

How Primary Care Providers Can Help Pediatric/AYA Cancer Survivors Thrive

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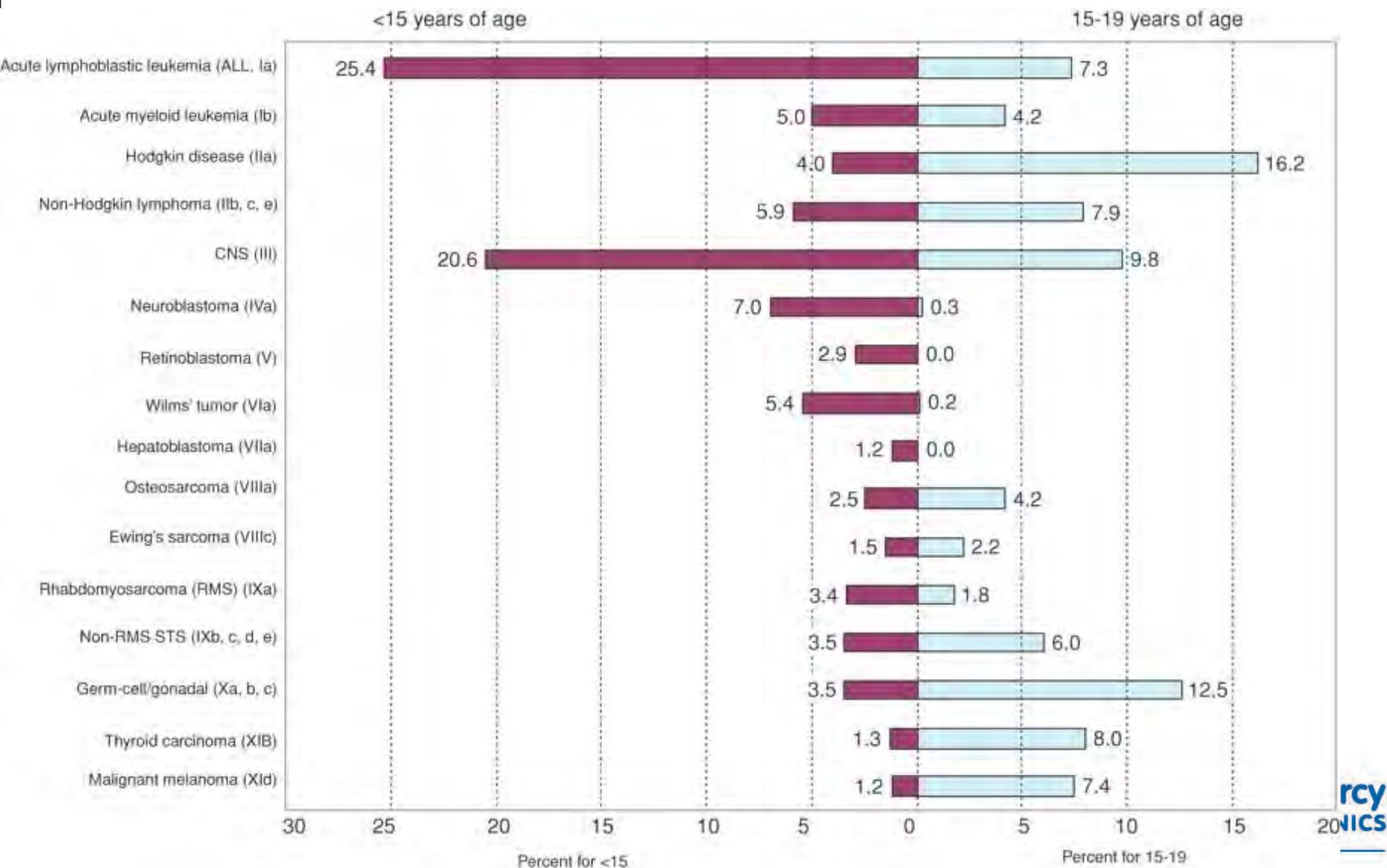


Outline

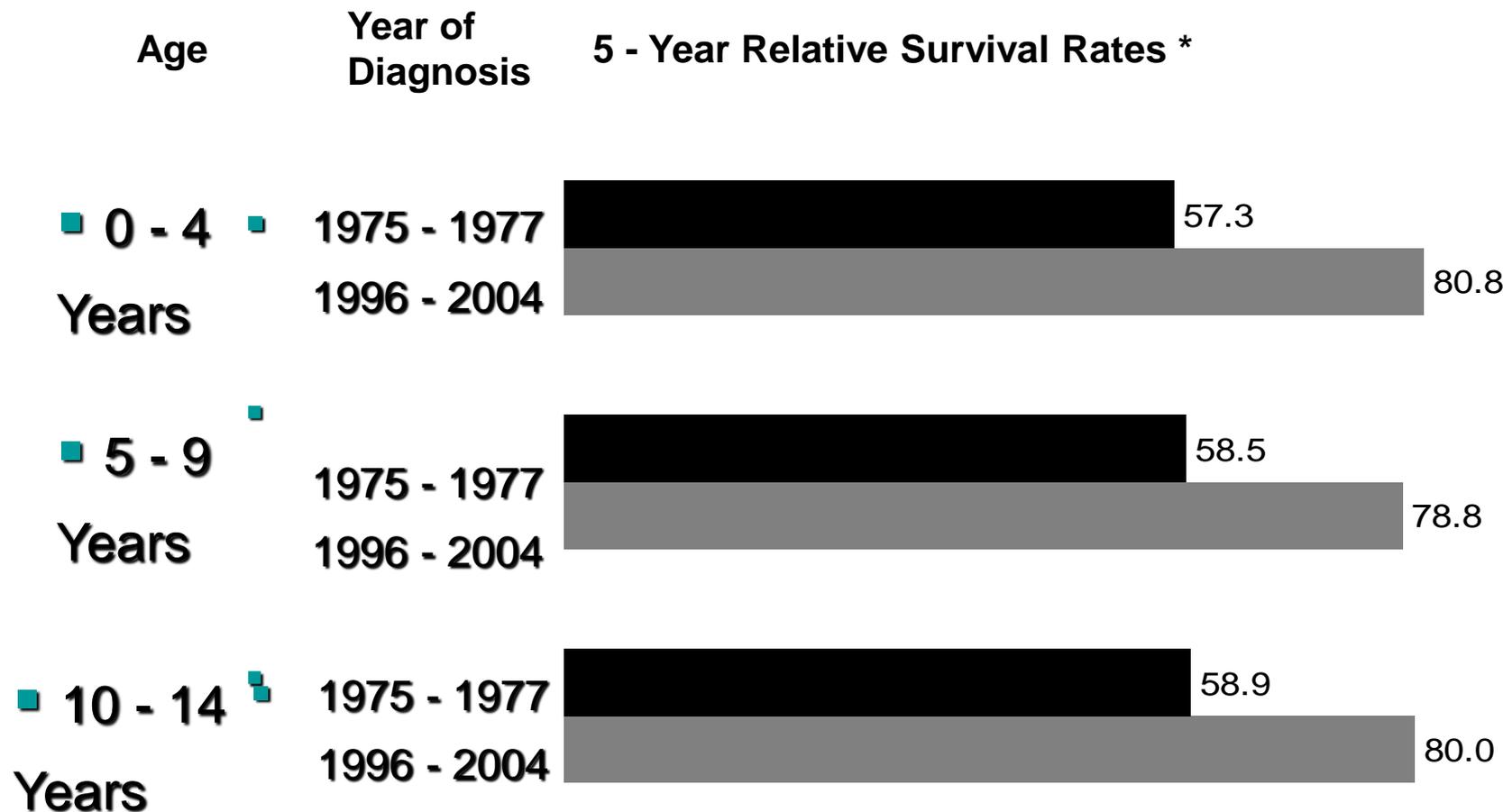
- What are late effects
- Information you need to know about a survivor
- How to access and use Children's Oncology Group guidelines
- Late Effects by organ system
- Secondary Malignancies



Incidence of Cancer by age group



Trends in Cancer Survival by Age Group, Children 0-14 Years, 1975-2004



*5-year relative survival rates, based on follow up of patients through 2005.

Source: Surveillance, Epidemiology, and End Results Program, 1975-2005, Division of Cancer Control and Population Sciences, National Cancer Institute, 2008.



Survivorship Epidemiology

- 13,500 new cases per year in U.S. of childhood and adolescent cancer (Howlander N et al SEER Cancer Statistics Review 1975-2010)
- Estimated that 1 in every 530 individuals between ages 20 and 50 are a survivor of pediatric/adolescent cancer (Ward et al. CA Cancer J Clin 2014; 64:83-103)
- Survivors are more aware of importance of quality comprehensive follow up care (Mulder et al Future Oncol 2013)



What are Late Effects?

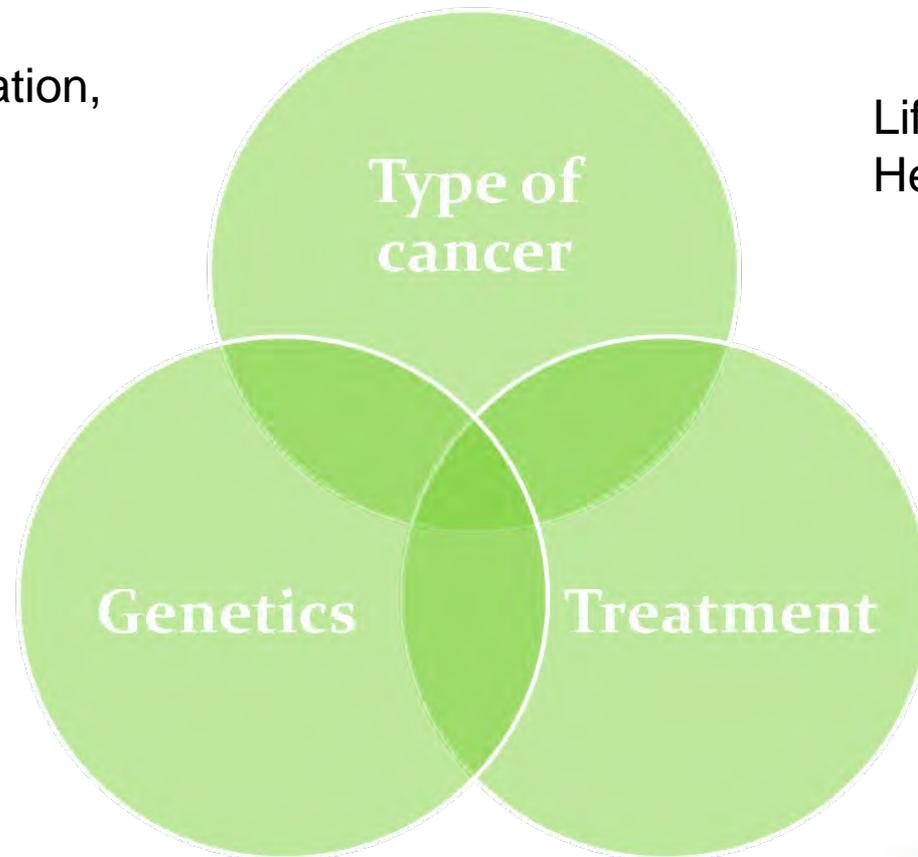
- Complications or disabilities from cancer, treatment or both
- Can be physical or emotional
- May resolve or become chronic problems
- Usually begin to appear in second decade of life



What Causes Late Effects?

Location, Location,
Location

Lifestyle
Health Behaviors

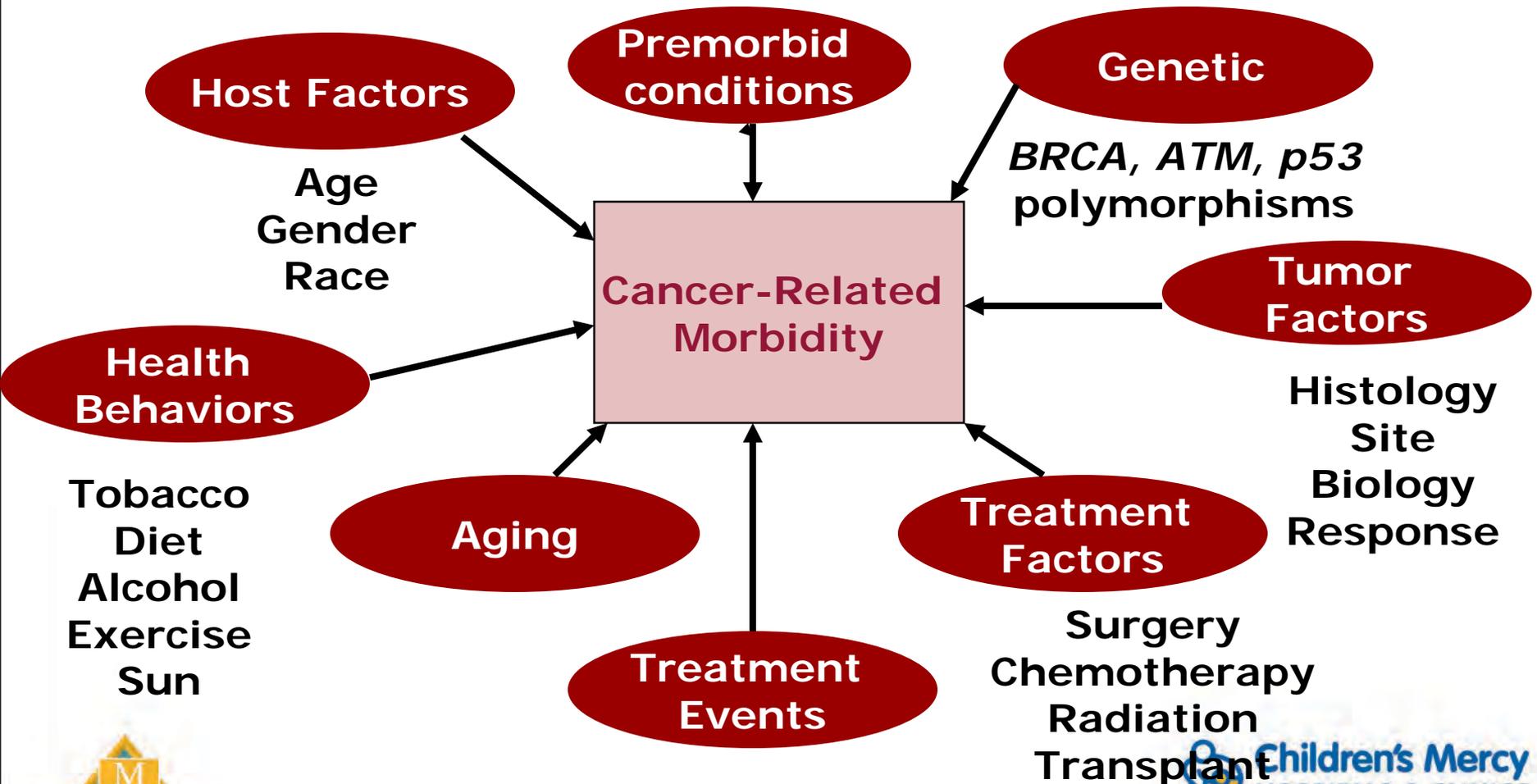


Age
Gender
Genes

Surgery
Chemotherapy
Radiation



Risk-based survivor care



How To Access Guidelines

<https://childrensoncologygroup.org/index.php/survivorshipguidelines>



COG Guidelines

- Guidelines are updated regularly
- Will change with new knowledge
- Working to decrease late effects with new therapies or decrease in therapy



Treatment summary & survivorship care plan

- All patients should receive an individualized survivorship care plan that includes a treatment summary
 - Organizational support for survivorship care
 - Institute of Medicine, American Cancer Society, American Society of Clinical Oncology, Children's Oncology Group
- American College of Surgeons Commission on Cancer
 - Mandate survivorship care plans for all survivors
 - 25% of all survivors by January 2016
 - 100% of all survivors by 2019

Blanch-Hartigan et al. Journal Clinical Oncology. 2014. Provision and Discussion of Survivorship Care Plans Among Cancer Survivors
Barton. Perspectives: Research in Context; A Cancer Journal for Clinicians. 2014. Oncologists and Primary Care Physicians Infrequently Provide Survivorship Care Plans
Commission on Cancer, 2011. Cancer Program Standards: Ensuring Patient-Centered Care.



Treatment Summaries:

- Minimum information to include:
 - Diagnosis, dates on/off therapy
 - Chemotherapy and cumulative doses
 - Radiation therapy with location and doses
 - Any other therapy (antibodies, bone marrow transplant, experimental treatment)
 - Surgeries
 - Complications and/or known late effects



Primary Diagnosis

Diagnosis Neuroblastoma,
Diagnosis Date 11-30-2006
Age Diagnosed 5 Years 7 Months
Comment

Date Therapy Completed
**Sites Involved/
Stage/Diagnostic Details**

02-05-2008
Stage IV, not N-myc
amplified

Pertinent History

presented with a 3 week history of back pain and a 1 week history of chest pain and some forced breathing. He was seen by his primary care provider who ordered a chest x-ray. The x-ray revealed a posterior mediastinal mass. He also presented with a history of decreased appetite, occasional difficulty breathing and low grade fevers. A chest CT confirmed the mediastinal mass. The initial biopsy of the mass showed ganglioneuroblastoma, however, bone marrow showed neuroblastoma cells. Initial work-up also revealed metastases to the thoracic and lumbar vertebra as well as right and left shoulder, right upper thigh, right pubic bone, right iliac wing and scattered areas in the abdomen.

Heredity

None

Relapses - None Indicated

Subsequent Malignant Neoplasm - None Indicated

Past Medical History

History of ADHD. History of systolic heart murmur. History of allergies and asthma. History of bipolar disorder.

Family History

Mother passed away from a brain tumor in 2006. Paternal grandmother with a history of breast cancer, possible skin cancer and diabetes. Paternal grandfather with history of high blood pressure and high cholesterol.



Surgeries - 2 surgeries entered

Date	Procedure	Site (if applicable)	Laterality (if applicable)	Surgeon/Institution	Comment
1 12-14-2006	Central venous catheter			Dr. George Holcomb/Children's Mercy Hospital	
2 11-30-2006	Other: Thorascopic removal of mediastinal mass			Dr. George Holcomb/Children's Mercy Hospital	

Chemotherapies - 7 chemotherapies entered

Drug Name	Route	Cumulative Dose	Date of Treatment	Comment
1 Vincristine	IV	7.2 mg/m2		
2 Cyclophosphamide	IV	16,800 mg/m2		
3 Doxorubicin	IV	300 mg/m2		
4 Etoposide (VP16)	IV	2,552 mg/m2		Includes doses given as part of conditioning regimen for stem cell infusion
5 Cisplatin	IV	400 mg/m2		
6 Carboplatin (myeloablative doses only)	IV	1,700 mg/m2		
7 Melphalan	IV	210 mg/m2		



Radiation - 2 radiation entered

Site/Field/Type	Laterality	Dates	Fractions	Dose per Fraction (Gy)*	Total Fractions	Initial Dose (Gy)*	Boost Dose (Gy)*/Site	Total Dose /w Boost (Gy)*
1 Thorax: Mantle		START: 07-30-2007 STOP: 08-14-2007	12	1.80Gy	12			21.60 Gy

Oncologist: Dr. Vickie Massey

Institution: Kansas City Cancer Center

Comment:

2 Extremities: Upper extremity	Right	START: 07-30-2007 STOP: 08-14-2007	12	1.80Gy	12			21.60 Gy
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Oncologist: Dr. Vickie Massey

Institution: Kansas City Cancer Center

Comment:

Type	Source	Date of Infusion	Conditioning Regimen(s)	Institution	Treating MD	Comment
1 Autologous	Peripheral blood stem cells	06-19-2007	Carboplatin	Children's Mercy Hospital	Dr. Jignesh Dalal	

 Was this patient ever diagnosed with **chronic** graft-versus-host disease (cGVHD)? **NO**
Other Therapeutic Modalities -
(Radioiodine, Systemic MIBG, Bioimmunotherapy) 5 other modalities

Therapy	Route	Cumulative Dose (if known)	Comment
1 Hematopoietic growth factors G-CSF	SQ		given after each round of chemo and post stem cell infusion
2 Other: Isotretinoin	PO	13,440 mg/m2	
3 Other: Monoclonal antibody: GD-2	IV	500 mg/m2	
4 Other: GM-CSF	IV	8.40 mg/m2	
5 Interleukin IL-2	IV	53.3 million IU/m2	

Passport for Care®

- Provider inputs information regarding treatment
- Program pulls in the recommended screening guidelines per COG Long-Term Follow-Up Guidelines
- Generates a survivorship care plan including treatment summary and recommended screening/evaluation for potential late effects
- Survivors can access their own treatment summaries/screening recommendations via patient portal



“The cancer experience is a process that extends throughout a lifetime, a looking glass through which all future health and illness behaviors of the survivor must be interpreted.”

~Dr. Kevin Oeffinger



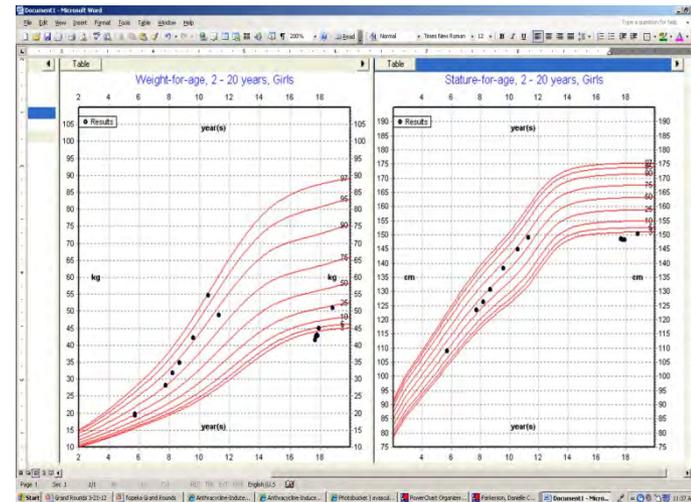
Endocrine

- Central Adrenal Insufficiency
 - Cranial irradiation
 - Screen for yearly for 15 yrs with 8 am cortisol and for sings/symptoms
- Hypothyroidism/ Thyroid nodule/cancer
 - Cranial irradiation, TBI and Thyroid irradiation (also risk for Hyperthyroidism)
 - Yearly history/TSH, free T4 and thyroid exam



Endocrine

- Growth Hormone deficiency
 - Monitor height/weight, BMI, Tanner staging every 6 months until growth complete/sexually mature
 - Refer to endocrine if height $<3^{\text{rd}}$ percentile, Drop >2 percentile channels, growth $<4\text{-}5$ cm/year, Lack of pubertal growth spurt



Endocrine

- Precocious Puberty
 - Cranial Irradiation
 - Hgt/wgt, tanner stage, testicular volume yearly until sexually mature
 - Refer if rapidly growing, accelerated puberty in girls <8 or boys < 9 years old
- Hypogonadism/Infertility
 - Cranial irradiation, TBI, thyroid irradiation, gonadal irradiation, alkylating agents, heavy metals
 - Tanner stage (until sexually mature), LH/FSH estradiol or testosterone (yearly starting age 13 F, 14 Males)



Endocrine

- Low bone mineral density
 - Corticosteroids
 - Anti-metabolites
 - Stem cell transplant
 - Obtain baseline DEXA
 - Refer to endocrinre if osteoporosis T score >2.5DS or hx of multiple fractures
- Hyperprolactionemia
 - High dose cranial RT (>40 gray) mid brain surgery or tumor in hypothalamic area
 - Prolactin levels prn symptoms



Endocrine

- Obesity/hyperlipidemia
- Metabolic syndrome
 - Cranial irradiation
 - TBI (for MS)
 - Fasting blood glucose/insulin/lipid profile
 - Q 2 yrs if overweight
 - Q 5 yrs if nml weight and prn



Neurocognitive

- Global dysfunction
 - Cranial irradiation (36 gy or more)
 - Intrathecal and high dose methotrexate
 - Educational and vocational progress
 - Formal neuropsychological evaluation in those receiving tx with higher doses cranial irradiation/extensive brain surgery



Neurological

- Treatment/disease complications
 - Seizures, ICP
- Peripheral Neuropathy
 - Vincristine/Vinblastine and cisplatin
- Cerebrovascular
 - Cranial irradiation

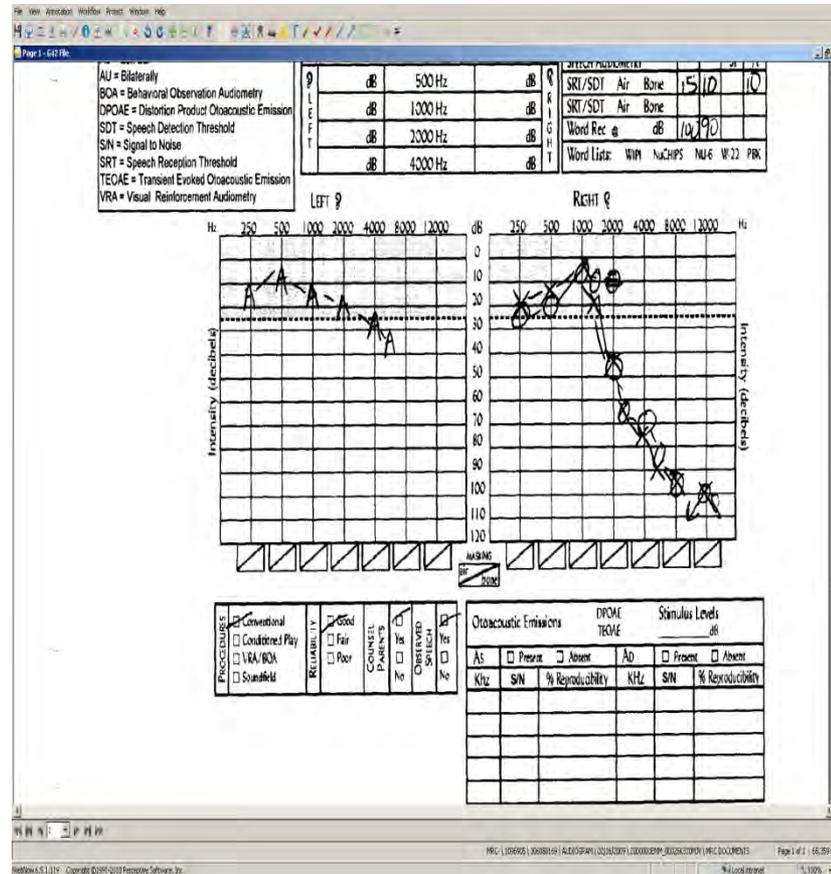


Eyes

- Vision
 - Retinoblastoma tx, Optic gliomas
- Cataracts
 - Steroids, busulfan, cranial RT, eye/orbital RT
 - Yearly Eye exams
- Other eye issues
 - Lacrimal duct atrophy, glaucoma, eye pain etc
 - Cranial RT, eye/orbital RT
 - Yearly Eye exams



Ears



- Ear wax
- Tympanosclerosis
- Hearing
 - Cisplatin, carboplatin (sensineural)
 - Radiation (conductive)

Heart: Screening Guidelines

Recommended Frequency of Echocardiogram		
Anthracycline Dose*	Radiation Dose**	Recommended Frequency
None	< 15 Gy or none	No screening
	≥ 15 - < 35 Gy	Every 5 years
	≥ 35 Gy	Every 2 years
< 250 mg/m ²	< 15 Gy or none	Every 5 years
	≥ 15 Gy	Every 2 years
≥ 250 mg/m ²	Any or none	Every 2 years

*Based on doxorubicin isotoxic equivalent dose. See dose conversion instructions in section 33.
 **Based on radiation dose with potential impact to heart (radiation to chest, abdomen, spine [thoracic, whole], TBI). See section 76.

If radiation dose > 15 Gy and or anthracycline exposure an EKG (include evaluation of QTc interval) at baseline at entry into long-term follow up; repeat as clinically indicated

Anthracycline Dose Equivalents

Doxorubicin: Multiply total dose x 1

Daunorubicin: Multiply total dose x 0.5

Epirubicin: Multiply total dose x 0.67

Idarubicin: Multiply total dose x 5

Mitoxantrone: Multiply total dose x 4



Heart: Modifying Risk

- Armstrong GT et al JCO 2013 found in multivariate analysis that hypertension or two or more cardiovascular risk factors (hypertension, dyslipidemia, diabetes, obesity) was significantly associated with cardiac-specific mortality in CCS
- Recommend regular cardiovascular exercise (At least 30-45 minutes 3-4 times a week); limit screen time to no more than 2 hours for our patients and monitor blood pressure



Lungs

Lung Volumes

- Data Actual %Predicted
- TLC: 8.04 102.7
- RV: 2.09 120.5
- RV/TLC: 25.9 110.1
- FRC: 3.61 99.3
- Raw:
- DLCO: 32.92 86.5
- DLCO adj: 32.05 84
- Hgb: 15.6
- MVV:
- SpO2: 98%
- Comments:
- Interpretation:
- Mild intrathoracic airflow obstruction; better after bronchodilator. Worse from 11/20/05. Normal lung volumes; similar to 11/30/05. Normal diffusion capacity, but reduced from 11/30/05. Normal oxygen saturation.



Lungs

- Pulmonary dysfunction
 - Surgery (such as lobectomy to treat metastatic disease)
- Pulmonary Fibrosis, Interstitial pneumonitis, restrictive or obstructive lung disease
 - Alkylating agents (busulfan, carmustine, lomustine, *bleomycin)
 - Radiation therapy (>15 gray)
 - Annual pulmonary exam
 - Question regarding respiratory symptoms/exercise tolerance
 - Baseline CXR and pulmonary function studies (repeat if abnormal esp prior to general anesthesia)



Lungs

- Other factors that contribute
 - Combination therapy
 - Younger age at therapy
 - Smoking
 - Atopic history



Kidneys

- Glomerular toxicity, tubular toxicity, renal insufficiency
 - Cisplatin and carboplatin
 - Ifosfamide (Fanconi's-like syndrome can lead to hypophosphatemic rickets)
 - Radiation injury (doses >12-14 gray)
 - Nephrectomy
 - Yearly blood pressure
 - Yearly UA in those at risk
 - Baseline BMP, mag, phos



Kidneys

- Hypertension
 - Study of 1442 long term survivors demonstrated hypertension in 14.8% of patients (Knijnenburg et al *Clin J Amer Soc Nephrol* 2012)
 - Average age was 19.8
 - Monitoring for hypertension important preventative measure



Bladder

- Radiation induced fibrosis limit bladder capacity and function
- Hemorrhagic cystitis
 - Pelvic radiation
 - Ifos/Cyclophos (rare)



Liver

- Hepatitis B (if transfused prior to 1972) and Hepatitis C (if transfused prior to 1993)
- Veno-occlusive disease - usually acute without long-term sequelae
 - Dactinomycin, mercaptopurine and thioguanine; HSCT

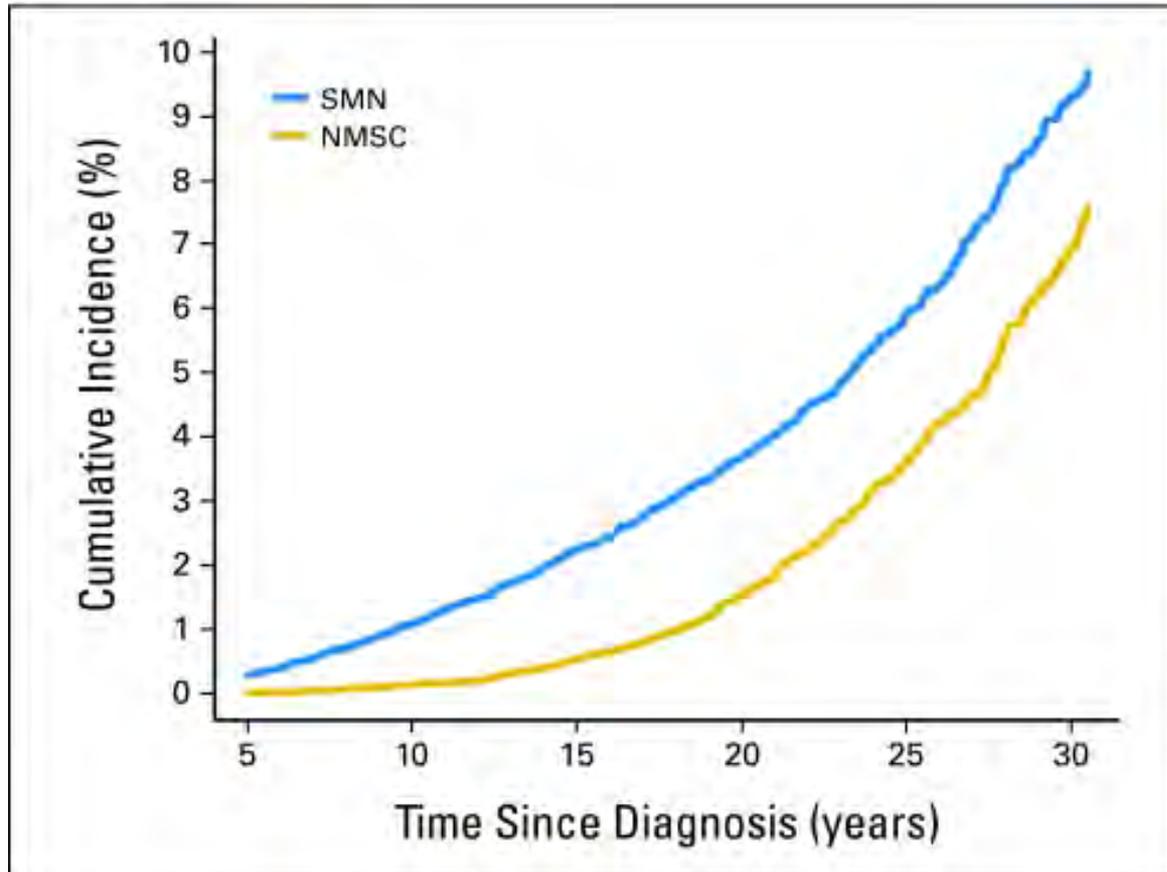


Psychosocial

- PTSD
- Depression and Anxiety
- Concerns about physical health, body image or self concept, access to life and health insurance



Secondary Neoplasms



Meadows et al JCO 2009



SNs

- Compared to the general population the largest risk excesses were observed for breast cancers (SIR16.2), bone cancers (SIR19.1), and thyroid cancers (SIR11.3)
- In an analysis of female breast cancer, the cumulative incidence at an attained age of 40 years was highest (12.9%) for survivors of HL treated with radiotherapy



Meadows et al JCO 2009



Risk Factors for SNs

- Higher doses of alkylating agents (cyclophosphamide, ifosfamide), epipodophyllotoxins (etoposide, tenoposide), anthracyclines
- Radiation therapy
- Age at diagnosis (younger age)
- Race (female survivors increased risk)



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