Introduction to Pediatric Neoplasms

FCDS EDUCATIONAL WEBCAST SERIES

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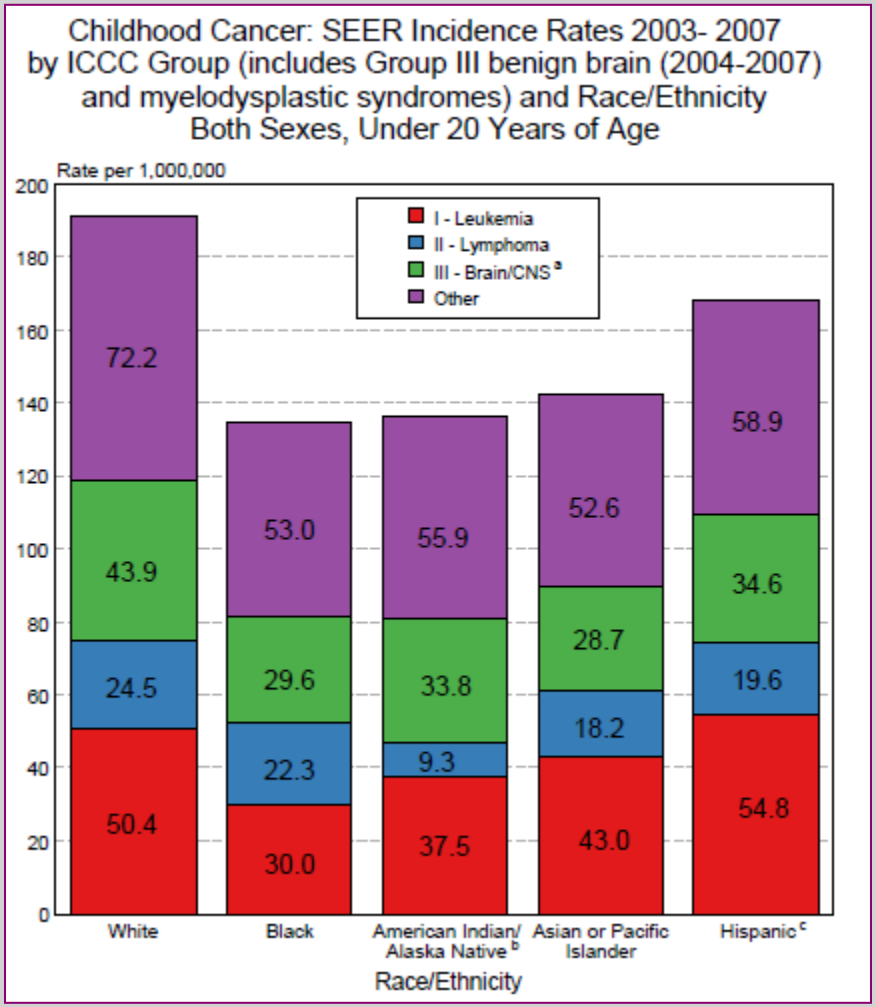
Program Outline

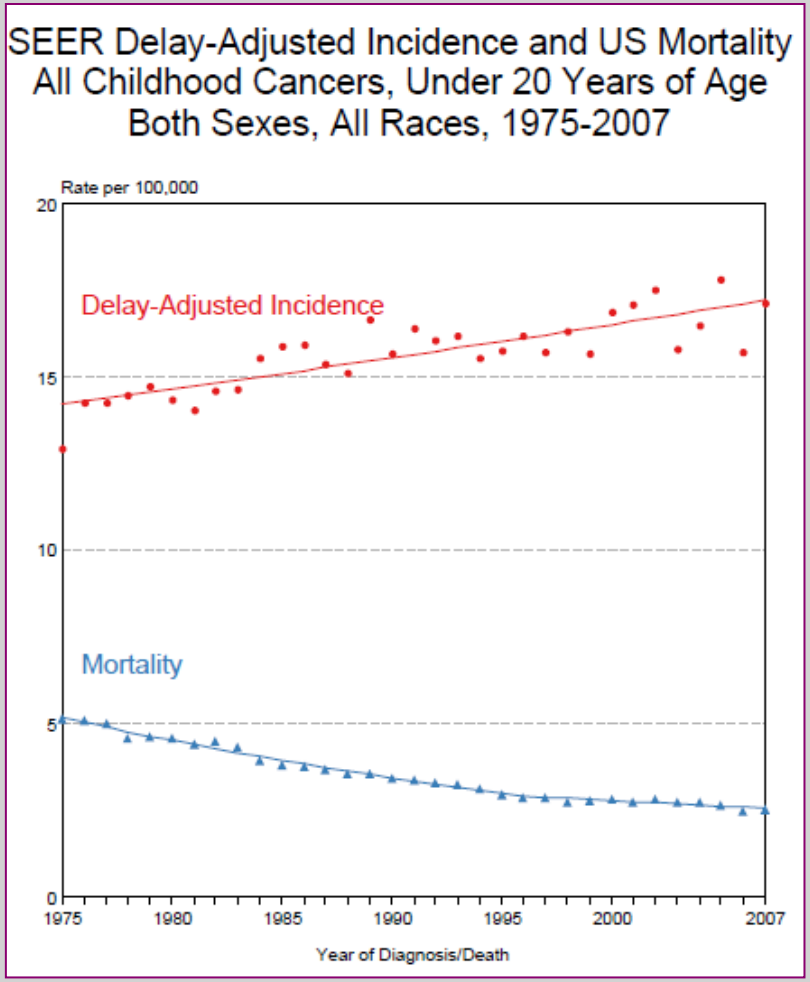
- Introduction
- Types of Pediatric Neoplasms
- Signs and Symptoms
- Causes and Risk Factors
- MPH Rules – Solid Tumors
- MPH Rules – Heme/Lymph Neoplasms
- Staging Pediatric Tumors
- Collaborative Stage Data Collection System
- Treatment Options
- Future Webcasts
- Q&A

Introduction



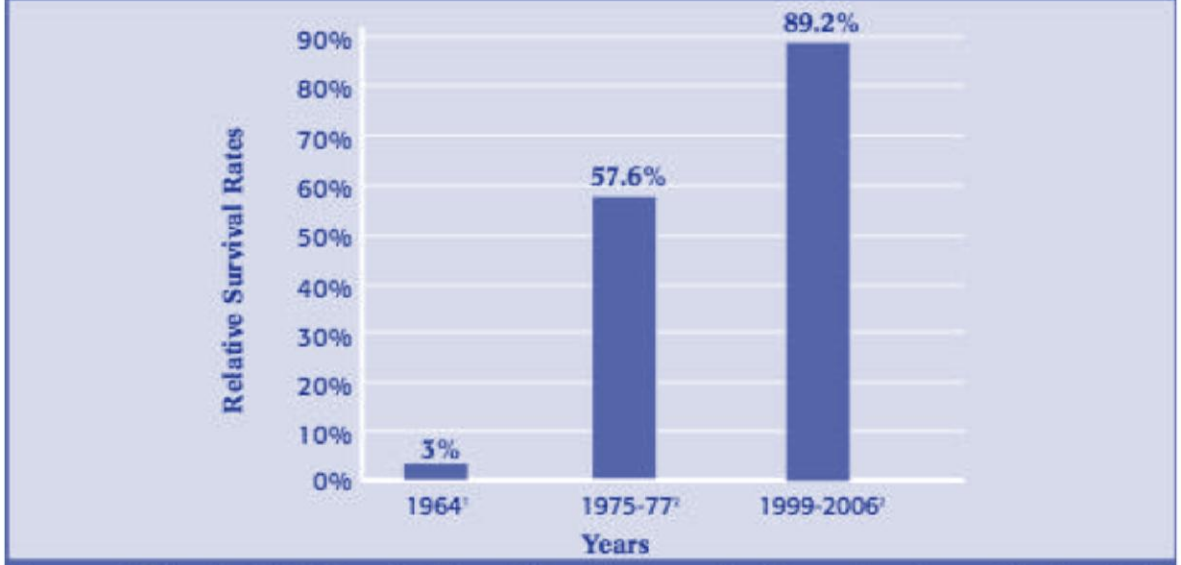
Source: SEER Cancer Statistics Review (CSR) 1975-2007

Introduction



Introduction

Figure 3. Five-Year Relative Survival Rates for Acute Lymphoblastic Leukemia in Children Under 15 Years, 1964-2006



Sources: 1. Zuelzer WW. Implications of long-term survivals in acute stem cell leukemia of childhood treated with composite cyclic therapy. *Blood*. 1964;24:477-494. 2. Surveillance, Epidemiology and End Results (SEER) Program. Cancer Statistics Review, 1975-2007. National Cancer Institute; 2010.

Introduction

Building on 50 Years of Cooperative Research

PEDIATRIC CLINICAL TRIAL ENROLLMENT	
5 and younger	> 90%
10 and younger	75-90%
10 to 15	50%
Adolescents aged 15 to 19	15-25%

Introduction

Building on 50 Years of Cooperative Research

1940s

Remission achieved in pediatric leukemia patients using an antifolate drug, aminopterin

Introduction

Building on 50 Years of Cooperative Research

1950s

- 6-mercaptopurine treats pediatric acute lymphoblastic leukemia
- Combination chemotherapy introduced by NCI researchers
- NCI begins funding pediatric cooperative clinical trials

Introduction

Building on 50 Years of Cooperative Research

1960s

- Dactinomycin first used to treat Wilms tumor
- National Wilms Tumor Study Group formed and multi-modality therapy first used in pediatric patients (surgery, radiation, chemo)
- Prophylaxis of occult central nervous system leukemia markedly improves outcome for children with ALL
- Laminar airflow technology creates "sterile rooms" for chemotherapy patients

Introduction

Building on 50 Years of Cooperative Research

1970s

- Intergroup Rhabdomyosarcoma Study Group Committee pioneers repetitive-course, multi-agent chemotherapy for advanced rhabdomyosarcoma
- First successful bone marrow transplant (BMT) for leukemia
- Knudson describes the 2-hit hypothesis for retinoblastoma to describe genetics and heredity of cancer

Introduction

Building on 50 Years of Cooperative Research

1980s

- First tumor-suppressor gene, in retinoblastoma, is cloned
- MYCN identified as a target of genomic amplification in neuroblastoma
- Adjuvant chemotherapy improves relapse-free survival for pediatric osteosarcoma
- Different treatment for lymphoblastic lymphoma vs other lymphomas are realized
- Platinum-based chemo improves response rates in pediatric germ cell tumors
- National Marrow Donor Program begins

Introduction

Building on 50 Years of Cooperative Research

1990s

- Autologous BMT and 13-cis-retinoic acid improve survival for neuroblastoma
- Characteristic fusion genes identified for pediatric solid tumors
- Combined ifosfamide and etoposide improve outcomes for Ewing sarcoma
- Long-term survival rates of 80-90% achieved for advanced Burkitt lymphoma
- Genetic test for thyroid cancer enables prophylactic thyroidectomy before age 2
- NCI-funded Childhood Cancer Survivors Study begins

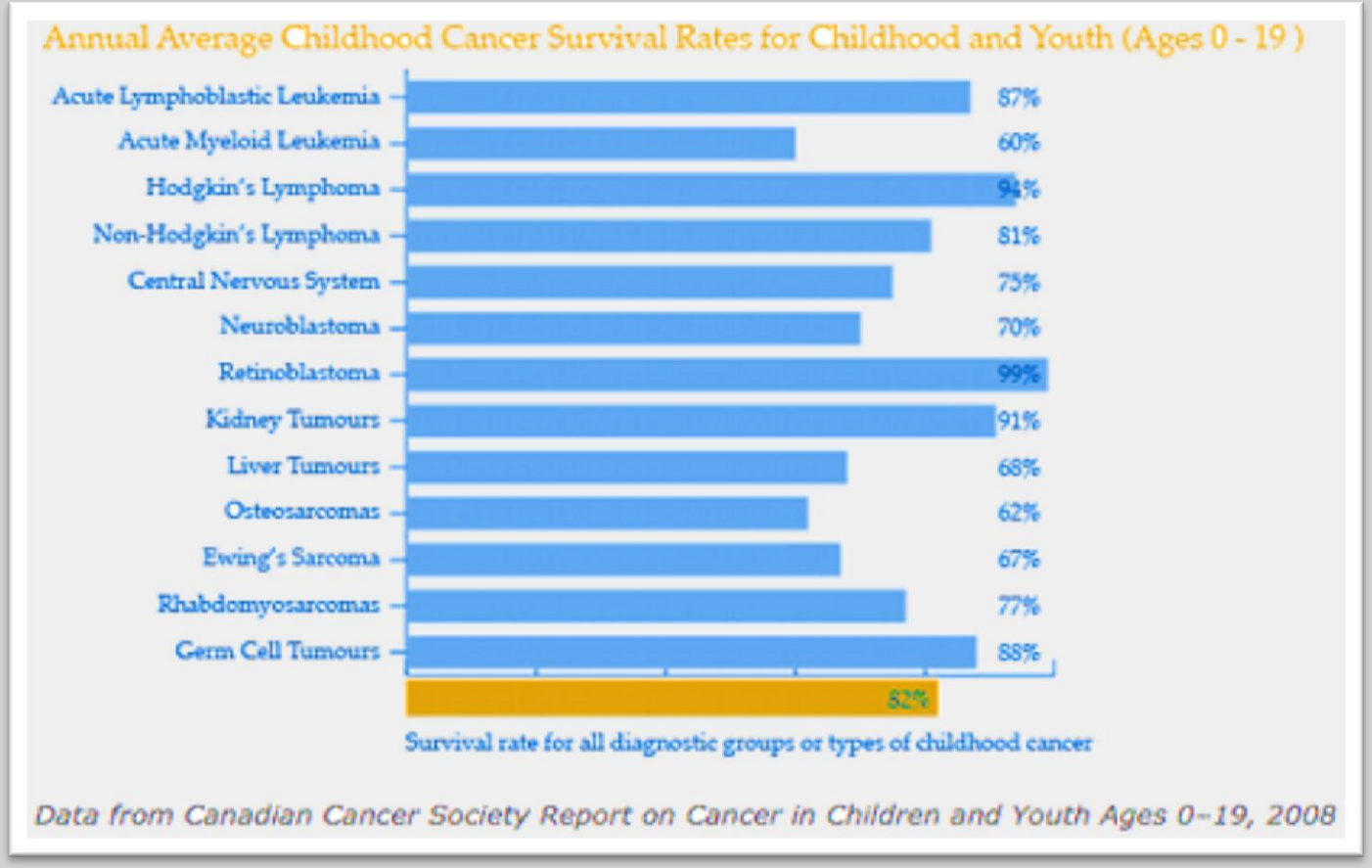
Introduction

Building on 50 Years of Cooperative Research

2000s

- Four legacy research groups merge as the Children's Oncology Group (COG)
- COG publishes long-term follow-up guidelines for pediatric cancer survivors
- Imatinib added to intensive chemotherapy improves early outcomes for Ph+ ALL
- 5-year survival rates for children with cancer (age 0-14 years) approach 80%

Introduction

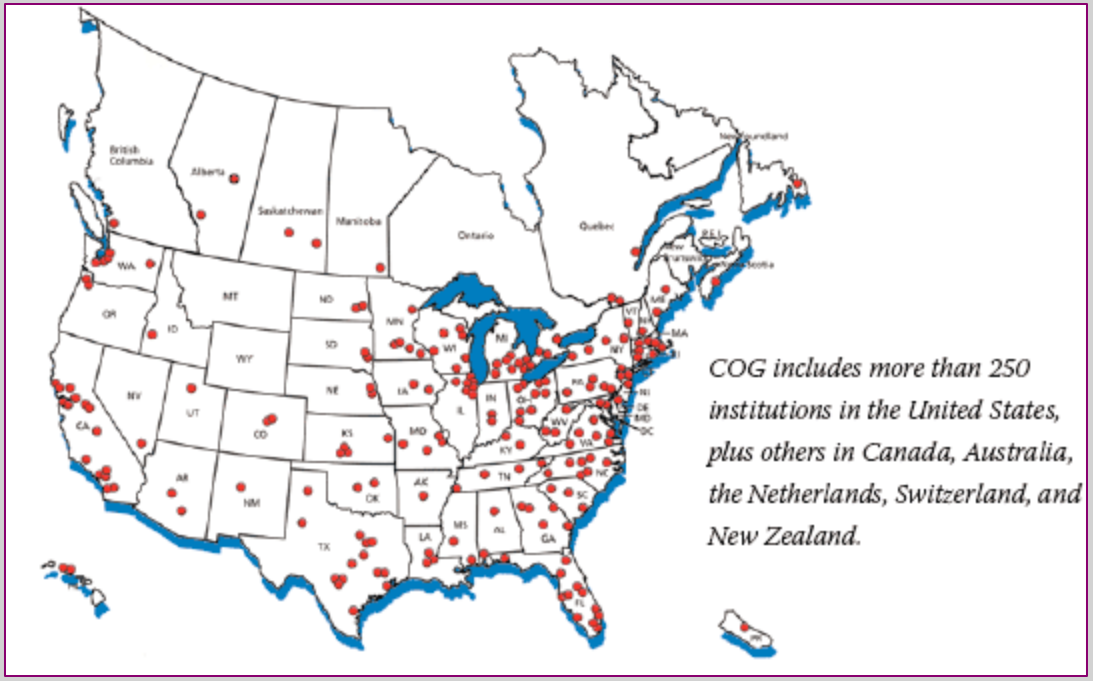


Pediatric Cancer Research
Pediatric Cancer Registries

Children's Oncology Group

CHILDREN'S ONCOLOGY GROUP

The world's childhood cancer experts



Pediatric Brain Tumor Consortium

Children's Oncology Group

Childhood Cancer Survivor Study

- Diagnosis 1970-1986
- 20,000 person cohort
- Survival at least 5 years
- Chance for long-term effects increase over time
- > 70% at least 1 chronic illness related to treatment
- > 25% have 3 or more chronic illnesses related to tx

Childhood Cancer Survivor Study

- Kidney Disease
- Second Cancers
- Cognitive Dysfunction
- Cardiovascular Disease
- Endocrine Abnormalities
- Musculoskeletal Conditions

Long-Term Active Follow-Up is CRITICAL…

Childhood Cancer Survivor Study

Health Effects	Predisposing Therapy	Clinical Manifestations
Oral/dental	Any chemotherapy in a patient who has not developed permanent dentition	Dental maldevelopment (tooth/root agenesis, microdontia, root thinning and shortening, enamel dysplasia)
	Radiation impacting oral cavity and salivary glands	Salivary gland dysfunction
		Xerostomia
		Accelerated dental decay
		Periodontal disease
Thyroid	Radiation impacting thyroid gland	Hypothyroidism
		Hyperthyroidism
		Thyroid nodules
Cardiovascular	Radiation impacting cardiovascular structures	Subclinical left ventricular dysfunction
		Cardiomyopathy
		Pericarditis
		Heart valve dysfunction
		Conduction disorder
		Coronary, carotid, subclavian vascular disease
		Myocardial infarction
		Stroke
	Anthracycline chemotherapy	Subclinical left ventricular dysfunction
		Cardiomyopathy
		Congestive heart failure

Childhood Cancer Survivor Study

Pulmonary	Radiation impacting the lungs	Subclinical pulmonary dysfunction
	Bleomycin	Pulmonary fibrosis
Musculoskeletal	Radiation of musculoskeletal tissues in any patient who is not skeletally mature	Growth impairment
	Glucocorticosteroids	Bone mineral density deficit
		Osteonecrosis
Reproductive	Alkylating agent chemotherapy	Hypogonadism
	Gonadal irradiation	Infertility
Immune	Splenectomy	Overwhelming post-splenectomy sepsis
Subsequent neoplasm or disease	Alkylating agent chemotherapy	Myelodysplasia/acute myeloid leukemia
	Epipodophyllotoxins	Myelodysplasia/acute myeloid leukemia
	Radiation	Solid benign and malignant neoplasms

Pediatric Cancer Registries

- COG – Childhood Cancer Research Network
- CDC NPCR – National Childhood Cancer Registry
- FAPTP – Florida Consortia Pediatric Cancer Registry
- Cancer Site/Type Specific Registries
- Bone Marrow Donor Registries
- National Children's Study
- Other

Florida Association of Pediatric Tumor Programs

FAPTP

and

The Florida Pediatric CCOP

Member Directory

3650 Spectrum Blvd, Suite 100, Tampa, FL 33612
(813) 396-9528 (813) 910-5928 Fax
faptp@epi.usf.edu flccop@epi.usf.edu
www.faptp.org

Table of Contents

*Member of the Florida Pediatric Community Clinical Oncology Program-CCOP
**Member only of the Florida Pediatric Community Clinical Oncology Program

Source: FAPTP

Florida Association of Pediatric Tumor Programs

http://faptp.epi.usf.edu

St. Joseph's Children's Hospital of Tampa

Children's Hospital at St. Mary's

MD Anderson Cancer Center Orlando
Supported by the Charles Lewis Institute
Part of Orlando Regional Healthcare

Children's Center for Cancer & Blood Diseases

Joe DiMaggio Children's Hospital at Memorial

Nemours Nemours Children's Clinic

all children's hospital

Baptist Health

UF&Shands The University Of Florida Health System

The Children's Hospital of Southwest Florida Lee Memorial Health System

Miami Children's Hospital
The Mary Ann Knight International Institute of Pediatrics
Founded as Variety Children's Hospital

Department of Pediatrics
University of Miami Miller School of Medicine

Broward Health Chris Evert Children's Hospital

Palms West Hospital

Source: FAPTP

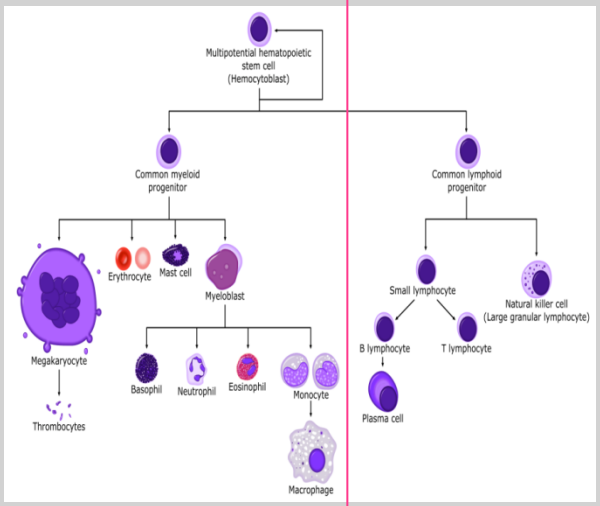
Types of Pediatric Neoplasms

Major Types of Pediatric Neoplasms

Childhood Cancer Incidence Rates (SEER) by ICCC Group 2001-2004 – All Sex, All Race	
Leukemia	44.2
Brain/CNS	27.4
Lymphoma	23.2
Soft Tissue	12.0
Germ Cell	11.8
Bone	8.9
Neuroblastoma	7.6
Renal	6.0
Retinoblastoma	3.0
Note: Rates are per 1,000,000 population	

Major Types of Pediatric Neoplasms

- Lymphoid Neoplasms
  - Hodgkin Lymphoma
  - Non-Hodgkin Lymphoma
  - Acute Lymphocytic Leukemia



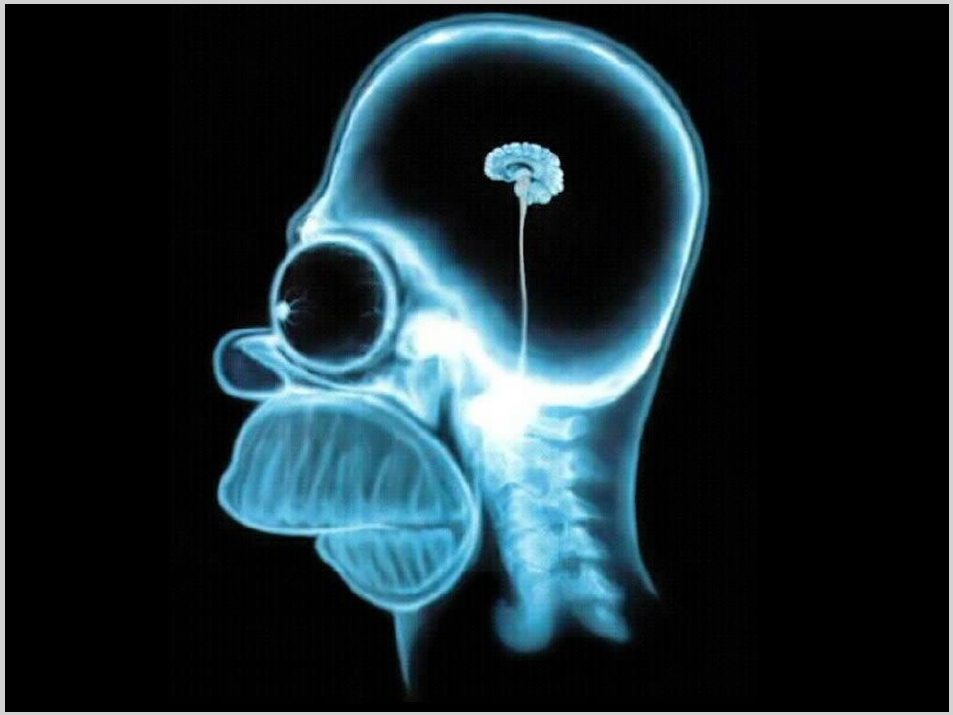
- Myeloid Neoplasms
  - Myeloid Leukemia Associated with Down Syndrome
  - Chronic Myeloid Leukemia
  - Acute Myeloid Leukemia

Major Types of Pediatric Neoplasms

- Brain and CNS –Non-Germ Cell Tumors
  - Astrocytoma
  - Glioblastoma
  - Ependymoma
  - Medulloblastoma
  - PNET – Primitive Neuroectodermal Tumor

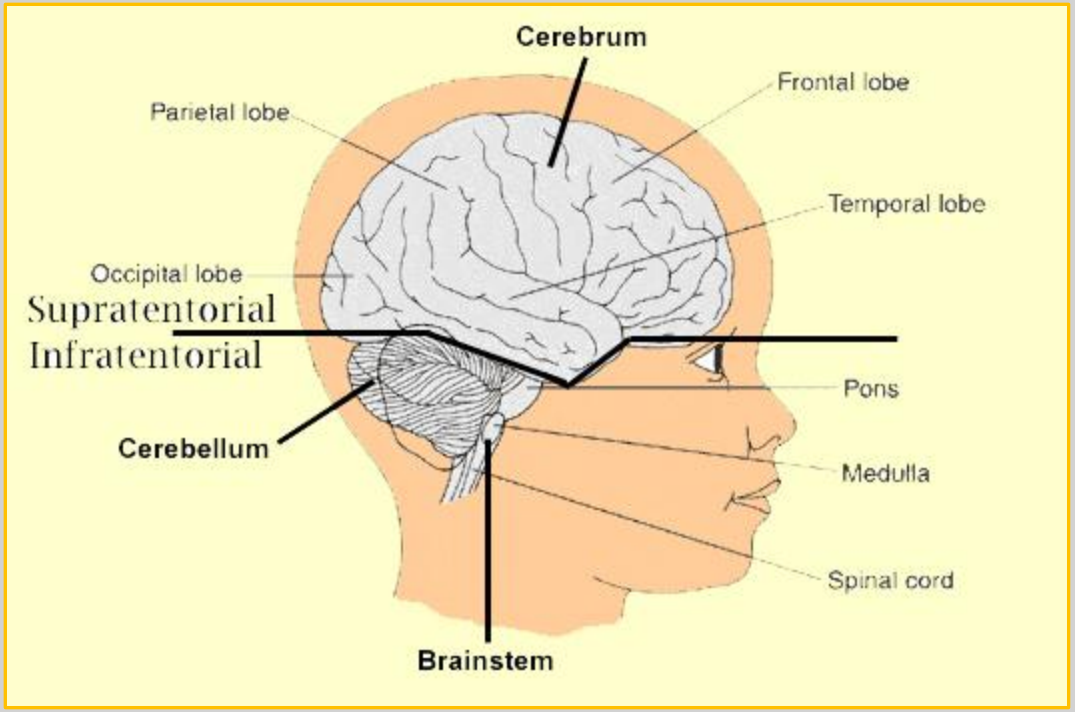
- Brain and CNS – Germ Cell Tumors
  - Atypical Teratoid/Rhabdoid Tumor
  - Mixed Germ Cell Tumor
  - Embryonal Tumor

Major Types of Pediatric Neoplasms



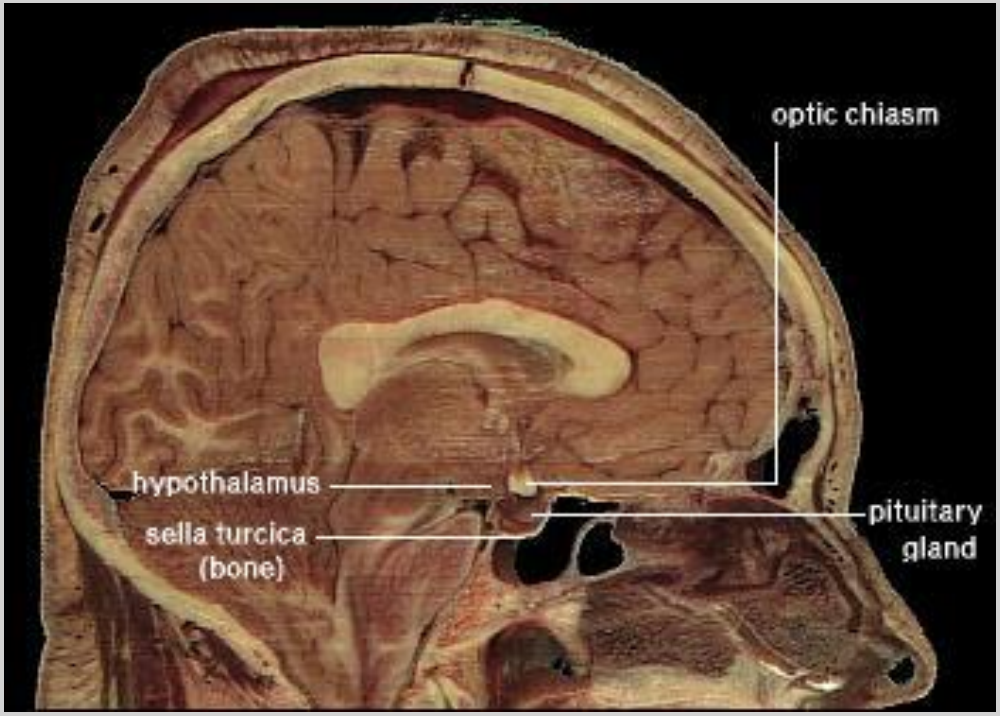
Source: The Simpsons – Homer Brain X-Ray

Major Types of Pediatric Neoplasms



Source: http://www.montekids.org/services/neurosurgery/neurologicaldisorders/brain_tumor/

Major Types of Pediatric Neoplasms



Source: http://www.vivo.colostate.edu/hbooks/pathphys/endocrine/hypopit/anatomy.html

Major Types of Pediatric Neoplasms

Pediatric Sarcoma	
Sarcoma – Bone	Sarcoma – Connective/Soft Tissue
Ewing Sarcoma – Undifferentiated pPNET	pPNET – PNET with Neural Differentiation
Osteosarcoma	Rhabdomyosarcoma
Odontogenic Sarcoma	Lymphangiosarcoma
Chondrosarcoma	Fibrosarcoma

Ewing Family of Tumors		
9473/3	PNET	Brain/CNS
9364/3	pPNET	Soft Tissue
9365/3	Askin Tumor	Soft Tissue
9260/3	Ewing Sarcoma	Bone
9260/3	Ewing Sarcoma – Extra Osseous	Soft Tissue

Major Types of Pediatric Neoplasms

Childhood Soft Tissue Sarcoma Treatment (PDQ®)

National Cancer Institute at the National Institutes of Health

	Age <5 y	Age 5–9 y	Age 10–14 y	Age 15–19 y	% of the Total Number of STS Cases <20 y	
Other specified soft tissue sarcomas	**198**	**220**	**512**	**856**	**38**	
Ewing tumor and Askin tumor of soft tissue	22	28	57	81		4
pPNET of soft tissue	21	19	29	42		2.4
Extrarenal rhabdoid tumor	37	3	8	3		1
Liposarcomas	5	6	22	66		2
Fibrohistiocytic tumors [a]	53	69	171	293		12
Leiomyosarcomas	13	19	22	57		2.4
Synovial sarcomas	12	39	133	204		8.3
Blood vessel tumors	15	7	11	33		1.4
Osseous and chondromatous neoplasms of soft tissue	1	5	9	16		0.6
Alveolar soft parts sarcoma	3	7	19	26		1
Miscellaneous soft tissue sarcomas	16	18	31	35		2
Unspecified soft tissue sarcomas	**70**	**58**	**136**	**163**	**9**	

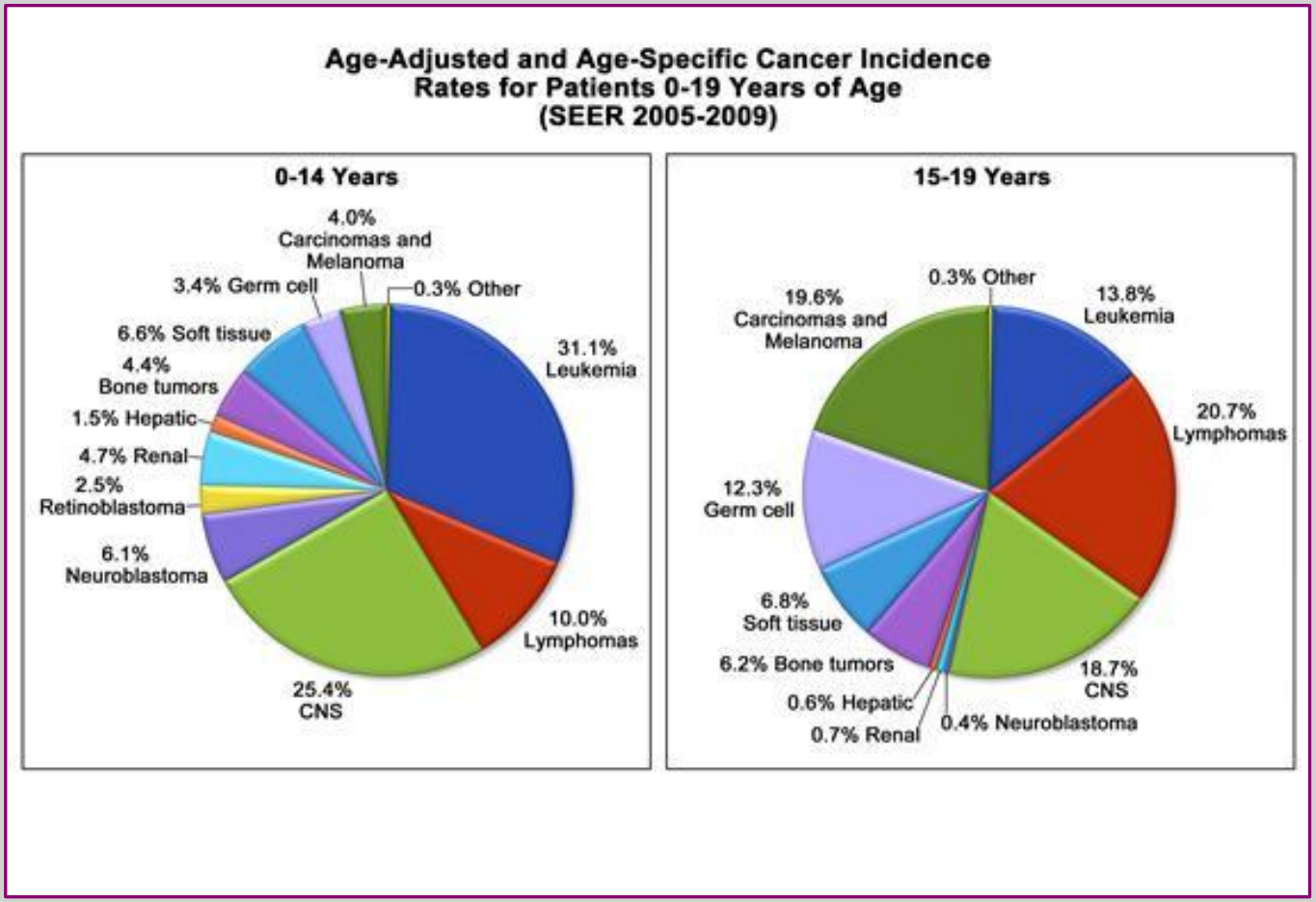
pPNET = peripheral primitive neuroectodermal tumors; SEER = Surveillance Epidemiology and End Results.

[a]*Dermatofibrosarcoma accounts for 75% of these cases.*

Major Types of Pediatric Neoplasms

- Langerhans Cell Histiocytosis
- Retinoblastoma
- Neuroblastoma
- Wilms Tumor
- Melanoma

Major Types of Pediatric Neoplasms



Signs and Symptoms

C ontinued, unexplained weight loss

H eadaches, often with early morning vomiting

I ncreased swelling or persistent pain in bones, joints, back, or legs

L ump or mass, especially in the abdomen, neck, chest, pelvis, or armpits

D evelopment of excessive bruising, bleeding, or rash

C onstant infections

A whitish color behind the pupil

N ausea which persists or vomiting without nausea

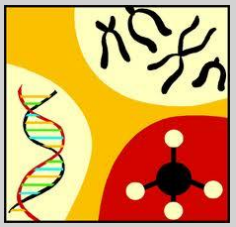
C onstant tiredness or noticeable paleness

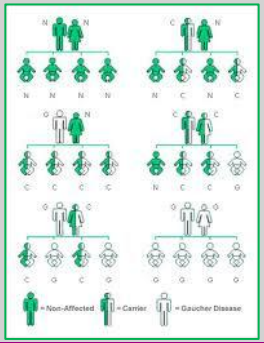
E ye or vision changes which occur suddenly and persist

R ecurrent or persistent fevers of unknown origin

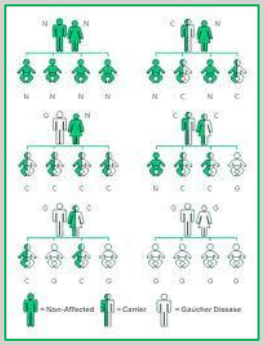
Causes and Risk Factors

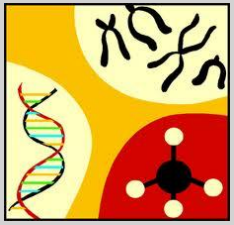
- Genetic Abnormalities
- Ionizing Radiation Exposure
- History of Chemotherapy and/or Radiation Therapy
- Infectious Agents Including Prenatal Infection
  - HIV
- Environmental Including Parental Exposure
  - Toxins
  - Solvents
  - Pesticides
  - Magnetic Fields
- Cancer Predisposition Syndromes
  - Down Syndrome
  - Li-Fraumeni Syndrome
  - Neurofiobromatosis
  - Gorlin Syndrome

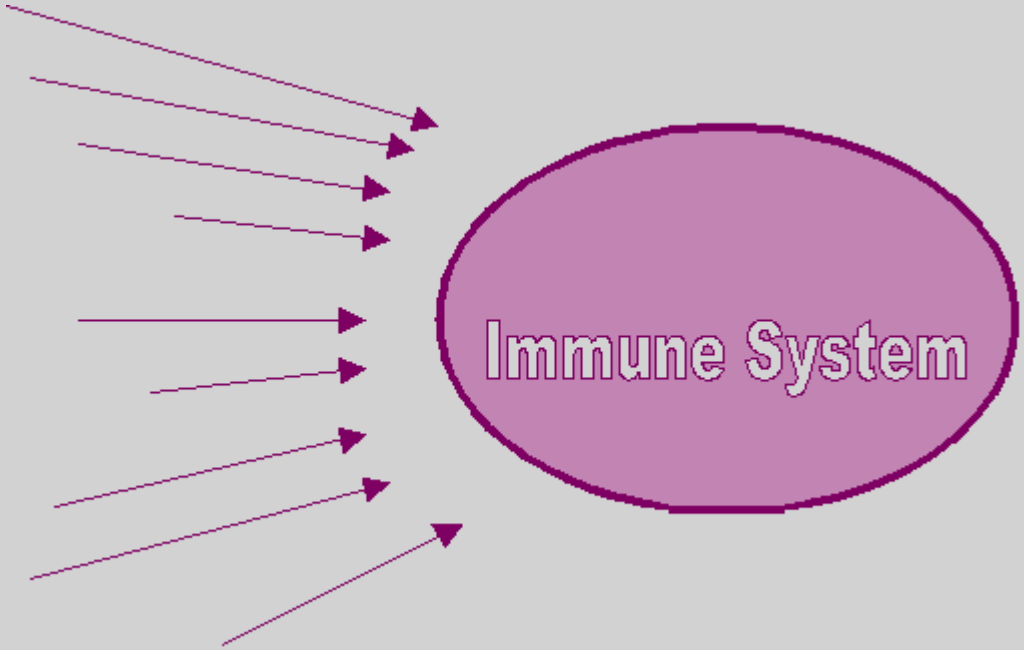




Causes and Risk Factors







MPH Rules – The Basics

1. Is the condition reportable?
2. How many cases do I abstract?
3. How do I code the primary site?
4. How do I code the histology?
5. How do I code the grade?

MPH Rules – Solid Tumors

- Identify the Primary Site

- Use Multiple Primary Rules
  - General Rules
  - Site-Specific Rules
    - Brain – Malignant
    - Brain – Benign/Borderline
    - Melanoma
    - Kidney
    - N/A – breast, colon, head & neck, lung, urinary system

MPH Rules – Solid Tumors

- Histology Coding Rules
- What Drives Treatment Decisions?
- Pediatric Pathology – Characteristics and Terminology
- Tumor Characteristic Testing
- Tumor Marker Testing
- Genetic Testing
- Profile

MPH Rules – Heme/Lymph Neoplasms

- Hodgkin Lymphoma
- Non-Hodgkin Lymphoma
- Acute Lymphoblastic Leukemia

- Acute Myeloid Leukemia
- Chronic Myeloid Leukemia
- Myeloid Leukemia Associated with Down Syndrome

- Langerhans Cell Histiocytosis – solitary/multifocal

MPH Rules – Heme/Lymph Neoplasms

Staging Pediatric Tumors

Staging Pediatric Tumors

- Wilms Tumor Study Group Staging
- International Neuroblastoma Staging System
- Children's Oncology Group Neuroblastoma Risk Grouping
- Intergroup Rhabdomyosarcoma Study Staging System
- Soft Tissue Sarcoma Tumor Pathological Grading System
- FNCLCC Grading System
- TNM Staging System

Collaborative Stage Data Collection System

CS Core Data Items and Site Specific Factors Used to Derive

- AJCC Cancer Stage
  - TNM 6th edition
  - TNM 7th edition
  - Clinical Stage
  - Pathologic Stage
  - Best Combined Stage
  - T, N, and M Core Elements
  - Anatomic/Prognostic Stage Group
- SEER Summary Stage 1977
- SEER Summary Stage 2000

NO Pediatric-Specific Staging Schema or SSFs

Staging is often Site/Type Specific or Clinical Trial-Specific

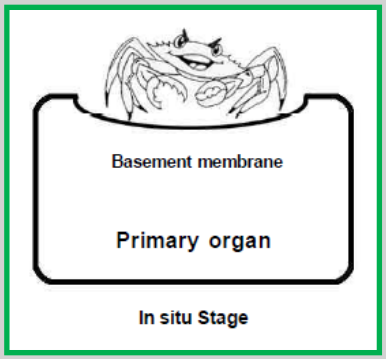
Collaborative Stage Version 2

TNM 7 Schema List (v.02.04)

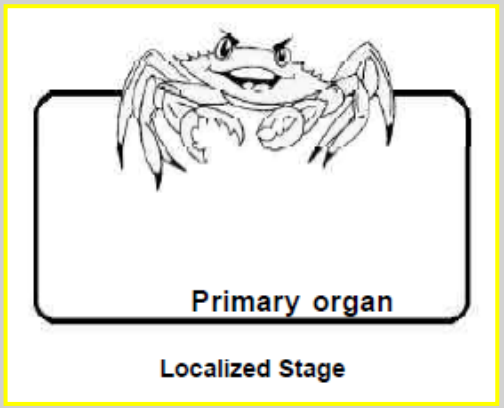
Natural Order • **Alphabetical Order**

AdnexaUterineOther
AdrenalGland
AmpullaVater
Anus
Appendix
BileDuctsDistal
BileDuctsIntraHepat
BileDuctsPerihilar
BiliaryOther
Bladder
Bone
Brain
Breast
BuccalMucosa
CarcinoidAppendix
Cervix
CNSOther
Colon
Conjunctiva
CorpusAdenosarcoma
CorpusCarcinoma
CorpusSarcoma
CysticDuct
DigestiveOther
EndocrineOther
EpiglottisAnterior
Esophagus
EsophagusGEJunction
EyeOther
FallopianTube
FloorMouth
Gallbladder
GenitalFemaleOther
GenitalMaleOther
GISTAppendix
GISTColon
GISTEsophagus
GISTPeritoneum
GISTRectum
GISTSmallIntestine
GISTStomach
GumLower
GumOther
GumUpper
HeartMediastinum
HemeRetic
Hypopharynx
IllDefinedOther
IntracranialGland
KaposiSarcoma
KidneyParenchyma
KidneyRenalPelvis
LacrimalGland
LacrimalSac
LarynxGlottic
LarynxOther
LarynxSubglottic
LarynxSupraglottic
LipLower
LipOther
LipUpper
Liver
Lung
Lymphoma
LymphomaOcularAdnexa
MelanomaBuccalMucosa
MelanomaChoroid
MelanomaCiliaryBody
MelanomaConjunctiva
MelanomaEpiglottisAnterior
MelanomaEyeOther
MelanomaFloorMouth
MelanomaGumLower
MelanomaGumOther
MelanomaGumUpper
MelanomaHypopharynx
MelanomaIris
MelanomaLarynxGlottic
MelanomaLarynxOther
MelanomaLarynxSubglottic
MelanomaLarynxSupraglottic
MelanomaLipLower
MelanomaLipOther
MelanomaLipUpper
MelanomaMouthOther
MelanomaNasalCavity
MelanomaNasopharynx
MelanomaOropharynx
MelanomaPalateHard
MelanomaPalateSoft
MelanomaPharynxOther
MelanomaSinusEthmoid
MelanomaSinusMaxillary
MelanomaSinusOther
MelanomaSkin
MelanomaTongueAnterior
MelanomaTongueBase
MerkelCellPenis
MerkelCellScrotum
MerkelCellSkin
MerkelCellVulva
MiddleEar
MouthOther
MycosisFungoides
MyelomaPlasmaCellDisorder
NasalCavity
Nasopharynx
NETAmpulla
NETColon
NETRectum
NETSmallIntestine
NETStomach
Orbit
Oropharynx
Ovary
PalateHard
PalateSoft
PancreasBodyTail
PancreasHead
PancreasOther
ParotidGland
Penis
Peritoneum
PeritoneumFemaleGen
PharyngealTonsil
PharynxOther
Placenta
Pleura
Prostate
Rectum
RespiratoryOther
Retinoblastoma
Retroperitoneum
SalivaryGlandOther
Scrotum
SinusEthmoid
SinusMaxillary
SinusOther
Skin
SkinEyelid
SmallIntestine
SoftTissue
Stomach
SubmandibularGland
Testis
Thyroid
TongueAnterior
TongueBase
Trachea
Urethra
UrinaryOther
Vagina
Vulva

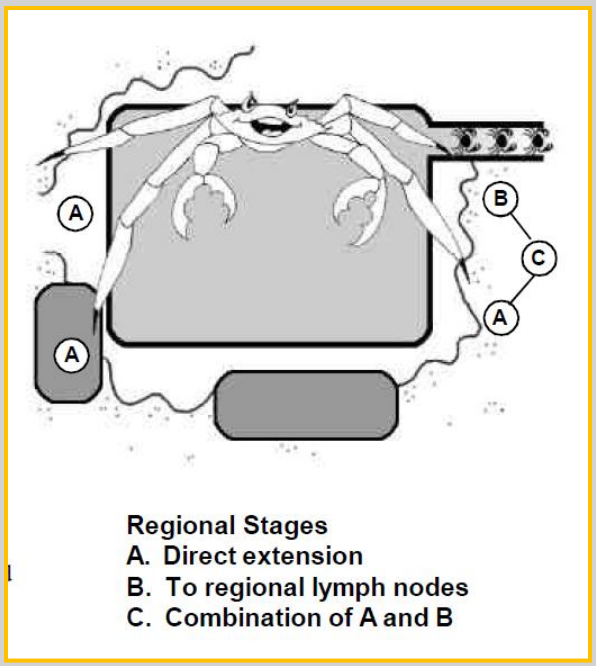
Solid Tumor Staging



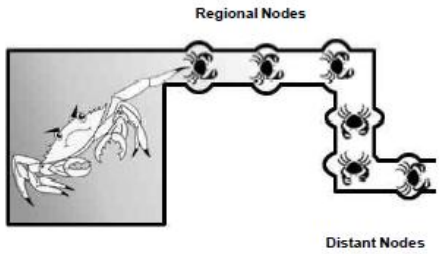
In situ Stage



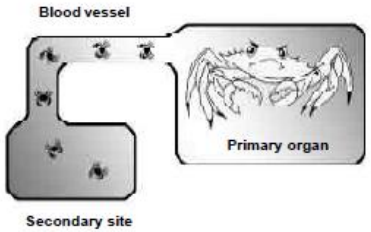
Localized Stage



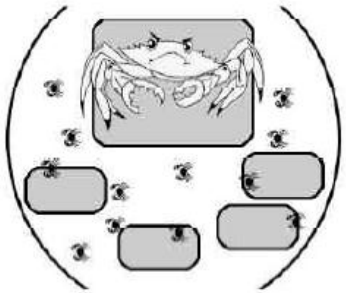
Regional Stages
A. Direct extension
B. To regional lymph nodes
C. Combination of A and B



Distant lymph node involvement



Blood-borne metastases



Implantation metastases

Source: SEER Summary Staging Manual 2000

Solid Tumor Staging - Example

- Wilms Tumor
- Stage I – 43%
  - Tumor is limited to the kidney
  - Tumor is completely resected.
  - The renal capsule is intact.
  - Tumor is not ruptured or biopsied prior to removal.
  - No involvement of renal sinus vessels.
- Stage II – 20%
  - Tumor is completely resected,
  - The tumor extends beyond the kidney as evidenced by any one of the following :
    - There is regional extension of the tumor (i.e., penetration of the renal sinus capsule).
    - Blood vessels in the nephrectomy specimen outside the renal parenchyma with tumor
- Stage III – 21%
  - Residual non-hematogenous tumor present following surgery confined to the abdomen
- Stage IV – 11%
  - hematogenous metastases (lung, liver, bone, brain),
  - Lymph node metastases outside the abdomino-pelvic region are present
- Stage V – 5%
  - bilateral involvement by tumor is present at diagnosis

Brain Tumor Staging

Brain and Cerebral Meninges

C70.0, C71.0-C71.9

- C70.0 Cerebral meninges
- C71.0 Cerebrum
- C71.1 Frontal lobe
- C71.2 Temporal lobe
- C71.3 Parietal lobe
- C71.4 Occipital lobe
- C71.5 Ventricle, NOS
- C71.6 Cerebellum, NOS
- C71.7 Brain stem
- C71.8 Overlapping lesion of brain
- C71.9 Brain, NOS
- Note 1: This schema is compatible with the AJCC 4th edition TNM scheme for brain, updated to include metastatic and site-specific information from the AJCC 7th edition. The AJCC opted not to recommend a TNM scheme in the 6th or 7th editions.
- Note 2: AJCC does not define TNM staging for this site.

CS Tumor Size	CS Site-Specific Factor 7
CS Extension	Surgical Resection
CS Tumor Size/Ext Eval = **9**	CS Site-Specific Factor 8
CS Lymph Nodes	Unifocal vs Multifocal Tumor
CS Lymph Nodes Eval = **9**	CS Site-Specific Factor 9 = **988**
Regional Nodes Positive = **99**	CS Site-Specific Factor 10 = **988**
Regional Nodes Examined = **99**	CS Site-Specific Factor 11 = **988**
CS Mets at DX	CS Site-Specific Factor 12 = **988**
CS Mets Eval = **9**	CS Site-Specific Factor 13 = **988**
CS Site-Specific Factor 1	CS Site-Specific Factor 14 = **988**
World Health Organization (WHO) Grade Classification	CS Site-Specific Factor 15 = **988**
CS Site-Specific Factor 2	CS Site-Specific Factor 16 = **988**
Ki-67/MIB-1 Labeling Index (LI): Brain	CS Site-Specific Factor 17 = **988**
CS Site-Specific Factor 3	CS Site-Specific Factor 18 = **988**
Functional Neurologic Status - Karnofsky Performance Scale (KPS)	CS Site-Specific Factor 19 = **988**
CS Site-Specific Factor 4	CS Site-Specific Factor 20 = **988**

Leukemia Staging

Code	Description
100	Localized disease: (Single/solitary/unifocal/isolated): May be coded for: Mast cell sarcoma (9740) Malignant histiocytosis (9750) Langerhans cell histiocytosis (9751) Histiocytic sarcoma (9755) Langerhans cell sarcoma (9756) Dendritic cell sarcoma (9757, 9758) Myeloid sarcoma (9930)
800	Systemic disease (All histologies including those in 100)
999	Unknown; extension not stated Primary tumor cannot be assessed Not documented in patient record

Lymphoma Staging

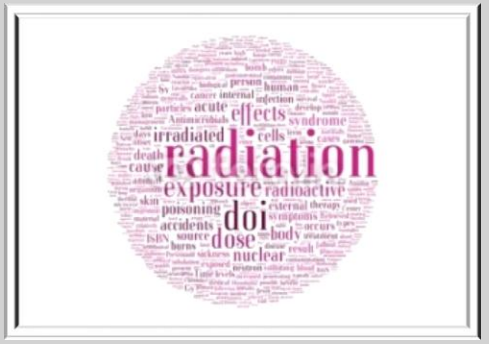
Stage	Description
[a]*Reprinted with permission from AJCC: Hodgkin and non-Hodgkin lymphomas. In: Edge SB, Byrd DR, Compton CC, et al., eds.: AJCC Cancer Staging Manual. 7th ed. New York, NY: Springer, 2010, pp 607-11.[15]*	
I	Involvement of a single lymphatic site (i.e., nodal region, Waldeyer's ring, thymus, or spleen) (I); or localized involvement of a single extralymphatic organ or site in the absence of any lymph node involvement (IE).
II	Involvement of two or more lymph node regions on the same side of the diaphragm (II); or localized involvement of a single extralymphatic organ or site in association with regional lymph node involvement with or without involvement of other lymph node regions on the same side of the diaphragm (IIE).
III	Involvement of lymph node regions on both sides of the diaphragm (III), which also may be accompanied by extralymphatic extension in association with adjacent lymph node involvement (IIIE) or by involvement of the spleen (IIIS) or both (IIIE,S).
IV	Diffuse or disseminated involvement of one or more extralymphatic organs, with or without associated lymph node involvement; or isolated extralymphatic organ involvement in the absence of adjacent regional lymph node involvement, but in conjunction with disease in distant site(s). Stage IV includes any involvement of the liver or bone marrow, lungs (other than by direct extension from another site), or cerebrospinal fluid.
Designations applicable to any stage	
A	No symptoms.
B	Fever (temperature >38°C), drenching night sweats, unexplained loss of >10% of body weight within the preceding 6 months.
E	Involvement of a single extranodal site that is contiguous or proximal to the known nodal site.
S	Splenic involvement.

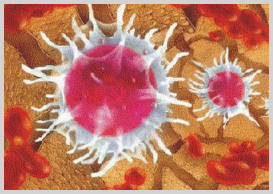
Source: http://cancer.gov – Pediatric Non-Hodgkin Lymphoma NCI PDQ for Health Professionals

Treatment

Treatment Options – Basic Concepts

- Surgery
- Chemotherapy
- Radiation Therapy
- Hormonal Therapy
- Combination Therapy
- Continuation Therapy
- Bone Marrow/Stem Cell Transplant





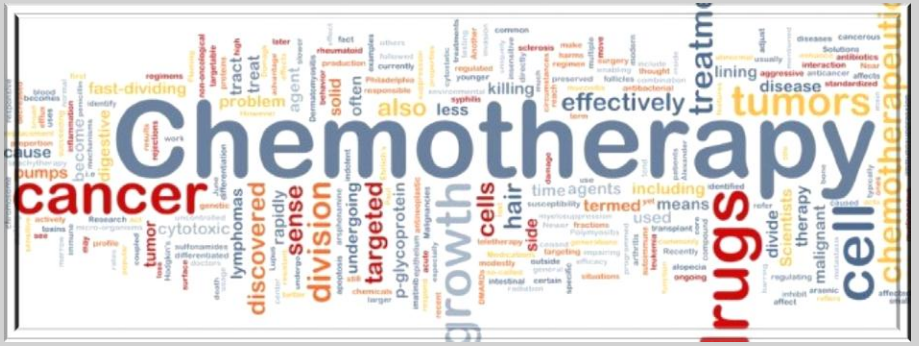


Image Source: http://greenplanetparadise.com and http://avinoamlerner.com

Treatment Options – Basic Concepts

- Pre-Induction Risk Assessment
- Induction Therapy
- Post-Induction Assessment
- Re-Induction Therapy
- Intensification/Consolidation Therapy
- Post-Consolidation Assessment
- BMT/Stem Cell Transplant
- Maintenance Therapy
- Maintenance Assessment

Treatment Options – Basic Concepts

- Risk-Based Treatment – Pre-Induction Risk
  - Patient Characteristics
    - Age at Diagnosis
    - WBC Count at Diagnosis
    - CNS Involvement
    - Gender
  - Neoplasm Characteristics
    - Morphology
    - Immunophenotype
    - Cytogenetics
  - Genetic Characteristics of Neoplasm
    - Philadelphia Chromosome Transloaction
    - MLL Translocations
    - CRLF2 and JAK Mutation

Source: http://cancer.gov – Pediatric Lymphoid Neoplasm NCI PDQ for Health

Treatment Options – Basic Concepts

- Risk-Based Treatment – Induction Failure
  - Patients at highest risk of induction failure:
    - T-cell phenotype (especially without a mediastinal mass).
    - B-precursor ALL with very high presenting leukocyte counts.
    - 11q23 rearrangement.
    - Older age.
    - Philadelphia chromosome
- Risk-Based Treatment – ReInduction/Consolidation
  - Re-Induction
  - Intensification
  - Consolidation
- Risk-Based Treatment – Sanctuary Sites
- Risk-Based Treatment – Maintenance Therapy

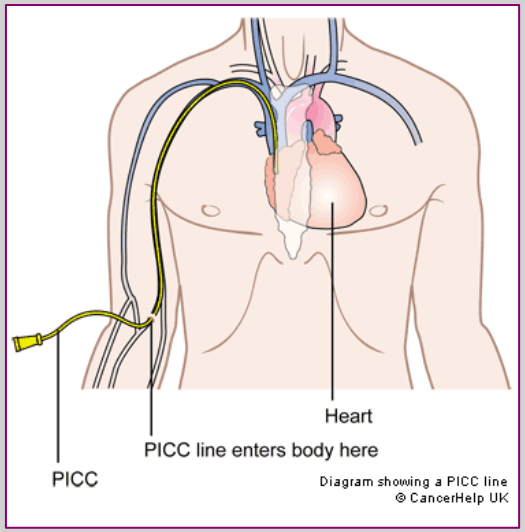
Source: http://cancer.gov – Pediatric Lymphoid Neoplasm NCI PDQ for Health

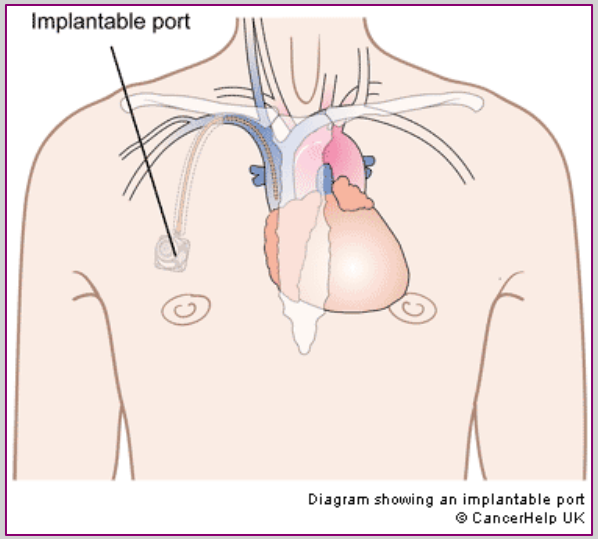
Treatment Options – Basic Concepts

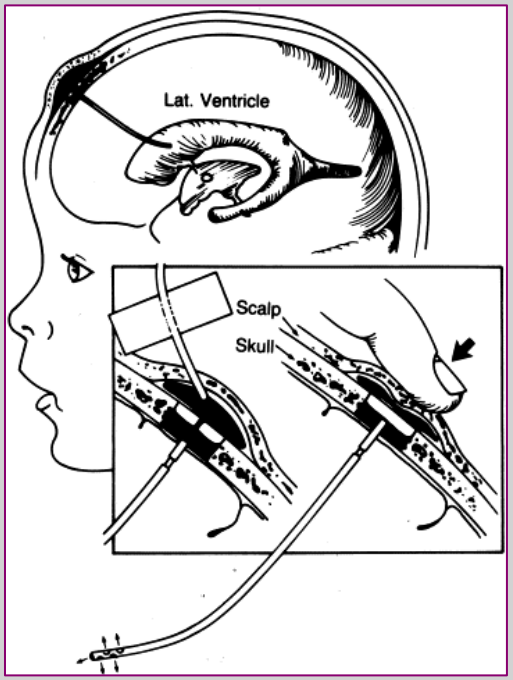
- Risk-Based Treatment Assessment
  - Low Risk Disease – Stage I, II – no B symptoms, no bulky disease
  - Intermediate Risk Disease – Stage I, II with B symptoms
  - Intermediate Risk Disease – Stage I, II with bulky disease
  - Intermediate Risk Disease – Stage IIIA, IVA
  - High Risk Disease – Stage IIIB, IVB
  - High Risk Disease – Poor response to initial chemotherapy

Source: http://cancer.gov – Pediatric Lymphoid Neoplasm NCI PDQ for Health

Treatment Options – Basic Concepts



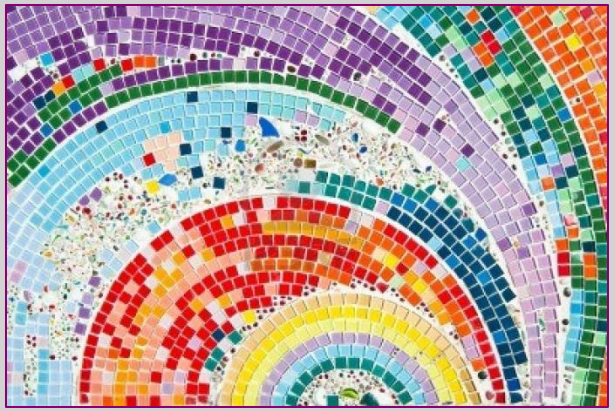




Images: http://www.sciencedirect.com/science and http://cancerhelpuk.org

Treatment Options – Lymphoid Neoplasms

- Hodgkin Lymphoma
- Non-Hodgkin Lymphoma
- Chronic Lymphocytic Leukemia
- Acute Lymphocytic Leukemia
- Other Lymphoid Neoplasm



Source: Mosaic Rainbow and Woodland Forest - http://www.etsy.com

Treatment Options – Lymphoma

Table 5. Low-Risk Disease (Stages I–IIA; No Bulky Disease; No B Symptoms)

Enlarge

Chemotherapy (No. of Cycles)[a]	Radiation (Gy)	Stage	No. of Patients	Event-Free Survival (No. of Years of Follow-up)	Survival (No. of Years of Follow-up)
VAMP (4) [38]	15-25.5, IFRT	CS I/II[b]	110	89 (10)	96 (10)
VAMP (4) [44]	25.5, IFRT/None	CS I/II[b]	41/47	88/89 (5)	100/100 (5)
COPP/ABV (4) [14,17]	21, IFRT/None	CS IA/B, IIA[c]	94/113	100/89 (10)[d]	97/96 (10)[d]
OEPA/OPPA (2) [18]	20-35, IFRT/None	I, IIA	281/113	94/97 (5)	N/A
ABVE (2-4) [47]	25.5, IFRT	IA, IIA, IIIA1	51	91 (6)	98 (6)

Source: http://cancer.gov – Pediatric Hodgkin Lymphoma NCI PDQ for Health Professionals

Treatment Options – Lymphoma

Table 6. Intermediate-Risk Disease (All Stage I and Stage II Patients Not Classified as Early Stage; Stage IIIA; Stage IVA)

Enlarge

Chemotherapy (No. of Cycles)[a]	Radiation (Gy)	Stage	No. of Patients	Event-Free Survival (No. of Years of Follow-up)	Survival (No. of Years of Follow-up)
COPP/ABV (6) [17]	21, IFRT/None	CS I/II[b], CS IIB, CS III	103/122	84/78 (10)[c]	100 (3)
OEPA/OPPA (2) + COPP (2) [18]	20–35, IFRT	II_EA, IIB, IIIA	212	92 (5)	N/A
OEPA/OPPA (2) + COPDAC (2) [37]	20–35, IFRT	II_EB, III_EA/B, IIIB, IVA/B	139	88.3 (5)	98.5 (5)
ABVE-PC (3–5) [32]	21, IFRT	IB, IIA, IIIA	53	84 (5)	95 (5)

Source: http://cancer.gov – Pediatric Hodgkin Lymphoma NCI PDQ for Health Professionals

Treatment Options – Lymphoma

Table 7. High-Risk Disease (Stages IIIB, IVB)

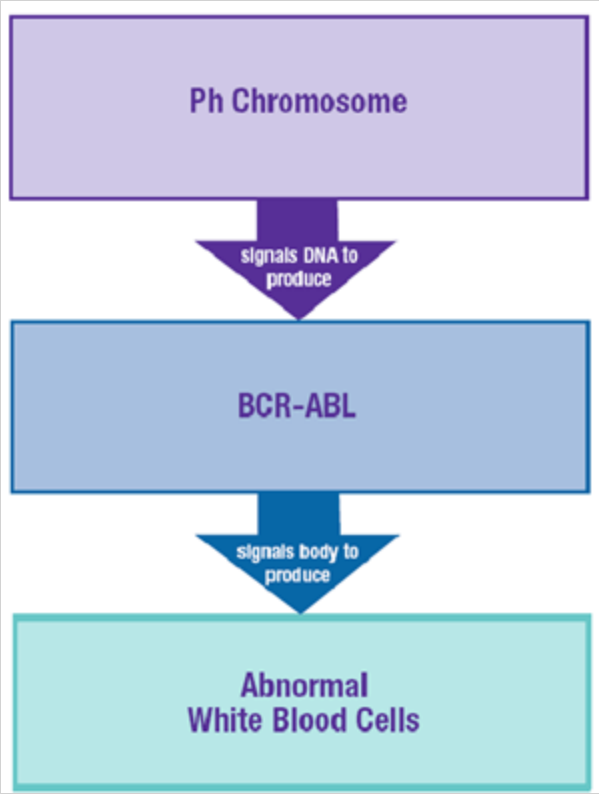
Enlarge

Chemotherapy (No. of Cycles)[a]	Radiation (Gy)	Stage	No. of Patients	Event-Free Survival (No. of Years of Follow-up)	Survival (No. of Years of Follow-up)
OEPA/OPPA (2) + COPP (4) [18]	20–35, IFRT	II_EB, III_EA/B, IIIB, IVA/B	265	91 (5)	N/A
OEPA/OPPA (2) + COPDAC (4) [37]	20–35, IFRT	II_EB, III_EA/B, IIIB, IVA/B	239	86.9 (5)	94.9 (5)
ABVE-PC (3-5) [32]	21, IFRT	IB, IIA, IIIA	163	85 (5)	95 (5)
BEACOPP (4); COPP/ABV (4) (RER; girls) [40]	None	IIB, IIIB, IV	38	94 (5)	97 (5)
BEACOPP (4); ABVD (2) (RER; boys) [40]	21, IFRT	IIB, IIIB, IV	34		
BEACOPP (8) (SER) [40]	21, IFRT	IIB, IIIB, IV	25		

Source: http://cancer.gov – Pediatric Hodgkin Lymphoma NCI PDQ for Health Professionals

Treatment Options – Myeloid Neoplasms

- Myeloid Leukemia Associated with Down Syndrome
- Chronic Myeloid Leukemia
- Acute Myeloid Leukemia
- Other Myeloid Neoplasm
- MPD/MPS/MDS



Source: http://cancer.gov – Pediatric Myeloid Neoplasm NCI PDQ for Health Professionals

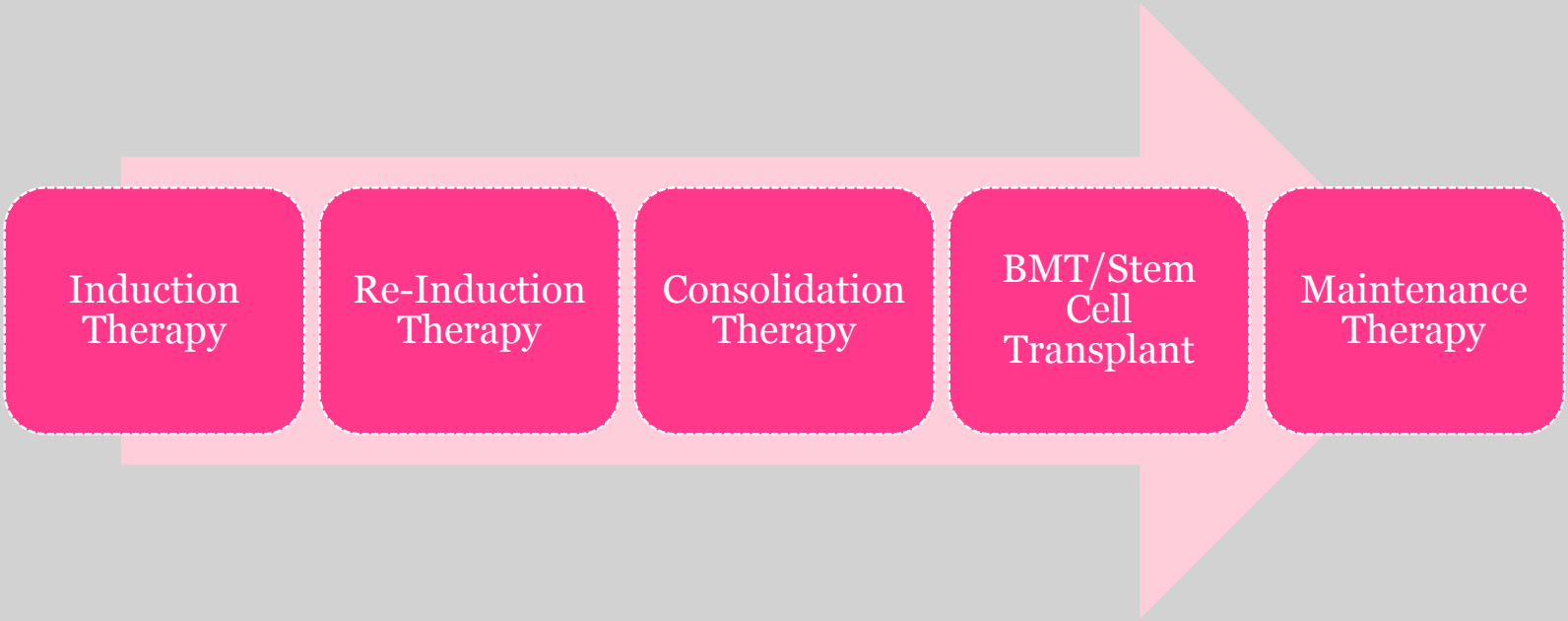
Treatment Options – CML/AML

- About **85%** of patients are **diagnosed in the chronic phase**
- The **accelerated phase** of CML is characterized by **10% - 19% blasts in the WBC of peripheral blood** (WHO)
  - Note: There are alternative ways to define the accelerated phase proposed by Sokal et al., the International Bone Marrow Transplant Registry, and MD Anderson.
- The **blast phase**, also referred to as blast crisis, is most often defined as **>20% blasts WBC of peripheral blood**

Source: http://cancer.gov – Pediatric Myeloid Neoplasm NCI PDQ for Health Professionals

Treatment Options – CML/AML

- Use same basic model as ALL – different agents



Source: http://cancer.gov – Pediatric Myeloid Neoplasm NCI PDQ for Health Professionals

Treatment Options – CML/AML

- Ph^+ chronic phase CML is typically treated with a tyrosine kinase inhibitor (TKI).
- TKIs include imatinib, nilotinib or dasatinib.
- All TKIs are given orally so there will be no "administration" documentation rather the patient will be given prescriptions
- Other treatment options include clinical trial or Hematopoietic Stem Cell Transplant [HSCT].

Source: http://cancer.gov – Pediatric Myeloid Neoplasm NCI PDQ for Health Professionals

Treatment Options – CML/AML

- Patients are evaluated for a cytogenetic response
- Treatment is based on response
  - Complete Response – no Ph^+ positive metaphases
  - Partial Response – 1 %-35% Ph^+ positive metaphases
  - Major Response – 0 %-35% Ph^+ positive metaphases
    - Complete + Partial
  - Minor - > 35% Ph^+ positive metaphases

Source: http://cancer.gov – Pediatric Myeloid Neoplasm NCI PDQ for Health Professionals

Treatment Options – CML/AML

- Patients achieving a complete hematologic response are continued on their current medication at the same dose.
- Patients who fail to achieve a complete hematologic response are evaluated for compliance, drug-drug interaction and possibly mutational status but generally are switched to an alternate TKI as second line treatment.
- Other treatment options include evaluation and discussion of HSCT and clinical trial.

Source: http://cancer.gov – Pediatric Myeloid Neoplasm NCI PDQ for Health Professionals

Treatment Options – CML/AML

- Growth Factors
  - filgrastim (Neupogen®)
  - pegfilgrastim (Neulasta ®)
- Diuretics (aldactone, hydrochlorothiazide [HCTZ]), steroids (prednisone 20mg/day x 3 for effusions)
- Topical steroids (hydrocortisone cream)
- Antidiarrheal agents (loperamide [Imodium®])
- Analgesics (acetaminophen, ibuprofen)

Source: http://cancer.gov – Pediatric Myeloid Neoplasm NCI PDQ for Health Professionals

Treatment Options – Brain and CNS

Treated Based on Histology and Location

Tumor Type	Pathologic Subtype	Staging and Treatment of Newly Diagnosed and Recurrent Disease
CNS = central nervous system.		
Astrocytomas and Other Tumors of Glial Origin		
– *Low-Grade Astrocytomas*	Diffuse fibrillary astrocytoma	Childhood Astrocytomas Treatment
	Gemistocytic astrocytoma	
	Oligoastrocytoma	
	Oligodendroglioma	
	Pilocytic astrocytoma	
	Pilomyxoid astrocytoma	
	Pleomorphic xanthoastrocytoma	
	Protoplasmic astrocytoma	
	Subependymal giant cell astrocytoma	
– *High-Grade Astrocytomas*	Anaplastic astrocytoma	Childhood Astrocytomas Treatment

Source: http://cancer.gov – Pediatric Brain Tumors NCI PDQ for Health Professionals

Treatment Options – Brain and CNS

Treated Based on Histology and Location

Tumor Type	Pathologic Subtype	Staging and Treatment of Newly Diagnosed and Recurrent Disease
	Anaplastic oligoastrocytoma	
	Anaplastic oligodendroglioma	
	Giant cell glioblastoma	
	Glioblastoma	
	Gliomatosis cerebri	
	Gliosarcoma	
Brain Stem Glioma		
	Diffuse intrinsic pontine gliomas	Childhood Brain Stem Glioma Treatment
	Focal or low-grade brain stem gliomas	
CNS Embryonal Tumors		
– *Medulloblastoma*	Anaplastic	Childhood CNS Embryonal Tumors Treatment
	Classic	
	Desmoplastic/nodular	
	Large cell	

Source: http://cancer.gov – Pediatric Brain Tumors NCI PDQ for Health Professionals

Treatment Options – Brain and CNS

Treated Based on Histology and Location

Tumor Type	Pathologic Subtype	Staging and Treatment of Newly Diagnosed and Recurrent Disease
	Medulloblastoma with extensive nodularity	
– *CNS Primitive Neuroectodermal Tumors (PNETs)*	CNS ganglioneuroblastoma	
	CNS neuroblastoma	
	Ependymoblastoma	
	Medulloepithelioma	
– *Tumors of the Pineal Region*	Pineal parenchymal tumor of intermediate differentiation	
	Pineoblastoma	
	Pineocytoma	
	Papillary tumor of the pineal region	
– *CNS Atypical Teratoid/Rhabdoid Tumor*		Childhood CNS Atypical Teratoid/Rhabdoid Tumor Treatment
CNS Germ Cell Tumors		
– *Germinomas*		Childhood CNS Germ Cell Tumors Treatment

Source: http://cancer.gov – Pediatric Brain Tumors NCI PDQ for Health Professionals

Treatment Options – Brain and CNS

Treated Based on Histology and Location

Tumor Type	Pathologic Subtype	Staging and Treatment of Newly Diagnosed and Recurrent Disease
– *Teratomas*	Immature teratomas	
	Mature teratomas	
	Teratomas with malignant transformation	
– *Non-Germinomatous Germ Cell Tumors*	Choriocarcinoma	
	Embryonal carcinoma	
	Mixed germ cell tumors	
	Yolk sac tumor	
Craniopharyngioma		Childhood Craniopharyngioma Treatment
Ependymoma		Childhood Ependymoma Treatment
Tumors of the Choroid Plexus		

Source: http://cancer.gov – Pediatric Brain Tumors NCI PDQ for Health Professionals

Treatment Options - Teratoid/Rhabdoid Tumor

- CNS
- Non-CNS

Rhabdoid Kids

http://www.bubbalove.org

- Both CNS and Non-CNS Involvement
- Rhabdomyosarcoma (see Sarcoma)
- Rhabdoid Tumor of Kidney

Source: http://cancer.gov – Atypical Teratoir/Rhabdoid Tumor NCI PDQ for Health Professionals

Treatment Options – Soft Tissue Sarcoma

- Primary Tumor Resection with Negative Margins
- Regional Lymph Node Involvement is Rare
- Radiation Therapy depends upon potential for surgery plus or minus chemotherapy to obtain local control
  - Age
  - Gender
  - Tumor site
  - Tumor size
  - Tumor grade

- Role for Adjuvant Chemotherapy Controversial
  - Vincristine, dactinomycin, cyclophosphamide, doxorubicin

Source: http://cancer.gov – Pediatric Soft Tissue Sarcoma NCI PDQ for Health Professionals

Treatment Options – Ewing Sarcoma

- Pre-Treatment Factors
  - Site of Tumor
  - Tumor Size or Volume
  - Age of Patient
  - Gender (favorable girls)
  - Metastases
  - Standard Cytogenetics
  - Detectable Fusion Transcripts

- Surgery
- Chemo – vincristine, doxorubicin, cyclophosphamide
- Radiation Therapy

Treatment Options – Wilms Tumor

- Preoperative chemotherapy prior to nephrectomy is indicated in the following situations:[10,17,20-23]
  - Metachronous bilateral Wilms tumor.
  - Wilms tumor in a solitary kidney.
  - Extension of tumor thrombus above the level of the hepatic veins.
  - Tumor involves contiguous structures whereby the only means of removing the kidney tumor requires removal of the other structures (e.g., spleen, pancreas, colon but excluding the adrenal gland).
  - Pulmonary compromise due to extensive pulmonary metastases.
- Patients with massive, nonresectable unilateral tumors, bilateral tumors, or venacaval tumor thrombus are candidates for preoperative chemotherapy

Treatment Options – Wilms Tumor

- Pre-Surgical Chemotherapy for High Risk Group
- Nephrectomy
- Chemotherapy
- Radiation Therapy

Table 2. Standard Chemotherapy Regimens for Wilms Tumor

Enlarge

Regimen Name	Regimen Description
Regimen EE-4A [1]	Vincristine, dactinomycin x 18 weeks postnephrectomy
Regimen DD-4A [1]	Vincristine, dactinomycin, doxorubicin x 24 weeks postnephrectomy
Regimen I [2]	Vincristine, doxorubicin, cyclophosphamide, etoposide x 24 weeks

Treatment Options – Neuroblastoma

- Low-Risk Neuroblastoma
  - Surgery
  - Chemo - carboplatin, cyclophoasphamide, doxorubicin, etoposide
- Intermediate-Risk Neuroblastoma
  - Surgery
  - Chemo as above x 2 cycles
  - Dose Intensive Multi-Agent Chemo
- High-Risk Neuroblastoma
  - Dose Intensive Multi-Agent Chemo as above plus ifosfamide, cisplatin
  - Surgery
- Response Assessment – then next steps

Treatment Options - Retinoblastoma

- Goals of Treatment
  - Eradicate the disease to save the patient's life.
  - Preserve as much vision as possible.
  - Decrease risk of late sequelae from treatment, particularly subsequent neoplasms.
- Enucleation
- Radiation Therapy (beam or brachytherapy)
- Local Treatments (Cryotherapy/Laser Therapy)
- Chemo – carboplatin, etoposide, vincristine
- Subteton (subconjunctival) Chemo - carboplatin
- Opthalmic Artery Infusion Chemo – topotecan, carboplatin

Late Effects of Treatment

- Childhood Cancer Survivors Study
  - Chance for long-term effects increase over time
  - > 70% at least 1 chronic illness related to treatment
  - > 25% have 3 or more chronic illnesses related to tx
  - Kidney Disease
  - Second Cancers
  - Cognitive Dysfunction
  - Cardiovascular Disease
  - Endocrine Abnormalities
  - Musculoskeletal Conditions

References and Resources

- National Cancer Institute Physician Data Query (PDQ) - Health Professionals
  - Childhood Cancers Fact Sheet
  - Childhood Acute Lymphoblastic Leukemia
  - Childhood Acute Myeloid Leukemia
  - Childhood Brain and Spinal Cord Tumors Overview
  - Childhood Astrocytoma
  - Childhood CNS Embryonal Tumors
  - Childhood CNS Atypical Teratoid/Rhabdoid Tumors
  - Childhood Hodgkin Lymphoma
  - Childhood Non-Hodgkin Lymphoma
  - Ewing Sarcoma
  - Childhood Soft Tissue Sarcoma
  - Childhood Rhabdomyosarcoma
  - Neuroblastoma
  - Wilms Tumor

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References and Resources

- Progress in Childhood Cancer: 50 Years of Research Collaboration, A Report from the Children's Oncology Group, *Semin Oncol*. 2008 October; 35(5): 484–493. doi:10.1053/j.seminoncol.2008.07.008.
- NCI Cancer Bulletin, Pediatric Oncology Partnerships are Models for Success, Volume 5/Number 6, March 18, 2008
- Advances in Neuroblastoma Risk Asessment and Treatment, Susan L Cohn, MD, University of Chicago Department of Pediatrics
- Florida Association of Pediatric Tumor Programs (FAPTP)
- Children's Oncology Group (COG)

Future Pediatric Oncology Webcasts

Questions