

*Clinical Practice in Pediatrics
6-8 September 2017*

MASSSES FROM HEAD TO TOE

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**CHILDREN'S
ONCOLOGY
GROUP**





คำแนะนำ

กรณีมือถือ / แท็บเล็ต

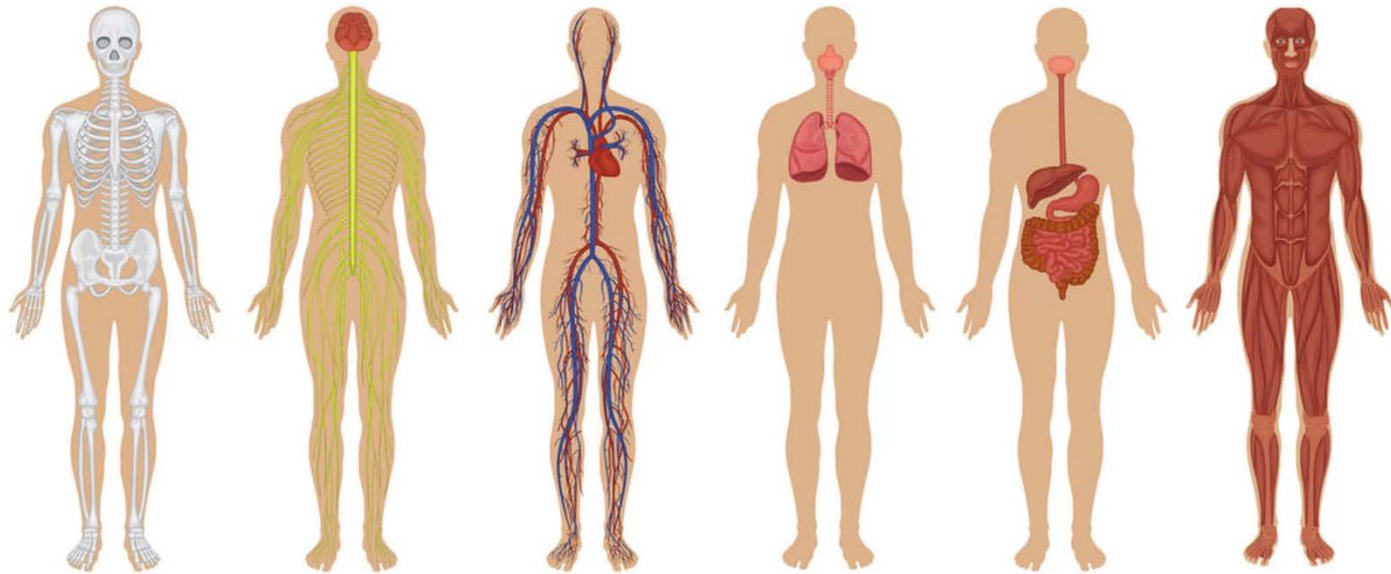
1. เปิดโปรแกรมอ่าน QR code จาก LINE หรือโปรแกรม QR code scanner (ดาวน์โหลดจาก Play store)
2. สแกน QR code จากนั้น เครื่องจะเปิดเอกสารโดยอัตโนมัติ
3. บันทึกเอกสารไว้ในเครื่อง โดยการคลิกปุ่มลูกศร ↓

กรณี notebook / PC

1. เปิด browser เช่น Chrome, internet explorer, Firefox ฯลฯ
2. พิมพ์ URL address ในช่องด้านบนสุด แล้วกดปุ่ม ENTER จากนั้น เครื่องจะเปิดเอกสารโดยอัตโนมัติ
3. บันทึกเอกสารไว้ในเครื่อง โดยการคลิกที่ปุ่มลูกศร ↓

MASS

Benign vs. Malignant



Benign masses

- Slow growing
- Firm or rubbery
- Painful
- Regular borders
- Solid or cystic consistency
- Mobile
- No infiltration
- No metastasis
- Capsulated

Malignant masses

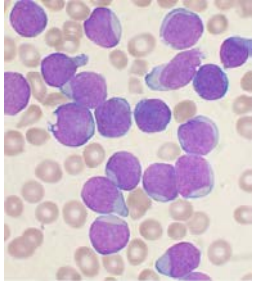
- Rapid growing
- Hard
- Painless'
- Irregular borders
- Solid consistency
- Fixed to skin/soft tissue
- Infiltrative
- Metastasis
- Non-capsulated

Differential Diagnosis

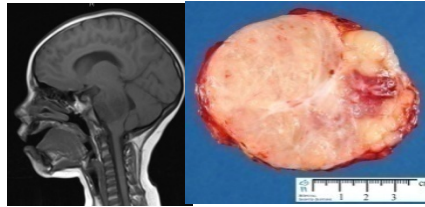
- Age
- Location
- Pattern of growth
- Constitutional symptoms
- Associated symptoms: pain, anemia etc.

Pediatric Malignancies

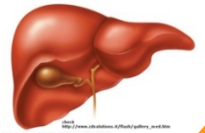
Leukemia



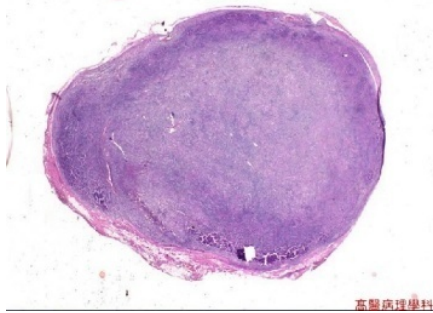
CNS tumors



Liver tumors



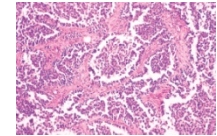
Lymphoma



Sarcomas

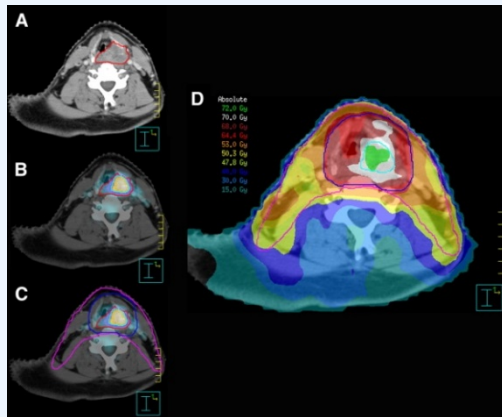


Embryonal tumors



Principle of Treatment in Pediatric ST

Local Control



Systemic Control





2 year old girl in
usual state of good
health until...

3 weeks before

- Vomiting, drowsiness
- Difficulty walking

A young child is seated in a stroller, wearing a light blue hat and a white face mask. The child is dressed in a purple top and a patterned skirt. The stroller has a pink and purple canopy. The background is blurred, suggesting an indoor setting.

What is the most appropriate investigation?

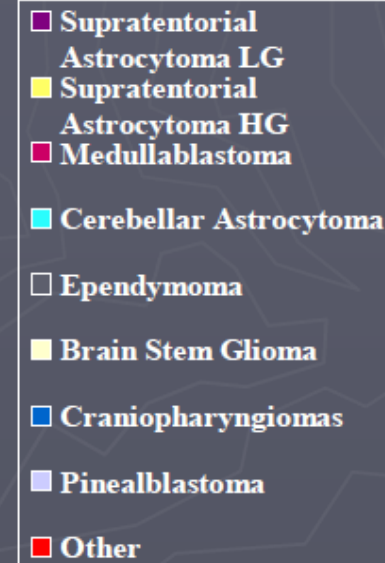
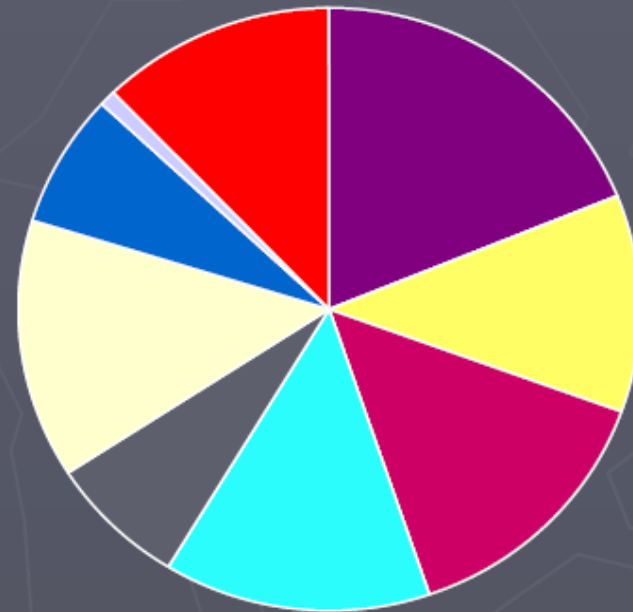
- A. MRI brain
- B. CT brain without contrast
- C. CT brain with contrast
- D. LP and CSF profile



.....

Brain Tumors

- ▶ Most common solid tumor
- ▶ Astrocytomas - most common family of brain tumors
 - Low grade astrocytomas, brainstem glioma, anaplastic astrocytoma and glioblastoma multiforme



Strother, D. R., Pollack, I. F., Fisher, P. G., Hunter, J. V., Woo, S. Y., Pomeroy, S. L., & Rorke, L. B. (2002). Tumors of the Central Nervous System. In P. A. Pizzo & D. G. Poplack (Eds.), *Principles and practice of pediatric oncology 4th Ed.* (pp. 752). Philadelphia: Lippincott Williams & Wilkins.

Hemispheric

Gliomas: 37%

Low-grade astrocytomas: 23%

High-grade astrocytomas: 11%

Other: 3%

Supratentorial

Midline:

1. Chiasmal gliomas: 4%

2. Craniopharyngiomas: 8%

3. Pineal region tumors: 2%

Midline

Posterior fossa:

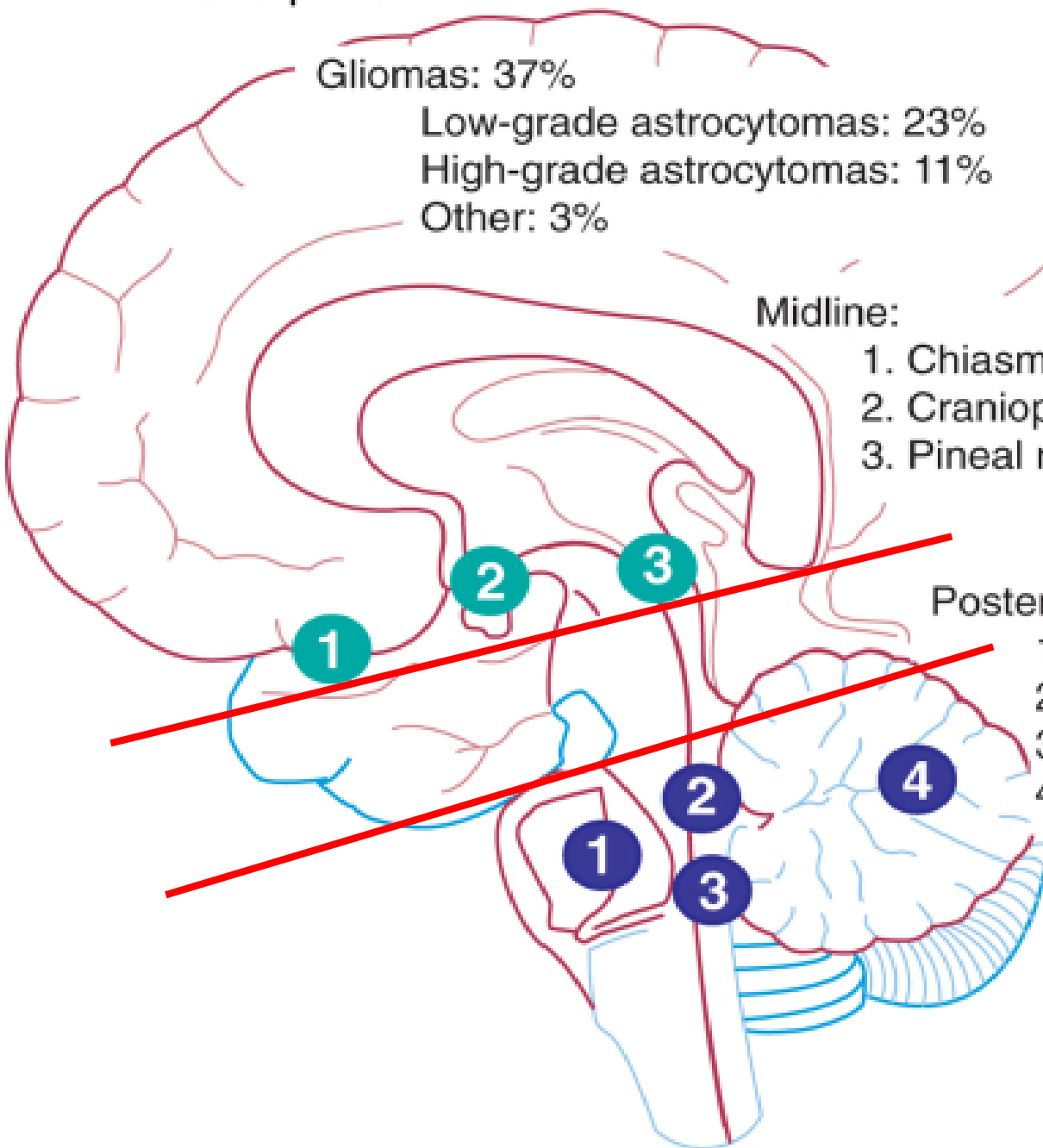
1. Brainstem gliomas: 15%

2. Medulloblastomas: 15%

3. Ependymomas: 4%

4. Cerebellar astrocytomas: 15%

Infratentorial



Presentation

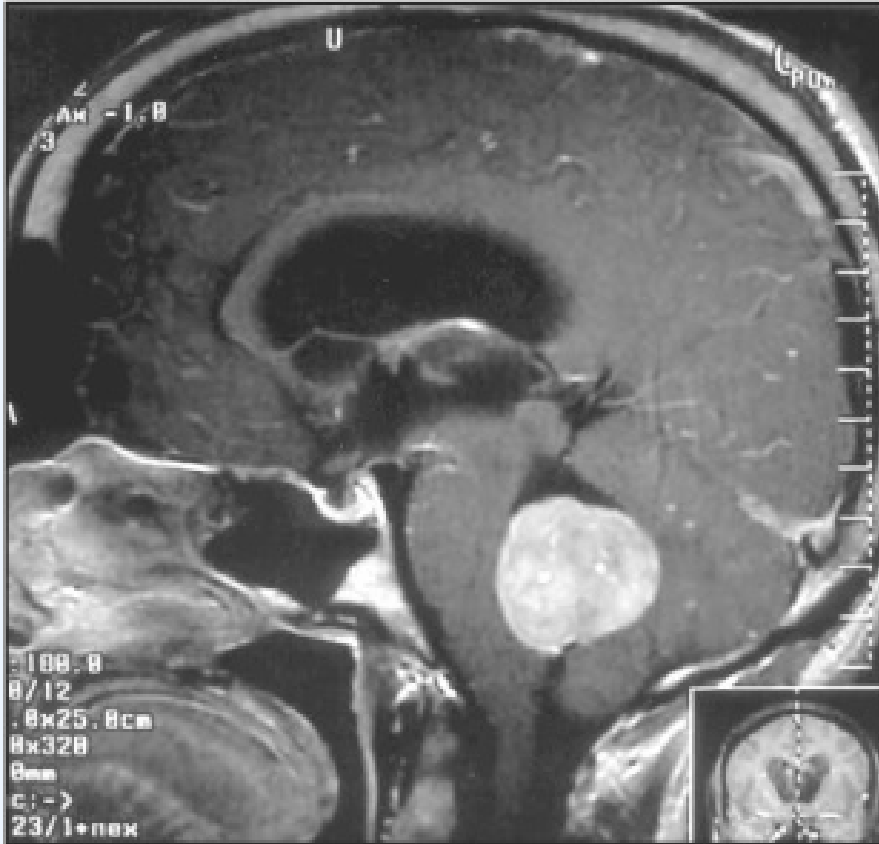
- Related to
 - Location
 - Size
 - Growth rate of tumor
- MCM is increased intra cranial pressure (47%)

Medulloblastoma

- Posterior fossa/cerebellar tumor
- Infratentorial
- Bimodal age : 3-4 yo and 6-9 yo
- 14-43% CNS seeding
- <4% distant metastasis outside CNS
- Genetic association
 - Li Fraumei syndrome (TP 53 mutation)
 - Turcot syndrome (APC mutation, 5q21-22) : associated with CA colon
 - Ataxia telangiectasia (ATM mutation)

Medulloblastoma

Clinical presentations



- Obstructive hydrocephalus
- Cerebellar dysfunction
- Infant :
 - Macrocephaly
 - Splitting suture
 - Bulging AF

Medulloblastoma

Treatment



- Obstructive hydrocephalus
- Cerebellar dysfunction
- Infant :
 - Macrocephaly
 - Splitting suture
 - Bulging AF

- Surgery
- RT :
 - Average risk : CSI 24 Gy
 - High risk : CSI 36 Gy } + whole PF boost 54-56 Gy
- Plus concurrent VCR weekly
- Chemotherapy
 - Improved survival
 - Decreased extracranial relapse



One-year old boy with history of recurrent otitis media and polyuria.

On examination cradle cap was noticed.





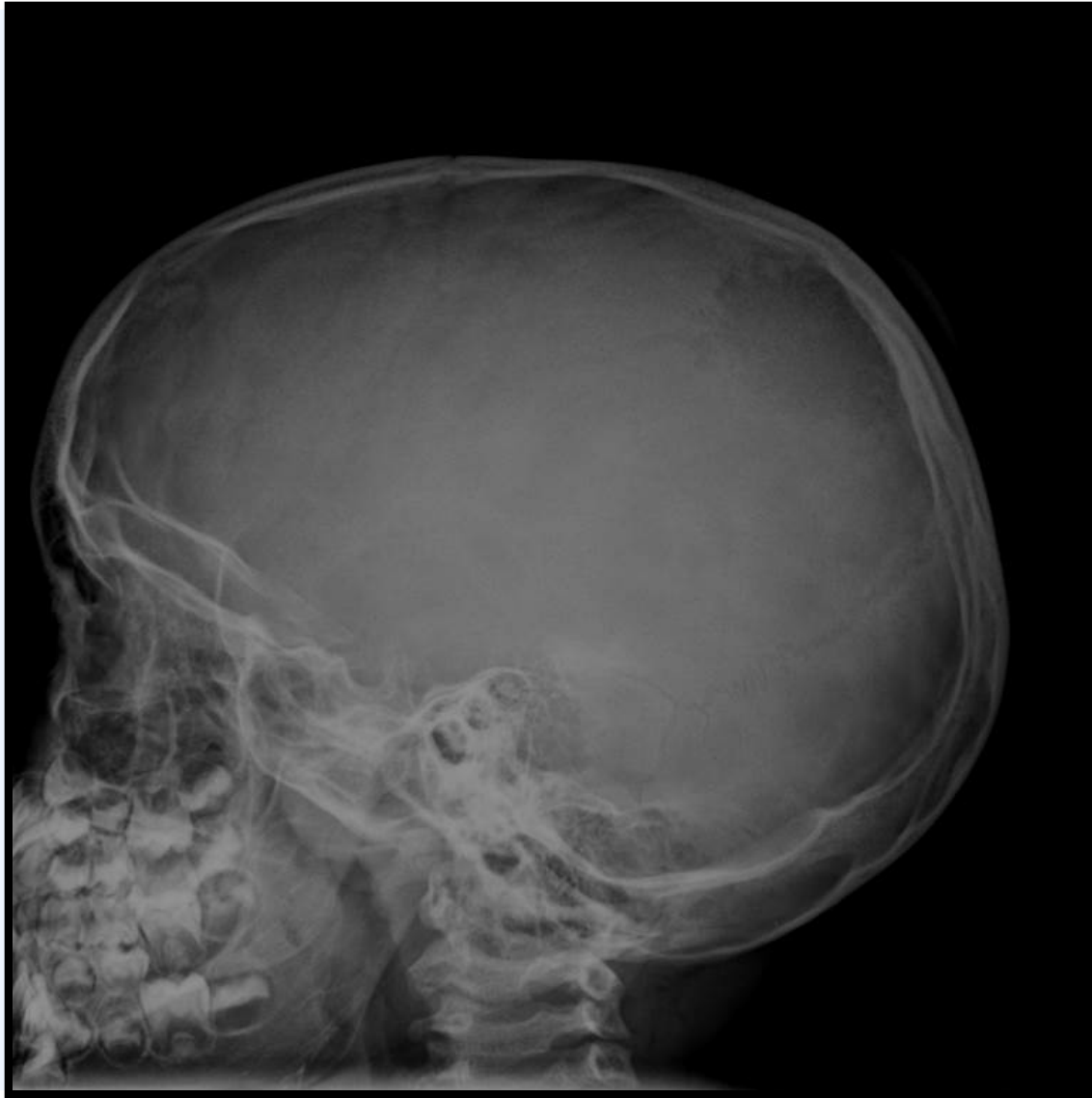
What is the most likely diagnosis?

- A. Acute leukemia
- B. Burkitt lymphoma
- C. Langerhans cell histiocytosis
- D. Neuroblastoma



What is the most appropriate further investigation?

- A. CBC with platelet count
- B. CT brain with contrast
- C. Blood chemistry
- D. Plain film skull



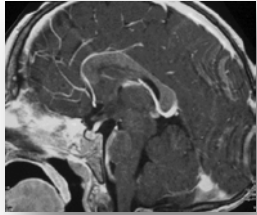
Classification of histiocytosis syndrome in children

Class	Syndrome
I Dendritic/histiocytic disorder	<ul style="list-style-type: none"> • Langerhans cell histiocytosis (LCH) • Non-LCH <ul style="list-style-type: none"> ○ Erdheim-Chester Disease – primary in adult ○ Juvenile xanthogranuloma (JXG) – occur in children and adult
II Macrophage/monocytoid disorder	<ul style="list-style-type: none"> • Rosai-Dorfman Disease • Hemophagocytic lymphohistiocytosis (HLH) <ul style="list-style-type: none"> ○ Primary HLH – genetic disorder ○ Secondary HLH- infectious associated hemophagocytic syndrome (IAHS)
III Malignant disorder	<ul style="list-style-type: none"> • Malignant histiocytosis (histiocytic sarcoma) • Monocytic/myelomonocytic leukemias

- Rare
- 8-9 cases per million/year in children
 - Same in adults
- 1/10th the incidence of childhood leukemia
- Male: Female ratio is 1:1
- Median age presentation is 30 months
- Patients may present from birth to the 9th decade

LCH

Organ System Involvement



Brain
Skull and craniofacial bones

- Neuroendocrine deficits
- Neurodegeneration

Chest

- Lung disease (infants, smokers)
- Thymus

Abdomen

- Liver
- Spleen
- GI tract

Skeleton

- Bones

Skin

- Cradle cap, seborrhea

Hematopoietic system
Lymph nodes

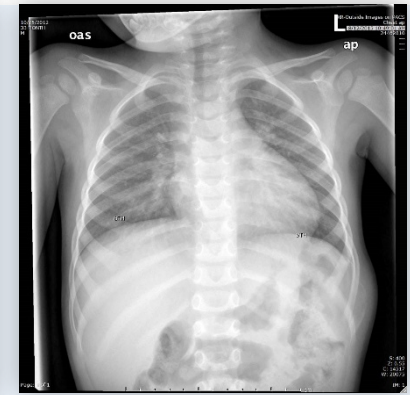
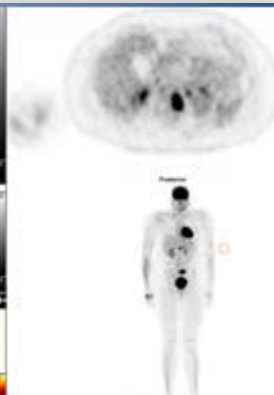
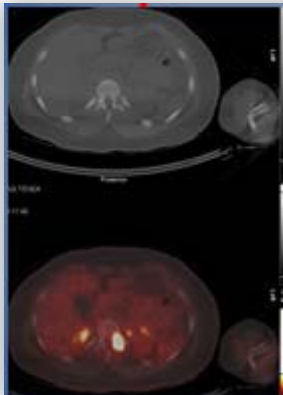
- pancytopenia, hypersplenism



LCH

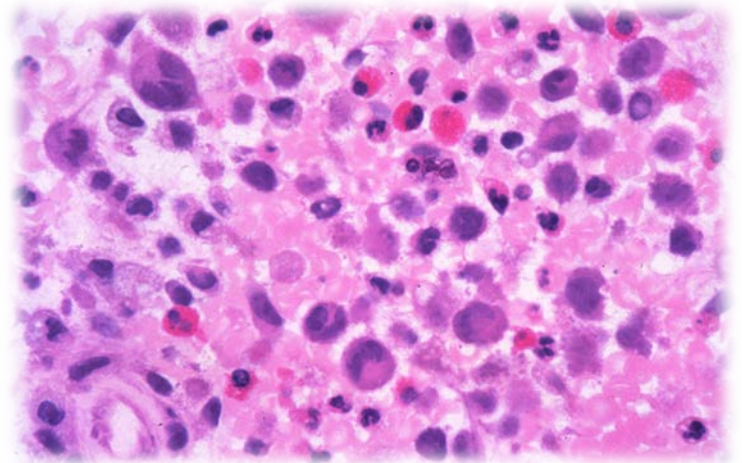
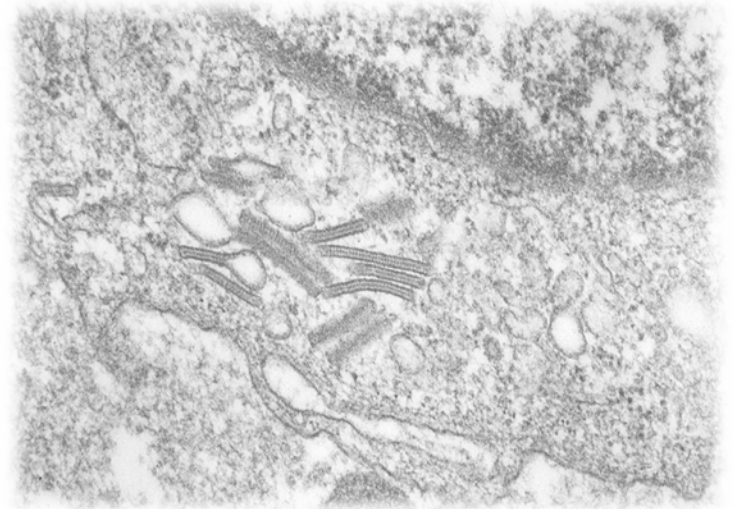
Investigations

- 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



LCH

Clinical Classification

- 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)	<ul style="list-style-type: none">• Bone UF (single bone) or MF (>1 bone)• Skin• LN (excluding draining LN of another LCH lesion)• <u>Lungs</u>• Special site (eg. Vertebrae, spine)• "CNS-risk"• Central nervous system (CNS)• Other (e.g. thyroid, thymus)

10 year-old boy with 1
week history of cough
and fatigue



What is the most likely diagnosis?

- A. Askin's tumor
- B. Rhabdomyosarcoma
- C. Ganglioneuroma
- D. Germ cell tumor
- E. Hodgkin's lymphoma



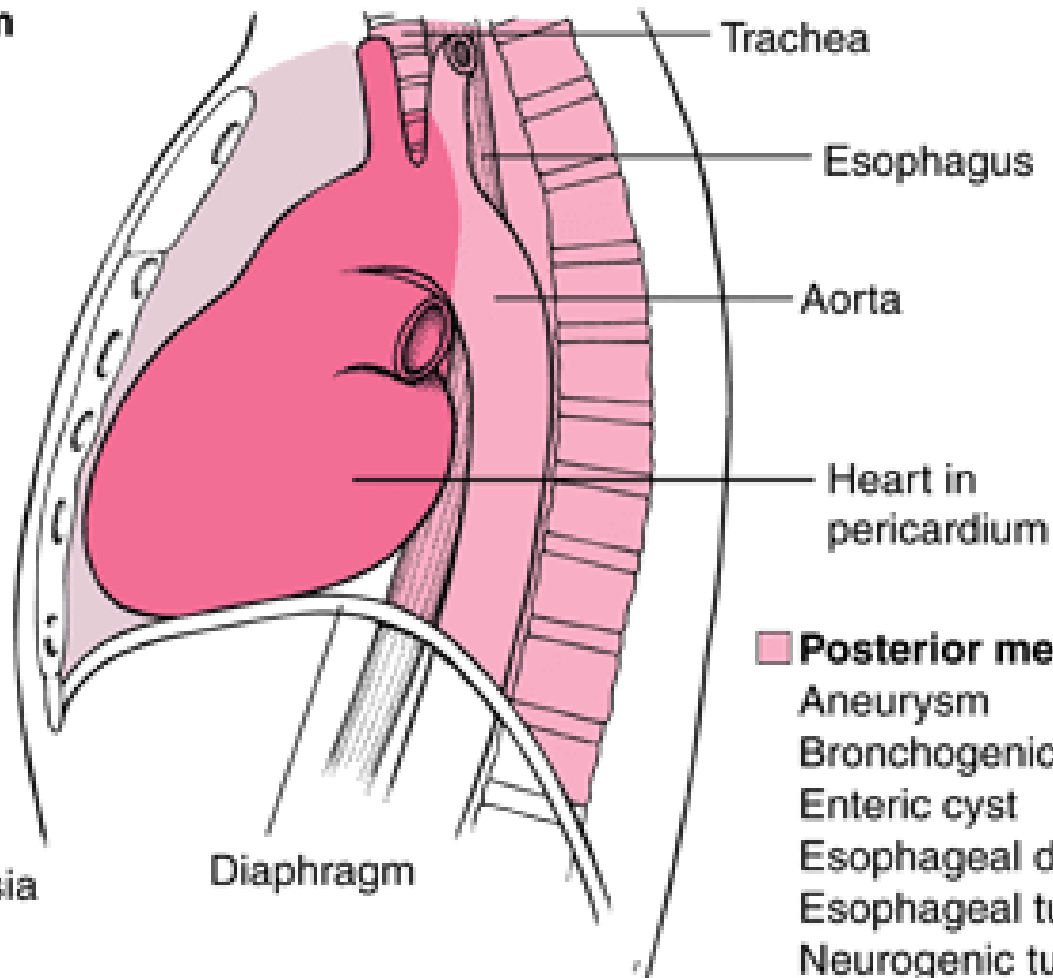
Mediastinal mass

Anterior mediastinum

- Aneurysm
- Angiomatous tumor
- Goiter
- Lipoma
- Lymphoma
- Morgagni hernia
- Parathyroid tumor
- Pericardial cyst
- Teratoma
- Thymoma
- Thyroid tumor

Middle mediastinum

- Bronchogenic cyst
- Bronchogenic tumor
- Lymph node hyperplasia
- Lymphoma
- Pleuropericardial cyst
- Vascular masses



Posterior mediastinum

- Aneurysm
- Bronchogenic tumor
- Enteric cyst
- Esophageal diverticula
- Esophageal tumor
- Neurogenic tumor

Mediastinal mass

DDx

Anterior mediastinal mass

"5T"

T cell lymphoma

T cell acute lymphoblastic
leukemia (T cell ALL)

Teratoma/Germ cell tumor

Thymoma

Thyroid gland

Middle mediastinal mass

Hodgkin's lymphoma

Bronchogenic cyst

Posterior mediastinal mass

"Neural crest cell tumors"

Neuroblastoma

Ganglioneuroma

Ganglioneuroblastoma

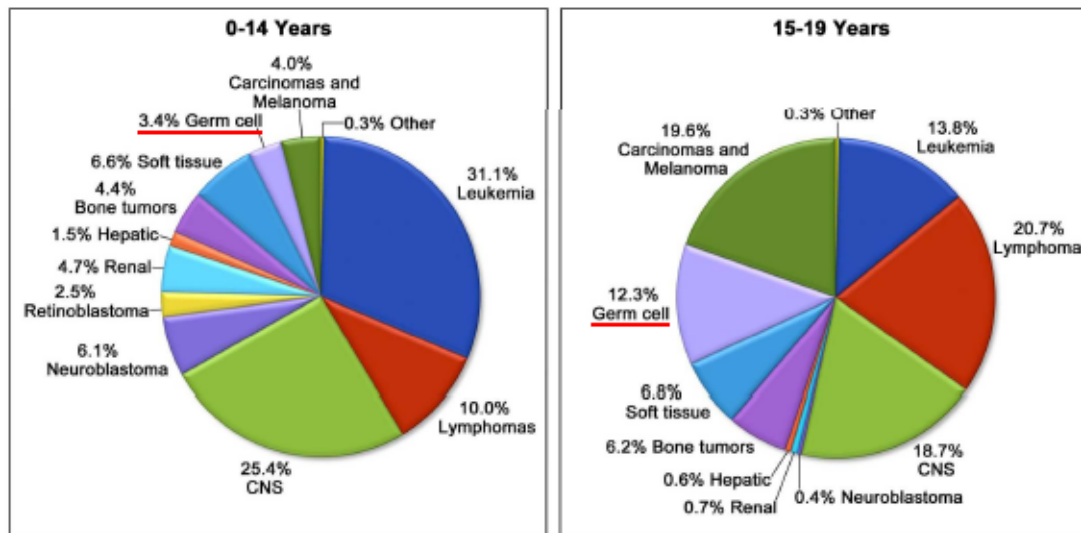
Neurofibroma

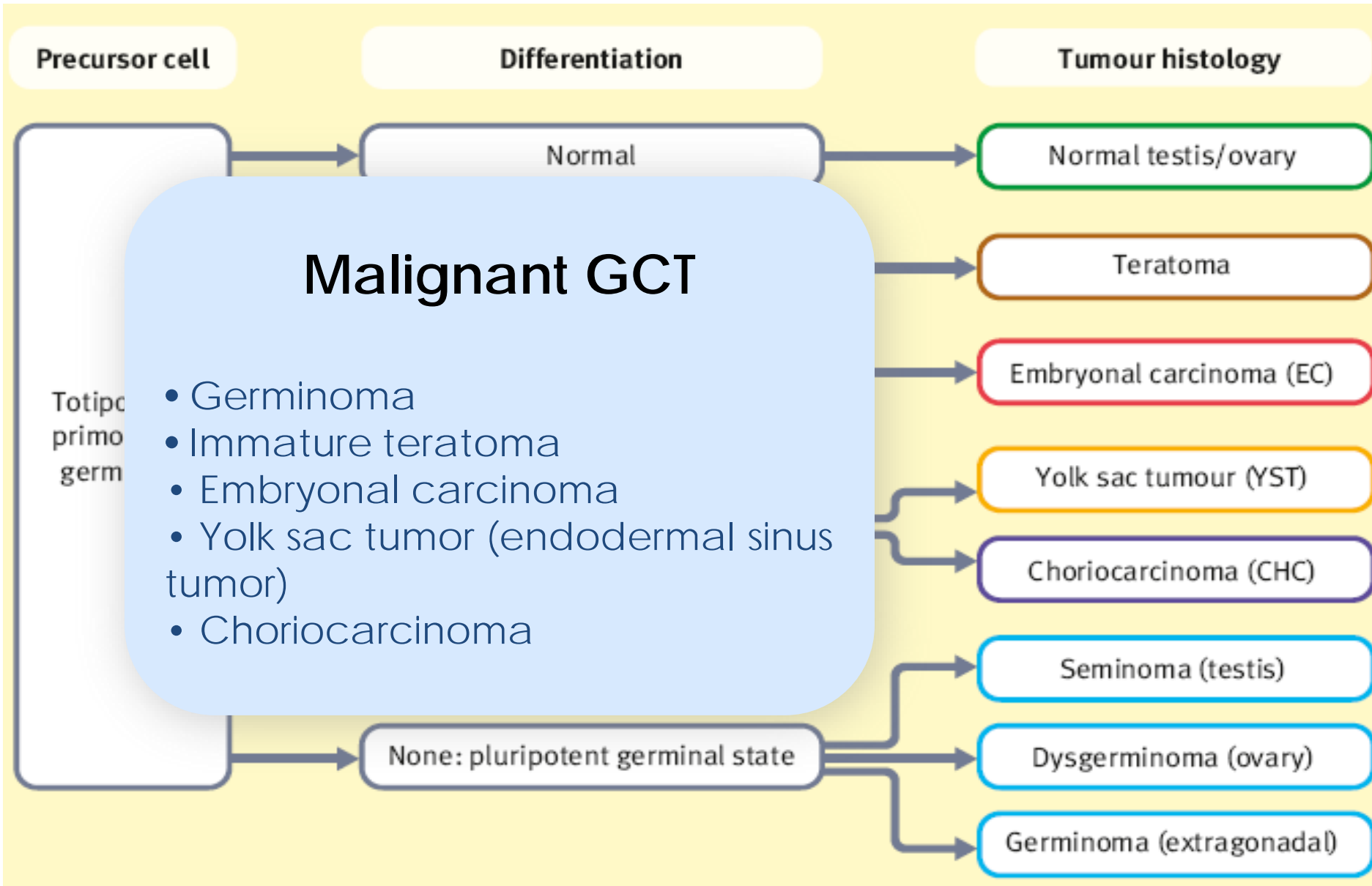
GERM CELL TUMORS



Pediatric Germ Cell Tumors

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





Germ Cell Tumors

Epidemiology and Sites

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

Gonadal	Extragenital
Ovarian	Mediastinum
Testis	Sacroccocygeal
	Retroperitoneum

Metastasis



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

Germ Cell Tumors

Investigations

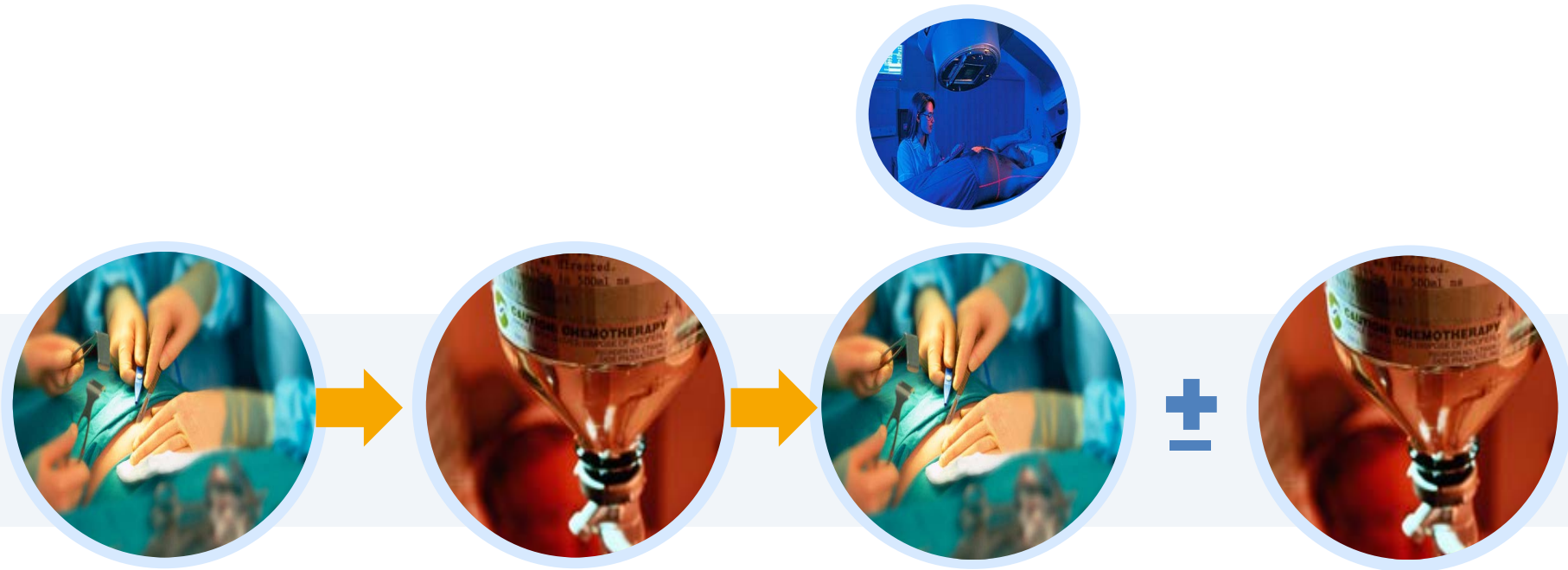
- CXR/CT/MRI primary site
- U/S (testis)
- Metastatic evaluation:
 - CT chest/Abd/pelvis
 - Bone scan
 - PET scan



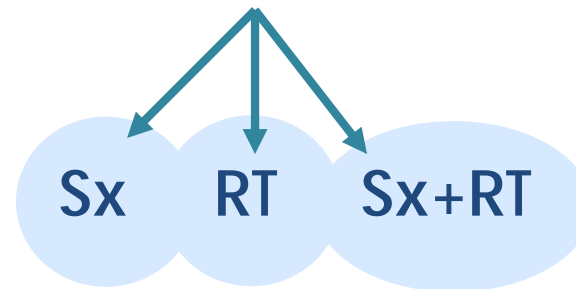
- Tumor markers : AFP (YST), β -hCG (embryonal, CC)
- Peritoneal cytology : 25% positive esp. in ovarian tumor

Germ Cell Tumors

Treatment



2nd Look Surgery





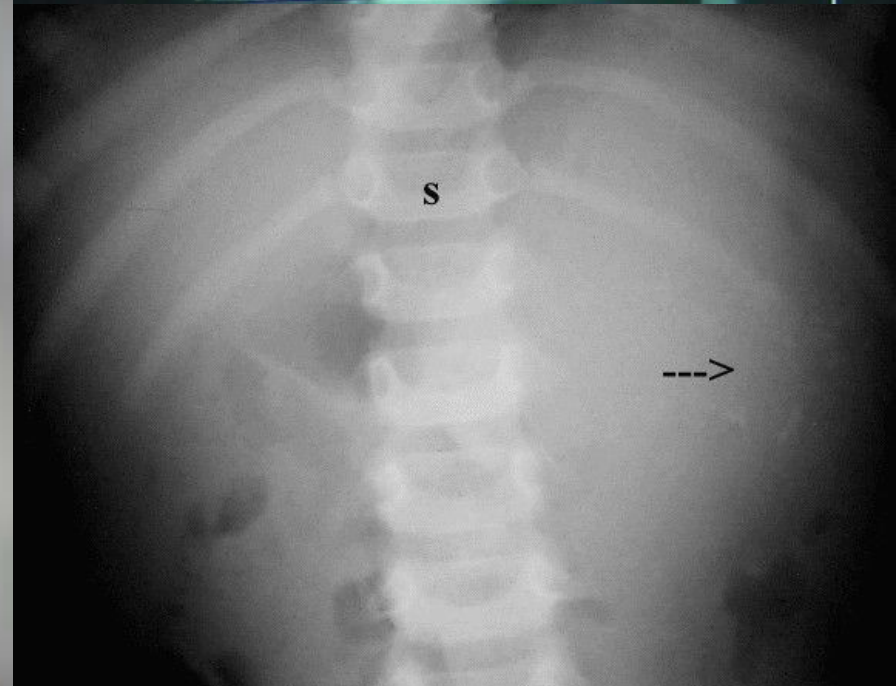
"1 year-old boy with an abdominal mass, pallor, ill-appearing"



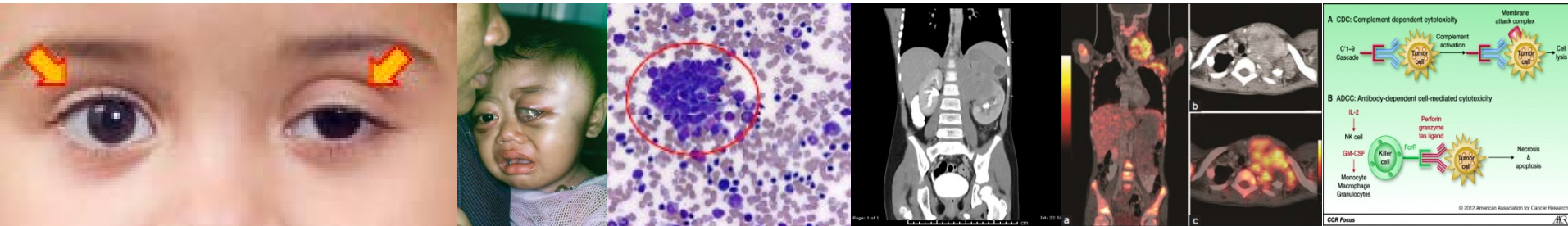
"1 year-old boy with an abdominal mass, pallor, ill-appearing

What is the most likely diagnosis?

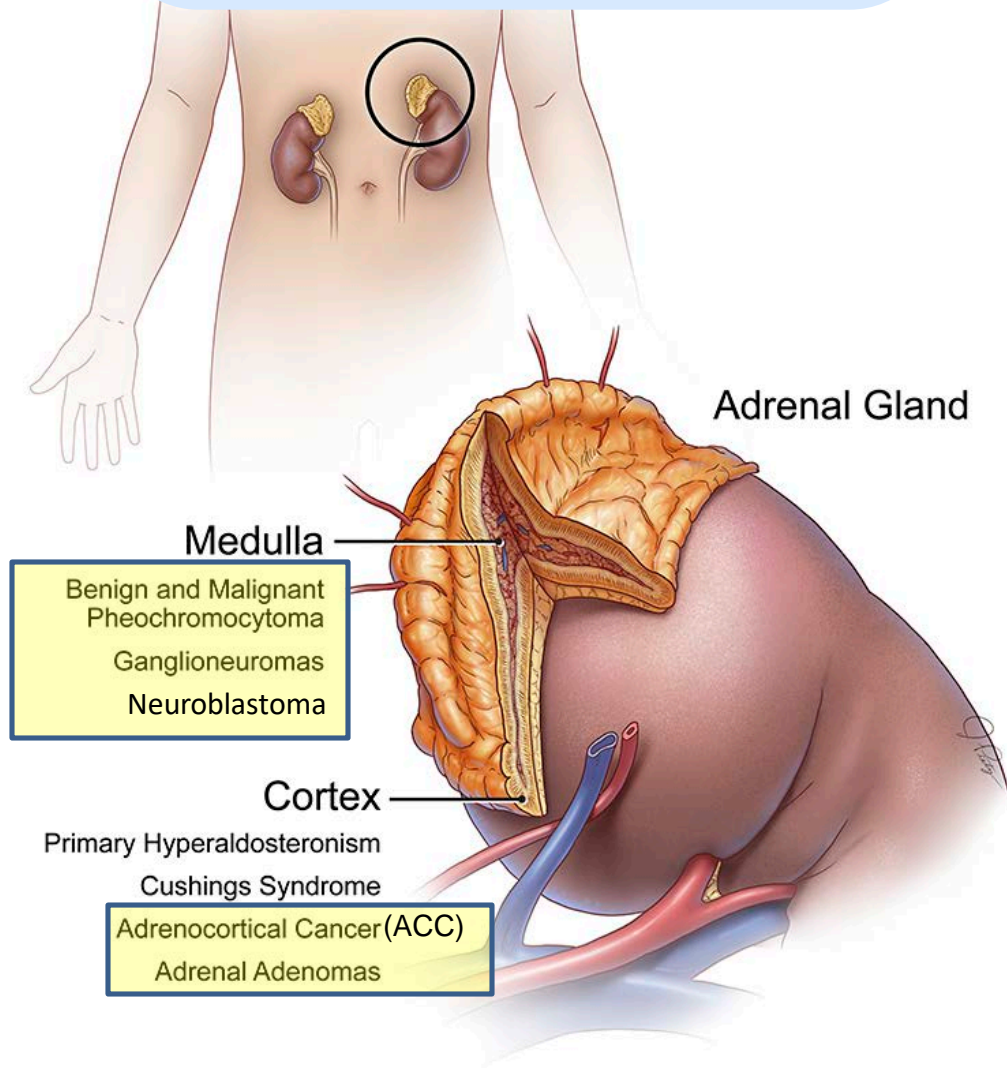
- A. Neuroblastoma
- B. Wilms tumor
- C. Malignant germ cell tumor
- D. hepatoblastoma
- E. Non-Hodgkin's lymphoma



NEUROBLASTOMA



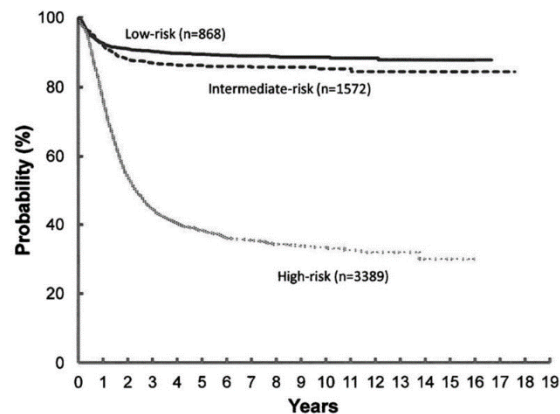
Adrenal Tumors



Neuroblastoma

Epidemiology

- MCM Extracranial malignant solid tumor in children
- Most frequent cancer diagnosis in infants 1/7,000 live births
- 7% of all cancer in children less than 15 yo
- Accounts of 15% of all pediatric cancer deaths
- ~50% present with HR disease



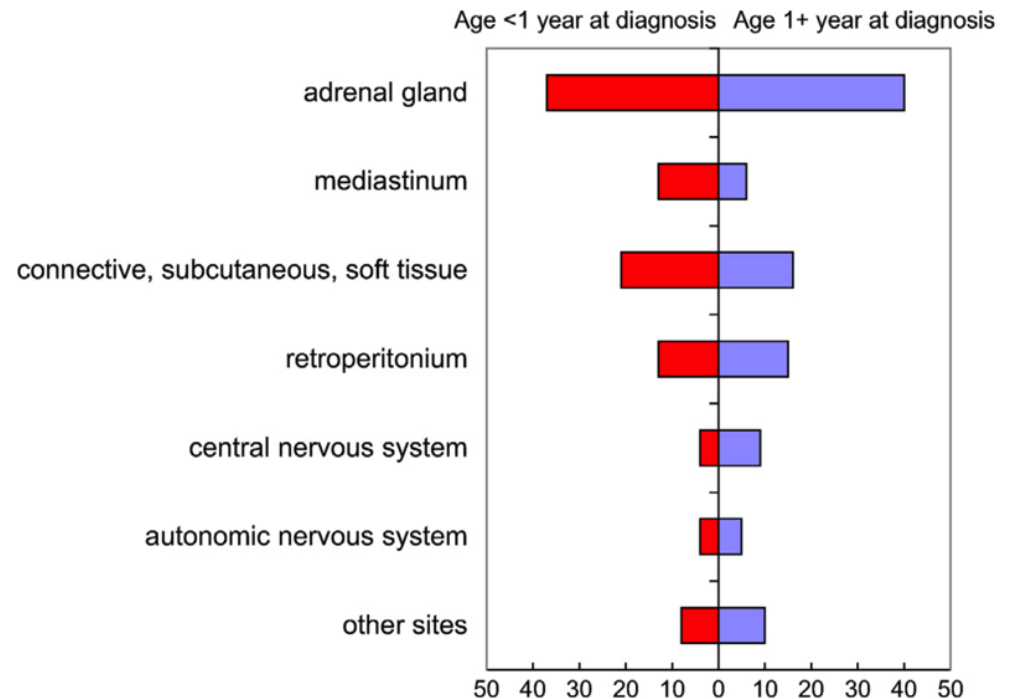
Neuroblastoma

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



Neuroblastoma

Clinical Presentation

- Asymptomatic mass
 - Neck
 - Thorax
 - Abdomen
 - Pelvis
- Horner's Syndrome (cervical mass)
- Spinal Cord Compression (medical emergency)
 - Back pain
 - Neurologic deficits
- "Raccoon eyes"
- Hepatomegaly
- Systemic symptoms
 - Weight loss
 - Irritability
 - Fever
 - Hypertension
 - Intractable diarrhea (VIP)
 - Opsoclonus/myoclonus
- Bone pain
 - Limp
 - Refusal to walk
- Pallor
- Skin lesions

Neuroblastoma

- Irritable child, tender
- Abdominal mass
: cross midline
- Bimanual palpation :
Negative
- Skin : blueberry muffin
- Eyes : raccoon eyes
- Urinary metabolites
- X-rays :
stippled calcifications
- IVP : Drooping-lily



Wilm's Tumor

- Asymptomatic
- Abdominal mass
: no cross midline
- Bimanual palpation :
Positive
- Hemihypertrophy, aniridia
- Ambiguous genitalia
mental retardation
- HT , hematuria
- GU anomalies, Beckwith-
Wiedemann syndrome
- CT/IVP : Claw

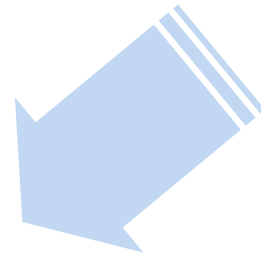
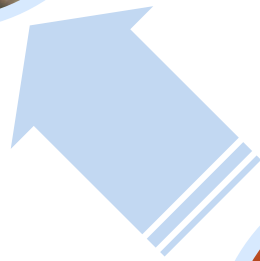
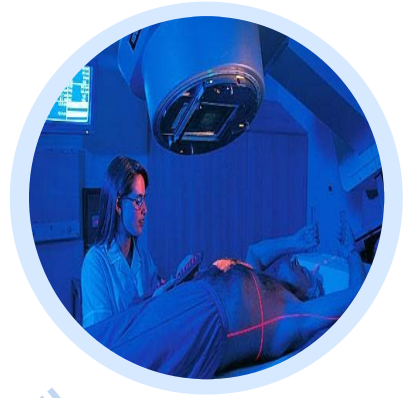
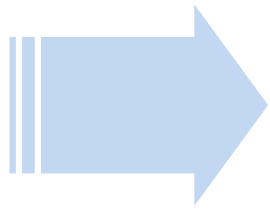
- **Urine catecholamine (VMA, HVA)**
*increased up to 78% and 83%, respectively**
- Serum NSE (non-specific)
- Imaging : plain films, U/S, CT, MRI
- Nuclear medicine
 - Bone scans
 - **MIBG scans** *positive up to 90% of cases*
 - PET scans
- Bilateral BMA, BM biopsy
- Tissue biopsy

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

With clinical support

Neuroblastoma

Treatment





"2 Years-old boy with an asymptomatic abdominal mass and hypertension"



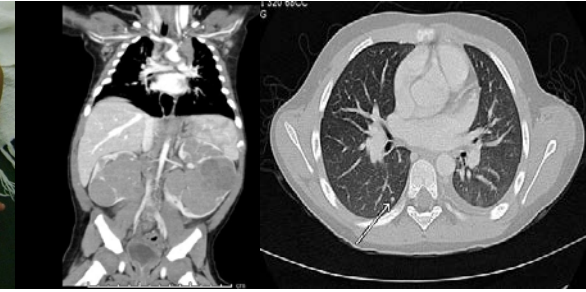
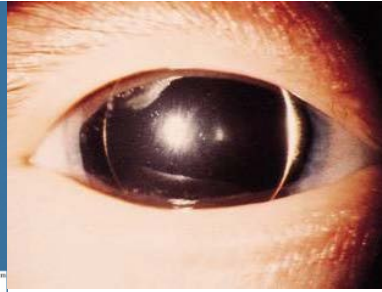
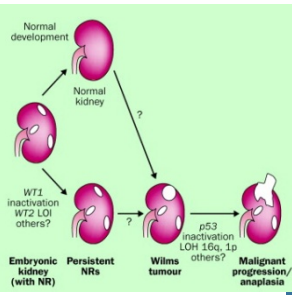


What is the most likely diagnosis?

- A. Neuroblastoma**
- B. Wilms' tumor**
- C. Malignant germ cell tumor**
- D. hepatoblastoma**
- E. Non-Hodgkin's lymphoma**

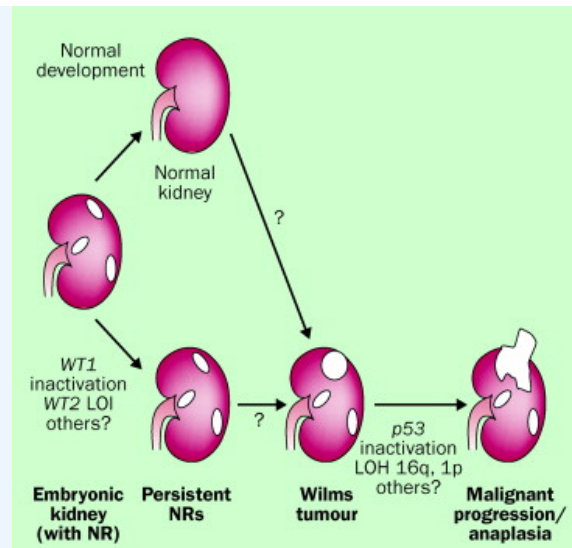


WILMS' TUMOR



Wilms' tumor

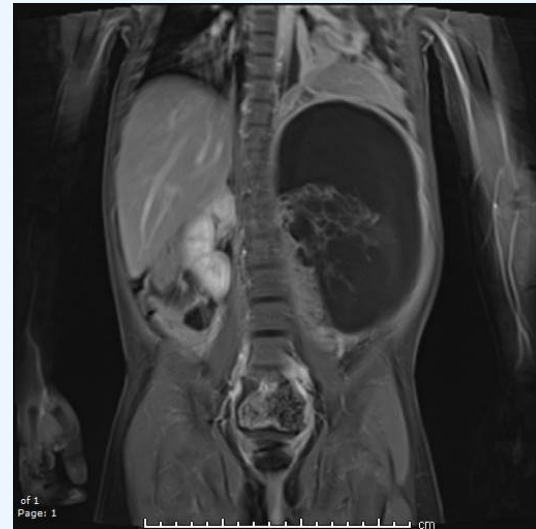
- MCM renal malignancy
- Peak age 3-4 years
- Embryonal neoplasm arising in kidneys



Wilms' tumor

Signs & Symptoms

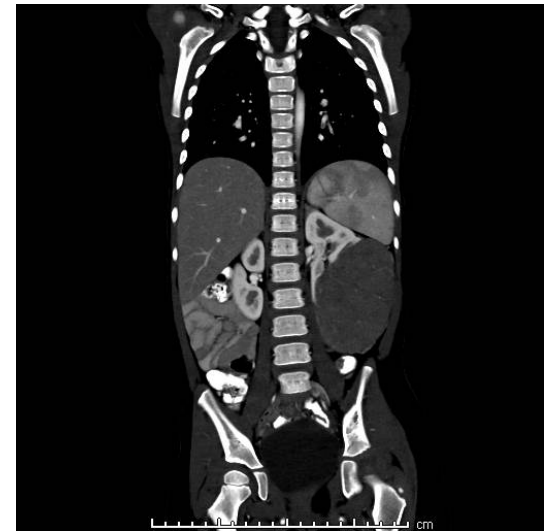
- A symptomless abdominal mass 60%
- Hematuria 30%
- HT 25%
- Polycythemia
- Acquired vWD <10%



Wilms' tumor

Investigations

- U/A
- BUN/Cr
- Coagulogram and bleeding time : acquired vWD
- U/S, CT scan
- CXR, CT chest

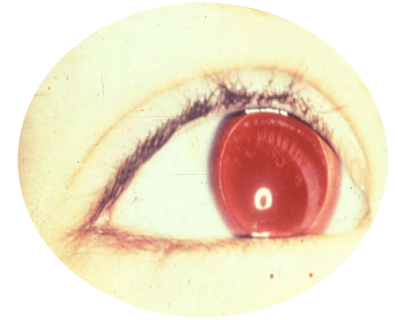


- BMA: Not necessary unless + evidence of BM invasion

Wilms' tumor

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)



Wilms' tumor

Principle of the treatment

CHILDREN'S
ONCOLOGY
GROUP

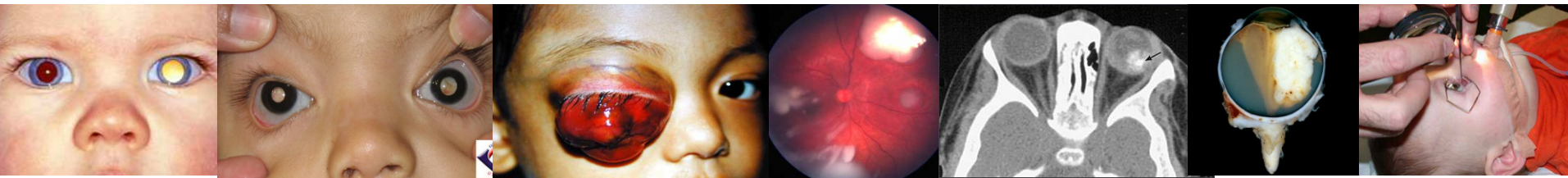


Except bilateral WT



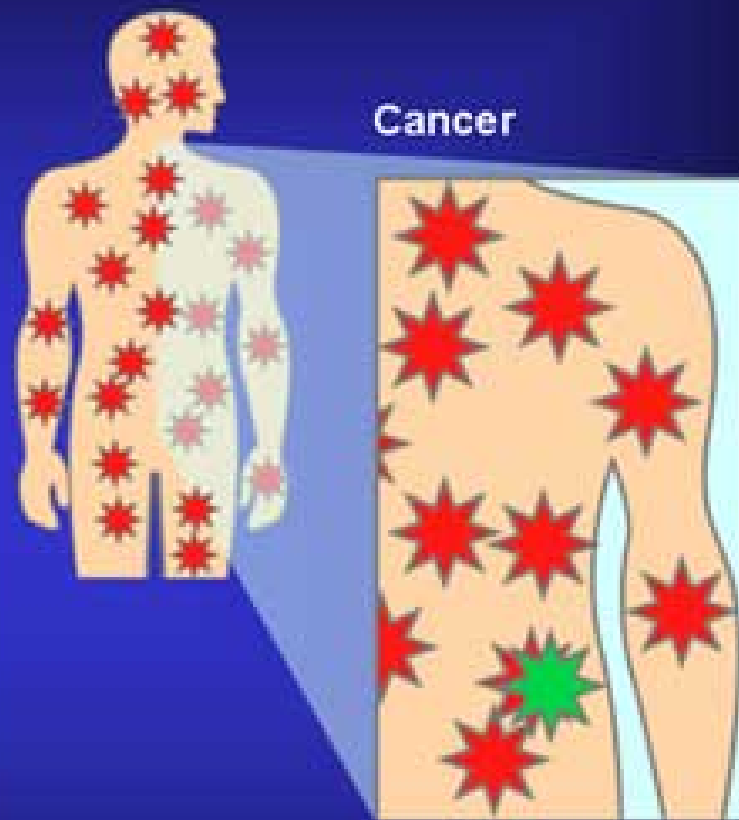
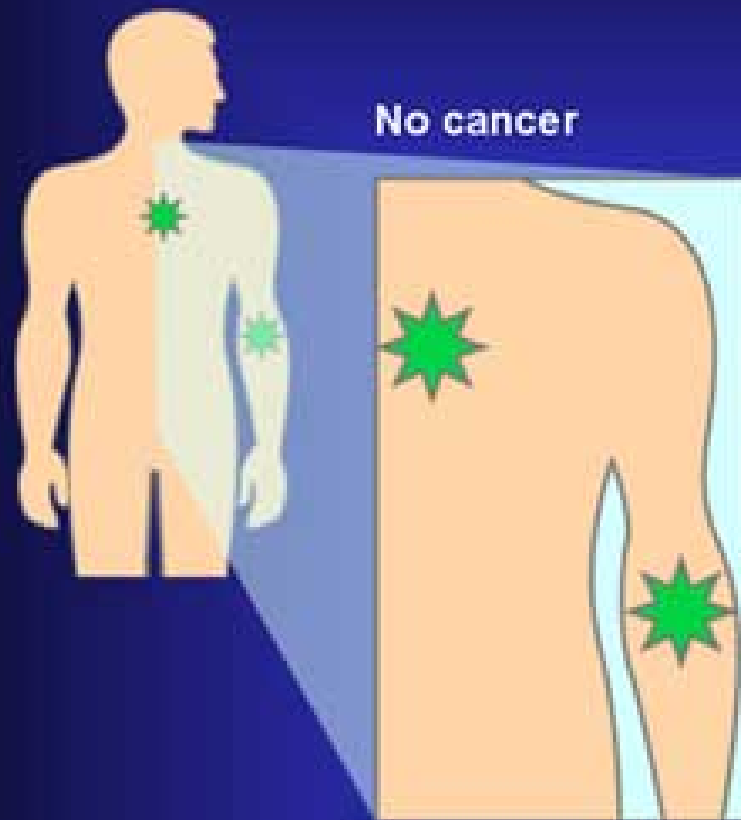
"2 months-old girl,
mom noticed
abnormal on photo
she has taken"

RETINOBLASTOMA



- Malignant tumor of retina
- MCM primary intraocular malignancy of childhood
- MCM occur < 2 yr of age
- Mutation in tumor suppressor gene retinoblastoma gene (RB 1 gene)
 - Germ cell mutation → Hereditary 40%
 - Somatic cell mutation → Non - Hereditary 60%
- Survival rate > 90%

Two-Hit Hypothesis



- ★ Germline mutation
- ★ Somatic mutation

If first hit is a germline mutation, second somatic mutation more likely to enable cancer

First hit is germline in heritable form and somatic in sporadic non-heritable form

Retinoblastoma

Clinical Presentations

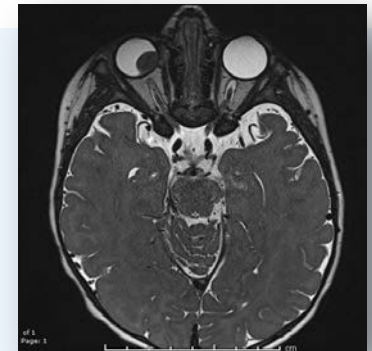
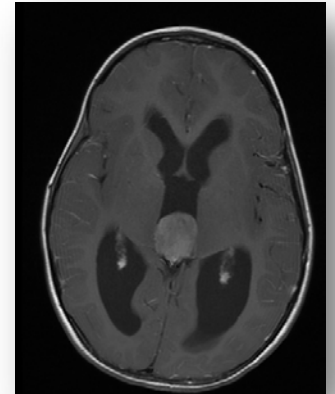
- Leukocoria : MCM
- Strabismus
- Painful, red eye
- Proptosis
- Trilateral retinoblastoma
- Metastasis :
 - Soft tissue extension
 - Hematogenous : brain, liver, BM, bone



Retinoblastoma

Investigations

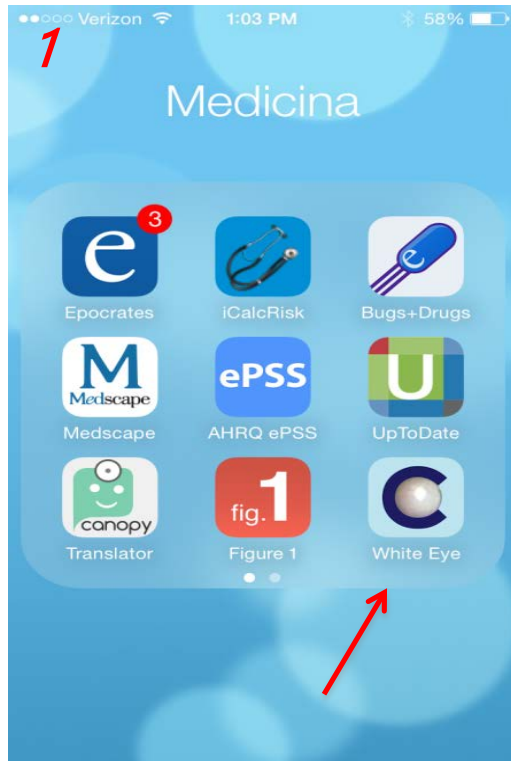
- EUA (Examination Under Anesthesia) by ophthalmologist
- MRI brain with orbit Bone scan
- BMA and biopsy
- CSF studies if suspected CNS disease



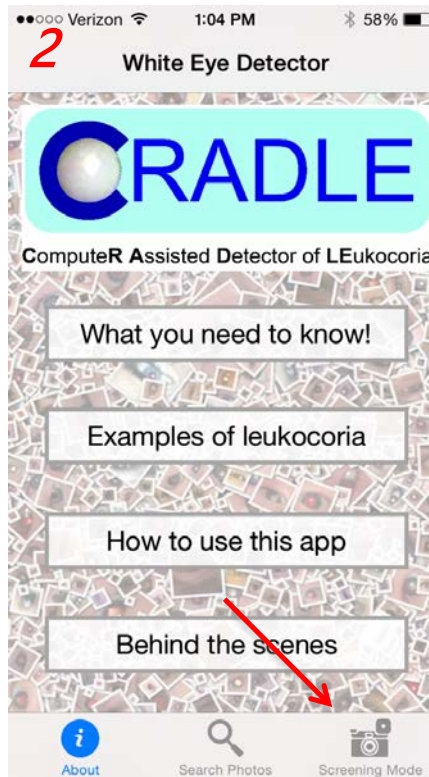
*Diagnosis made during EUA
Pathology not necessary*

CRADLE

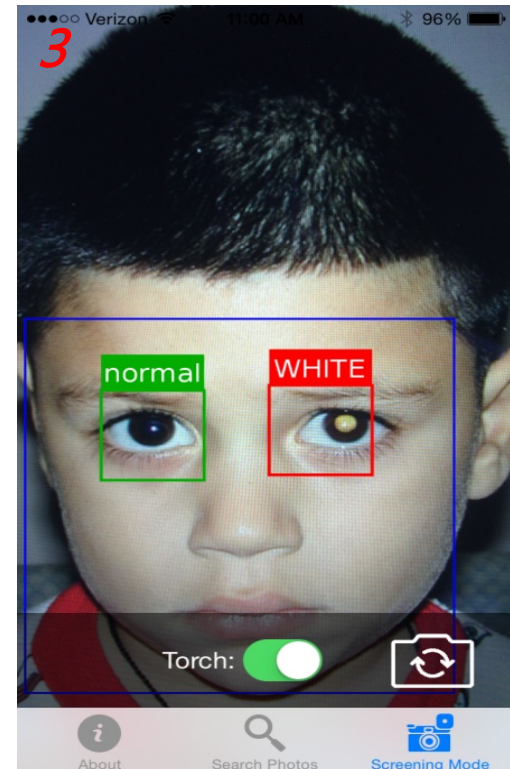
Computer Assisted Detector of LEukocoria



Open the App White Eye



Choose the option "Screening Mode."



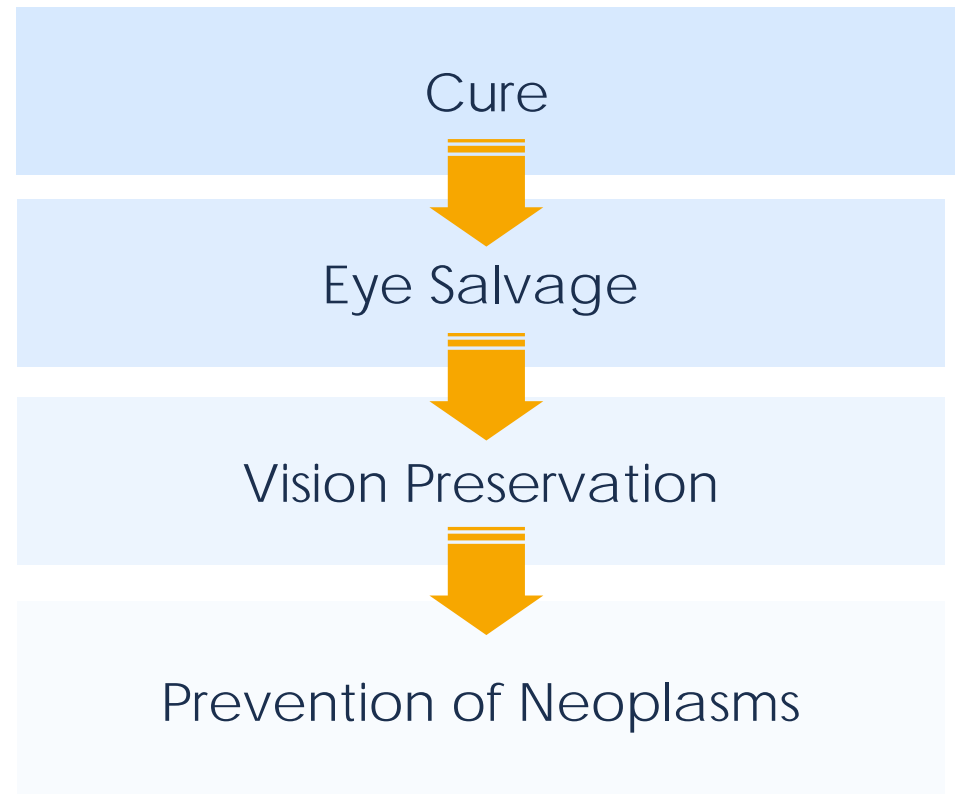
Retinoblastoma

Treatment

Multidisciplinary Team

- Pediatric Oncologist
- Ophthalmologist
- Radiation Oncologist
- Infrastructure
- Supportive care

Priorities in Treatment





“8 years-old boy
with
growing mass”

**What is the most likely
diagnosis ?**

- A. Rhabdomyosarcoma
- B. Neuroblastoma
- C. Langerhans cell histiocytosis
- D. Burkitt lymphoma

RHABDOMYOSARCOMA



Rhabdomyosarcoma

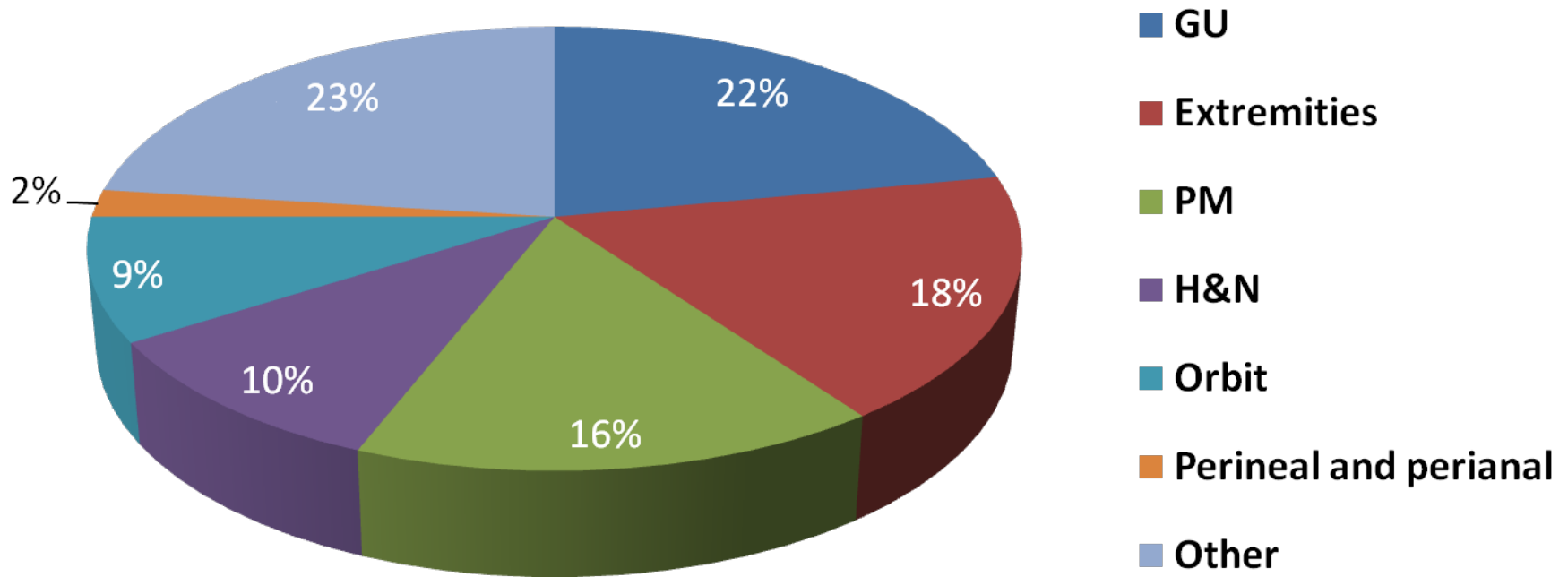
Epidemiology

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



Rhabdomyosarcoma

Primary Sites



Rhabdomyosarcoma

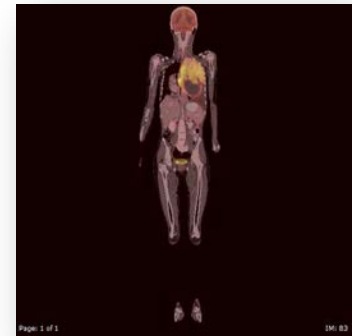
Disease Characteristics

Primary site	Frequency (%)	Symptoms and signs	Predominant pathologic subtype
Head and neck	35	Proptosis	Embryonal
Orbit	9	Cranial nerve palsies; aural or sinus obstruction +/- drainage	
Parameningeal	16	Painless, progressively enlarging mass	
Other	10		
Genitourinary	22	Hematuria, urinary obstruction	Embryonal (botryoid variant in bladder and vagina)
Bladder and prostate	13	Pelvic mass, grape liked mass, vaginal discharge	
Vagina and uterus	2	Painless mass	
Paratesticular	7		
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

Rhabdomyosarcoma

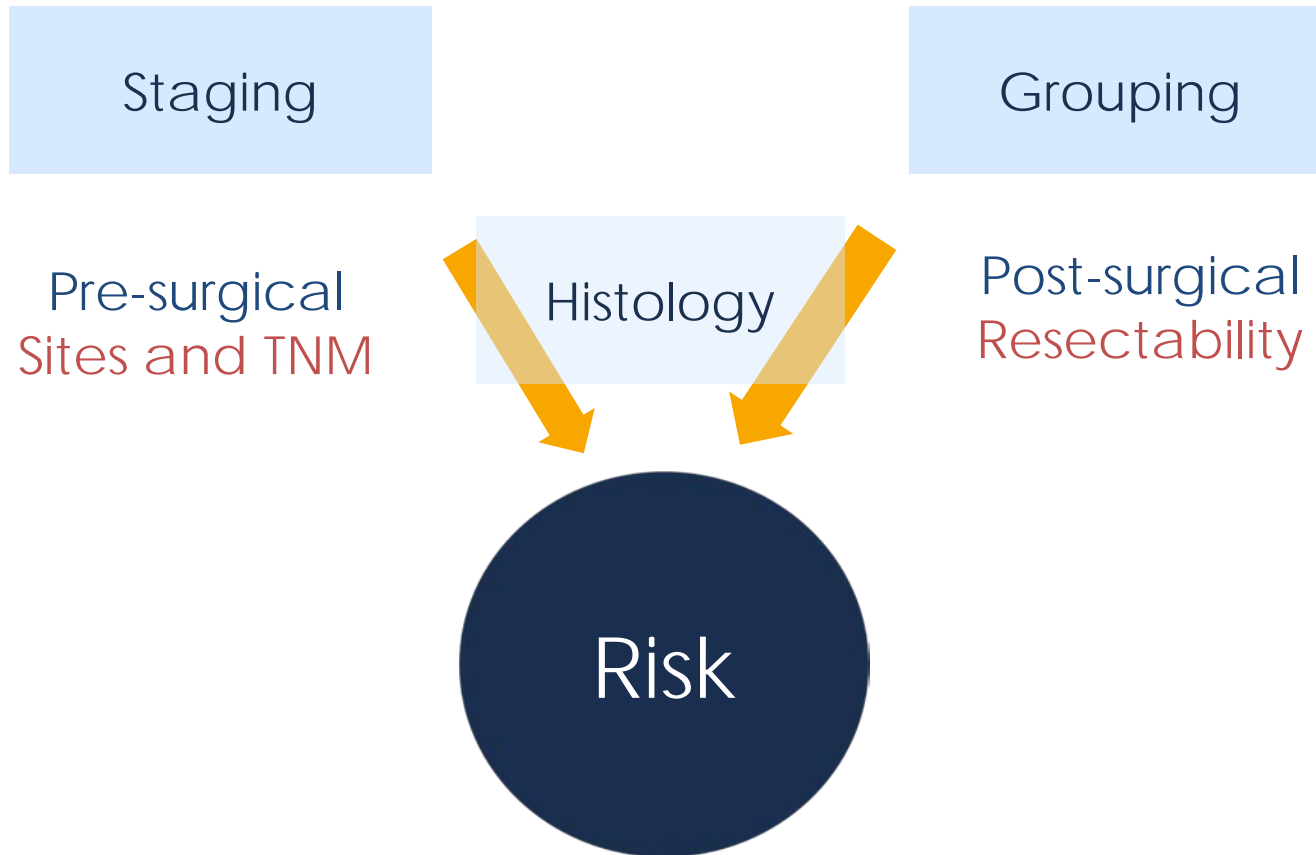
Investigations

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



Rhabdomyosarcoma

Risk Stratification



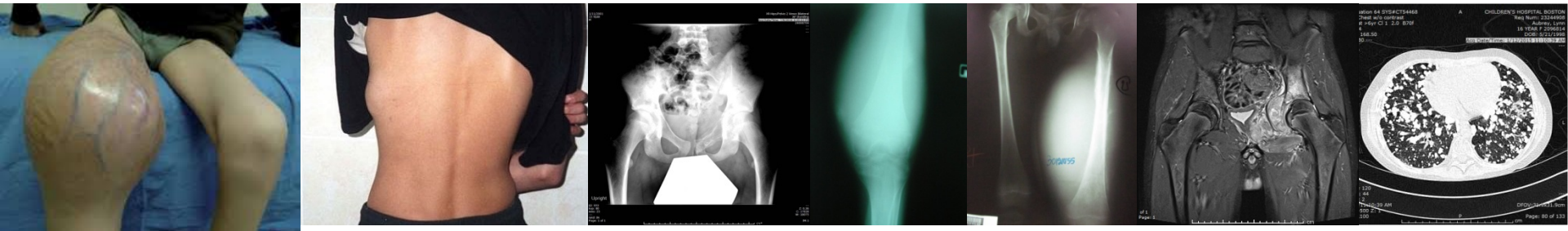


“9 years-old boy
with growing
mass and pain ”

**What is the most likely
diagnosis ?**

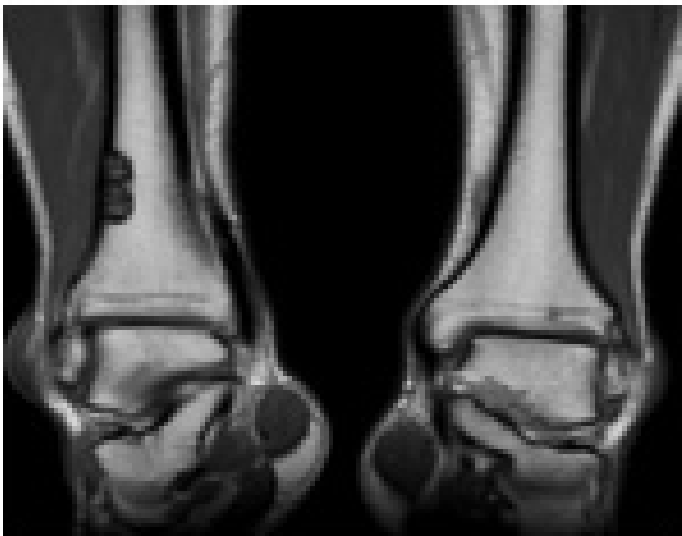
- A. Ewing's sarcoma
- B. Osteosarcoma
- C. Rhabdomyosarcoma
- D. Hemangioma
- E. Lymphoma

MALIGNANT BONE TUMORS



Bone Tumors in Children

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



Osteosarcoma



Ewing sarcoma



Malignant Bone Tumors

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

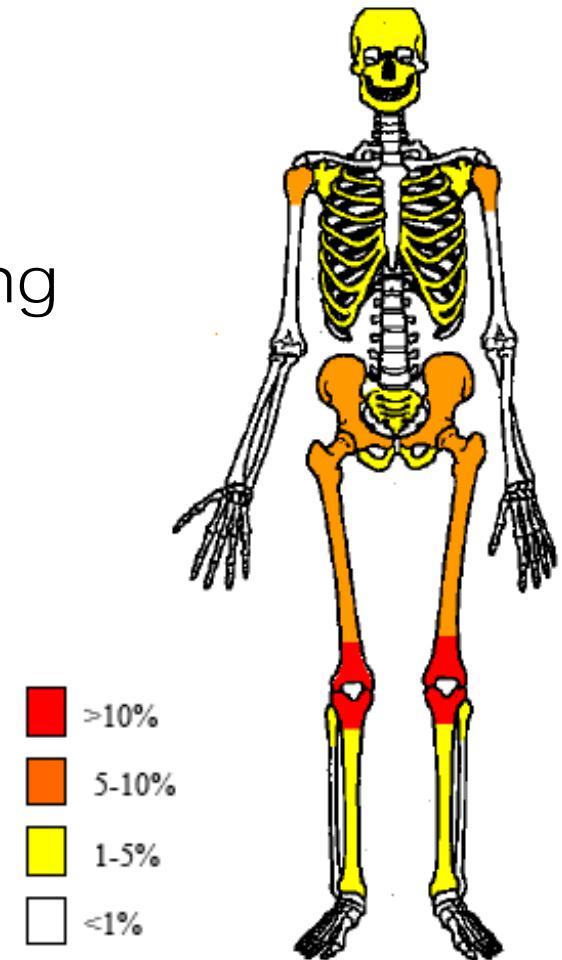
Malignant Bone Tumors

	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	<ul style="list-style-type: none"> • Sunburst pattern • Calcification 	<ul style="list-style-type: none"> • Moth-eaten lytic lesion • Onion skin
	<ul style="list-style-type: none"> • 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

Clinical Presentation

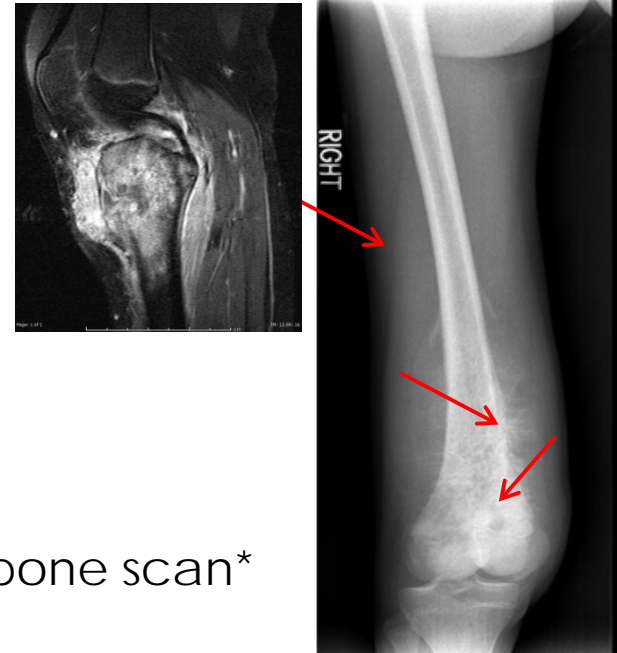
- Local pain (90%)
- Local swelling (50%)
- Decreased range of motion, limping (45%)
- Pathologic fracture (8%)
- Lab
 - Elevated LDH 30%
 - Elevated ALP 40%



Osteosarcoma

Investigations

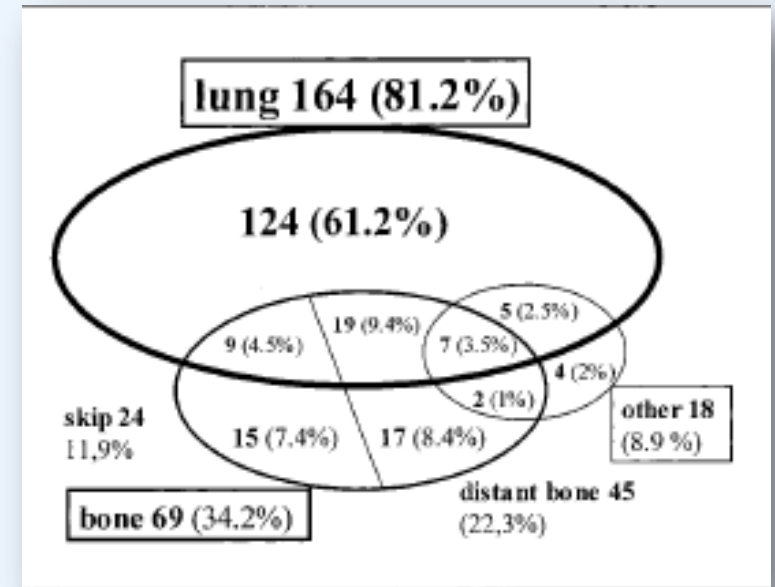
- Plain film at primary and bone met site(s)
- CXR
- MRI of primary tumor
- CT chest
- Bone scan
- PET scan: (recommend) evaluation for metastatic disease (bone, lung)
 - PET/CT more sensitive and accurate than bone scan*
 - Combined use improves sensitivity*
- Biopsy
 - Requires planning for later resection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



Osteosarcoma

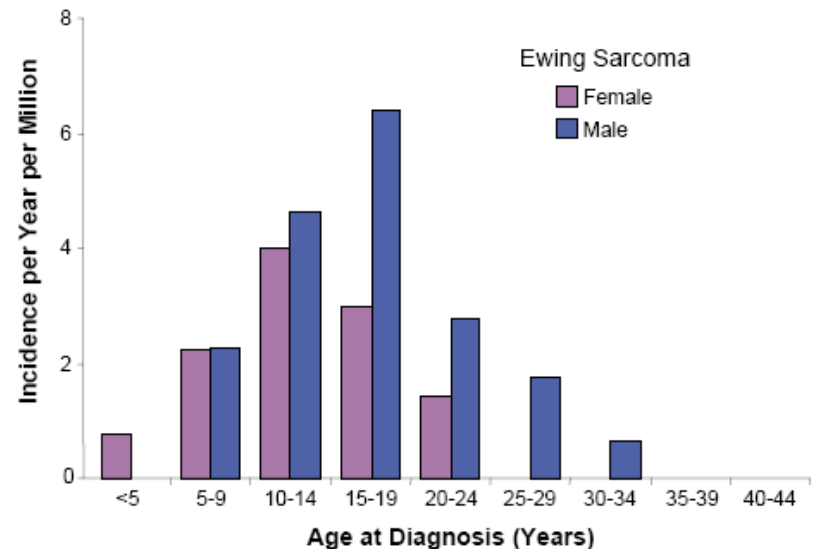
Staging

- Localized
- Metastatic
 - 15-20% metas at presentation
 - Lungs
 - Bone:
 - distant and skip lesions
 - Combined



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



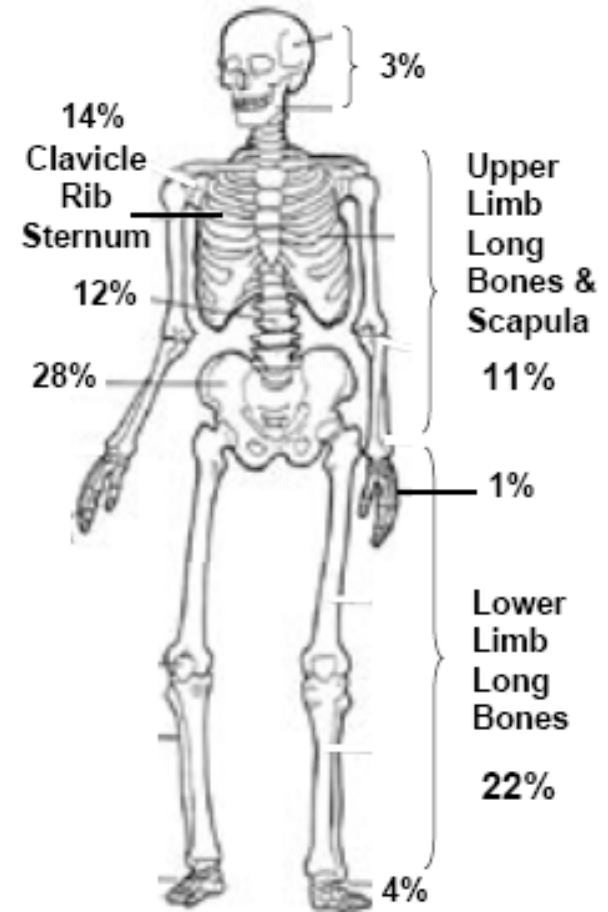
- Age: median age 15 years
- Race: significant higher incidence in Caucasians
- Presenting symptoms
 - Pain
 - Soft tissue mass
 - Median time to diagnosis 3 – 9 months
 - Constitutional symptoms: fever, weight loss, malaise
 - LAB: LDH increased (marker of advance disease)



ESFT

Site of Origin

- Bone primaries (75%)
Axial=extremities
 - Pelvis
 - Long bones
 - Other axial sites
- Soft tissue primaries (25%)
 - Paraspinal
 - Chest wall
 - Various other sites



ESFT

Investigations

Primary site

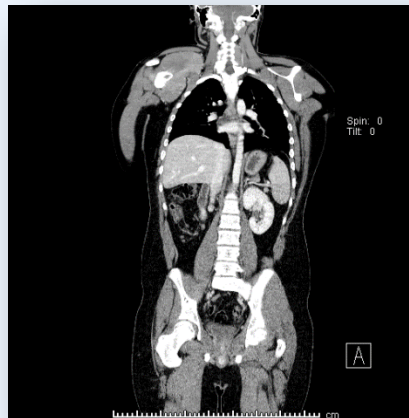
- Plain film
- MRI of affected region



Metastasis detection and staging

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

Tissue biopsy



ESFT

Bone Sarcoma Treatment



**CHILDREN'S
ONCOLOGY
GROUP**

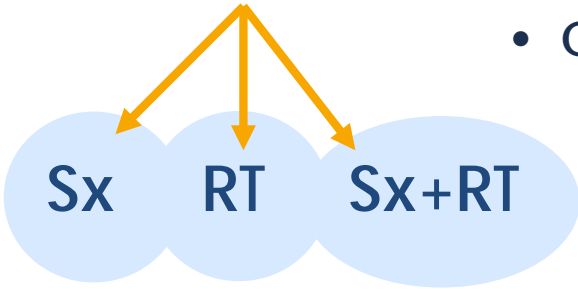
**THAI
POG**
Thai Pediatric Oncology Group



- Neoadjuvant
- Chemotherapy

- Local Control

- Adjuvant
- Chemotherapy



Thank You



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