
<td>Treatment Factors: Cranial radiation, Eye radiation, Radiomimetic chemotherapy (e.g., doxorubicin, daunomycin)</td>
<td>Treatment Factors: Radiation dose to eye ≥ 30 Gy, Radiation fraction ≥ 2 Gy</td>
<td><strong>HISTORY</strong>&lt;br&gt;Dry eyes (burning, itching, foreign body sensation, inflammation) &lt;br&gt;Yearly</td>
<td><strong>Health Links</strong>&lt;br&gt;Eye Health&lt;br&gt;<strong>Considerations for Further Testing and Intervention</strong>&lt;br&gt;Supportive care with artificial tears. Schirmer's testing as clinically indicated. Ongoing ophthalmology follow-up for identified problems. Consider every six month ophthalmology evaluation for patients with corneal damage.</td>
</tr>
</tbody>
</table>

#### System = Ocular  
**Score = 1**

### SECTION 99 REFERENCES

## HEMATOPOIETIC CELL TRANSPLANT

<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>100</td>
<td>HCT with any history of Chronic GVHD</td>
<td>Xerostomia</td>
<td>Treatment Factors: Head and neck radiation involving the parotid gland</td>
<td>Treatment Factors: Salivary gland radiation dose ≥ 30 Gy, Use of azathioprine for cGVHD management</td>
<td>HISTORY: Xerostomia</td>
<td>Info Link: More common with active cGVHD; effects may persist after cGVHD resolves.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Salivary gland dysfunction</td>
<td>Dental caries</td>
<td>Medical Conditions: High grade of cGVHD</td>
<td>Xerostomia</td>
<td>Yearly</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Periodontal disease</td>
<td>Oral cancer (squamous cell carcinoma)</td>
<td></td>
<td>Oral exam</td>
<td>Yearly</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Dental exam and cleaning</td>
<td>Every 6 months</td>
</tr>
</tbody>
</table>

### Treatment Factors
- Head and neck radiation involving the parotid gland
- Higher radiation doses
- Radiomimetic chemotherapy (e.g., doxorubicin, dacarbazine)

### Medical Conditions
- High grade of cGVHD

### Screening
- Dental exam and cleaning every 6 months

### Historic Data

### System = Dental
**Score = 1**

### Section 100 References
<table>
<thead>
<tr>
<th>Section</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>101</td>
<td>HCT with <em>any history of Chronic GVHD</em></td>
<td>Pulmonary toxicity Bronchiolitis obliterans Chronic bronchitis Bronchiectasis</td>
<td>Treatment Factors Chest radiation TBI Pulmonary toxic chemotherapy: - Bleomycin - Busulfan - Carmustine (BCNU) - Lomustine (CCNU)</td>
<td>Medical Conditions Prolonged immunosuppression related to cGVHD and its treatment</td>
<td>HISTORY Cough SOB DOE Wheezing Yearly</td>
<td><strong>Health Links</strong> Pulmonary Health <strong>Resources</strong> Extensive information regarding smoking cessation is available for patients on the NCI's website: <a href="http://www.smokefree.gov">www.smokefree.gov</a> <strong>Counseling</strong> Counsel regarding tobacco avoidance/smoking cessation. Patients who desire to SCUBA dive should be advised to obtain medical clearance from a pulmonologist. <strong>Considerations for Further Testing and Intervention</strong> 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.</td>
</tr>
</tbody>
</table>

| SYSTEM = Pulmonary | SCORE = 1 |

**Info Link:** More common with active cGVHD; effects may persist after cGVHD resolves.

**Medical Conditions**
- Prolonged immunosuppression related to cGVHD and its treatment

**Treatment Factors**
- Chest radiation
- TBI
- Pulmonary toxic chemotherapy:
  - Bleomycin
  - Busulfan
  - Carmustine (BCNU)
  - Lomustine (CCNU)

**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.

**Health Counseling Further Considerations**
- **Health Links** Pulmonary Health
- **Resources** Extensive information regarding smoking cessation is available for patients on the NCI's website: [www.smokefree.gov](http://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.
## SECTION 101 REFERENCES


### HEMATOPOIETIC CELL TRANSPLANT

#### WITH CHRONIC GVHD (cont)

<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling Further Considerations</th>
</tr>
</thead>
</table>
| 102   | HCT with any history of Chronic GVHD | Immuneologic complications Secretory IgA deficiency Hypogammaglobulinemia Decreased B cells T cell dysfunction Chronic infections (e.g., conjunctivitis, sinusitis, and bronchitis associated with chronic GVHD) | 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. |

### SECTION 102 REFERENCES

HEMATOPOIETIC CELL TRANSPLANT

WITH CHRONIC GVHD (cont)

<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>103</td>
<td>HCT with currently active Chronic GVHD</td>
<td>Functional asplenia</td>
<td>At risk for life-threatening infection with encapsulated organisms (e.g., Haemophilus influenzae, Streptococcus pneumoniae, meningococcus)</td>
<td>Splenic radiation</td>
<td>Hypogammaglobulinemia</td>
<td>Physical exam at time of febrile illness to evaluate degree of illness and potential source of infection</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Treatment Factors</td>
<td></td>
<td></td>
<td>When febrile T ≥ 101°F as indicated for patients with active chronic GVHD</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Ongoing immunosuppression</td>
<td></td>
<td></td>
<td>Blood culture</td>
</tr>
</tbody>
</table>

SYSTEM = Immune
SCORE = 1

SECTION 103 REFERENCES


## HEMATOPOIETIC CELL TRANSPLANT WITH CHRONIC GVHD (cont)

<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>104</td>
<td>HCT with any history of Chronic GVHD</td>
<td>Esophageal stricture</td>
<td>Treatment Factors</td>
<td>Treatment Factors</td>
<td>HISTORY</td>
<td>Health Links</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Radiation involving the esophagus</td>
<td>Radiation dose ≥ 40 Gy</td>
<td>Dysphagia</td>
<td>Gastrointestinal Health</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Radiomimetic chemotherapy (e.g., doxorubicin, dactinomycin)</td>
<td>Medical Conditions</td>
<td>Heartburn</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Gastroesophageal reflux</td>
<td>Gut GVHD</td>
<td>Yearly</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>History of Candida esophagitis</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Medical Conditions
- Gastroesophageal reflux
- History of Candida esophagitis

### Treatment Factors
- Radiation dose ≥ 40 Gy
- Medical Conditions
  - Gut GVHD

### Health Counseling Further Considerations
- Surgery and/or gastroenterology consultation for symptomatic patients.

### SECTION 104 REFERENCES


<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>105</td>
<td>HCT with any history of Chronic GVHD</td>
<td>Vaginal fibrosis/stenosis</td>
<td>Treatment Factors Pelvic radiation</td>
<td>HISTORY</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**SECTION 105 REFERENCES**


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

**SYSTEM = Musculoskeletal**

**SCORE = 1**

**SECTION 106 REFERENCES**


**SURGERY**

<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>107</td>
<td>Amputation</td>
<td>Amputation-related complications</td>
<td>Host Factors Skeletally immature/ growing children</td>
<td>HISTORY Phantom pain Functional and activity limitations Yearly</td>
<td>PHYSICAL Residual limb integrity Yearly</td>
<td>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.</td>
</tr>
</tbody>
</table>

**AMPUTATION**

<table>
<thead>
<tr>
<th>Host Factors</th>
<th>Treatment Factors Site of amputation: Hemipelvectomy &gt; Trans-femur amputation &gt; Trans-tibia amputation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medical Conditions Obesity Diabetes Poor residual limb healing</td>
<td>Medical Conditions Obesity Diabetes Poor residual limb healing</td>
</tr>
</tbody>
</table>

**SCREENING**

- Prosthetic evaluation Every 6 months until skeletally mature, then yearly.

**SYSTEM = Musculoskeletal**

**SCORE = 1**

---

**SECTION 107 REFERENCES**

### Central Venous Catheter

<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>108</td>
<td>Central venous catheter</td>
<td>Thrombosis Vascular insufficiency Infection of retained cuff or line tract</td>
<td></td>
<td></td>
<td>HISTORY Tenderness or swelling at previous catheter site Yearly and as clinically indicated.</td>
<td>SYSTEM = Cardiovascular</td>
</tr>
</tbody>
</table>

### Section 108 References

## CYSTECTOMY

<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>109</td>
<td>Cystectomy</td>
<td>Cystectomy-related complications</td>
<td>Chronic urinary tract infection</td>
<td>Vitamin B12 level</td>
<td>Yearly evaluation</td>
<td>Urology evaluation Yearly Vitamin B12 level Yearly starting 5 years after cystectomy (patients with ileal enterocystoplasty only)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Renal dysfunction</td>
<td></td>
<td></td>
<td>Health Links Cystectomy Kidney Health</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Vesicouretal reflux</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Hydronephrosis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Reservoir calculi</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Spontaneous neobladder perforation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Vitamin B12/folate/carotene deficiency (patients with ileal enterocystoplasty only)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Reservoir calculi</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>are stones in the neobladder (a reservoir for urine usually constructed of ileum/colon).</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### SECTION 109 REFERENCES


### HEALTH LINKS

- Cystectomy
- Kidney Health

### SYSTEM = Urinary

### SCORE =

- Chronic urinary tract infection: 1
- Renal dysfunction: 1
- Vesicouretal reflux: 1
- Hydronephrosis: 1
- Spontaneous neobladder perforation: 1
- Reservoir calculi: 2A
- Vitamin B12/folate/carotene deficiency: 2B
<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>110</td>
<td>Enucleation</td>
<td>Impaired cosmesis</td>
<td>Host Factors</td>
<td>Younger age at enucleation</td>
<td>Screening Evaluation by oculist</td>
<td>Health Links Eye Health</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Poor prosthetic fit</td>
<td></td>
<td>Treatment Factors</td>
<td>Evaluation by ophthalmologist</td>
<td>Psychological consultation in patients with emotional difficulties related to cosmetic and visual impairment. Vocational rehabilitation referral as indicated.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Orbital hypoplasia</td>
<td></td>
<td>Combined with radiation</td>
<td>Yearly</td>
<td>SYSTEM = Ocular</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>SCORE = 1</td>
</tr>
</tbody>
</table>

**SECTION 110 REFERENCES**

<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>111</td>
<td>Hysterectomy (female)</td>
<td>Pelvic floor dysfunction Urinary incontinence Sexual dysfunction</td>
<td></td>
<td></td>
<td>HISTORY</td>
<td>Pelvic floor dysfunction Urinary incontinence Sexual dysfunction</td>
</tr>
</tbody>
</table>

**Info Link**: For patients who also underwent oophorectomy, see also: Section 123 (unilateral oophorectomy) or Section 124 (bilateral oophorectomy).

**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

---

**SECTION 111 REFERENCES**


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

**SECTION 112 REFERENCES**


<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>113</td>
<td>Limb sparing procedure</td>
<td>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)</td>
<td>Host Factors Younger age at surgery Rapid growth spurt Skeletally immature Treatment Factors Tibial endoprosthesi 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</td>
<td>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.</td>
<td>HEALTH</td>
<td>Limb Sparing Procedures Counseling 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-pharmaceutical 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.</td>
</tr>
</tbody>
</table>

**SECTION 113 REFERENCES**


### Surgeries

<table>
<thead>
<tr>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Host Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Nephrectomy</strong></td>
<td>Renal toxicity</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Proteinuria</td>
<td></td>
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</tr>
<tr>
<td></td>
<td>Hyperfiltration</td>
<td></td>
<td></td>
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</tr>
<tr>
<td></td>
<td>Renal insufficiency</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Hydrocele</td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td><strong>Info Link:</strong></td>
<td>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.</td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

#### Host Factors

- Denys-Drash syndrome
- WAGR syndrome
- Hypospadias
- Cryptorchidism
- Bilateral Wilms tumor

#### Treatment Factors

<table>
<thead>
<tr>
<th>Combined with other nephrotoxic therapy, such as:</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Cisplatin</td>
</tr>
<tr>
<td>- Carboplatin</td>
</tr>
<tr>
<td>- Ifosfamide</td>
</tr>
<tr>
<td>- Aminoglycosides</td>
</tr>
<tr>
<td>- Amphoterin</td>
</tr>
<tr>
<td>- Immunosuppressants</td>
</tr>
<tr>
<td>- Methotrexate</td>
</tr>
<tr>
<td>- Radiation impacting the kidneys</td>
</tr>
</tbody>
</table>

#### Physical

**Blood pressure**

**Testicular exam to evaluate for hydrocele**

Yearly

**Screening**

**BUN**

**Creatinine**

**Na, K, Cl, CO₂**

**Ca, Mg, PO₄**

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

**Urinalysis**

Yearly

### Host Factors

- Denys-Drash syndrome
- WAGR syndrome
- Bilateral Wilms tumor

### Treatment Factors

<table>
<thead>
<tr>
<th>Combined with other nephrotoxic therapy, such as:</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Cisplatin</td>
</tr>
<tr>
<td>- Carboplatin</td>
</tr>
<tr>
<td>- Ifosfamide</td>
</tr>
<tr>
<td>- Aminoglycosides</td>
</tr>
<tr>
<td>- Amphoterin</td>
</tr>
<tr>
<td>- Immunosuppressants</td>
</tr>
<tr>
<td>- Methotrexate</td>
</tr>
<tr>
<td>- Radiation impacting the kidneys</td>
</tr>
</tbody>
</table>

#### Physical

**Blood pressure**

Yearly

**Screening**

**BUN**

**Creatinine**

**Na, K, Cl, CO₂**

**Ca, Mg, PO₄**

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

**Urinalysis**

Yearly

### Health Counseling Further Considerations

**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**
### SECTION 114 REFERENCES


**SECTION 115 REFERENCES**


### NEUROSURGERY - BRAIN (cont)

<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>116</td>
<td>Neurosurgery - Brain</td>
<td>Motor and/or sensory deficits&lt;br&gt;Paralysis&lt;br&gt;Movement disorders&lt;br&gt;Ataxia&lt;br&gt;Eye problems (oculomotor nerve palsies, gaze paresis, nystagmus, papilledema, optic atrophy)</td>
<td>Host Factors&lt;br&gt;Primary CNS tumor&lt;br&gt;Medical Conditions&lt;br&gt;Hydrocephalus</td>
<td>Host Factors&lt;br&gt;Optic pathway tumor&lt;br&gt;Hypothalamic tumor&lt;br&gt;Suprasellar tumor (eye problems)</td>
<td><strong>SCREENING</strong>&lt;br&gt;<strong>Evaluation by neurologist</strong>&lt;br&gt;Yearly, until 2 to 3 years after surgery or stable; continue to monitor if symptoms persist.&lt;br&gt;<strong>Evaluation by psychiatrist/rehabilitation medicine specialist</strong>&lt;br&gt;Yearly, or more frequently as clinically indicated in patients with motor dysfunction.</td>
<td>Considerations for Further Testing and Intervention&lt;br&gt;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.</td>
</tr>
</tbody>
</table>

### SECTION 116 REFERENCES


### NEUROSURGERY - BRAIN (cont)

<table>
<thead>
<tr>
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<th>Periodic Evaluation</th>
<th>Health Counseling Further Considerations</th>
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</thead>
</table>
| 117   | Neurosurgery - Brain | Seizures               | Host Factors |                     | Screening          | SYSTEM = CNS  
Score = 1                                     |

#### SCREENING
- Evaluation by neurologist
- Every 6 months for patients with seizure disorder.

#### SECTION 117 REFERENCES

<table>
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<tbody>
<tr>
<td>118</td>
<td>Neurosurgery - Brain</td>
<td>Hydrocephalus</td>
<td>Host Factors</td>
<td>Primary CNS tumor</td>
<td>SCREENING</td>
<td>Counseling Further Testing and Intervention</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Shunt malfunction</td>
<td></td>
<td></td>
<td>Abdominal x-ray</td>
<td>Education patient/family regarding potential symptoms of shunt malfunction.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>After pubertal growth spurt for patients with shunts to assure distal shunt tubing in peritoneum.</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Evaluation by neurosurgeon</td>
<td>Yearly for patients with shunts.</td>
</tr>
</tbody>
</table>

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

**SECTION 118 REFERENCES**

### NEUROSURGERY - SPINAL CORD

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<thead>
<tr>
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<th>Potential Late Effects</th>
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<th>Highest Risk Factors</th>
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<th>Health Counseling Further Considerations</th>
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</thead>
<tbody>
<tr>
<td>119</td>
<td>Neurosurgery - Spinal cord</td>
<td>Neurogenic bladder Urinary incontinence</td>
<td>Host Factors Tumor adjacent to or compressing spinal cord or cauda equina</td>
<td>Host Factors Injury above the level of the sacrum</td>
<td>HISTORY Hematuria Urinary urgency/frequency Urinary incontinence/retention Dysuria Nocturia Abnormal urinary stream Yearly</td>
<td>Health Links Neurogenic Bladder Counseling Counsel regarding adequate fluid intake, regular voiding, seeking medical attention for symptoms of voiding dysfunction or urinary tract infection, and compliance with recommended bladder catheterization regimen. Considerations for Further Testing and Intervention Urologic consultation for patients with dysfunctional voiding or recurrent urinary tract infections.</td>
</tr>
</tbody>
</table>

#### NEUROSURGERY

**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.

---

**SECTION 119 REFERENCES**


### 120 Neurosurgery - Spinal cord

<table>
<thead>
<tr>
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<th>Health Counseling Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neurogenic bowel</td>
<td>Fecal incontinence</td>
<td>Host Factors Tumor adjacent to or compressing spinal cord or cauda equina</td>
<td>Host Factors Injury above the level of the sacrum</td>
<td><strong>HISTORY</strong> Chronic constipation Fecal soiling Yearly <strong>PHYSICAL</strong> Rectal exam As clinically indicated</td>
<td><strong>Counseling</strong> Counsel regarding benefits of adherence to bowel regimen, including adequate hydration, fiber, laxatives/enemas as clinically indicated. <strong>Considerations for Further Testing and Intervention</strong> GI consultation to establish bowel regimen for patients with chronic impaction or fecal soiling.</td>
</tr>
</tbody>
</table>

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<table>
<thead>
<tr>
<th>#</th>
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<th>Potential Late Effects</th>
<th>Risk Factors</th>
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<th>Periodic Evaluation</th>
<th>Health Counseling Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>121</td>
<td>Neurosurgery - Spinal cord (Male)</td>
<td>Sexual dysfunction (Male) Erectile dysfunction</td>
<td>Host Factors Tumor adjacent to or compressing spinal cord or cauda equina</td>
<td>Host Factors Injury above the level of the sacrum</td>
<td>HISTORY Sexual function (erections, nocturnal emissions, libido) Medication use impacting sexual function Yearly</td>
<td>Health Links Male Health Issues Resources <a href="http://www.urologychannel.com">www.urologychannel.com</a> Considerations for Further Testing and Intervention Urologic consultation in patients with positive history. SYSTEM = CNS SCORE = 2A</td>
</tr>
<tr>
<td>121</td>
<td>Neurosurgery - Spinal cord (Female)</td>
<td>Sexual dysfunction (Female)</td>
<td>Host Factors Tumor adjacent to or compressing spinal cord or cauda equina</td>
<td>Host Factors Injury above the level of the sacrum</td>
<td>HISTORY Dyspareunia Altered or diminished sensation, loss of sensation Medication use impacting sexual function Yearly</td>
<td>SYSTEM = CNS SCORE = 2A</td>
</tr>
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</table>

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<tr>
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<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling Further Considerations</th>
</tr>
</thead>
</table>
| 122  | Oophoropexy          | Oophoropexy-related complications  
Inability to conceive despite normal ovarian function  
Dyspareunia  
Symptomatic ovarian cysts  
Bowel obstruction  
Pelvic adhesions | Treatment Factors  
Ovarian radiation  
Tubo-ovarian dislocation, especially with lateral ovarian transposition | **HISTORY**  
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**
### Section 123

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<thead>
<tr>
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<th>Potential Late Effects</th>
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<th>Health Counseling Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>123</td>
<td>Oophorectomy (unilateral)</td>
<td>Premature menopause</td>
<td>Health Behaviors Smoking</td>
<td>Treatment Factors Combined with: - Pelvic radiation - Alkylating agents - TBI</td>
<td>HISTORY Pubertal (onset, tempo) Menstrual/pregnancy history Sexual function (vaginal dryness, libido) Medication use impacting sexual function Yearly</td>
<td>Health Links Female Health Issues Resources American Society for Reproductive Medicine (<a href="http://www.asrm.org">www.asrm.org</a>) Fertile Hope (<a href="http://www.fertilehope.org">www.fertilehope.org</a>) Counseling Counsel currently menstruating women to be cautious about delaying childbearing. Counsel regarding need for contraception. Considerations for Further Testing and Intervention Refer to reproductive endocrinology for counseling regarding oocyte cryopreservation in patients wishing to preserve options for future fertility.</td>
</tr>
</tbody>
</table>

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

#### Treatment Factors Combined with:
- Pelvic radiation
- Alkylating agents
- TBI

#### 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.

---

### References

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## ORCHIECTOMY

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<tbody>
<tr>
<td>125 (Male)</td>
<td>Orchiectomy</td>
<td>Hypogonadism, Infertility</td>
<td>Treatment Factors&lt;br&gt;Unilateral orchiectomy combined with pelvic or testicular radiation and/or alkylating agents</td>
<td>Treatment Factors&lt;br&gt;Bilateral orchiectomy</td>
<td><strong>HISTORY</strong>&lt;br&gt;Pubertal (onset, tempo)&lt;br&gt;Sexual function (erections, nocturnal emissions, libido)&lt;br&gt;Medication use impacting sexual function&lt;br&gt;Yearly</td>
<td><strong>Health Links</strong>&lt;br&gt;Male Health Issues&lt;br&gt;&lt;br&gt;<strong>Counseling</strong>&lt;br&gt;For patients with single testis - counsel to wear athletic supporter with protective cup during athletic activities.&lt;br&gt;&lt;br&gt;<strong>Considerations for Further Testing and Intervention</strong>&lt;br&gt;Consider surgical placement of testicular prosthesis. For <strong>patients with unilateral orchiectomy</strong>: 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 <strong>patients with bilateral orchiectomy</strong>: Refer boys with post-surgical hypogonadism after bilateral orchiectomy to endocrinology at age 11 for initiation of hormonal replacement therapy to initiate puberty.</td>
</tr>
</tbody>
</table>

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**SECTION 125 REFERENCES**


### SURGERY

<table>
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<tr>
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<th>Therapeutic Agent(s)</th>
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<tbody>
<tr>
<td>126</td>
<td>Pelvic surgery</td>
<td>Cystectomy</td>
<td>Urinary incontinence Urinary tract obstruction</td>
<td>Host Factors Tumor adjacent to or compressing spinal cord or cauda equina</td>
<td>History Hematuria Urinary urgency/frequency Urinary incontinence/retention Dysuria Nocturia Abnormal urinary stream Yearly</td>
<td>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.</td>
</tr>
</tbody>
</table>

### PELVIC SURGERY

#### 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.

### SECTION 126 REFERENCES


<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling Further Considerations</th>
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</thead>
<tbody>
<tr>
<td>127</td>
<td>Pelvic surgery</td>
<td>Fecal incontinence</td>
<td>Host Factors</td>
<td>Radiation to the bladder, pelvis, or spine</td>
<td>HISTORY Chronic constipation, fecal soiling Yearly</td>
<td>Counsel regarding benefits of adherence to bowel regimen, including adequate hydration, fiber, laxatives/enemas as clinically indicated.</td>
</tr>
<tr>
<td></td>
<td>Cystectomy</td>
<td></td>
<td></td>
<td></td>
<td>PHYSICAL Rectal exam As clinically indicated</td>
<td>Considerations for Further Testing and Intervention GI consultation to establish bowel regimen for patients with chronic impaction or fecal soiling.</td>
</tr>
</tbody>
</table>

### SECTION 127 REFERENCES

<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>128</td>
<td>Pelvic surgery</td>
<td>Sexual dysfunction</td>
<td>Treatment Factors</td>
<td>Host Factors</td>
<td>HISTORY</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Cystectomy</td>
<td>(Male)</td>
<td>Retroperitoneal node dissection</td>
<td>Extensive presacral tumor resection</td>
<td>Sexual function (erectations, nocturnal emissions, libido)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Retropertitoneal tumor resection</td>
<td>Cystectomy</td>
<td>Radiation dose ≥ 55 Gy to penile bulb in adult and ≥ 45 Gy in prepubertal child</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Cystectomy</td>
<td>Radiation to bladder, pelvis, or spine</td>
<td>Medication use impacting sexual function</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Radical prostatectomy</td>
<td>Radiation to bladder, pelvis, or spine</td>
<td>Quality of ejaculation (frothy white urine with first void after intercourse suggests retrograde ejaculation)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Tumor adjacent to spine</td>
<td>Medical Conditions</td>
<td>Yearly</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Hypogonadism</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Sexual dysfunction (Female)</td>
<td>Host Factors</td>
<td>HISTORY</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Chronic GVHD</td>
<td>Extensive presacral tumor</td>
<td>Sexual function (erectations, nocturnal emissions, libido)</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Hypogonadism</td>
<td>Cystectomy</td>
<td>Radiation dose ≥ 55 Gy to penile bulb in adult and ≥ 45 Gy in prepubertal child</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Tumor adjacent to spine</td>
<td>Radiation to bladder, pelvis, or spine</td>
<td>Medication use impacting sexual function</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Medical Conditions</td>
<td>Radiation to bladder, pelvis, or spine</td>
<td>Quality of ejaculation (frothy white urine with first void after intercourse suggests retrograde ejaculation)</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Hypogonadism</td>
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<td>Yearly</td>
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<th>Health Counseling Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>129 (Male)</td>
<td>Pelvic surgery Cystectomy</td>
<td>Hydrocele</td>
<td>Treatment Factors Retroperitoneal node dissection</td>
<td></td>
<td>PHYSICAL Testicular exam to evaluate for hydrocele Yearly</td>
<td>Considerations for Further Testing and Intervention Urologic consultation for patients with hydrocele.</td>
</tr>
</tbody>
</table>

**SYSTEM = Urinary**

**SCORE = 1**

**SECTION 129 REFERENCES**

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<tr>
<td>130</td>
<td>Pulmonary lobectomy, Pulmonary metastasectomy, Pulmonary wedge resection</td>
<td>Pulmonary dysfunction</td>
<td>Treatment Factors: Combined with pulmonary toxic therapy - Bleomycin - Busulfan - Carmustine (BCNU) - Lomustine (CCNU)</td>
<td>Treatment Factors: Combined with: - Chest radiation - TBI</td>
<td>HISTORY: Cough, SOB, DOE, Wheezing Yearly</td>
<td>HEALTH LINKS: Pulmonary Health Resources: Extensive information regarding smoking cessation is available for patients on the NCI’s website: <a href="http://www.smokefree.gov">www.smokefree.gov</a> Counseling: Counsel regarding tobacco avoidance/smoking cessation. 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</td>
</tr>
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</table>

**SECTION 130 REFERENCES**


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<tr>
<th>Sec #</th>
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<tr>
<td>131</td>
<td>Splenectomy</td>
<td>Asplenia</td>
<td>At risk for life-threatening infection with encapsulated organisms (e.g., Haemophilus influenzae, streptococcus pneumoniae, meningococcus)</td>
<td></td>
<td>PHYSICAL</td>
<td>Splenic Precautions</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Blood culture</td>
<td>Medical alert bracelet/card noting asplenia. Counsel to avoid malaria and tick bites if living in or visiting endemic areas.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>When febrile $T \geq 101^\circ F$</td>
<td>Considerations for Further Testing and Intervention</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>In patients with $T \geq 101^\circ F$ (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 $\geq 104^\circ F$; 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 $\geq 10$ years old at $\geq 5$ years after previous dose (AAP-CIDP Recommendations, 2003). Discuss with dental provider potential need for antibiotic prophylaxis based on planned procedure.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>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.</td>
</tr>
</tbody>
</table>
SECTION 131 REFERENCES


### 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).

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<tr>
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<td>Thyroidectomy</td>
<td>Hypothyroidism</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

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

Yearly: Consider more frequent screening during periods of rapid growth.

**PHYSICAL**
- Height
- Weight
- Hair and skin
- Thyroid exam

Yearly: Consider more frequent screening during periods of rapid growth.

**SCREENING**
- TSH
- Free T4

Yearly: Consider more frequent screening during periods of rapid growth.

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

### SECTION 132 REFERENCES


<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>133</td>
<td>Radioiodine therapy (I-131 thyroid ablation)</td>
<td>Lacrimal duct atrophy</td>
<td></td>
<td></td>
<td>HISTORY</td>
<td>Excessive tearing, Yearly</td>
</tr>
</tbody>
</table>

SYSTEM = Ocular
SCORE = 2A

**SECTION 133 REFERENCES**


### OTHER THERAPEUTIC MODALITIES

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<tr>
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<th>Therapeutic Agent(s)</th>
<th>Potential Late Effects</th>
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<th>Health Counseling Further Considerations</th>
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<tbody>
<tr>
<td>134</td>
<td>Radioiodine therapy (I-131 thyroid ablation)</td>
<td>Hypothyroidism</td>
<td></td>
<td></td>
<td>HISTORY</td>
<td></td>
</tr>
</tbody>
</table>

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

Yearly; Consider more frequent screening during periods of rapid growth.

**PHYSICAL**

- Height
- Weight
- Hair and skin
- Thyroid exam

Yearly; Consider more frequent screening during periods of rapid growth.

**SCREENING**

- TSH
- Free T4

Yearly; Consider more frequent screening during periods of rapid growth.

**SYSTEM =** Endocrine/Metabolic

**SCORE =** 2A

**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.

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**SECTION 134 REFERENCES**


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<tr>
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<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>135</td>
<td>Systemic MIBG (in therapeutic doses)</td>
<td>Hypothyroidism</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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

**SYSTEMIC RADIATION (cont)**

**Reference**

### Bioimmunotherapy

<table>
<thead>
<tr>
<th>Therapy (Agent(s))</th>
<th>Potential Late Effects</th>
<th>Risk Factors</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bioimmunotherapy</td>
<td>Insufficient information currently available regarding late effects of biological agents</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**SECTION 136 REFERENCES**

No information currently available regarding late effects.
<table>
<thead>
<tr>
<th>Sec #</th>
<th>Organ</th>
<th>At Risk Population</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling Further Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>137</td>
<td>Breast</td>
<td>Over age 40</td>
<td>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</td>
<td><strong>PATIENTS AT STANDARD RISK (ACS Recommendation)</strong>&lt;br&gt;<strong>PHYSICAL</strong>&lt;br&gt;Clinical breast exam Every 3 years between ages 20-39, then yearly beginning at age 40 <strong>SCREENING</strong>&lt;br&gt;Mammogram Yearly, beginning at age 40</td>
<td>Health Links&lt;br&gt;Breast Cancer (for patients at highest risk only)&lt;br&gt;Counseling&lt;br&gt;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.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Family history of breast cancer in first degree relative</td>
<td></td>
<td><strong>PATIENTS AT HIGHEST RISK</strong>&lt;br&gt;<strong>PHYSICAL</strong>&lt;br&gt;BRACA1, BRACA2, ATM mutation</td>
<td>Considerations for Further Testing and Intervention&lt;br&gt;Surgery and/or oncology consultation as clinically indicated.</td>
</tr>
<tr>
<td></td>
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<td>Early onset of menstruation</td>
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<tr>
<td></td>
<td></td>
<td>Late onset of menopause (age 55 or older)</td>
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<tr>
<td></td>
<td></td>
<td>Older than 30 at birth of first child</td>
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<tr>
<td></td>
<td></td>
<td>Never pregnant</td>
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<tr>
<td></td>
<td></td>
<td>Obesity</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>Previous breast biopsy with atypical hyperplasia</td>
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<tr>
<td></td>
<td></td>
<td>Hormone replacement therapy</td>
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</tbody>
</table>

Info Link:<br>*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.

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.
CANCER SCREENING GUIDELINES

BREAST CANCER (cont)

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

SECTION 137 REFERENCES


## CANCER SCREENING GUIDELINES

<table>
<thead>
<tr>
<th>Sec #</th>
<th>Organ</th>
<th>At Risk Population</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling Further Considerations</th>
</tr>
</thead>
</table>
| 138   | 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)** | **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 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. |

### SECTION 138 REFERENCES

### Colorectal Cancer Screening Guidelines

<table>
<thead>
<tr>
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<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling Further Considerations</th>
</tr>
</thead>
</table>
| 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) - Paraortic - Flank/Hemilithroma (right, left) - Whole abdomen - Inverted Y - Pelvic - Vaginal - Prostate - Bladder - Iliac - Femoral - Femoral - STLI - TBI* | **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 | *Important:* Reports on colorectal cancer 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 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.  
**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 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. |
## SECTION 139 REFERENCES


### ENDOMETRIAL CANCER

#### Section 140

<table>
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<tr>
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</thead>
<tbody>
<tr>
<td>140</td>
<td>Endometrial</td>
<td>Obesity&lt;br&gt;Older age&lt;br&gt;Unopposed estrogen therapy&lt;br&gt;Tamoxifen&lt;br&gt;Diabetes&lt;br&gt;Hypertension&lt;br&gt;High fat diet&lt;br&gt;Early menopause&lt;br&gt;Late menopause&lt;br&gt;Nulliparity&lt;br&gt;Infertility&lt;br&gt;Failure to ovulate</td>
<td>History of/at risk for hereditary nonpolyposis colon cancer (HNPCC)</td>
<td><strong>PATIENTS AT HIGHEST RISK</strong> (ACS Recommendation)&lt;br&gt;&lt;br&gt;&lt;strong&gt;SCREENING&lt;/strong&gt;&lt;br&gt;Endometrial biopsy&lt;br&gt;Yearly, beginning at age 35 for patients at highest risk</td>
<td>Health Links&lt;br&gt;Reducing the Risk of Second Cancers</td>
</tr>
</tbody>
</table>

#### Section 140 References

### LUNG CANCER

**Organ**: Lung  
**At Risk Population**: Smoking  
Workplace exposures to asbestos, arsenic, radiation  
Second hand smoke (in non-smokers)  
**Highest Risk Factors**: 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 Counseling Further Considerations**
- 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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### SECTION 141 REFERENCES

<table>
<thead>
<tr>
<th>Sec #</th>
<th>Organ</th>
<th>At Risk Population</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
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</table>
### Prostate Cancer Screening Guidelines

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<thead>
<tr>
<th>Sec #</th>
<th>Organ</th>
<th>At Risk Population</th>
<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
<th>Health Counseling Further Considerations</th>
</tr>
</thead>
</table>
| 143   | 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 | Health Links 
Reducing the Risk of Second Cancers 
Considerations for Further Testing and Intervention 
Urology and/or oncology consultation as clinically indicated. |

**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.

### Section 143 References

### CANCER SCREENING GUIDELINES

#### SKIN CANCER

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</thead>
<tbody>
<tr>
<td>144</td>
<td>Skin</td>
<td>Light skin color, Chronic exposure to sun, Atypical moles or ≥ 50 moles</td>
<td>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</td>
<td><strong>PATIENTS AT STANDARD RISK</strong>&lt;br&gt;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.</td>
<td><strong>Health Links</strong>&lt;br&gt;Reducing the Risk of Second Cancers&lt;br&gt;Skin Health&lt;br&gt;Considerations for Further Testing and Intervention&lt;br&gt;Surgery, dermatology, and/or oncology consultation as clinically indicated.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td><strong>PATIENTS AT HIGHEST RISK</strong>&lt;br&gt;<strong>PHYSICAL</strong>&lt;br&gt;Skin self exam&lt;br&gt;Monthly&lt;br&gt;Dermatologic exam with attention to skin lesions and pigmented nevi in radiation field&lt;br&gt;Yearly</td>
<td></td>
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#### SECTION 144 REFERENCES

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<th>Organ</th>
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<th>Highest Risk Factors</th>
<th>Periodic Evaluation</th>
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</thead>
<tbody>
<tr>
<td>145</td>
<td>Testicular</td>
<td>Young males</td>
<td>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</td>
<td>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.</td>
<td></td>
</tr>
</tbody>
</table>

**SECTION 145 REFERENCES**


Any Cancer Experience

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/uspstf.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) or EBMT Guidelines (http://www.nature.com/bmt/journal/v23/n7/pdf/1701641a.pdf).

Section 146 References
