Pediatric Cancer & Hematologic Disorder
PedHemOnc-PMK

'H o p e'

Oncology II:
Solid Tumors

Intensive Review in Pediatrics 2019
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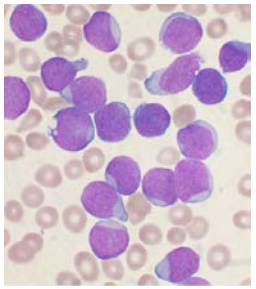
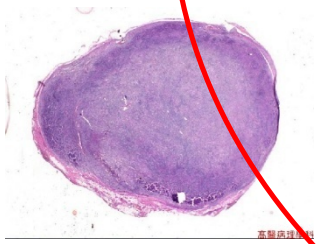
Pediatric Malignancies

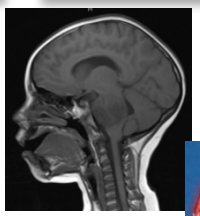
Leukemia

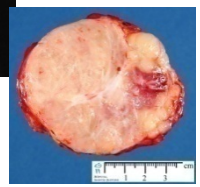


Lymphoma

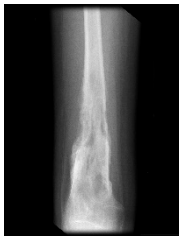


CNS tumors

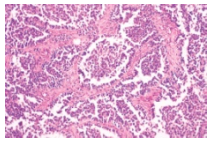


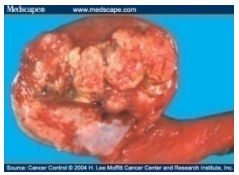


Sarcomas

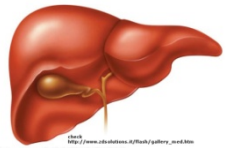


Embryonal tumors

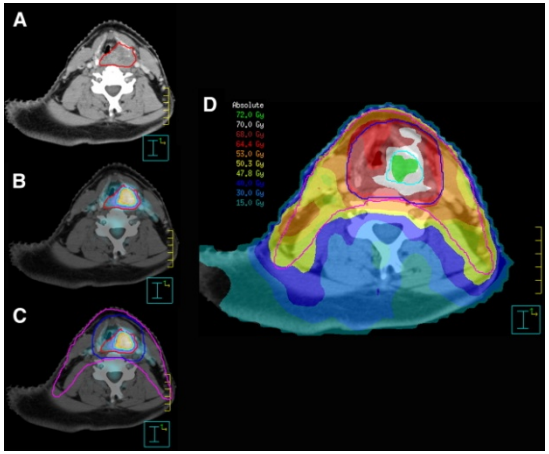




Liver tumors



Principle of treatment in Pediatric ST

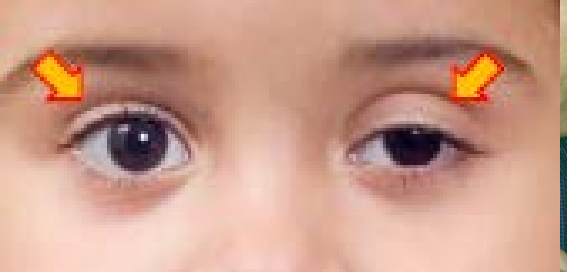


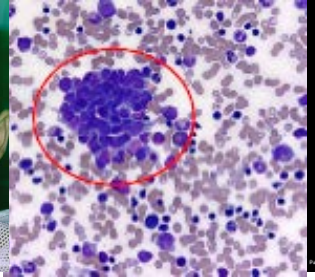
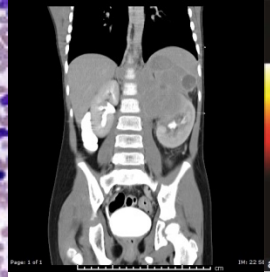
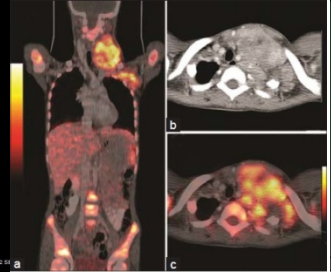
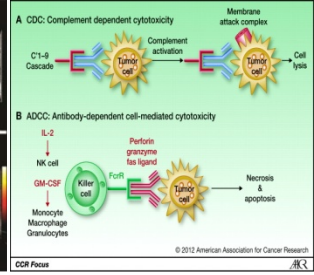
Local control

Systemic control

What’re Solid Tumors!!!

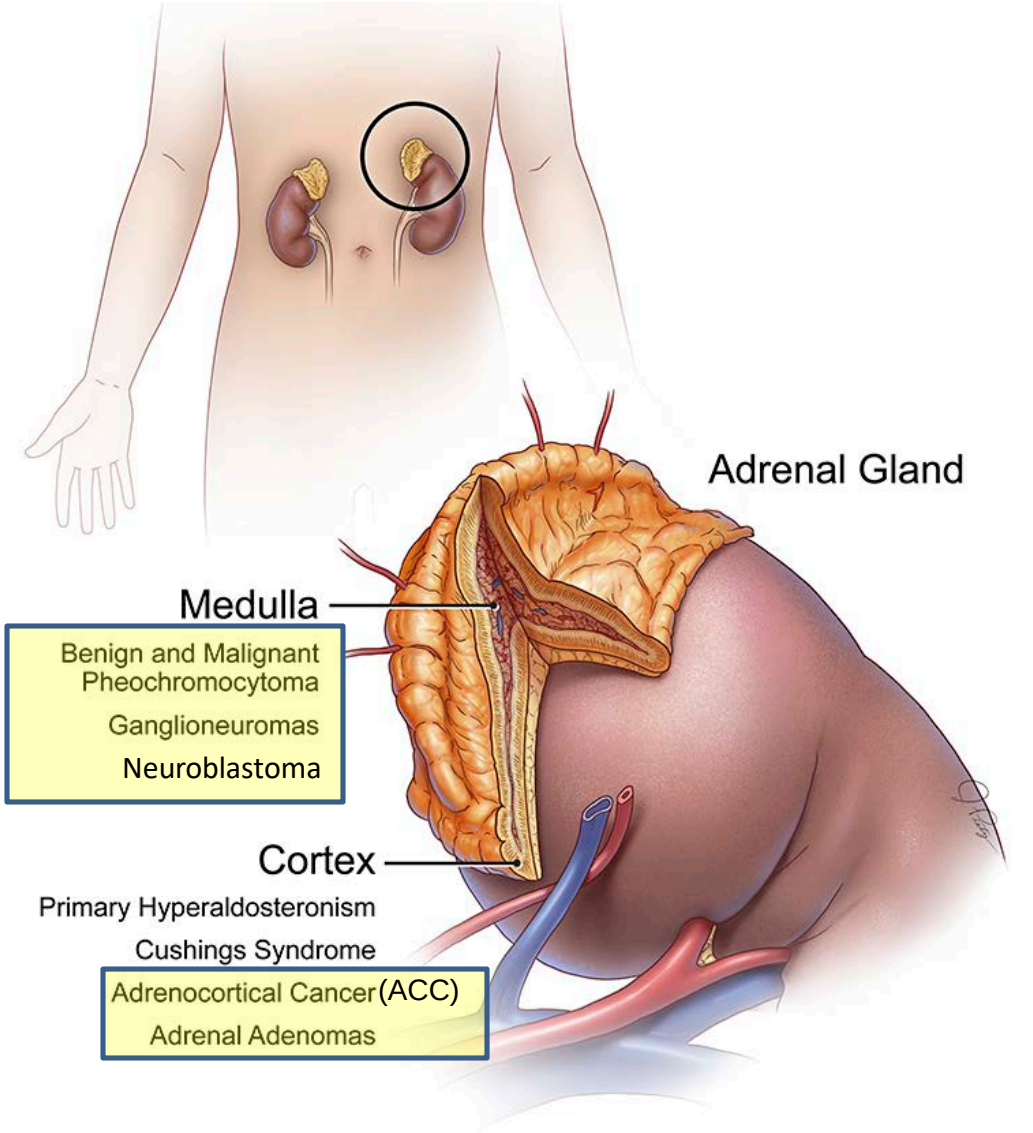
- Neuroblastoma
- Wilm’s Tumor
- Hepatoblastoma
- Retinoblastoma
- Rhabdomyosarcoma
- Malignant Bone Tumors
- Germ Cell Tumors

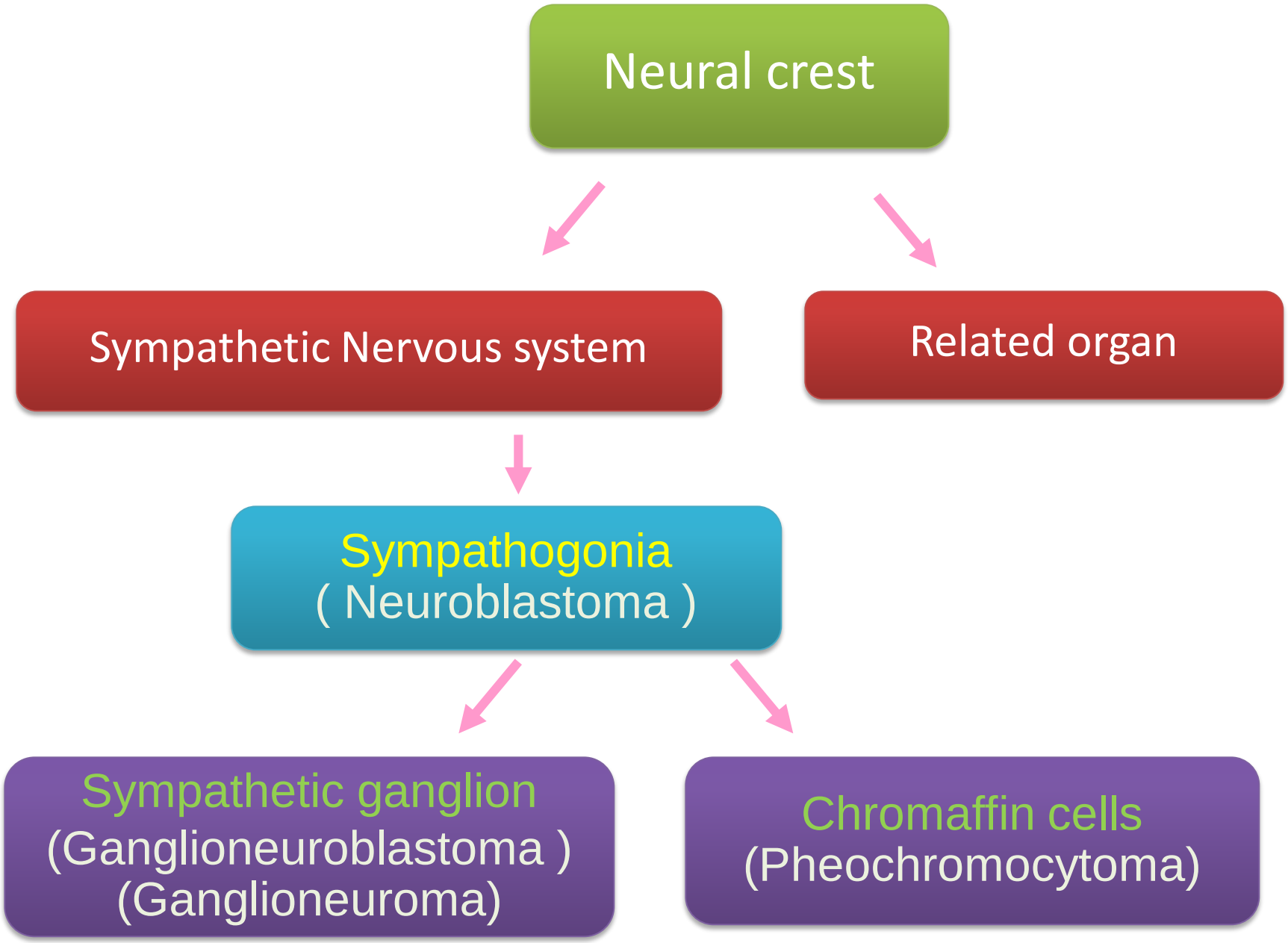


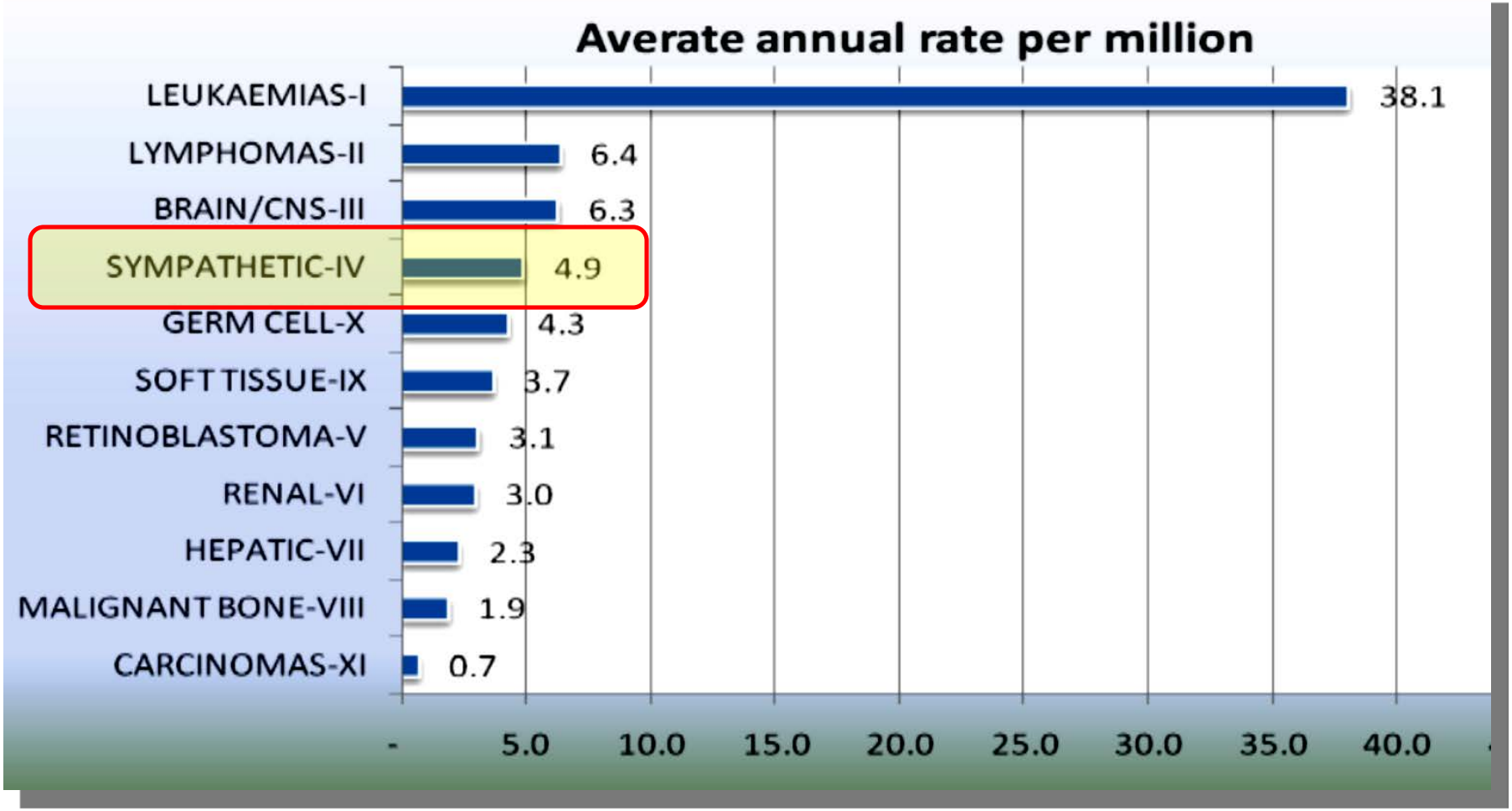
Neuroblastoma

Adrenal tumors




Neural crest
Sympathetic Nervous system
Related organ
Sympathogonia
(Neuroblastoma)
Sympathetic ganglion
(Ganglioneuroblastoma)
(Ganglioneuroma)
Chromaffin cells
(Pheochromocytoma)

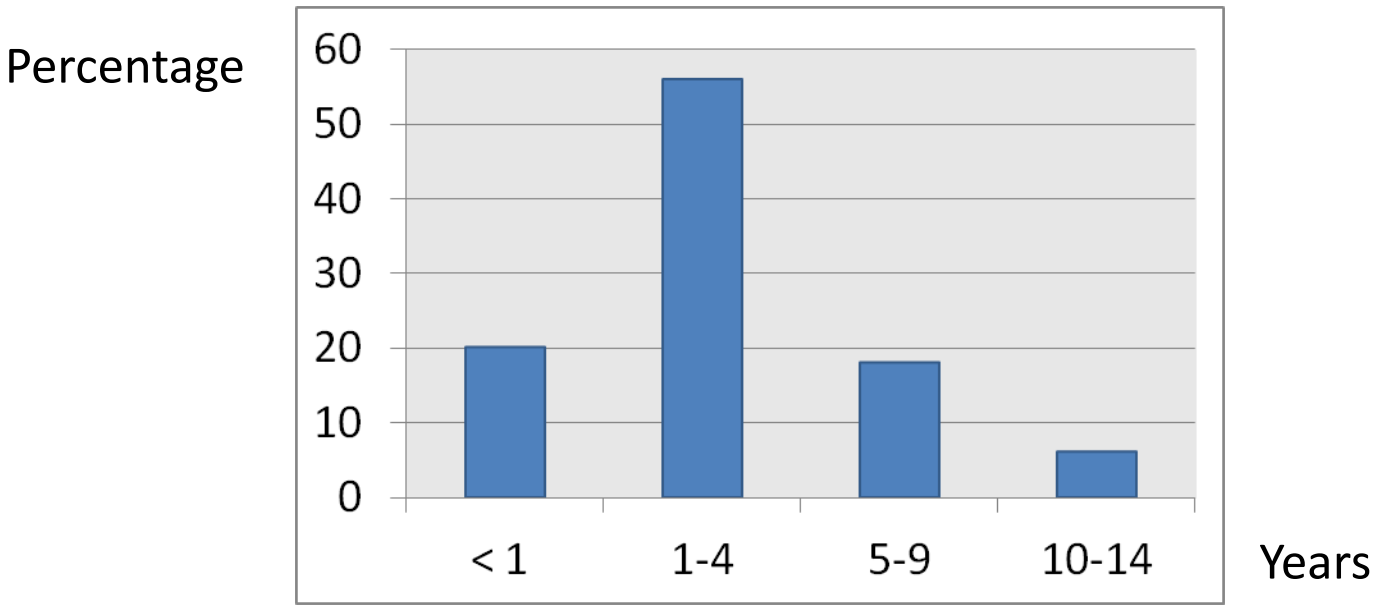
Incidence of Childhood Malignancy in Thailand



Wiangnon S, et al. APJCP. 2011;12(9):2215-20

Epidemiology of Neuroblastoma in Thailand

- Most common Extracranial malignant solid tumor in children
- Most common age: 1-4 years
- >50% present with high risk disease



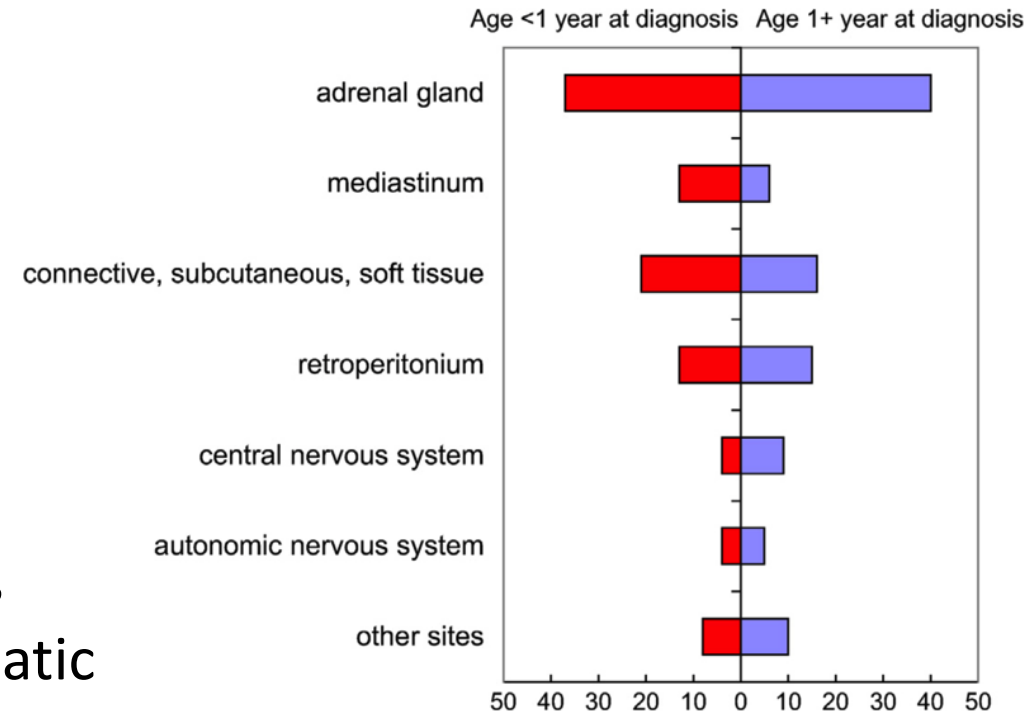
Wiangnon S, et al. APJCP. 2011;12(9):2215-20

Genetic alterations

- MYCN-amplification
- LOH 1p, 11q, 14q
- ALK
- PHOX2B
  - Hirschsprung disease
  - Decreased esophageal motility
  - Congenital hypoventilation syndrome

Clinical Presentation

- Anywhere along sympathetic chain
- 50% with distant metastases (bone, bone marrow, liver)

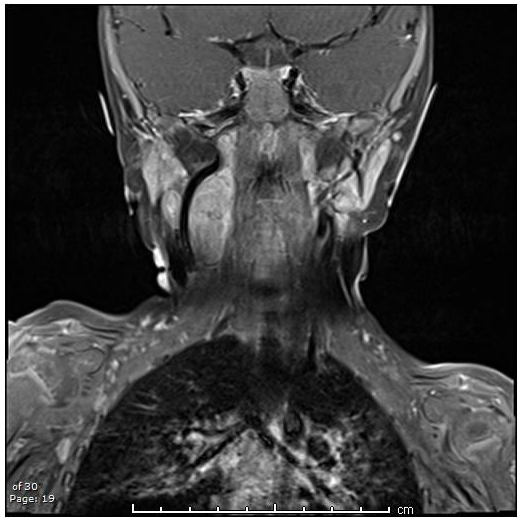


Stage 4S in infants
- Typically favorable
- Can spontaneously regress
- Can be treated if symptomatic

Irwin and Park. Pediatr Clin N Am 2015;62:225–256.

Paraneoplastic syndromes

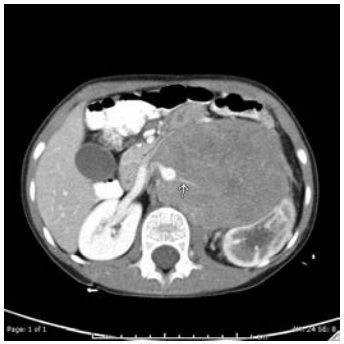
- Opsoclonus myoclonus ataxia syndrome (only 2-3%)
  - Favorable prognosis, but long term disability is likely
- Vasoactive Intestinal Peptide (VIP) Syndrome : Kerner-Morrison syndrome
  - Chronic diarrhea and FTT

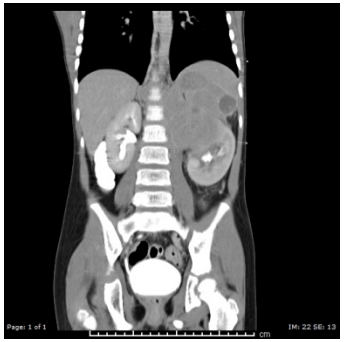


Neuroblastoma	Wilm's tumor
● Irritable child, tender	● Asymptomatic
● Abdominal mass : cross midline	● Abdominal mass : no cross midline
● Bimanual palpation : Negative	● Bimanual palpation : Positive
● Skin : blueberry muffin	● Syndromes: BWS, WARG, DDS; Hemihypertrophy, GU anomalies, Ambiguous genitalia, mental retardation
● Eyes : raccoon eyes	● Aniridia
● Urinary metabolites: diarrhea	● HT , hematuria
● X-rays : stippled calcifications	● no calcification

Investigations

- Urine catecholamine (VMA, HVA) *increased up to 78% and 83%, respectively**
- Serum NSE (non-specific)
- Imaging : plain films, U/S, CT, MRI
- Nuclear medicine
  - Bone scans
  - MIBG scans *positive up to 90-95% of cases*
  - PET scans
- Bilateral BMA, BM biopsy
- Tissue biopsy

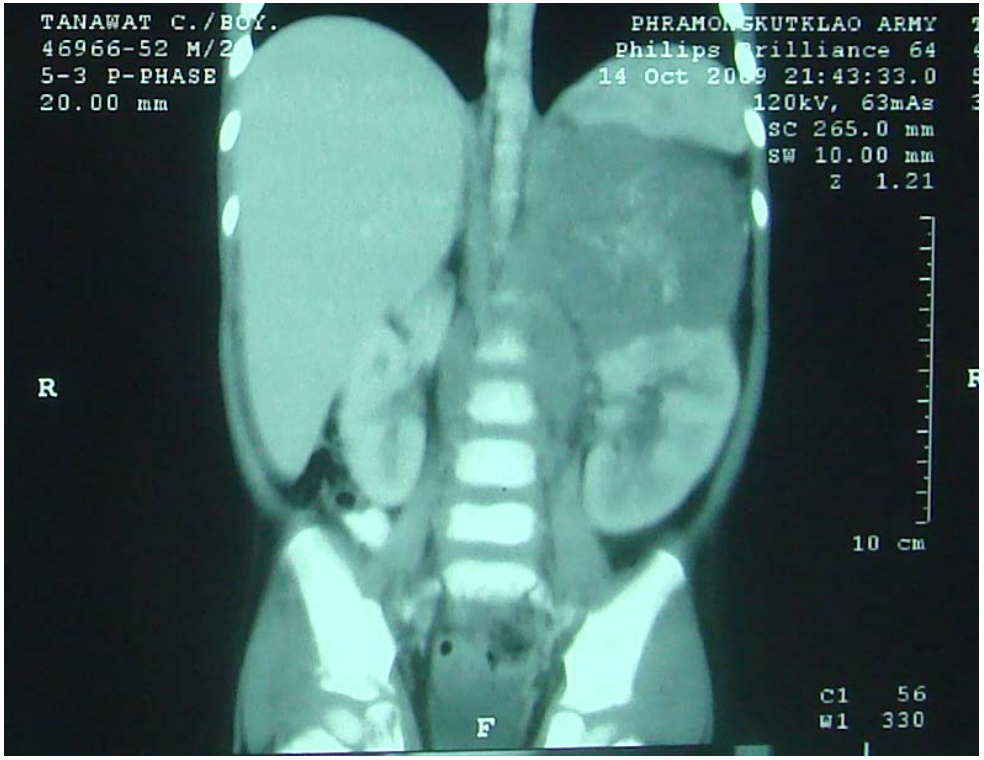


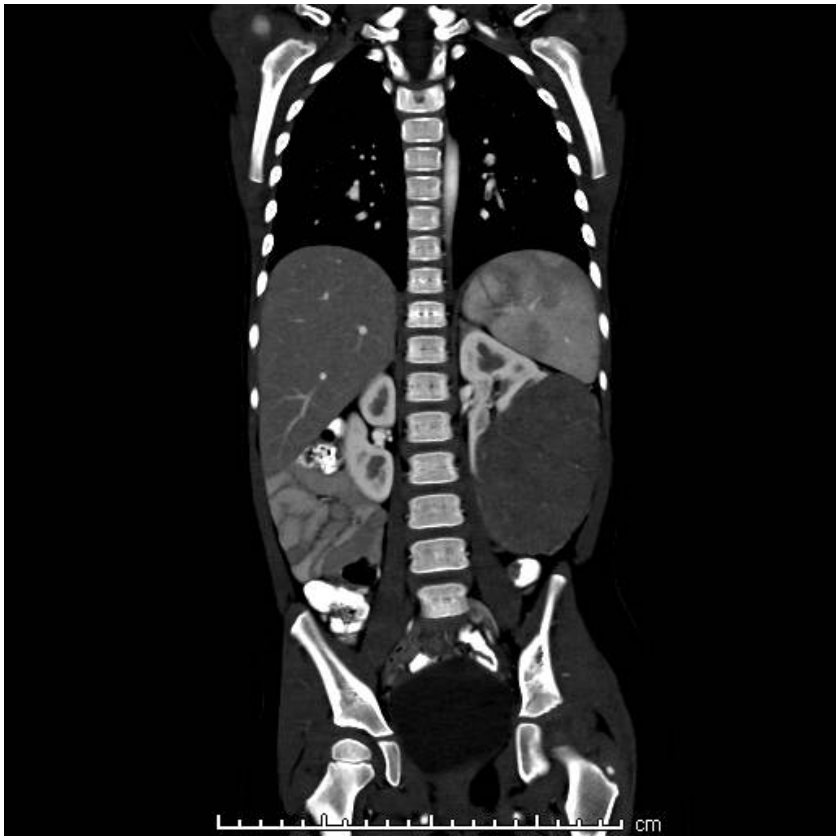


*Tonini et al., JCO, Vol 15;1,1997: pp 85-93

Quiz

Neuroblastoma





Wilms' tumor

Diagnosis of neuroblastoma

- Tissue diagnosis is definite

- Bone marrow aspirate positive for pseudo-rosette formation, small round blue cell + Elevation of Urine catecholamine

  With clinical support

NSE=*Non-specific* enolase
Also positive in other NE tumors, EWS, germinomas, WT

International Neuroblastoma Risk Group (INRG) Staging System

- Pretreatment classification
- Based on imaging criteria
- Locoregional disease extension based on image-defined risk factors (IDRF); L1, L2
- M= stage 4
- Ms (<18mo)= stage 4S (<12mo)

ANBL 1232 for non HR neuroblastoma

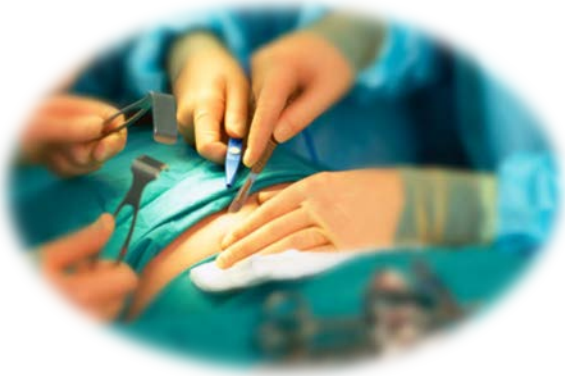
Pre-treatment risk classification modified by ThaiPOG

INRG Stage	Age (months)	Tumor histology	Tumor differentiation	MYCN	Shimada histology	Pre-treatment risk group
L1/L2	Any	GN maturing GNB intermixed	Any	Any	Any	Very low
L1	Any	Any, except GN maturing or GNB intermixed	Any	Non-Amp		Very low
				Amp	Any	High
L2	<18	Any, except GN maturing or GNB intermixed	Any	Non-Amp	Favorable	Low
					Unfavorable	Standard
	≥18	GNB nodular; Neuroblastoma	Differentiating	Non-Amp	Favorable	Low
					Unfavorable	Standard
			Poorly differentiated or undifferentiated		Any	Standard
	Any	Any	Any	Amp		High
M	<18	Any	Any	Non-Amp		Standard
				Amp	Any	High
	≥18			Any		High
MS	<18	Any	Any	Non-Amp	Favorable	Very low
					Unfavorable	High
				Amp	Any	High

Abbreviation: GN= Ganglioneuroma; GNB= Ganglioneuroblastoma; Non-Amp = MYCN non-amplified; Amp=MYCN amplified.

VLR, LR, IR, HR

Principle of neuroblastoma treatment



Treatment of Low- and IR (non-HR)

- Excellent outcome
- Reduction therapy aims to *decrease therapy-related toxicities* with maintaining EFS and OS

High risk "Kitchen sink"

Induction

6 cycles
Intensive CMT

- Cisplatin
- Cyclophosphamide
- Doxorubicin
- Etoposide
- Topotecan
- Vincristine

Local control

RT
Surgery

Consolidation

HDSCT with SC rescue**

MIBG Rx**

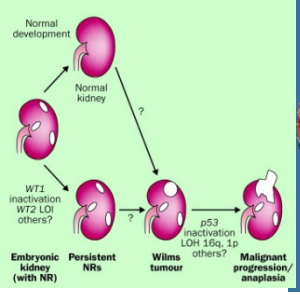
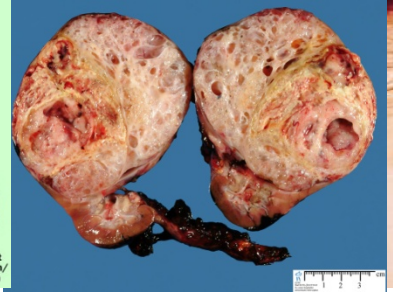
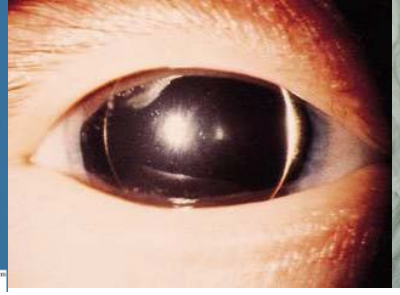
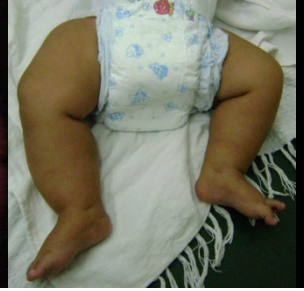
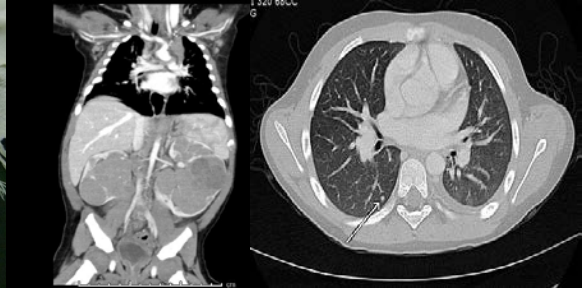
Myeloablative regimens
- Carbo/etoposide/melphalan (CEM)
- Busulfan/melphalan (BUMEL)
- Thiotepa/cyclophosphamide plus carbo/etoposide/melphalan

Maintenance
(MRD treatment)

Cis-RA and Chimeric anti-GD2 monoclonal Ab (ch14.18)

RT

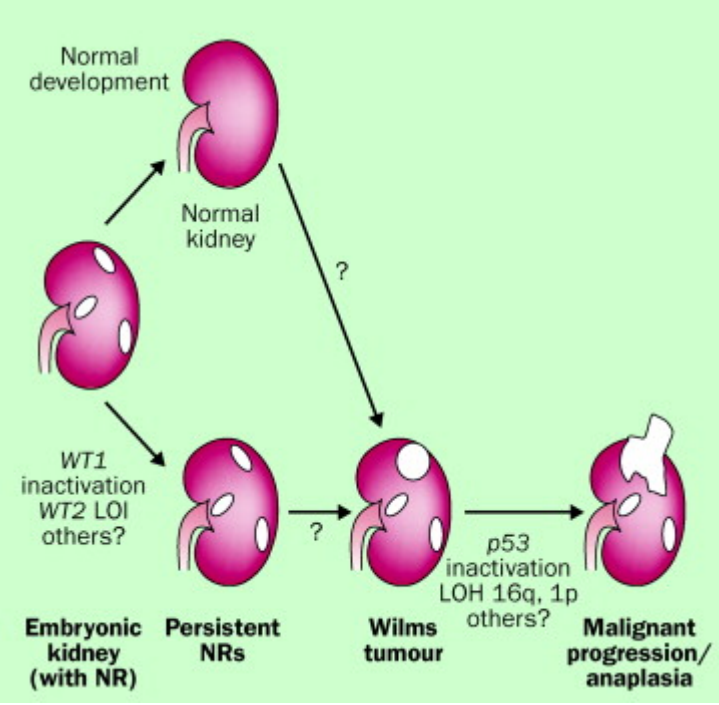
***Ongoing studies*


Normal development
Normal kidney
?
WT1 inactivation WT2 LOI others?
?
p53 inactivation LOH 16q, 1p others?
Embryonic kidney (with NR)
Persistent NRs
Wilms tumour
Malignant progression/ anaplasia





Wilm’s Tumor

Wilm's tumor

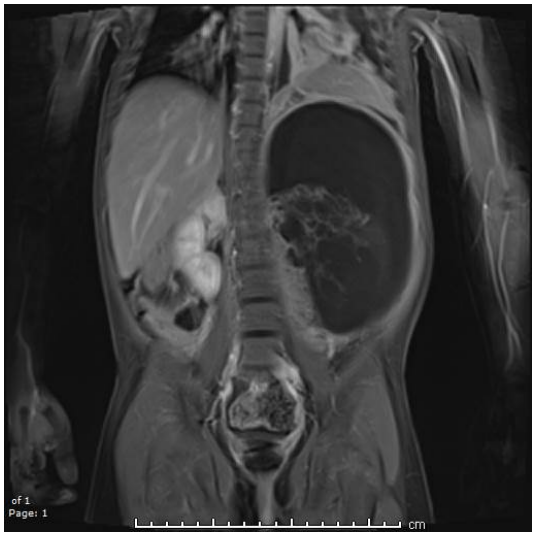
- MCM renal malignancy
- Peak age 3-4 years
- Embryonal neoplasm arising in kidneys



Kalapurakal et al.,Lancet Oncol 2004; 5: 37–46

Signs & Symptoms

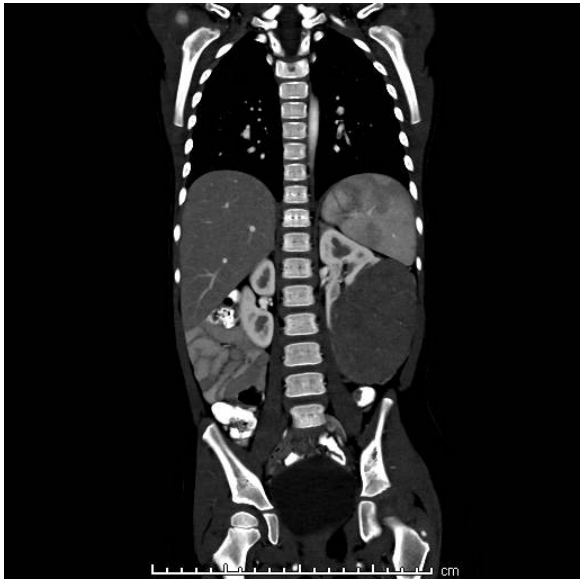
- A symptomless abdominal mass 60%
- Hematuria 30%
- HT 25%
- Polycythemia
- Acquired vWD <10%



Investigations

- U/A
- BUN/Cr
- Coagulogram and bleeding time : acquired vWD

- U/S, CT scan
- CXR, CT chest

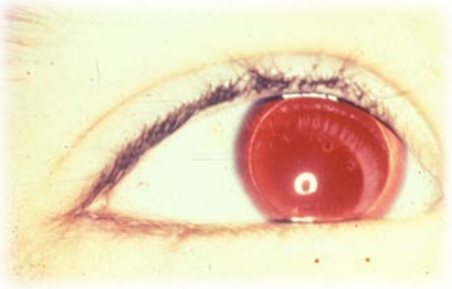


- BMA: Not necessary unless + evidence of BM invasion

Associated congenital anomalies

- 13-28%
- Beckwith – Wiedemann syndrome
- WAGR syndrome

  (Wilm's tumor, aniridia, GU anomaly, retardation)



- Denys-Drash syndrome:

  undermasculinized reproductive organs in boys, gonadoblastoma, end-stage renal disease (diffuse mesangial sclerosis)

Table 1. Syndromes and genetic loci associated with Wilms' tumour

Syndrome	Locus	Implicated genes
WAGR	11p13	*WT1*
Denys-Drash	11p13	*WT1*
Beckwith-Wiedemann	11p15	*IGF2, H19, p57*^{KIP}
Simpson-Golabi-Behmel	Xq26	*GPC3*
Li-Fraumeni	17p13	*p53*
Hyperparathyroid jaw tumour	1q21–q31	*HRPT2*
Neurofibromatosis	17q11	*NF1*
Sotos	5q35	*NSD1*
Bloom	15q26	*BLM*
Perlman	?	?
Mosaic variegated aneuploidy	?	?
Trisomy 18	18	?

Kalapurakal et al.,Lancet Oncol 2004; 5: 37–46

Patterns of Spread

Local :

- Through renal capsule-into peri-renal fat
- Blood vessels-tumor thrombi
- Regional LN

Hematogenous Metastases :

- Lung (80%) : renal v. -> IVC -> lung
- Liver (15%)
- Brain/bone for CCSK and RTK

Principle of Wims' tumor treatment

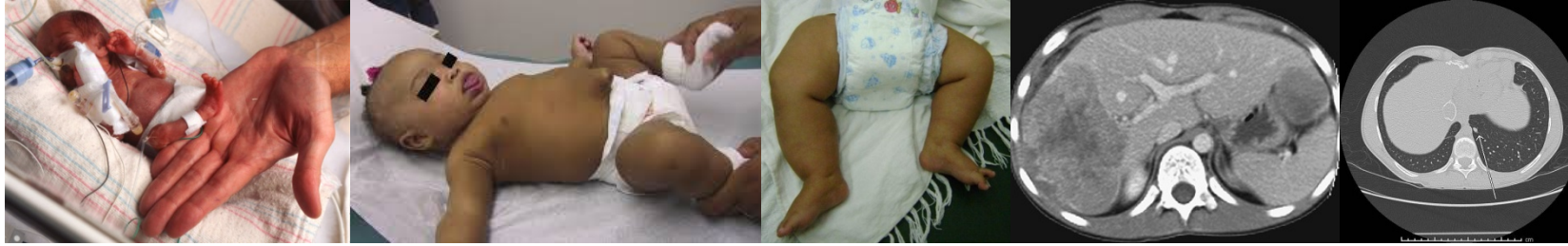
CHILDREN'S ONCOLOGY GROUP

THAI POG
Thai Pediatric Oncology Group

Except bilateral WT

SOCIÉTÉ INTERNATIONALE D'ONCOLOGIE PÉDIATRIQUE
SIOP
INTERNATIONAL SOCIETY OF PAEDIATRIC ONCOLOGY

beat hepato blastoma



Liver tumors

Epidemiology

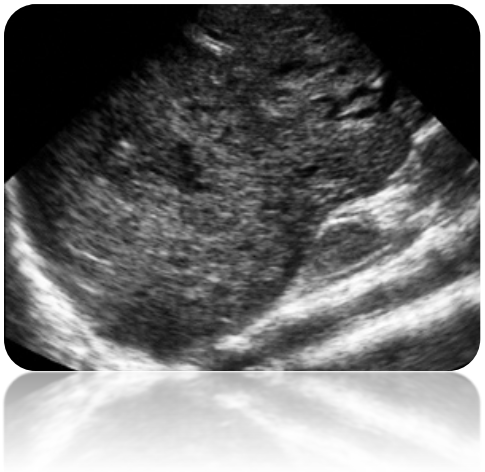
Hepatoblastoma	HCC
• 1.6 cases per million children/year • MCM primary malignant tumor of liver • >2/3 of all liver tumors • 90% of malignant liver tumors in children <4 years of age	• 0.8 cases per million children/year ages 0-14 years • 1.5 cases per million children/year ages 15-19 years • Incidence varies dependent upon HBV vaccination rates

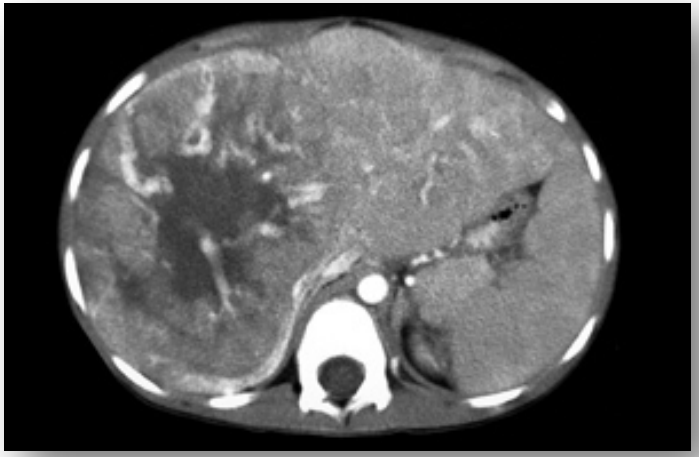
Hepatoblastoma

- Signs & Symptoms
  - Abdominal mass
  - Thrombocytosis
  - Not affect liver function
  - Metastasis : Lung

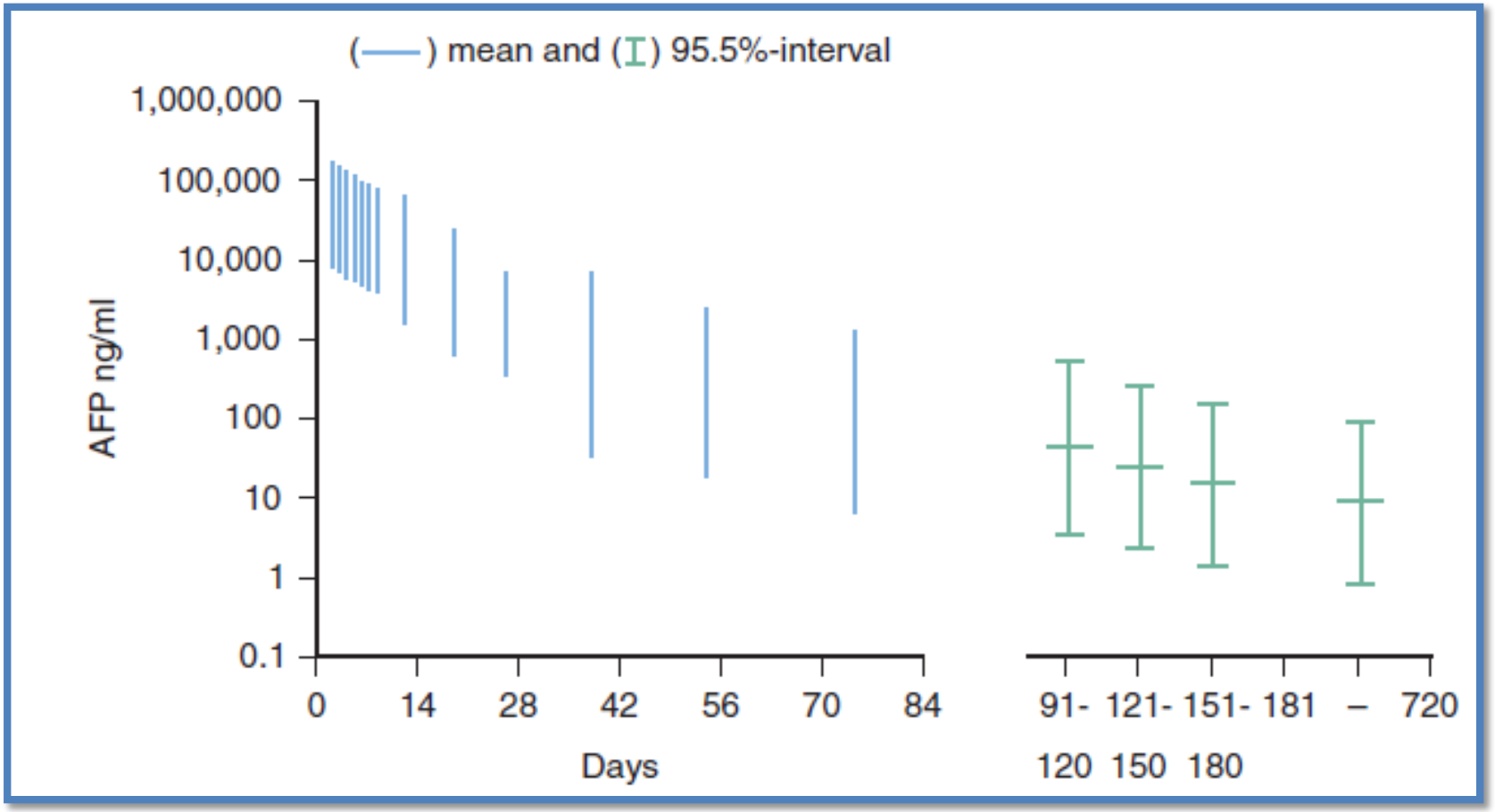
Investigations

- CBC : Thrombocytosis
- LFT
- Fibrinogen, coagulogram
- AFP
- U/S, CT abdomen
- CXR, CT chest
- MRI
- PET scan





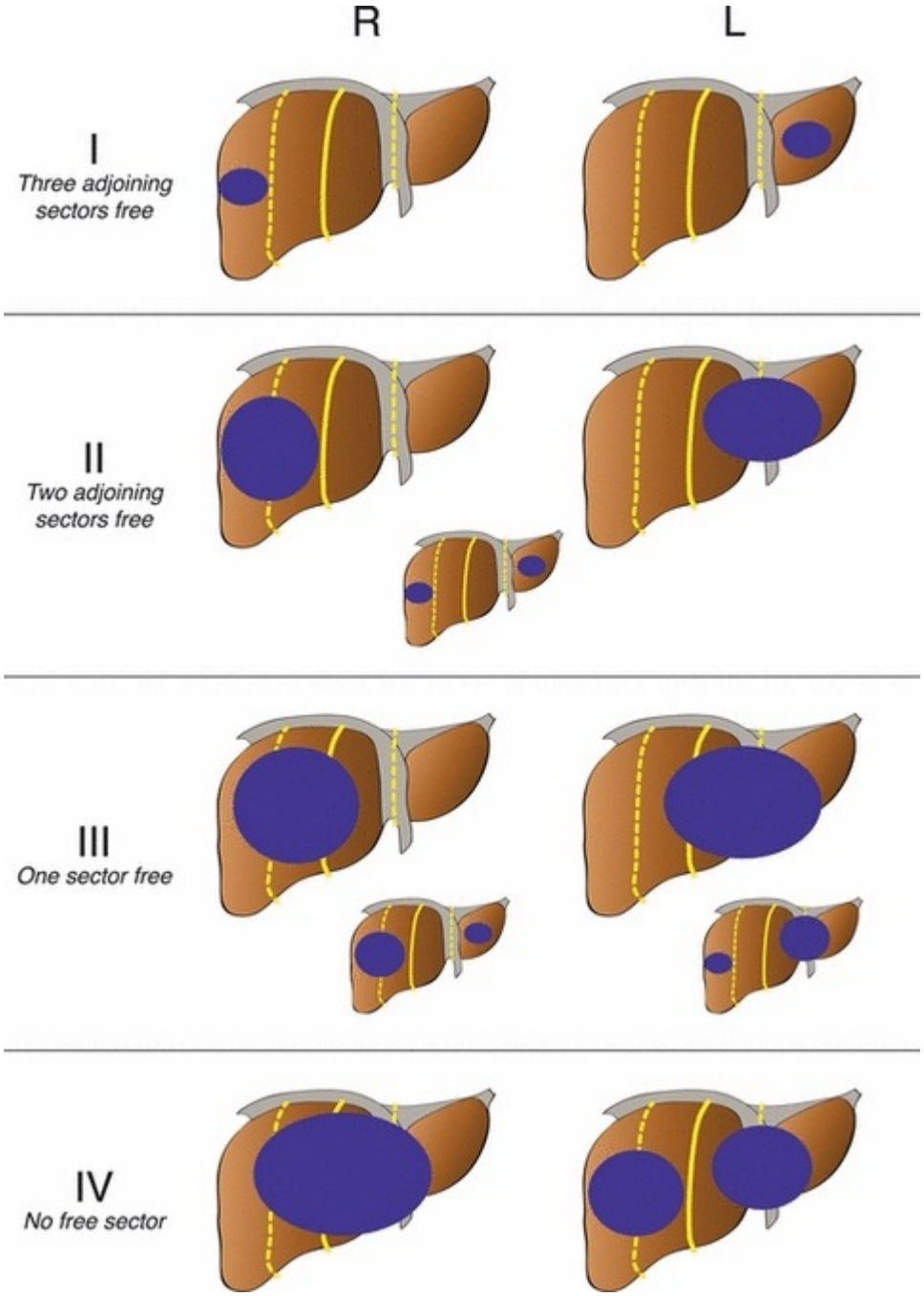
Serum AFP values in term babies



Blohm et al., Pediatr Hematol Oncol 15:135–142, 1998.

Indication for biopsy

1. Age <6 months, or >3 years
   - Biopsy is mandatory because of the wide differential diagnosis of hepatic masses and the possible confounding effect of an “elevated” serum AFP level if age <6 months, and because of the risk of misdiagnosing HCC if age >3 years
2. Age 6 months - 3 years
   - Biopsy is not required if typical radiological finding of hepatoblastoma and elevated AFP (>100 ng/ml) are present



Pretext staging

Principle of hepatoblastoma treatment

CHILDREN'S ONCOLOGY GROUP

THAI POG
Thai Pediatric Oncology Group

C5VD

RT : effective dose exceeds hepatic tolerance

SIOPEL

THAI POG
Thai Pediatric Oncology Group

PLADO: Cis/Dox/Carbo

AFP response after treatment of HB

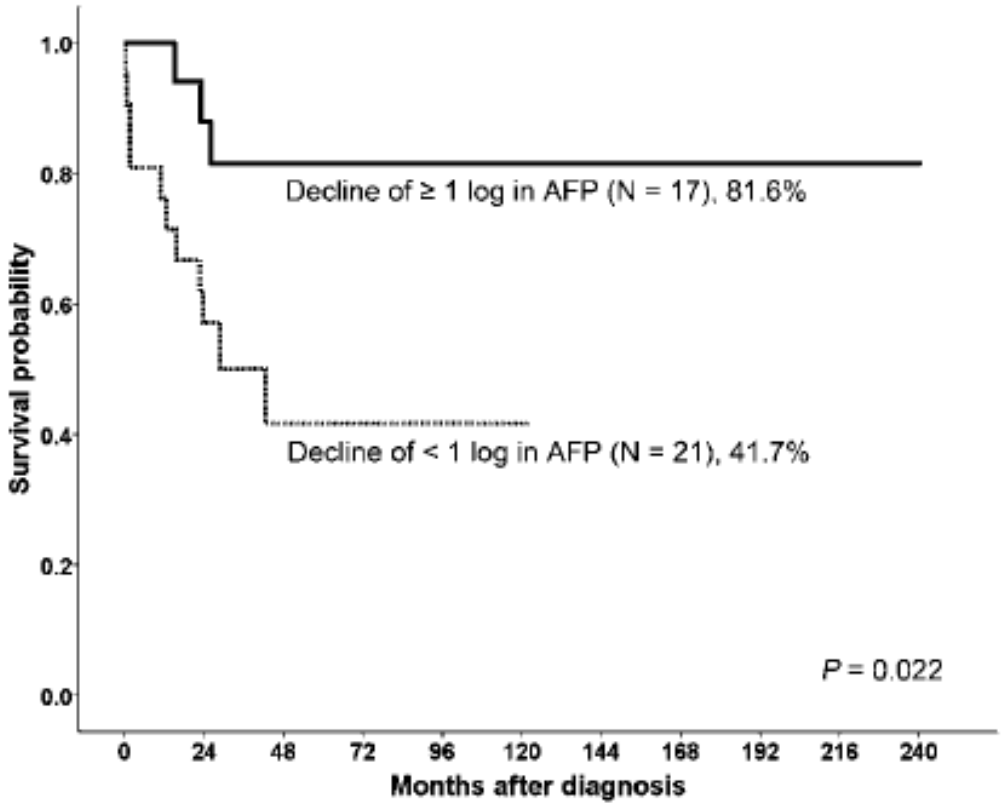
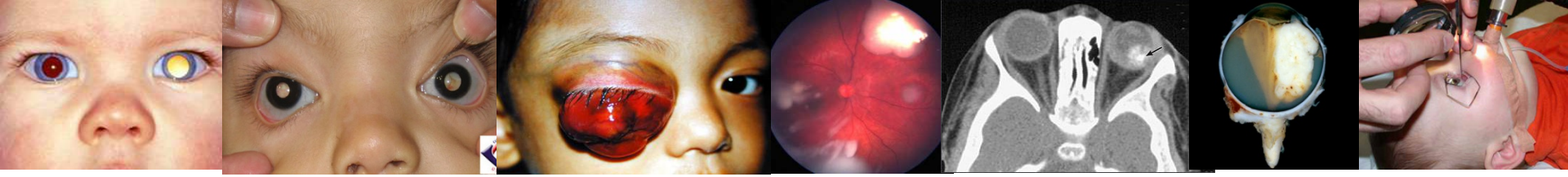


Fig. 3. Disease-free survival probability among 38 patients, who received preoperative chemotherapy, relative to magnitude of change in AFP level after the first cycle of chemotherapy.

Koh et al., Pediatr Blood Cancer, 2011



Retinoblastoma

Epidemiology

- Malignant tumor of retina
- MCM primary intraocular malignancy of childhood
- Mutation in tumor suppressor gene retinoblastoma gene (RB 1 gene)
  - Germ cell mutation → Hereditary 40%
  - Somatic cell mutation → Non – Hereditary 60%
- Survival rate > 90%

Genetic

- Hereditary
  - 85% bilateral, 15% unilateral
  - Multifocal lesion in unilateral
  - Unifocal lesion with family history
- Non – hereditary
  - 85-95% unifocal lesion with no family history

- 40% bilateral (germline RB1 mutations
  - 25% inherited, 75% sporadic
- 60% unilateral
  - 10-15% will have RB1 mutation

Clinical Presentations

- Leukocoria : MCM
- Strabismus
- Painful, red eye
- Proptosis
- Trilateral retinoblastoma
- Metastasis :
  - Soft tissue extension
  - Hematogenous : brain, liver, BM, bone

10 mo-old boy mom noticed an abnormal from a picture that has been taken recently

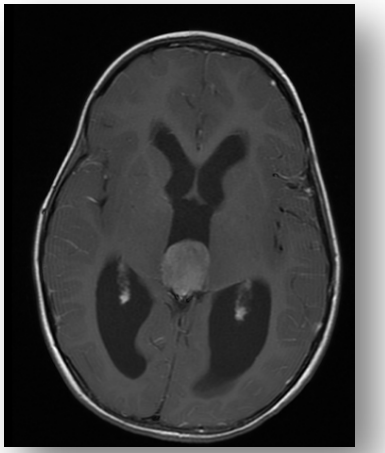
What should we do next???

- Obtain family history
- Complete PE
- EUA (Examination Under Anesthesia) by opthalmologist

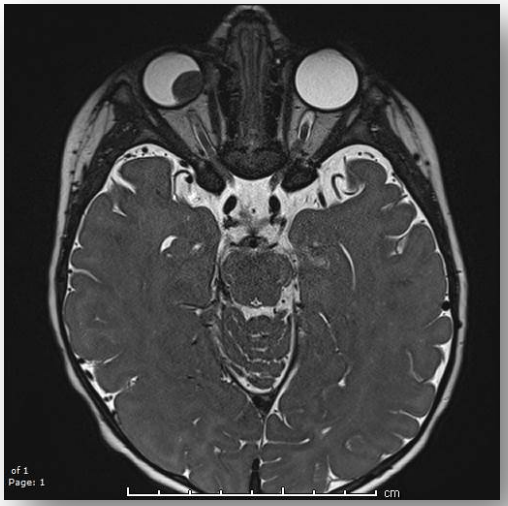
Diagnosis made during EUA
Pathology not necessary

Investigations

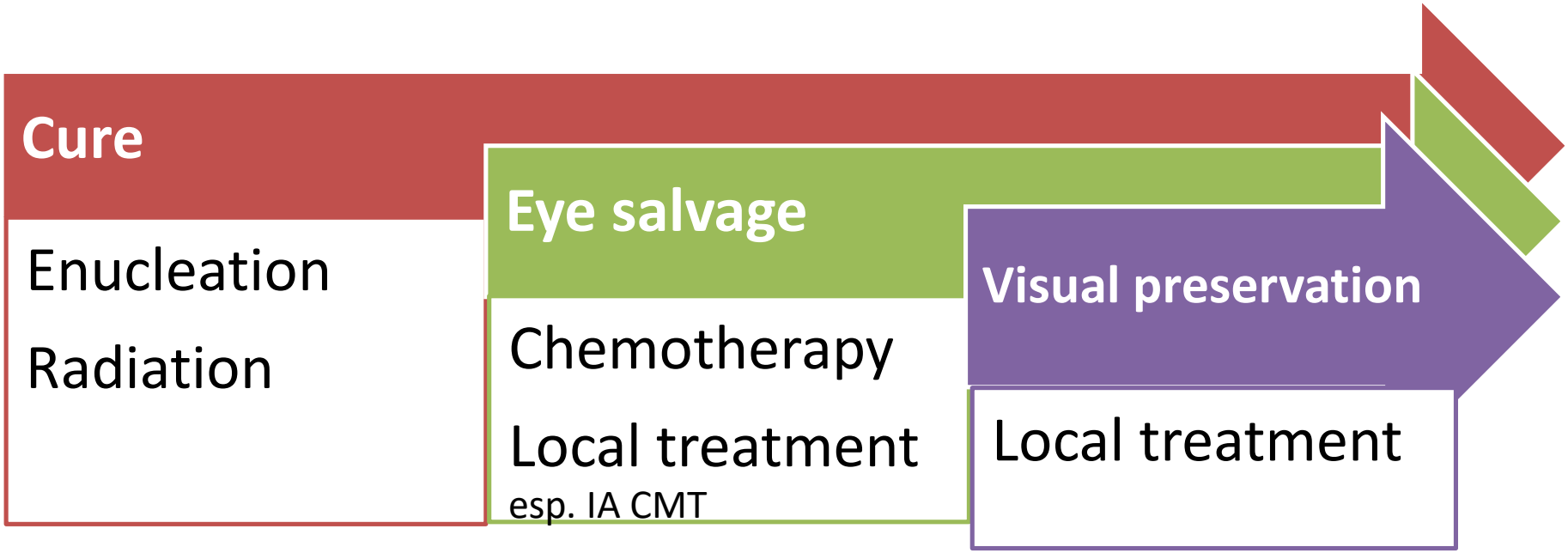
- MRI brain with orbit include pineal gland
- Bone scan
- BMA and biopsy
- CSF studies if suspected CNS disease



- Germline RB1 mutation testing!!



RB treatment strategies

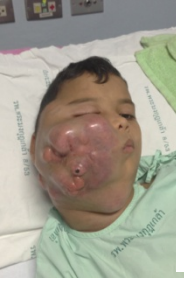


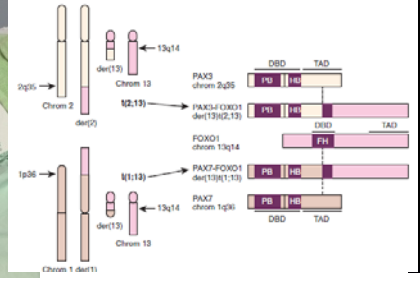
- Primary goal is to preserve life
- Secondary goal of preserving vision

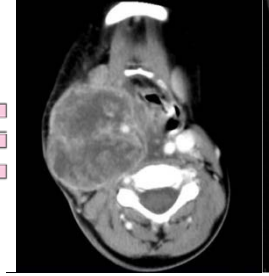
Second Malignancies in Retinoblastoma Survivors

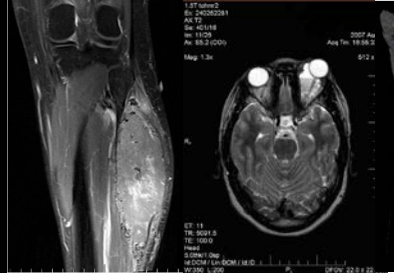
- Most are radiation-induced
  - 60-70% head and neck area
  - Dose-effect
  - Age-effect (higher risk for < 1 yo)

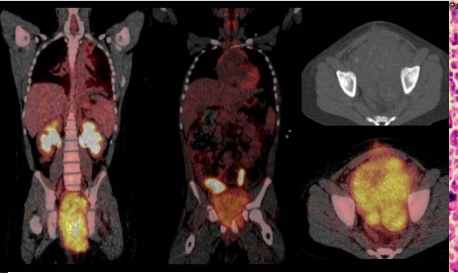
- Malignancies:
  - Osteosarcoma (25-40%): Most common inside and outside irradiated field
  - Soft tissue sarcomas (10-15%): Inside > outside irradiated field (leiomyosarcoma > fibrosarcoma > MFH > STS NOS > RMS)
  - Melanoma and other skin cancers (15-20%)
  - Lung cancer and other common cancers of adulthood

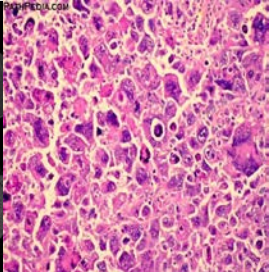








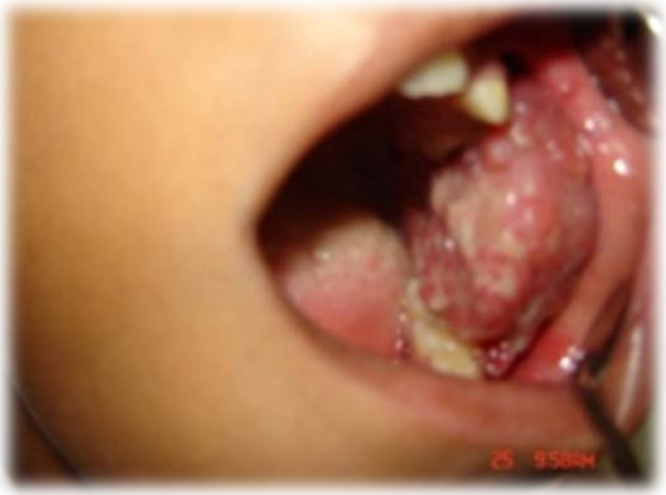




Rhabdomyosarcoma

Epidemiology

- Soft tissue tumor of mesenchymal origin
- Incidence: 4.5/1 million children
- 6-8% of all childhood cancers



Disease characteristics

Primary site	Frequency (%)	Symptoms and signs	Predominant pathologic subtype
Head and neck	**35**		Embryonal
Orbit	9	Proptosis	
Parameningeal	16	Cranial nerve palsies; aural or sinus obstruction +/- drainage	
Other	10	Painless, progressively enlarging mass	
Genitourinary	**22**		Embryonal (botryoid variant in bladder and vagina)
Bladder and prostate	13	Hematuria, urinary obstruction	
Vagina and uterus	2	Pelvic mass, grape liked mass, vaginal discharge	
Paratesticular	7	Painless mass	
Extremities	**18**	Affects adolescents; swelling of affected body part	Alveolar (50%)
Perineal and perianal (PRMS)	**2**	Mass	Alveolar (60-80%)
Other	**23**	Mass	Embryonal, alveolar

Prognostic Factors

- TNM
  - Diameter ≤ 5cm with improved survival (correlation between size and BSA*)
  - Metastasis and regional LN involvement
- Resectability
- Age: 1-9 yo have best prognosis
- Sites of primary tumor
- Histopathology

* Ferrari et al., JCO, 2009

Prognostic Factors : Sites of primary tumor

Favorable

- Orbit
- GU non bladder, non prostate
- H&N non parameningeal
- Biliary tract

Unfavorable

- Bladder
- Prostate
- Parameningeal
- Extremities
- (Perineal and perianal)*

*Casey at al., Int J Radiation Oncol Biol, 2014
Fuchs et al., Annals of Surgery, 2014

Prognostic Factors : Histopathology

Favorable

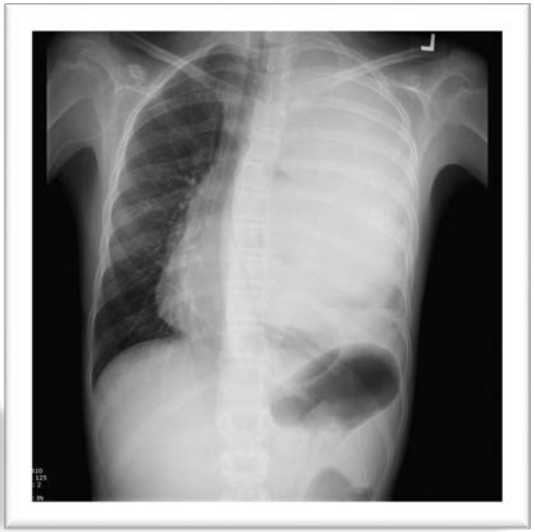
- Embryonal
- Botryoid (under mucosa of the vagina, bladder, nasopharynx and biliart tract)
- Spindle cell (mostly at paratesticular site)

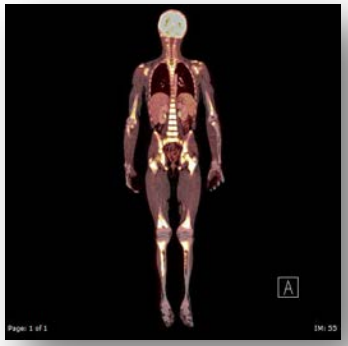
Unfavorable

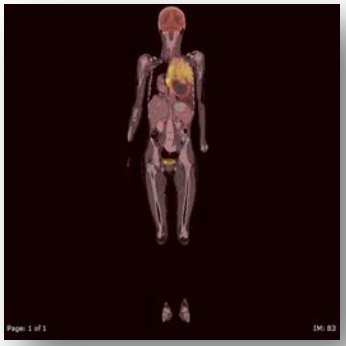
- Alveolar
- Anaplastic* (not influence treatment)

Investigations

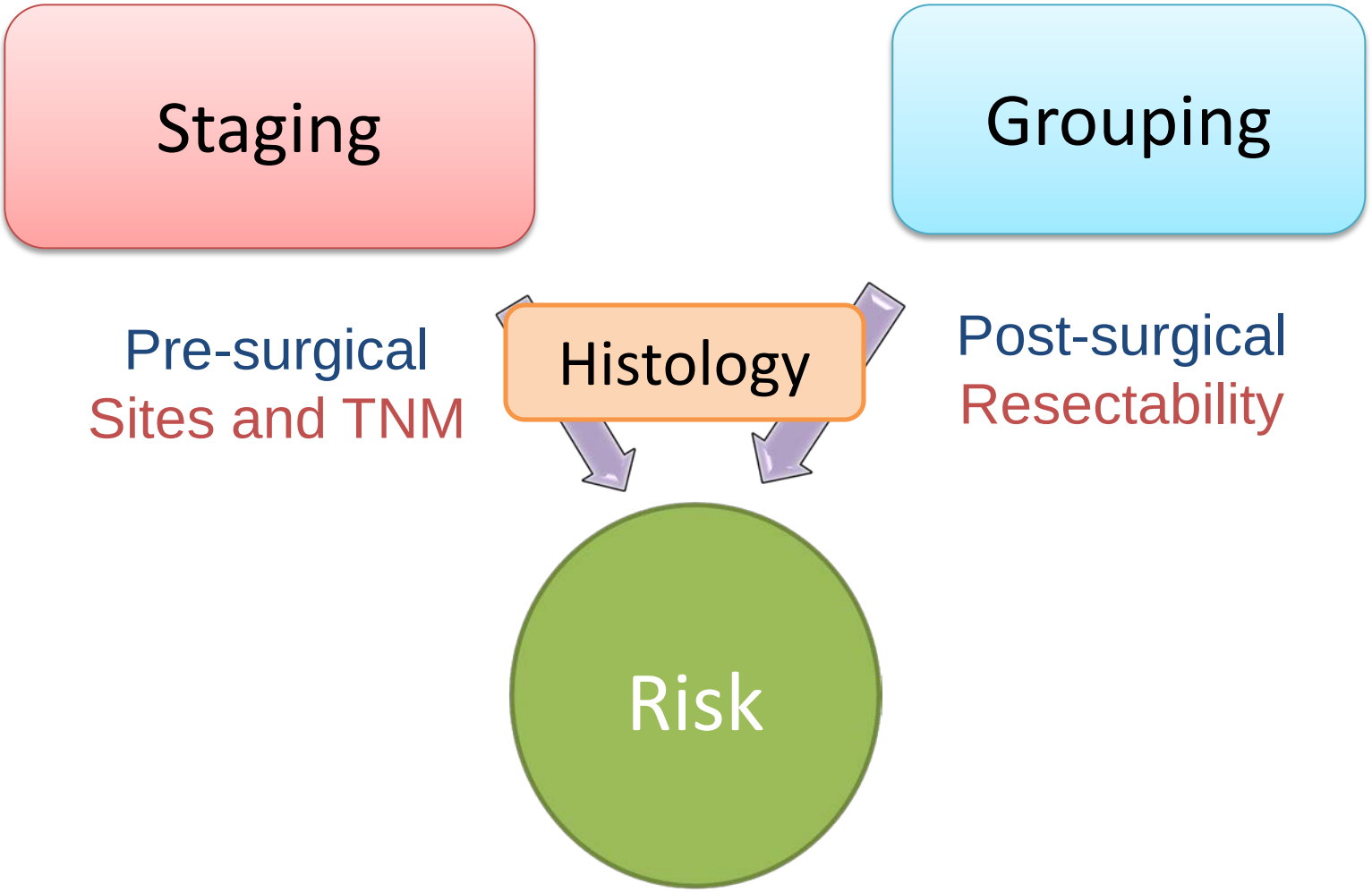
- CT/ MRI primary lesion
- CT chest, CXR
- CT abdomen include pelvis
- Bone scan
- PET scan
- BMA & BM biopsy
- Biopsy: malignant spindle cell
  - ARMS with extremities lesions → sentinel LN Bx



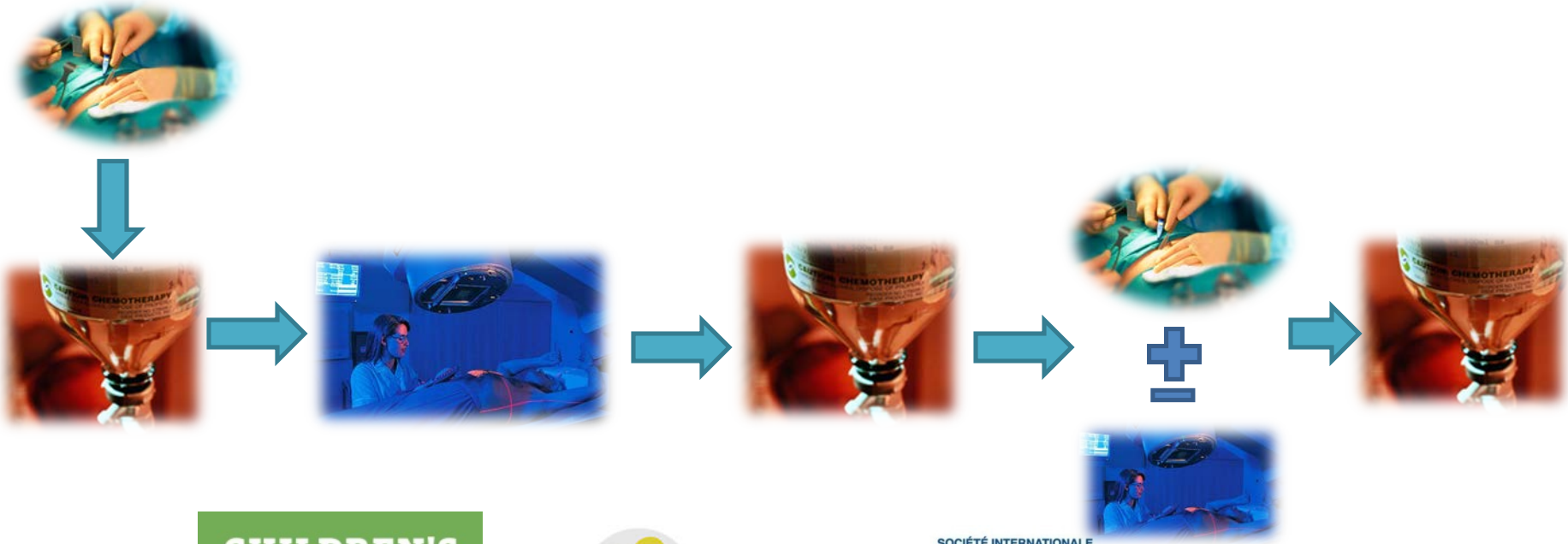




Risk Stratification



Principle of rhabdomyosarcoma treatment



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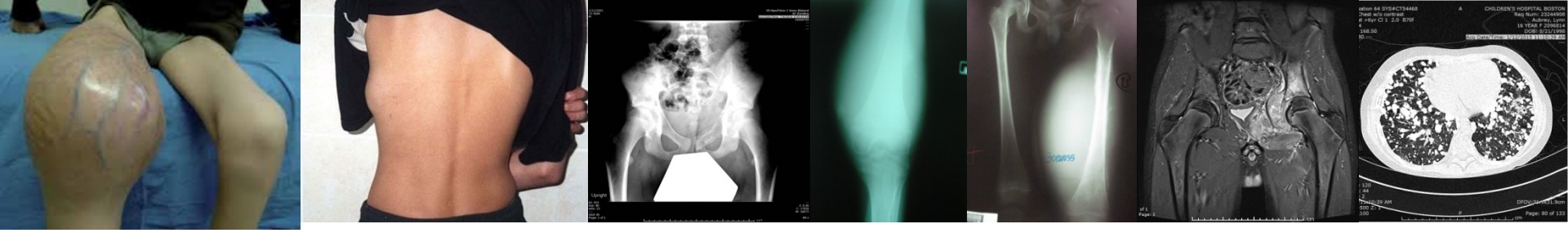
SIOP
INTERNATIONAL SOCIETY OF PAEDIATRIC ONCOLOGY

LR: avoid harmful treatment

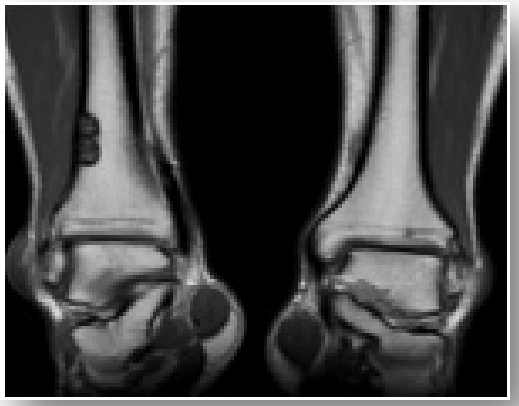
HR: "Kitchen sink" dose intense with interval compress to improve outcome

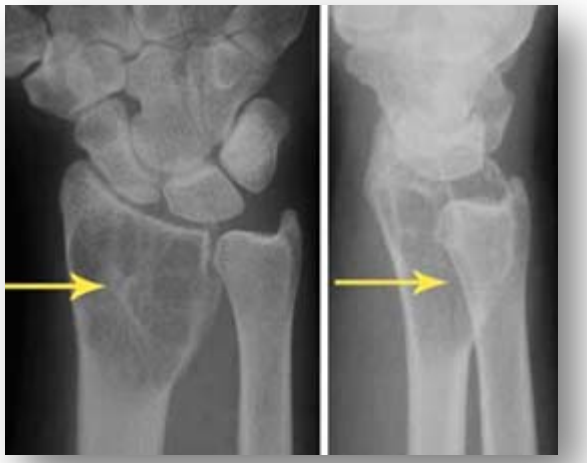


Malignant Bone Tumors

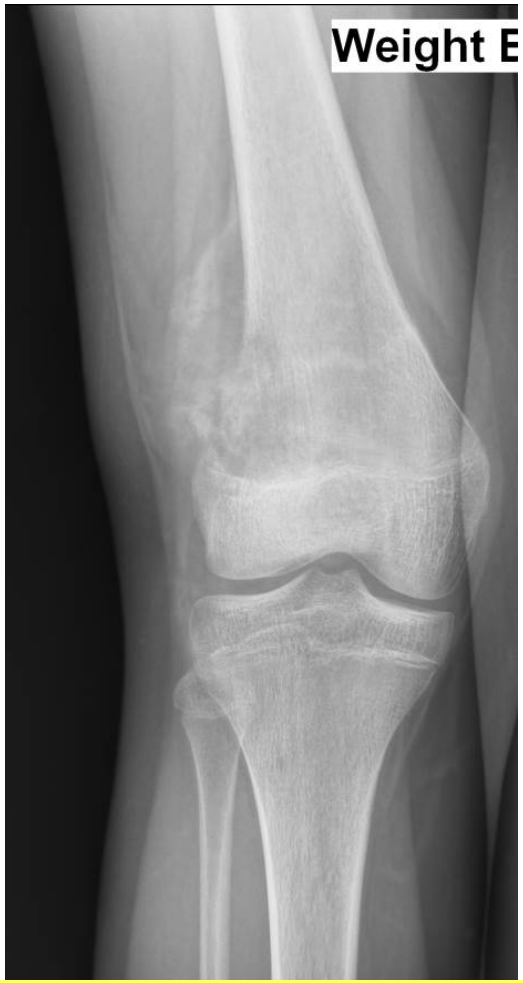
Bone Tumors in Children

- Only half of bone lesions in children are malignant
- Other half benign or nonneoplastic lesions

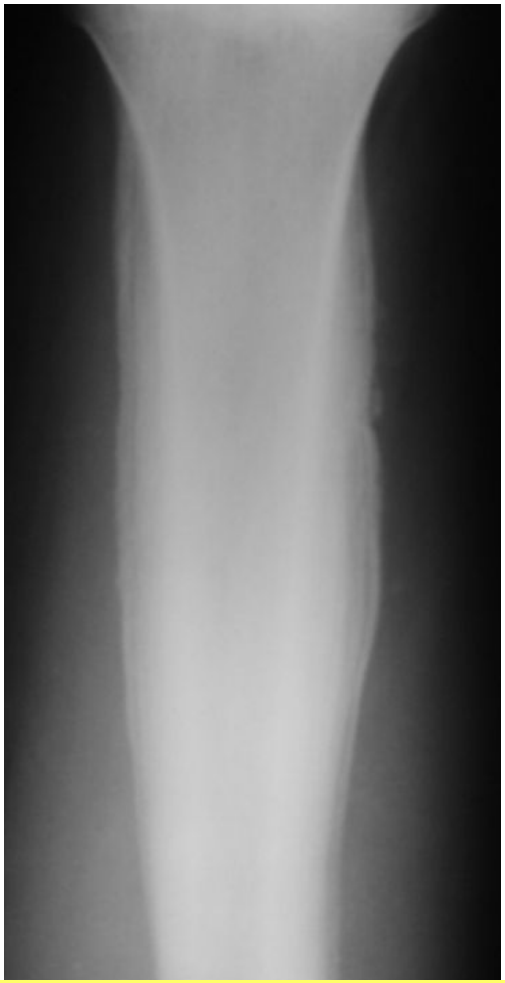




QUIZ



Osteosarcoma



Ewing sarcoma

Malignant Bone Tumors

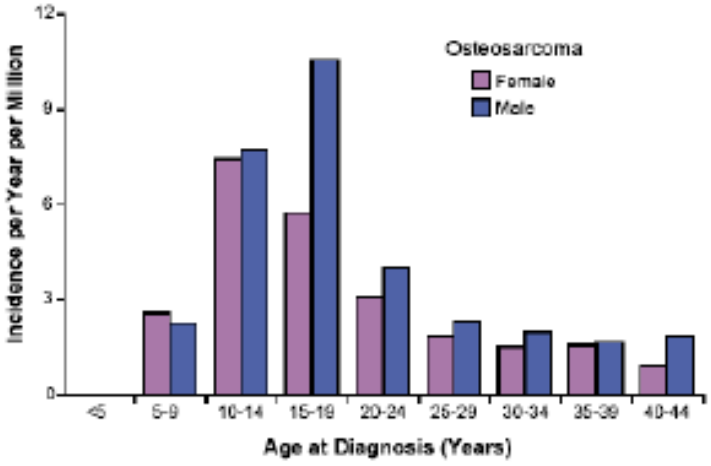
	Osteosarcoma	Ewing's Sarcoma
Age < 5yr Adolescent Adult > 40 yr	 Very rare Peak Yes	 Common Peak Very rare
Race	Asian> Caucasian	Caucasian>>>>>>> Asian
History Previous RT Family Hx	 Ye LFS, RB1	 No No
Constitutional symptoms	No	Yes
Location	Bone	Bone, soft tissue, renal
Skip lesion	Uncommon	Common
Metastasis	Lung	Lung, bone, BM

Malignant Bone Tumors

	Osteosarcoma	Ewing's Sarcoma
Bone	Long bones	Long and Flat bones (Pelvis, skull, ribs)
Site	Metaphysis	Diaphysis
Genetic	p53 gene mutation	Oncogene activation (EWS)
Radiologic findings	• Sunburst pattern • Calcification	• Moth-eaten lytic lesion • Onion skin
	• Periosteal reaction • Codman's triangle	
LAB	↑ALP CBC-normal	Normal ALP CBC-abnormal (if BM+)
PATH	Malignant spindle cell Malignant osteoid +	Small round blue cell No malignant osteoid
RT	Resistance	Responsive

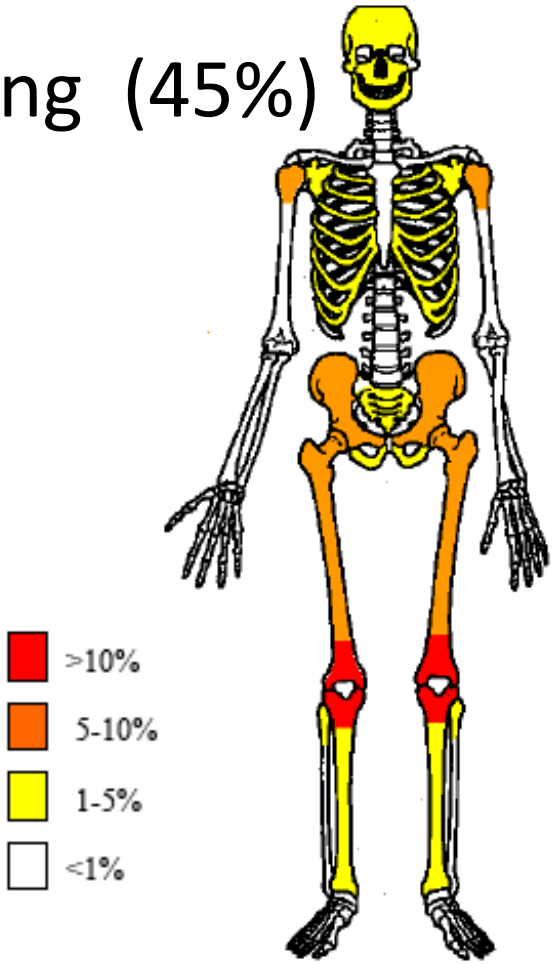
Osteosarcoma

- MCM primary malignant bone tumor in children
- Rare : < 10 years of age
- Genetic predisposing syndrome
  - Li-Fraumeni syndrome (p53)
  - Hereditary RB (RB1)
- Radiation therapy
  - 3% of all osteosarcoma
  - Long latency > 10 years
  - Potentiated by prior chemotherapy (alkylators, anthracyclines)



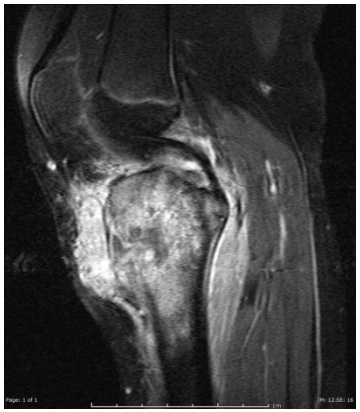
Clinical presentation

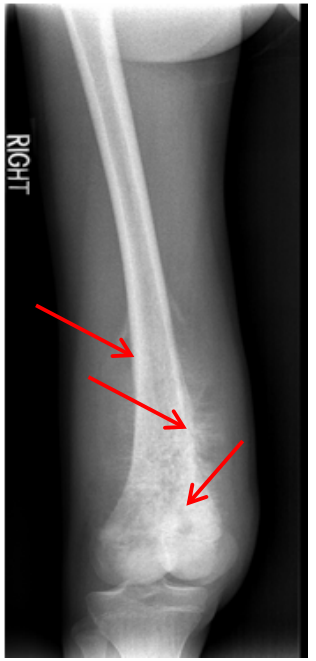
- Local pain (90%)
- Local swelling (50%)
- Decreased range of motion, limping (45%)
- Pathologic fracture (8%)
- Lab
  - Elevated LDH 30%
  - Elevated ALP 40%



Investigations

- Plain film at primary and bone met site(s)
- CXR
- MRI of primary tumor
- CT chest
- Bone scan
- PET scan: (recommend) evaluation for metastatic disease (bone, lung)
  - PET/CT more sensitive and accurate than bone scan*
  - Combined use improves sensitivity*
- Biopsy
  - Requires planning for later resection of biopsy tract



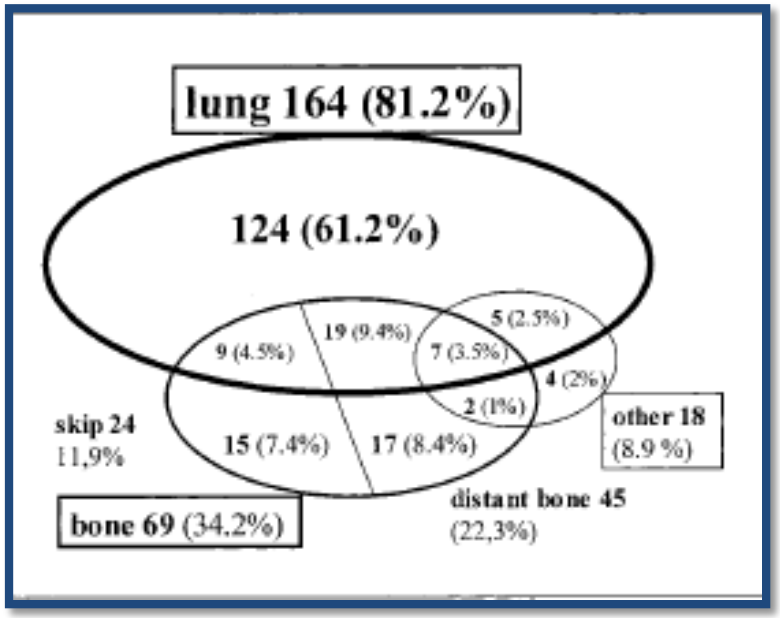


*Byun BH et al, Skeletal Radiol 2013
Meyer et al., Pediatr Blood Cancer 2008;51:163–170

Staging

- Localized
- Metastatic
  - 15-20% metas at presentation
  - Lungs
  - Bone:

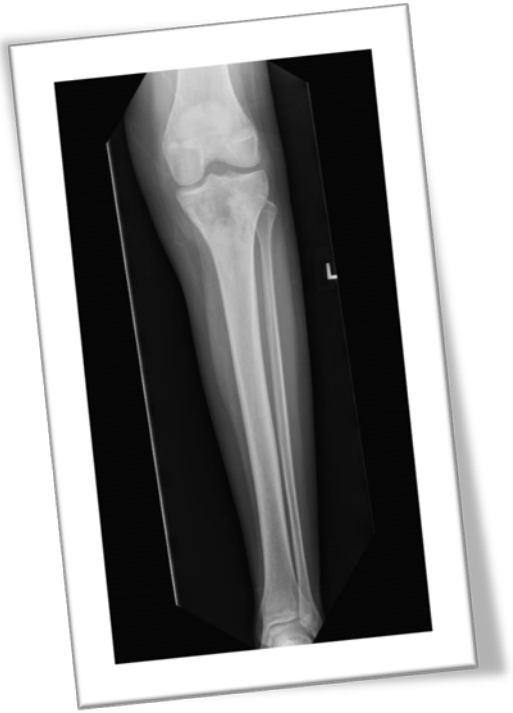
    distant and skip lesions
  - Combined

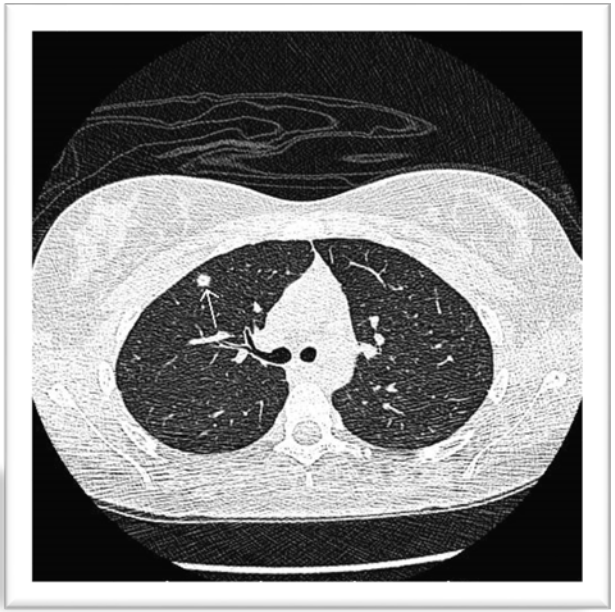


Kager L et al. J Clin Oncol 2003

5y OS in osteosarcoma

- Localized osteosarcoma ~ 70%
  - If CMT response ≥90% TN → increased to 80%
- Metastatic osteosarcoma ~ 25%





Principle of osteosarcoma treatment

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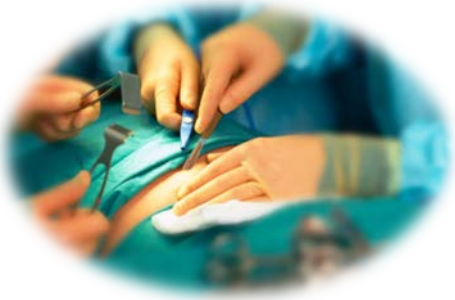


Neoadjuvant Chemotherapy

MAP

Local Control

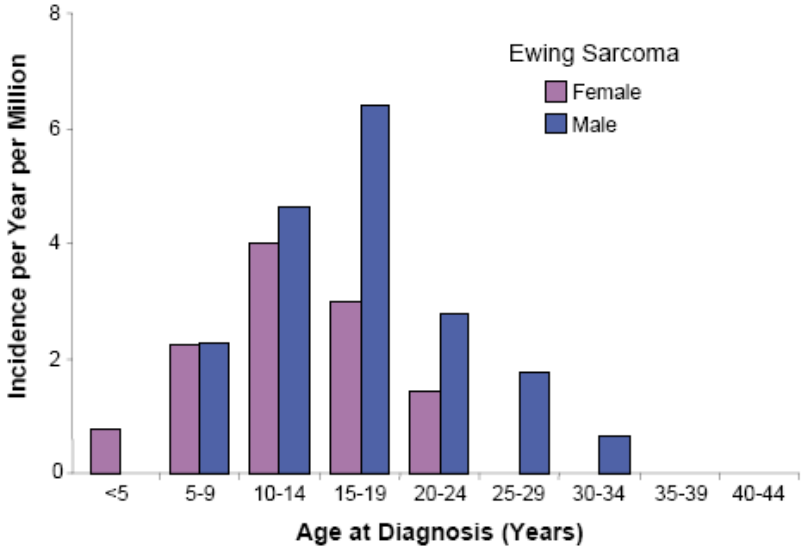
TN indicated prognosis but not changing the treatment

Adjuvant Chemotherapy

MAP

Ewing Sarcoma Family of Tumors (ESFT)

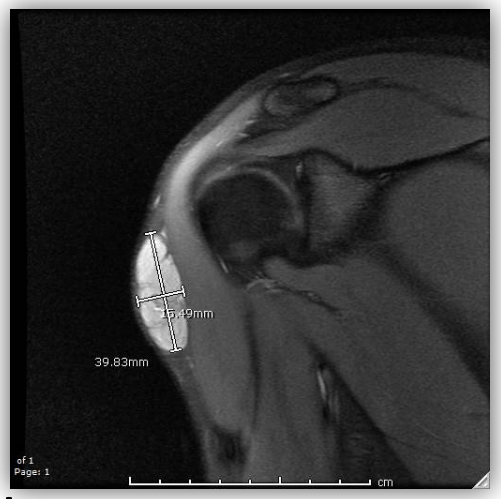
- Majority present in the 2nd decade of life
- 2nd MCM bone malignancy in children
- Bone, soft tissue, Askin's tumor or PNET
- Metastasis: 25% of patients present with metastases
  - Lung 38%
  - Bone 31%
  - BM 11%
  - Other unusual sites



Mascarenhas et al., 2006
SEER Data 1975-1999

Clinical presentation

- Age: median age 15 years
- Race: significant higher incidence in Caucasians
- Presenting symptoms
  - Pain
  - Soft tissue mass
  - Median time to diagnosis 3 – 9 months
  - Constitutional symptoms: fever, weight loss, malaise
  - LAB: LDH increased (marker of advance disease)

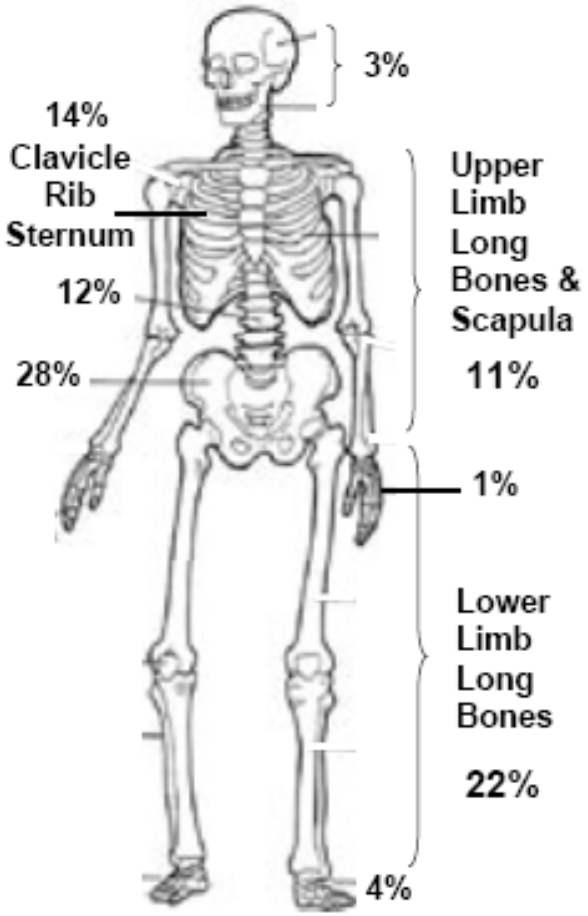


Site of Origin

- Bone primaries (75%)

  Axial=extremities

  - Pelvis
  - Long bones
  - Other axial sites
- Soft tissue primaries (25%)
  - Paraspinal
  - Chest wall
  - Various other sites



Mascarenhas et al., 2006
SEER Data 1975-1999

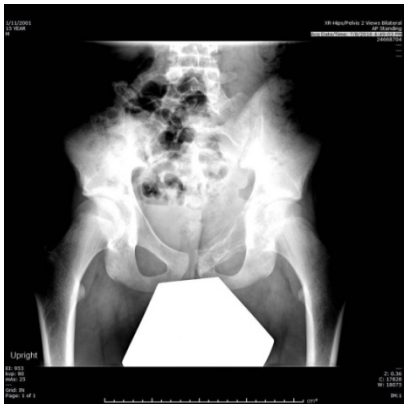
Biology

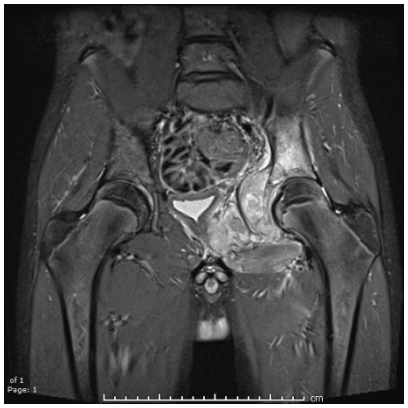
Tumor Type	Translocation	Fusion Gene	
Ewing sarcoma	t(11;22)(q24;q12)	*EWSR1/FLI1*	80-95%
	t(21;22)(q22;q12)	*EWSR1/ERG*	5-10%
	t(7;22)(p22;q12)	*EWSR1/ETV1*	
	t(17;22)(q12;q12)	*EWSR1/ETV4*	
	t(2;22)(q35;q12)	*EWSR1/FEV*	
	t(16;21)(p11;q22)	*TLS/ERG*	
	t(2;16)(q35;p11)	*TLS/FEV*	
Ewing-like sarcoma	t(20;22)(q13;q12) (NB: can occur in ring chromosome and may be amplified)	*EWSR1/NFATC2* *EWSR1/POU5F1*	
	t(6;22)(p21;q12)	*EWSR1/SMARCA5*	
	t(4;22)(q31;q12)	*EWSR1/ZSG*	
	Submicroscopic inv(22) in t(1;22)(p36.1;q12)		
	t(2;22)(q31;q12)	*EWSR1/SP3*	
	t(4;19)(q35;q13)	*CIC/DUX4*	
	inv(X)(p11.4;p11.22)	*BCOR/CCNB3*	

Investigations

Primary site

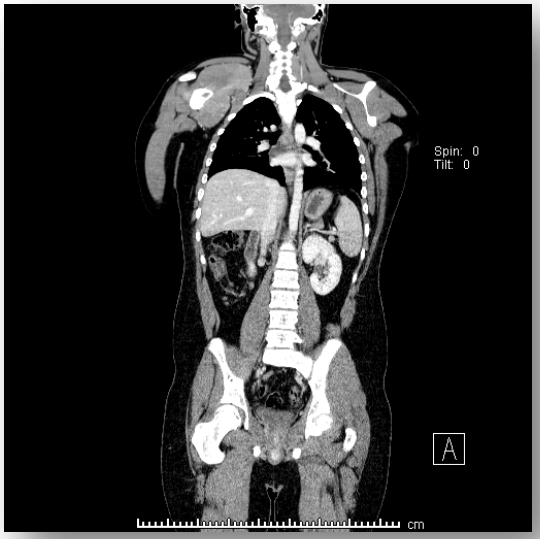
- Plain film
- MRI of affected region

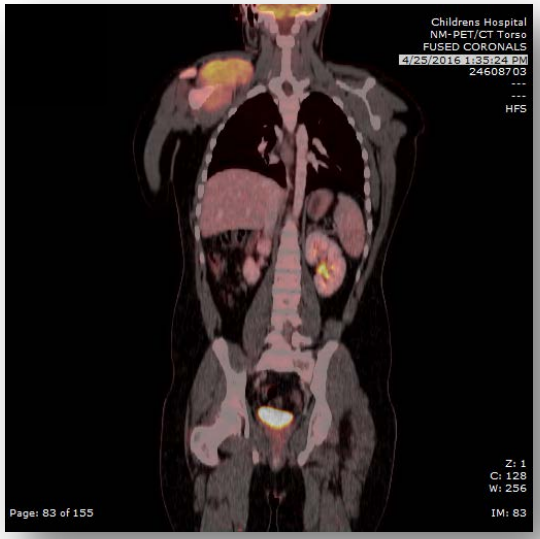




Metastasis detection and staging

- CT chest
- Bone scan
- Bilateral BM biopsy
- PET scan

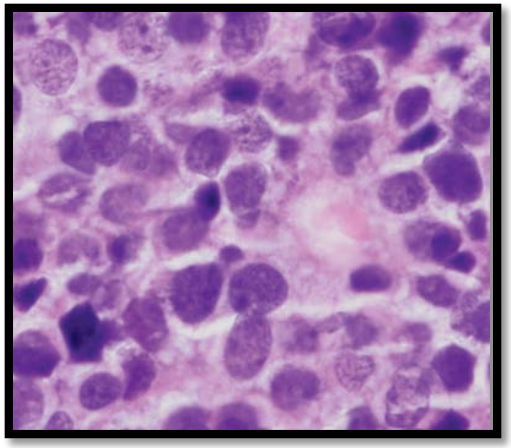




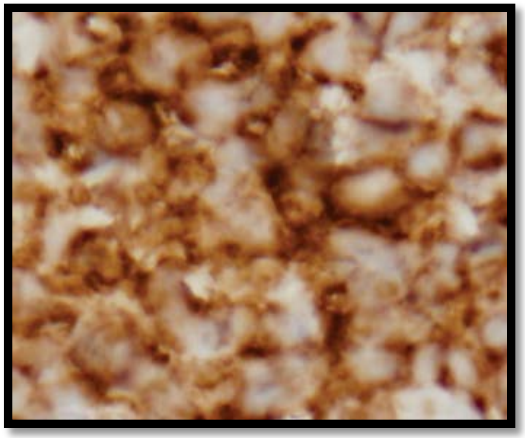
Tissue biopsy

Diagnosis-Pathology

- Small round blue cell tumor



- Neural differentiation with PNET
- Nearly universal membranous CD99 expression
- Molecular diagnostics
  - Cytogenetics
  - FISH
  - PCR



CD 99

Principle of EWS treatment

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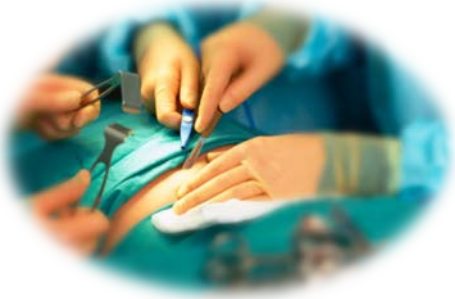
THAI POG
Thai Pediatric Oncology Group

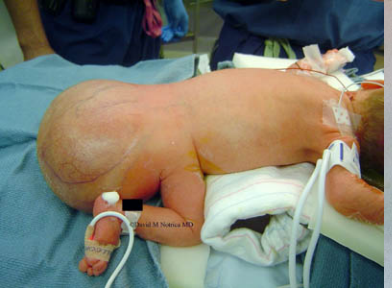
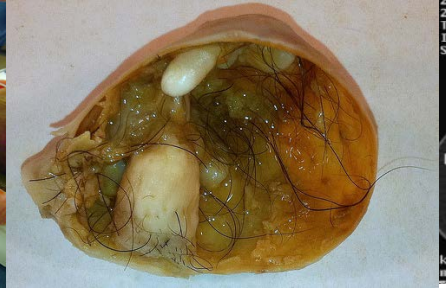
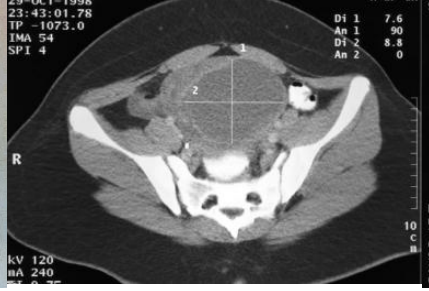


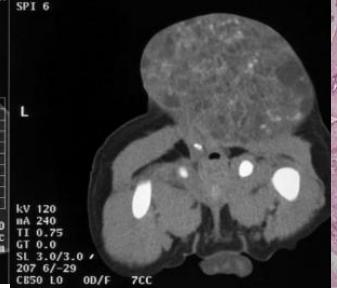
Neoadjuvant Chemotherapy

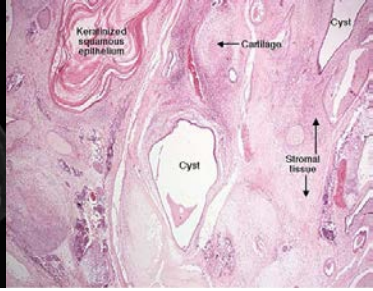
Local Control

Sx RT Sx+RT

Adjuvant Chemotherapy

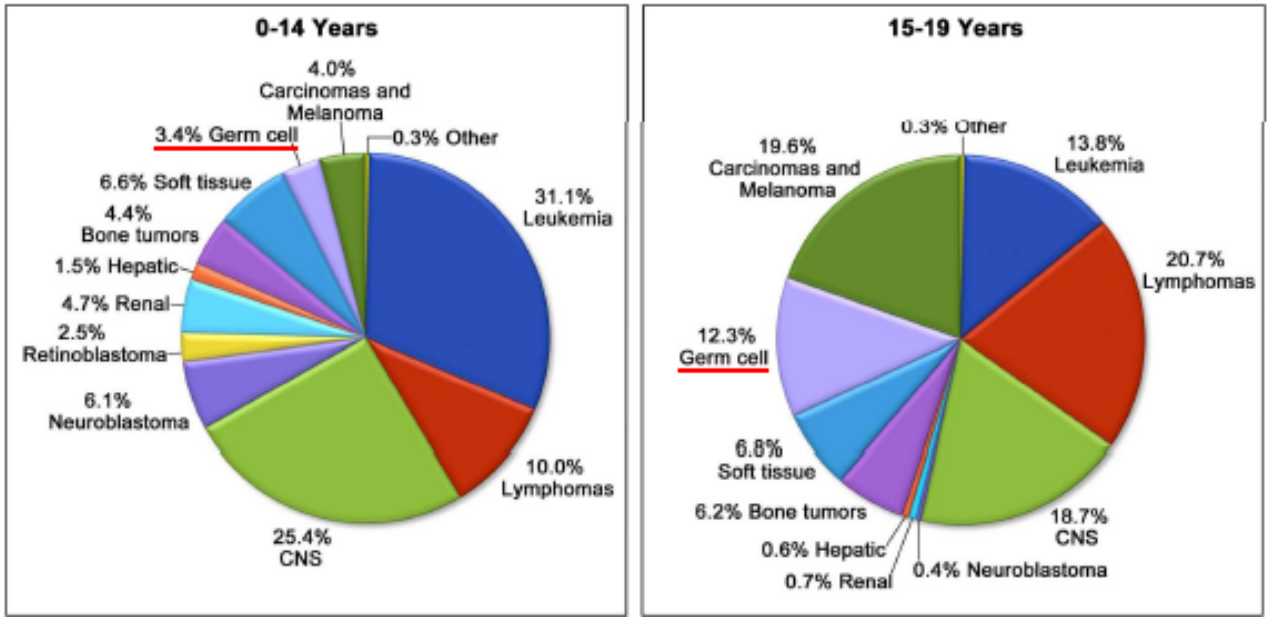




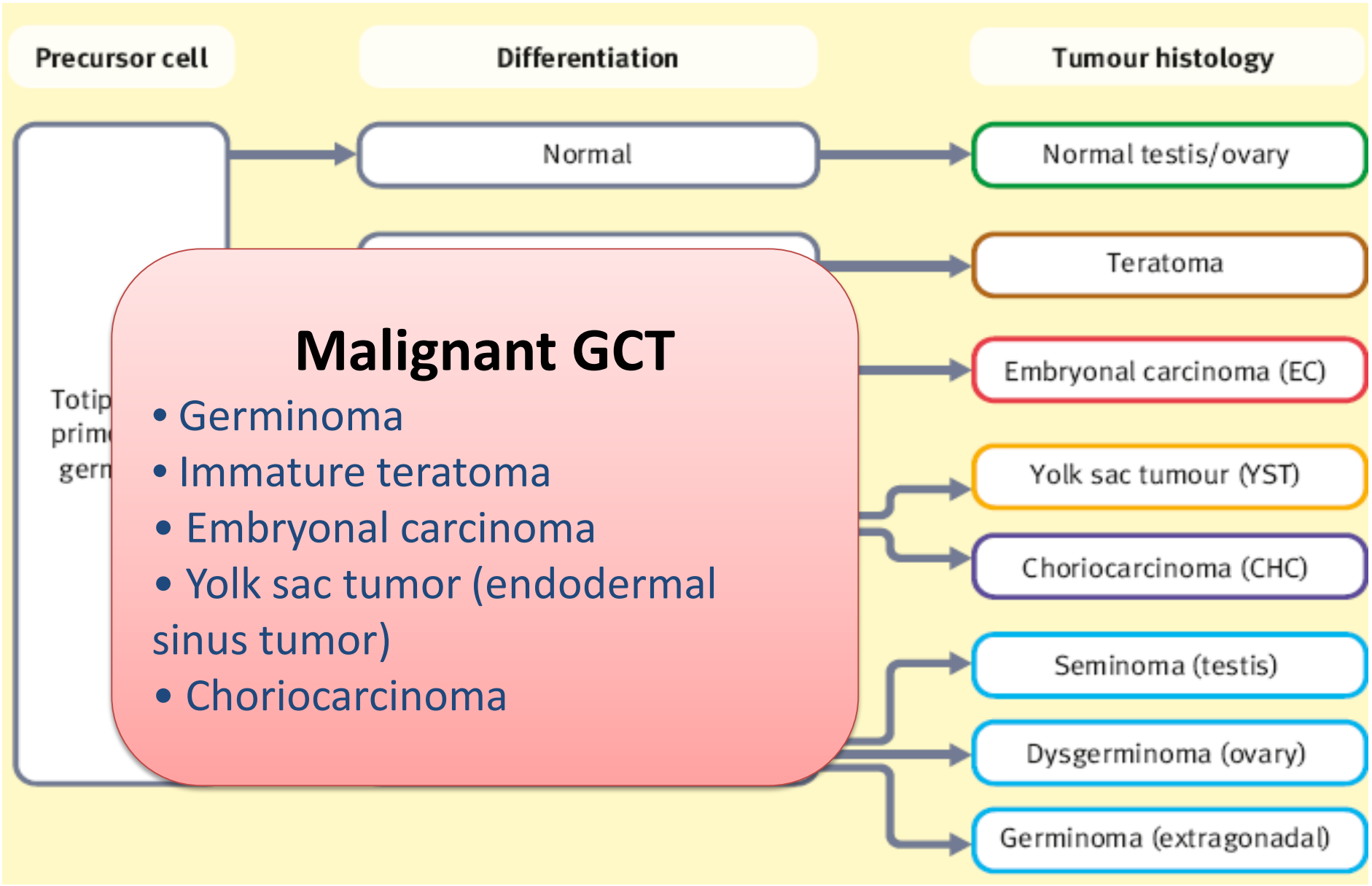
Germ Cell Tumors

Pediatric Germ Cell Tumors

- Heterogeneous in presentation, pathology, prognosis
  - Different biologic behavior by age, site of presentation



National Cancer Institute



Murray & Nicholson, Paediatrics and Child Health, 2010

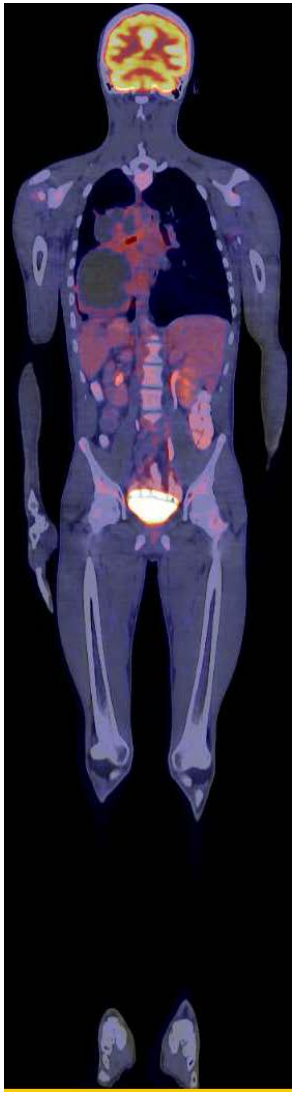
Epidemiology and sites

- 2-3 % of childhood malignancies
- 2.4 cases per million children
- Bimodal age distribution

Gonadal	Extragonadal
Ovarian	Medistinum
Testis	Sacrococcygeal
	Retroperitoneum

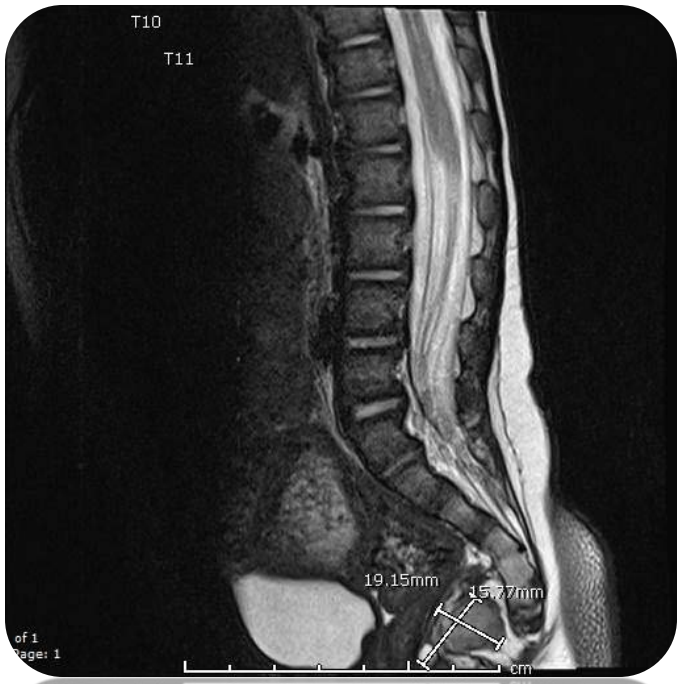
Metastasis

- Lungs
- Liver
- LN
- CNS
- Bone
- BM (less commonly)



Investigations

- CXR/CT/MRI primary site
- U/S (testis)
- Metastatic evaluation:
  - CT chest/Abd/pelvis
  - Bone scan
  - PET scan



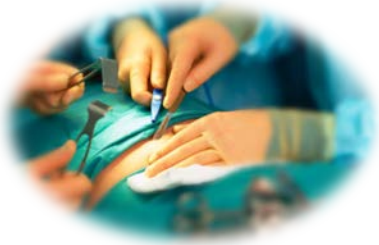
- Tumor markers : AFP (YST), β-hCG (embryonal, CC)
- Peritoneal cytology : 25% positive esp. in ovarian tumor

Tumor markers in GCT

Pathology	Sites	Tumor markers		
		AFP	ß-hCG	PLAP
Germinoma	Ovary: dysgerminoma Testis: Seminoma Ant. mediastinum	-	-	+
Mature teratoma	Sacrococcygeal Mediastinum gonad	-	-	-
Immature teratoma		+/-	-	-
Embryonal Carcinoma	Testis (young adult)	+	+++	+/-
Yolk sac tumor (Endodermal sinus tumor)	Testis (infant) Ovary Presacral	+++	-	-
Choriocarcinoma	Ovary Mediastinum Pineal region	-	+	-

Adapted from Nathan and Oski's Hematology and Oncology of Infancy and Childhood 8th ed, 2015

Principle of GCT treatment



PEB

2nd look surgery

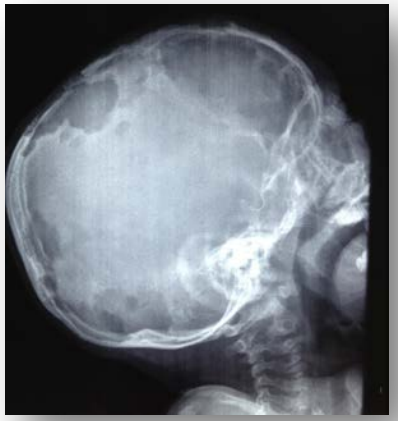
Sx RT Sx+RT

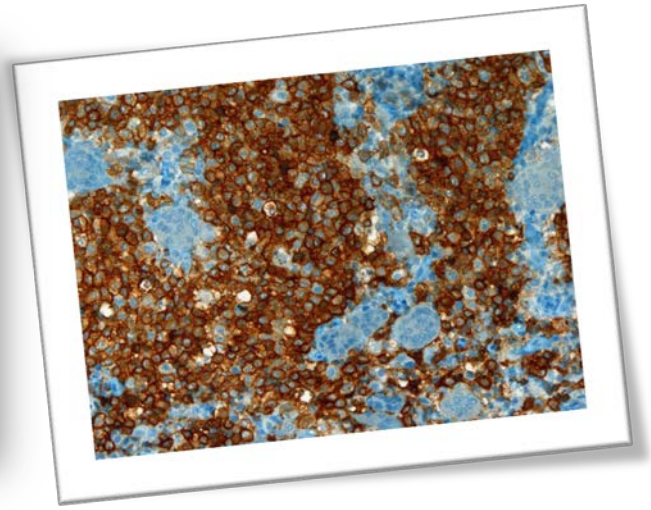
PEB

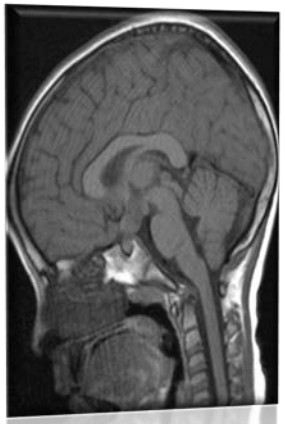
Treatment of Pediatric Germ Cell Tumors

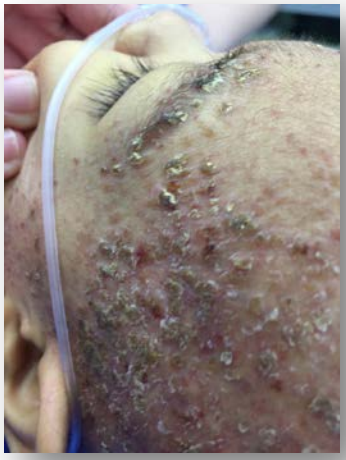
Risk	Stages	Rx	Overall survival
Low	Immature teratoma Stage 1 testis*	Surgery	>95%
Intermediate	Stage 2-4 testis Stage 1-4 ovary Stage 1-2 extragonadal	Surgery + CMT	>90%
High	Stage 3-4 extragonadal		70-75%

* Stage I testicular: EFS 70-80%, OS >95%









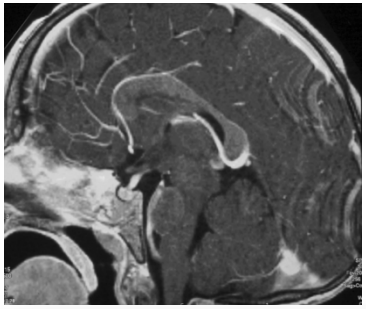
Langerhans Cell Histiocytosis

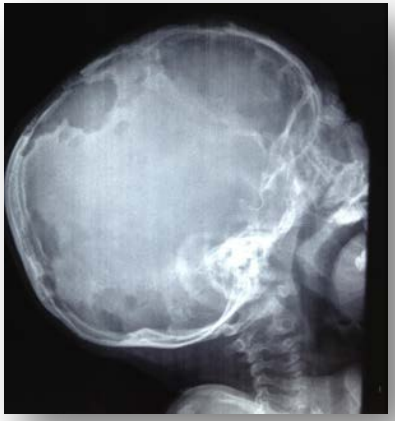
Classification of histiocytosis syndrome in children

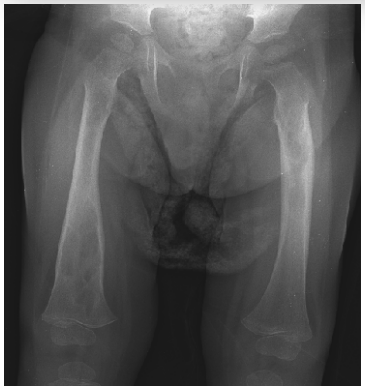
Class	Syndrome
I Dendritic/histiocytic disorder	• Langerhans cell histiocytosis (LCH) • Non-LCH o Erdheim-Chester Disease – primary in adult o Juvenile xanthogranuloma (JXG) – occur in children and adult
II Macrophage/monocytoid disorder	• Rosai-Dorfman Disease • Hemophagocytic lymphohistiocytosis (HLH) o Primary HLH – genetic disorder o Secondary HLH- infectious associated hemophagocytic syndrome (IAHS)
III Malignant disorder	• Malignant histiocytosis (histiocytic sarcoma) • Monocytic/myelomonocytic leukemias

Adapted from http://www.cancer.gov/cancertopics/pdq/treatment/lchistio/HealthProfessional

Organ system involvement in LCH



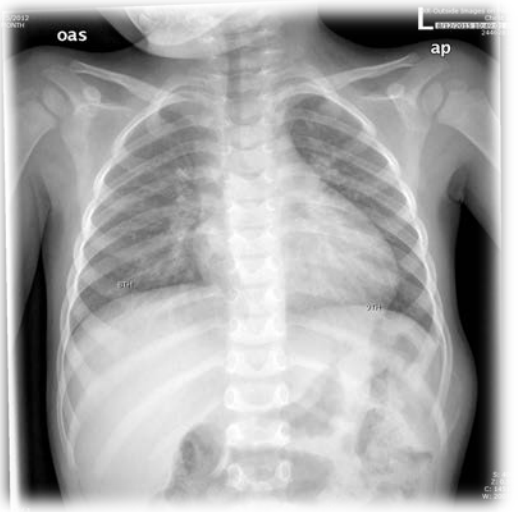


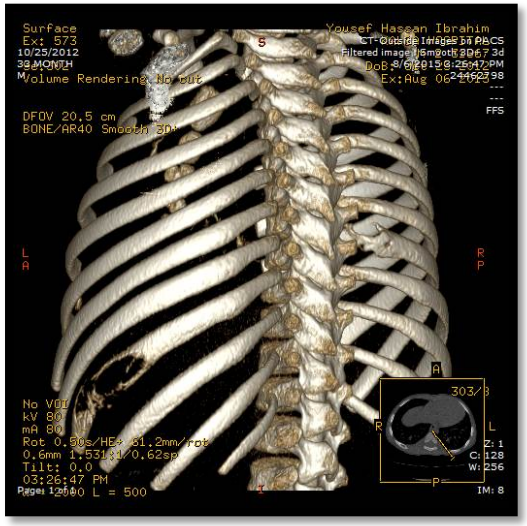


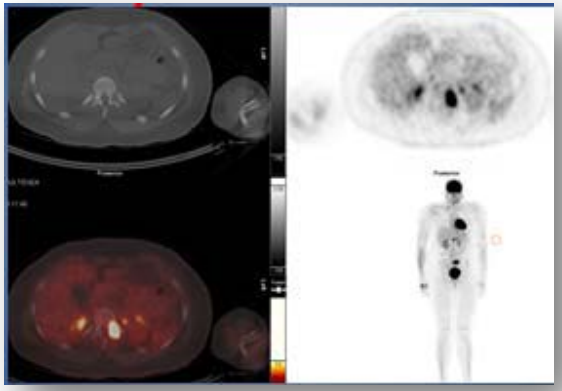
Brain	Neuroendocrine deficits Neurodegeneration
Skull and craniofacial bones	
Chest	Lung disease (infants, smokers) Thymus
Abdomen	Liver Spleen GI tract
Skeleton	Bones
Skin	Cradle cap, seborrhea
Hematopoietic system	pancytopenia, hypersplenism
Lymph nodes	

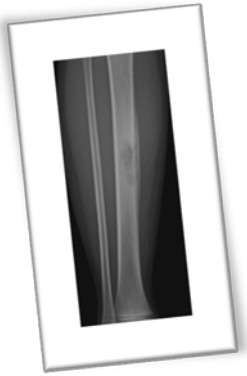
Investigations

- Plain film skull
- Plain x-ray of primary lesion
- Bone survey
- CT/MRI primary lesion
- Abdominal ultrasound
- MRI pituitary
- PET scan : almost always positive in LCH
- CBC, blood chem



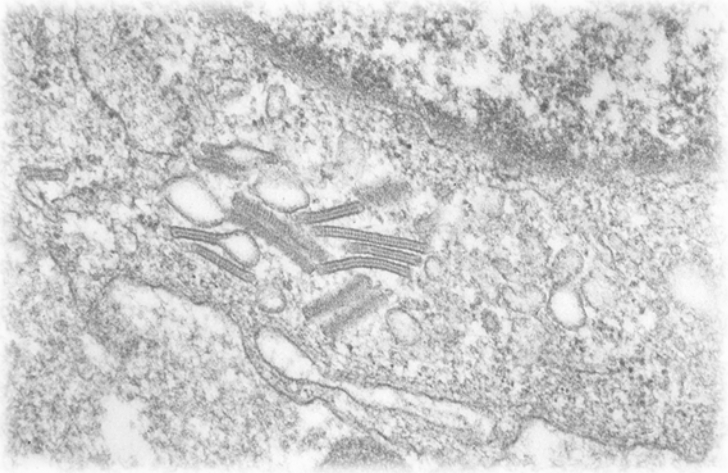


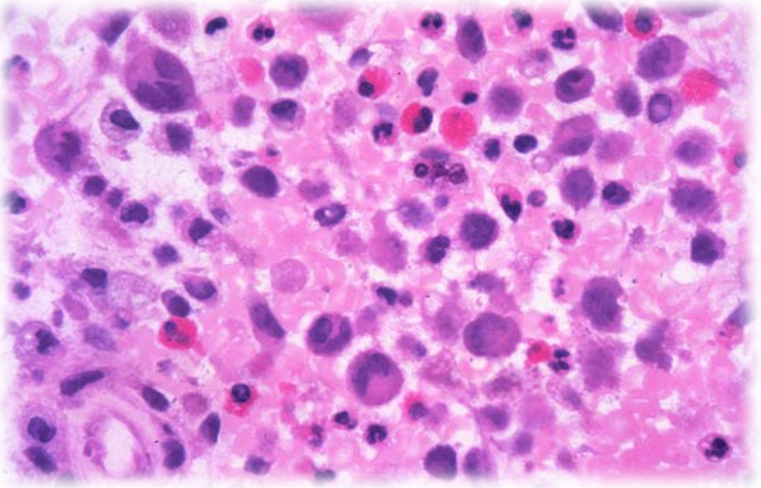




Diagnostic Histopathology

- Uniform regardless of clinical severity:
  - Diagnosis:
    - CD1a, Langerin (CD 207), S-100
    - EM: Birbeck granules





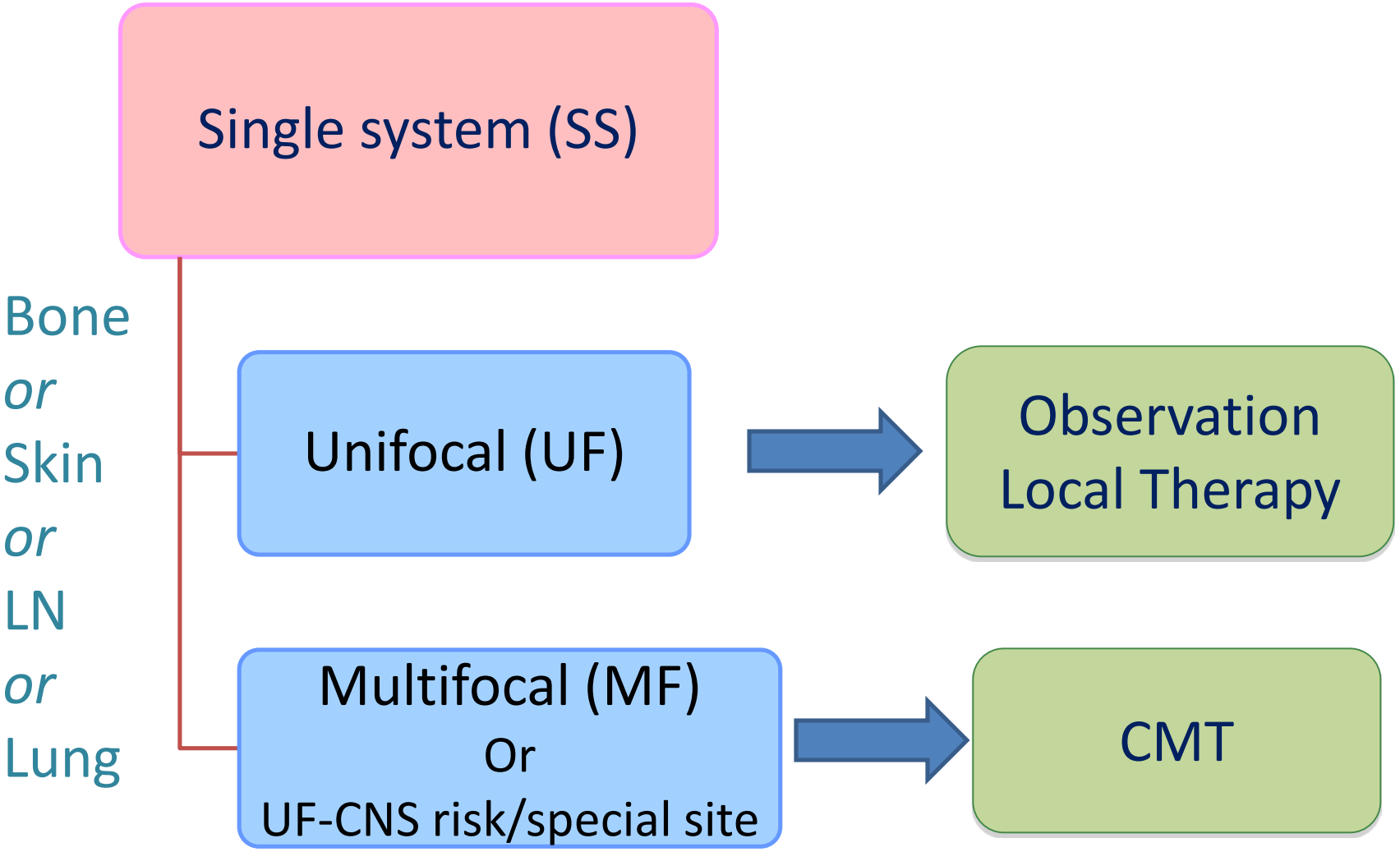
Clinical Classification of LCH patients

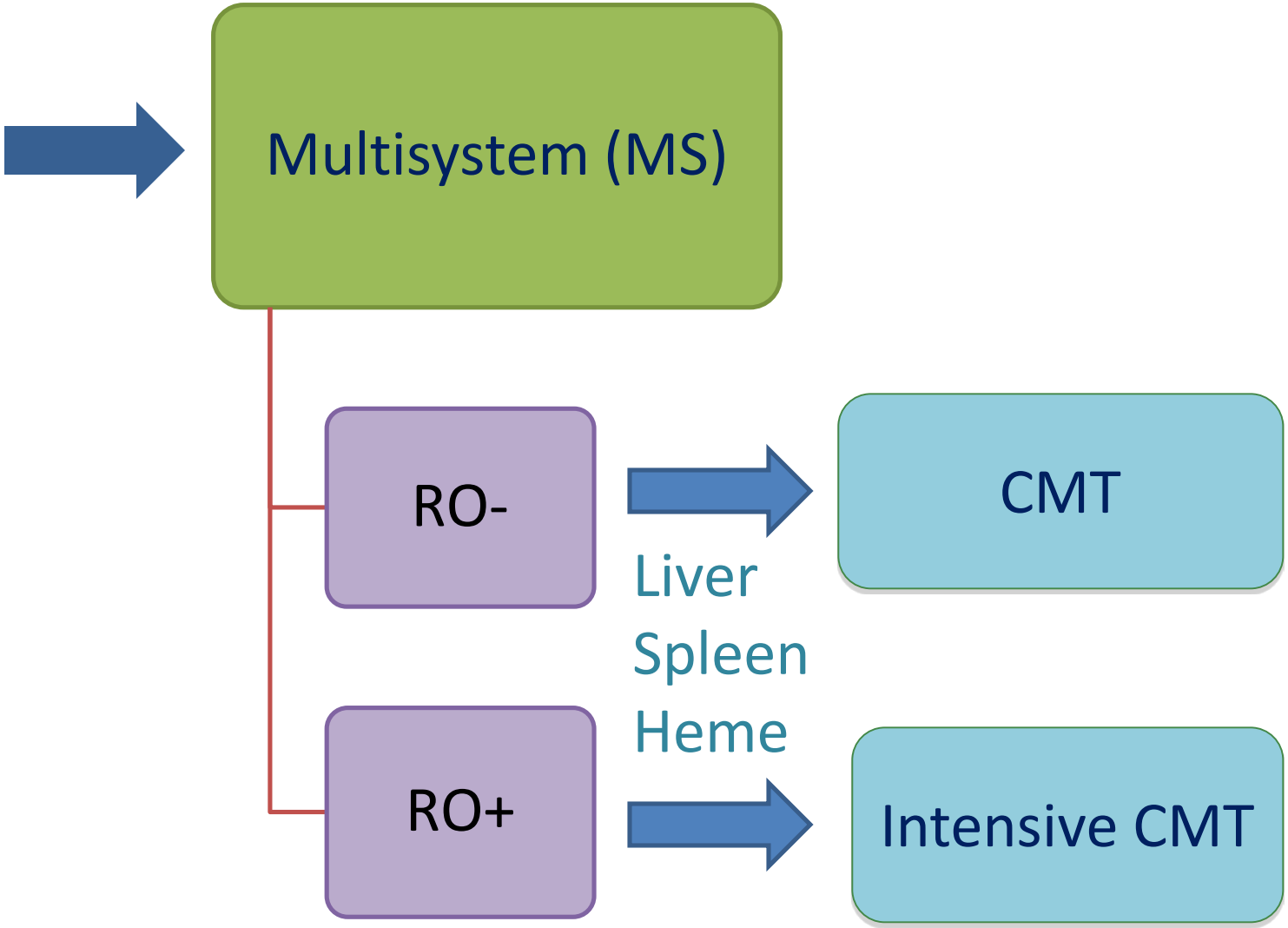
- LCH-IV

Clinical Classification	Involved System	Involved Organs
Multisystem LCH (MS-LCH) (Group 1)	≥ 2	RO+/- (e.g. hemato, liver, and/or spleen)
Single System LCH (SS-LCH) (Group 2)	1 (UF/MF)	• Bone UF (single bone) or MF (>1 bone) • Skin • LN (excluding draining LN of another LCH lesion) • Lungs • Special site (eg. Vertebrae, spine) • "CNS-risk" • Central nervous system (CNS) • Other (e.g. thyroid, thymus)

HISTIOCYTE SOCIETY

Treatment


Single system (SS)
Bone
or
Skin
or
LN
or
Lung
Unifocal (UF)
Observation
Local Therapy
Multifocal (MF)
Or
UF-CNS risk/special site
CMT


Multisystem (MS)
RO-
RO+
Liver
Spleen
Heme
CMT
Intensive CMT

Indications for Systemic Therapy

- SS-LCH with
  - CSN-risk lesions
  - Multifocal bone lesions
  - “Special Site” lesions
- MS-LCH with/without involvement of risk organs

for

children with cancer

www.pedhemeoncpmk.com