

CHEMOTHERAPY					ANTHRACYCLINE ANTIBIOTICS (cont)	
Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
34 (female)	<b>ANTHRACYCLINE ANTIBIOTICS</b> Daunorubicin Doxorubicin Epirubicin Idarubicin Mitoxantrone	<b>Cardiac toxicity</b> Cardiomyopathy Arrhythmias Subclinical left ventricular dysfunction	<b>Treatment Factors</b> Combined with radiation involving the heart Combined with other cardiotoxic chemotherapy - Cyclophosphamide conditioning for HCT - Amsacrine  <b>Medical Conditions</b> Obesity Congenital heart disease Febrile illness Pregnancy Hypertension Diabetes mellitus  <b>Health Behaviors</b> Isometric exercise Smoking Drug use (e.g., cocaine, diet pills, ephedra, mahuang)	<b>Host Factors</b> Female sex Black/of African descent Younger than age 5 years at time of treatment  <b>Treatment Factors</b> Higher cumulative anthracycline doses: - $\geq 550$ mg/m <sup>2</sup> in patients 18 years or older at time of treatment - $\geq 300$ mg/m <sup>2</sup> in patients younger than 18 years at time of treatment - Any dose in infant - Chest radiation $\geq 30$ Gy Longer time elapsed	<b>HISTORY</b> <b>SOB</b> <b>DOE</b> <b>Orthopnea</b> <b>Chest pain</b> <b>Palpitations</b> <b>If under 25 yrs: abdominal symptoms (nausea, vomiting)</b> Yearly  <b>Info Link</b> • Exertional intolerance is uncommon in patients younger than 25 years old. • Abdominal symptoms (nausea, emesis) may be observed more frequently than exertional dyspnea or chest pain in younger patients.	<b>Health Links</b> <b>Heart Health</b> <b>Cardiovascular Risk Factors</b>  <b>Counseling</b> Counsel patients with prolonged QTc interval about use of medications that may further prolong the QTc interval (e.g., tricyclic anti-depressants, antifungals, macrolide antibiotics, metronidazole). Counsel regarding maintaining appropriate weight, blood pressure and heart-healthy diet. Counsel regarding appropriate exercise. Aerobic exercise is generally safe and should be encouraged for most patients. Intensive isometric activities (e.g., heavy weight lifting, wrestling) should generally be avoided. High repetition weight lifting involving lighter weights is more likely to be safe. The number of repetitions should be limited to that which the survivor can perform with ease. Patients who choose to engage in strenuous or varsity team sports should discuss appropriate guidelines and a plan for ongoing monitoring with a cardiologist.
	<b>Info Link (Mitoxantrone):</b> Although Mitoxantrone technically belongs to the anthracenedione class of anti-tumor antibiotics, it is related to the anthracycline family and is included here because of its cardiotoxic potential.	<b>Info Link</b> • Dose levels correlating with cardiotoxicity are derived from adult studies. • Childhood cancer patients exhibit clinical and subclinical toxicity at lower levels. • Certain conditions (such as isometric exercise, pregnancy, and viral infections) have been anecdotally reported to precipitate cardiac decompensation. • Prospective studies are needed to better define the contribution of these factors to cardiac disease risk.			<b>PHYSICAL</b> <b>Cardiac murmur</b> <b>S3, S4</b> <b>Increased P2 sound</b> <b>Pericardial rub</b> <b>Rales</b> <b>Wheezes</b> <b>Jugular venous distension</b> <b>Peripheral edema</b> Yearly  <b>SCREENING</b> <b>ECHO (or comparable imaging to evaluate cardiac function)</b> Baseline at entry into long-term follow-up, then periodically based on age at treatment, radiation dose, and cumulative anthracycline dose.  <b>EKG (include evaluation of QTc interval)</b> Baseline at entry into long-term follow-up, repeat as clinically indicated.	<b>Considerations for Further Testing and Intervention</b> Cardiology consultation in patients with subclinical abnormalities on screening evaluations, left ventricular dysfunction, dysrhythmia, or prolonged QTc interval. Consider excess risk of intensive isometric exercise program in any high risk patient (defined as needing screening every 1 or 2 years). Additional cardiology evaluation in patients who received $\geq 300$ mg/m <sup>2</sup> or $< 300$ mg/m <sup>2</sup> plus chest radiation who are pregnant or planning pregnancy. Evaluation to include an echocardiogram before and periodically during pregnancy (especially during third trimester) and monitoring during labor and delivery due to risk of cardiac failure.
	<b>Info Link (Dose Conversion):</b> • Pediatric studies of anthracycline cardiotoxicity typically describe risks based on combined cumulative doses of doxorubicin. There is a paucity of literature to support isotoxic dose conversion. • To gauge the frequency of screening, use the following formulas to convert to doxorubicin isotoxic equivalents prior to calculating total cumulative anthracycline dose. <b>Doxorubicin:</b> Multiply total dose x 1 <b>Daunorubicin:</b> Multiply total dose x 1 <b>Epirubicin:</b> Multiply total dose x 0.67 <b>Idarubicin:</b> Multiply total dose x 5 <b>Mitoxantrone:</b> Multiply total dose x 4 • Clinical judgment should ultimately be used to determine indicated screening for individual patients.					<b>SYSTEM = Cardiovascular</b> <b>SCORE = 1</b>

RADIATION				POTENTIAL IMPACT TO BREAST		
Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
77 (female)	<p>≥ 10 Gy to: Subtotal Lymphoid Irradiation (STLI) Axilla Chest (thorax) Extended Mantle Mantle Mediastinal Mini-Mantle Whole lung Total Body Irradiation (TBI)* Total Lymphoid Irradiation (TLI)</p> <p><b>Info Link</b></p> <ul style="list-style-type: none"> <li>• <i>*Important:</i> The risk of breast cancer in patients who received 10–19 Gy of radiation with potential impact to the breast or those who received TBI alone is of a lower magnitude compared to those who received ≥ 20 Gy of radiation with potential impact to the breast (e.g., thorax, axilla).</li> <li>• <i>Monitoring of patients who received 10–19 Gy of radiation with potential impact to the breast, or those who received TBI without additional radiation, should be determined on an individual basis.</i></li> <li>• After the clinician discusses the benefits and risks/harms of screening with the patient, if a decision is made to screen, then follow the recommendations for patients who received ≥ 20 Gy.</li> </ul>	<p><b>Breast cancer</b></p>	<p><b>Host Factors</b> Family history of breast cancer</p> <p><b>Treatment Factors</b> Higher radiation dose Longer time since radiation (&gt; 5 years) Decreased risk in women treated with alkylating agents</p>	<p><b>Host Factors</b> <i>BRCA1, BRCA2, ATM</i> mutation</p>	<p><b>PHYSICAL</b></p> <p><b>Breast exam</b> Yearly, beginning at puberty until age 25, then every 6 months</p> <p><b>SCREENING</b></p> <p>≥ 20 Gy Mammogram Yearly, beginning 8 years after radiation or at age 25, whichever occurs last.</p> <p><b>Breast MRI</b> Yearly, as an adjunct to mammography beginning 8 years after radiation or at age 25, whichever occurs last.</p> <p><b>10–19 Gy or TBI alone</b> Clinician to discuss benefits and risks/harms of screening with patient. If decision is made to screen, then follow screening recommendations for ≥ 20 Gy.</p> <p><b>Info Link</b></p> <ul style="list-style-type: none"> <li>• Mammography is currently limited in its ability to evaluate the premenopausal breast.</li> <li>• MRI is now recommended as an adjunct to mammography in women treated with chest radiation for childhood cancer similar to screening of other populations at high risk for breast cancer (e.g., premenopausal known or likely carriers of gene mutation of known penetrance).</li> <li>• The upper age limit at which both modalities should be used for breast cancer surveillance has not been established.</li> </ul>	<p><b>Health Links</b> <b>Breast Cancer</b></p> <p><b>Counseling</b> Teach breast self-exam and counsel to perform monthly beginning at puberty.</p> <p><b>Considerations for Further Testing and Intervention</b> Surgical consultation for diagnostic procedure in patients with breast mass or suspicious radiographic finding. Decisions regarding the use of HRT should be based on current literature and should take into consideration the risk/benefit ratio for individual patients.</p> <div> <p>SYSTEM = SMN</p> <p>SCORE = 1</p> </div>

**Figure 3.** Guidelines for patients with a history of treatment for Hodgkin lymphoma who are at risk for the potential late adverse effects of cardiotoxicity and breast cancer. From the Children's Oncology Group's *Long-Term Follow-Up Guidelines for Survivors of Childhood, Adolescent, and Young Adult Cancers*, Version 4.0, October 2013. Used with permission.