Solid Tumors in Children

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Pediatric Hematology-Oncology

Childhood Solid tumors

Brain tumor 20% (intracranial CNS tumor)

Neuroblastoma 7% (extracranial CNS tumor)

Wilms tumor 6%

Rhabdomyosarcoma 4%

& other soft tissue sarcomas 3%

Retinoblastoma 3%

Germ cell tumors 3%

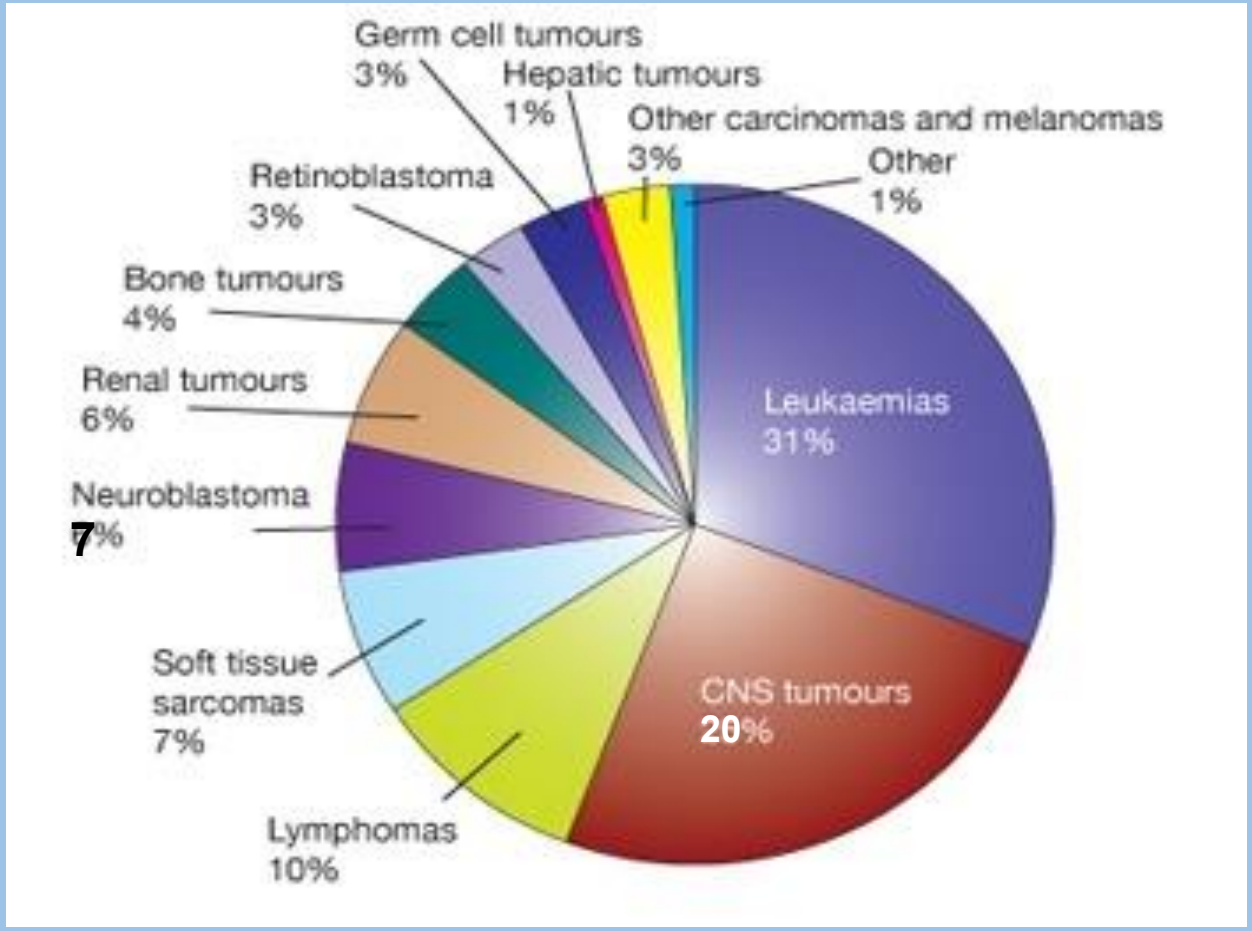
Osteosarcoma 2%

Ewing sarcoma 1%

Hepatoblastoma 1%

Others

Types of Childhood Malignancy



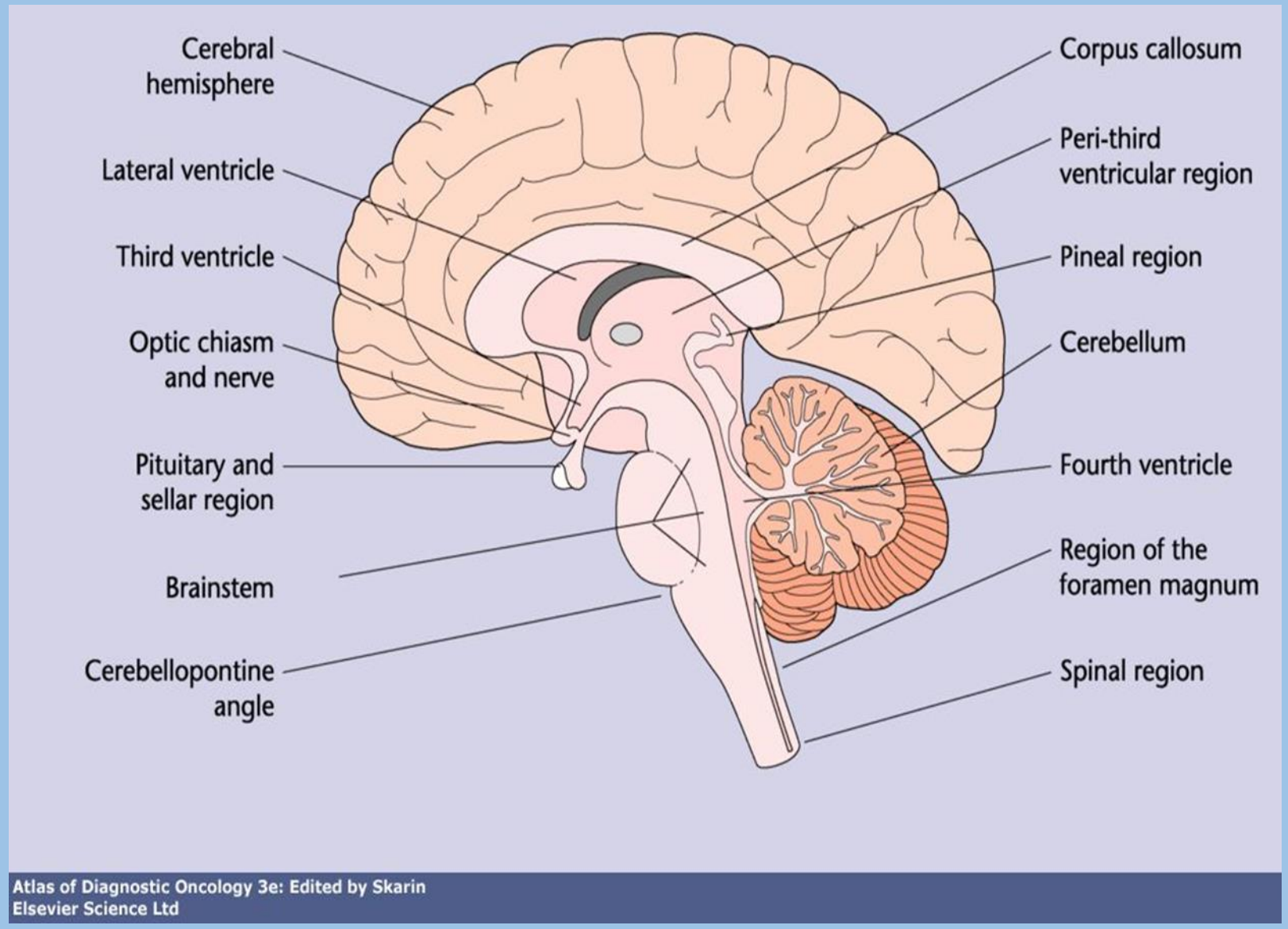
Brain tumor

It is a growth of cells in the brain that multiplies in an abnormal, uncontrollable way.

It is the most common solid tumor in children and the Second childhood malignancy after leukemia

(Because leukemia & Lymphoma are **hematological malignancy**, not solid tumor)

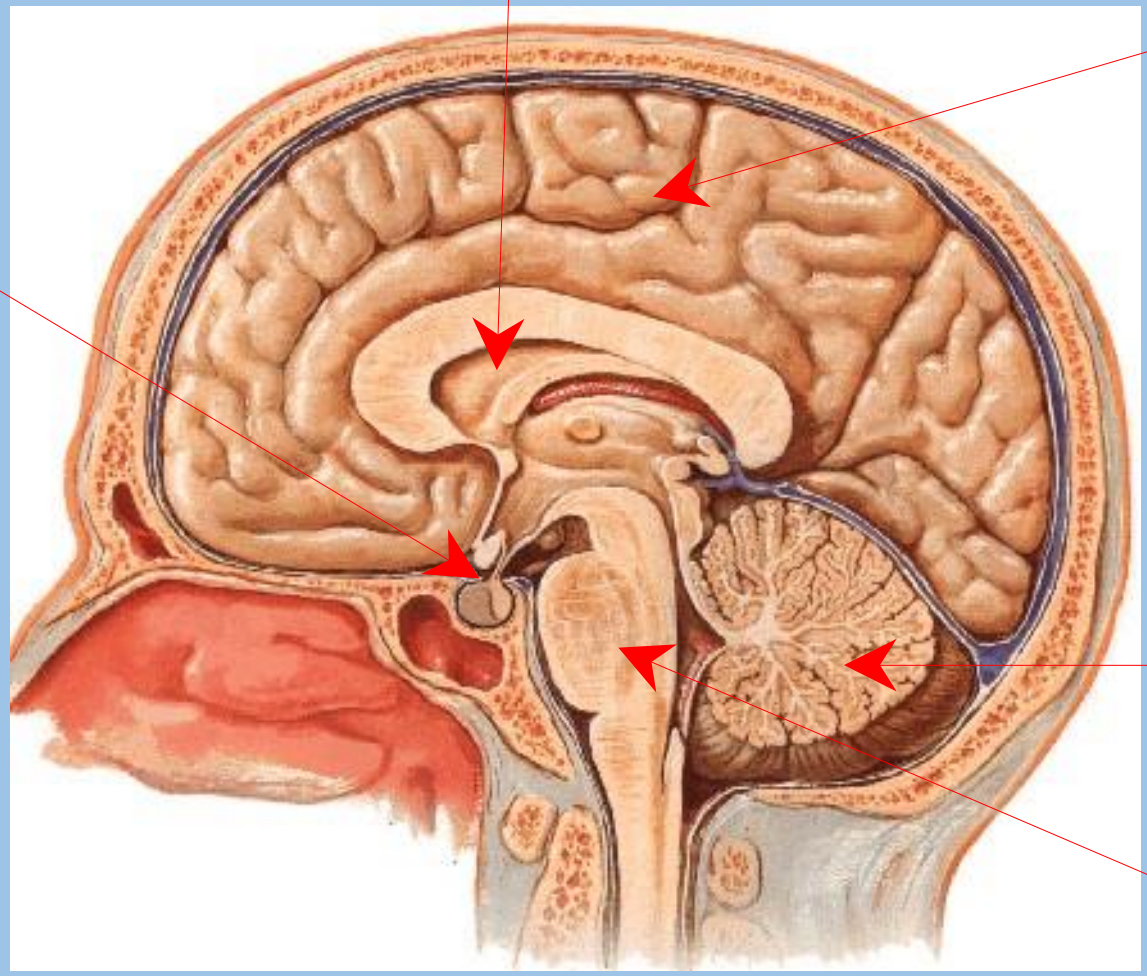
It accounts for **20%** of all pediatric cancers,
More frequent in males than females



Atlas of Diagnostic Oncology 3e: Edited by Skarin
Elsevier Science Ltd

Sella/

Suprasellar



Cerebral hemisphere

Post. fossa

Brain stem

- **Infratentorial lesions** (60 – 70%) mainly at posterior fossa:

1. Cerebellum (Medulloblastoma, Astrocytoma, Meningioma)
2. Brain stem (Astrocytoma, Ependymoma, Glioblastoma)

- **Supratentorial lesions** (30 – 40%):

1. Cerebral hemisphere (Astrocytoma, Ependymoma, Glioblastoma, Meningioma)
2. Sella or chiasm (Craniopharyngioma, Pituitary adenoma, Optic nerve glioma)

Association between primary CNS tumors and following conditions/ genetic disorders:

- **1. Neurofibromatosis (NF) type 1 and 2**
- **2. Tuberous sclerosis**
- 3. Von Hippel- Lindau syndrome
- 4. Gordlin's, Cowden's, Turcot's syndromes
- 5. Li-Fraumeni syndrome (mutation of suppressor oncogene p53)
- 6. Deletion of chromosome 17 or 20 (medulloblastoma)
- 7. Exposition of the brain to ionizing radiation i.e. after cranial radiotherapy in leukemia

Clinical presentation of brain tumor depends on:

Age

anatomical site

Tumor type

raised intracranial pressure (ICP)

Sign & symptoms in nfants and younger children:

Irritability

Failure to thrive,

Anorexia and vomiting

Regression of developmental milestones Hydrocephalus: dilated ventricles; increase head circumference with widened sutures and a tense anterior fontanelle, sun-setting sign

Common signs & symptoms of brain tumor in elder children:

- **Headaches**, more severe at morning, can be dull and constant, or throbbing
- **Vomiting**
- Confusion
- Drowsiness
- **Seizures (fits)**
- **Papilledema**
- **Ataxia**
- Mental or behavioural changes, such as memory problems or personality change
- **Poor school performance**
- Progressive weakness or paralysis at one side of the body (motor deficit)
- Sensory deficit
- Dysphasia
- **Visual disturbance**, inability to abduct the eye
- speech problems
- Neuroendocrine symptoms of precious puberty,

Symptoms may acute or may develop very slowly over time.

Symptoms and signs according to anatomical site of brain tumor

Infratentorial (60 – 70%)

- **posterior fossa** – ataxia, nystagmus, dysmetria (presents as clumsiness or worse handwriting)

- **brainstem** – multiple cranial nerve palsies, hemiparesis, spasticity, mood changes

- **Spinal (2 – 5%)**

  primary intramedullary – pain (local back and root pain),

  motor and sensory disturbance

  spinal metastases – scoliosis, sphincter (bowel, bladder) disturbances,

  reflex changes

Symptoms and signs according to anatomical site of brain tumor

Supratentorial (30-40%)

- **Cerebral hemisphere:** hemiparesis, spasticity, seizures (focal or generalized)
- **para/suprasellar**: endocrinopathy (growth failure, diabetes insipidus, pubertal abnormality)
- **Hypothalamus:** diencephalic syndrome (infants), developmental and behavioural abnormalities
- **Optic pathway:** visual field acuity, color vision deficits, optic atrophy, nystagmus, head tilt
- **Pineal:** Parinaud's syndrome, sleep abnormalities
- **Thalamus**, **basal ganglia:** pain, sensory loss, memory disturbances

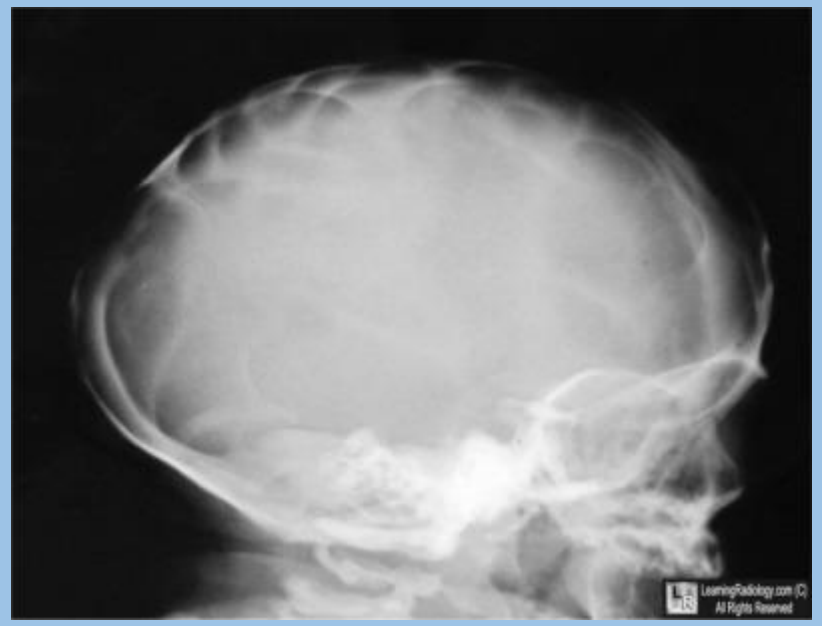
Differential diagnosis of brain tumor

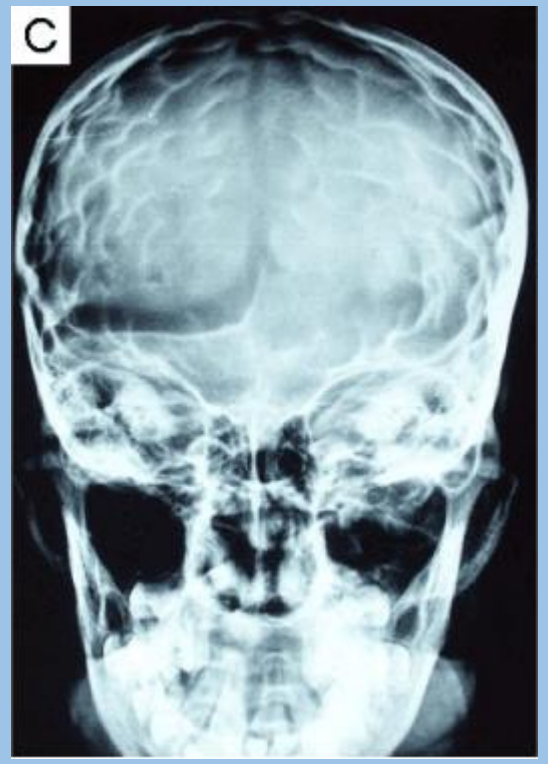
Brain abscess
Intracranial haemorrhage
Benign tumors: Pituitary adenoma, Craniopharyngioma, Meningioma, Acoustic neuroma, Dermoid tumor
Arteriovenous malformations
Pseudotumor cerebri
Aneurysm
Vasculitis

Investigations for brain tumors

* **Skull X ray**: silver biting appearance
* **MRI** of brain and spine to find out dissemination
* **CSF** (Cerebrospinal fluid) analysis for malignant cells
* **Biopsy**

Skull X-ray; Silver biting appearance





Treatment of Brain Tumor

Neurosurgical excision and histopathological examination

Radiotherapy

Chemotherapy

Symptomatic treatment:

Steroids for brain oedema

Analgesia for pain

Antiemetic for nausea

Pilocytic Astrocytoma (Juvenile)

Most common pediatric brain tumor: 40 – 50% of brain tumors.
60% located in posterior fossa.
age 5 – 15 years

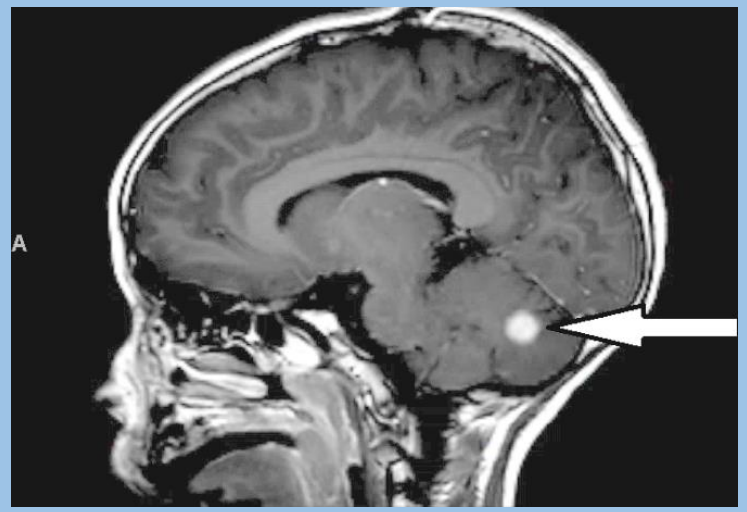
M = F

Signs & Symptoms:

increased ICP as headache, vomiting, papilledema (84%),

Cerebellar signs as Ataxia,

Hydrocephalus (85%)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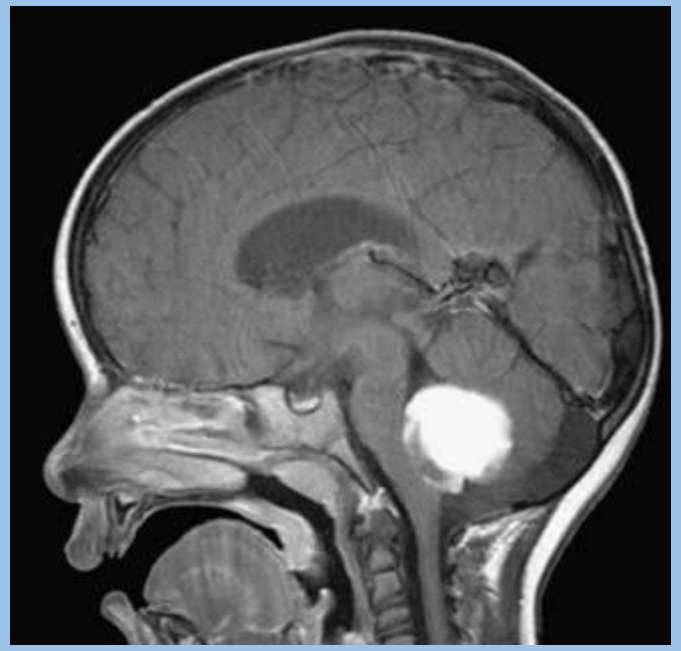
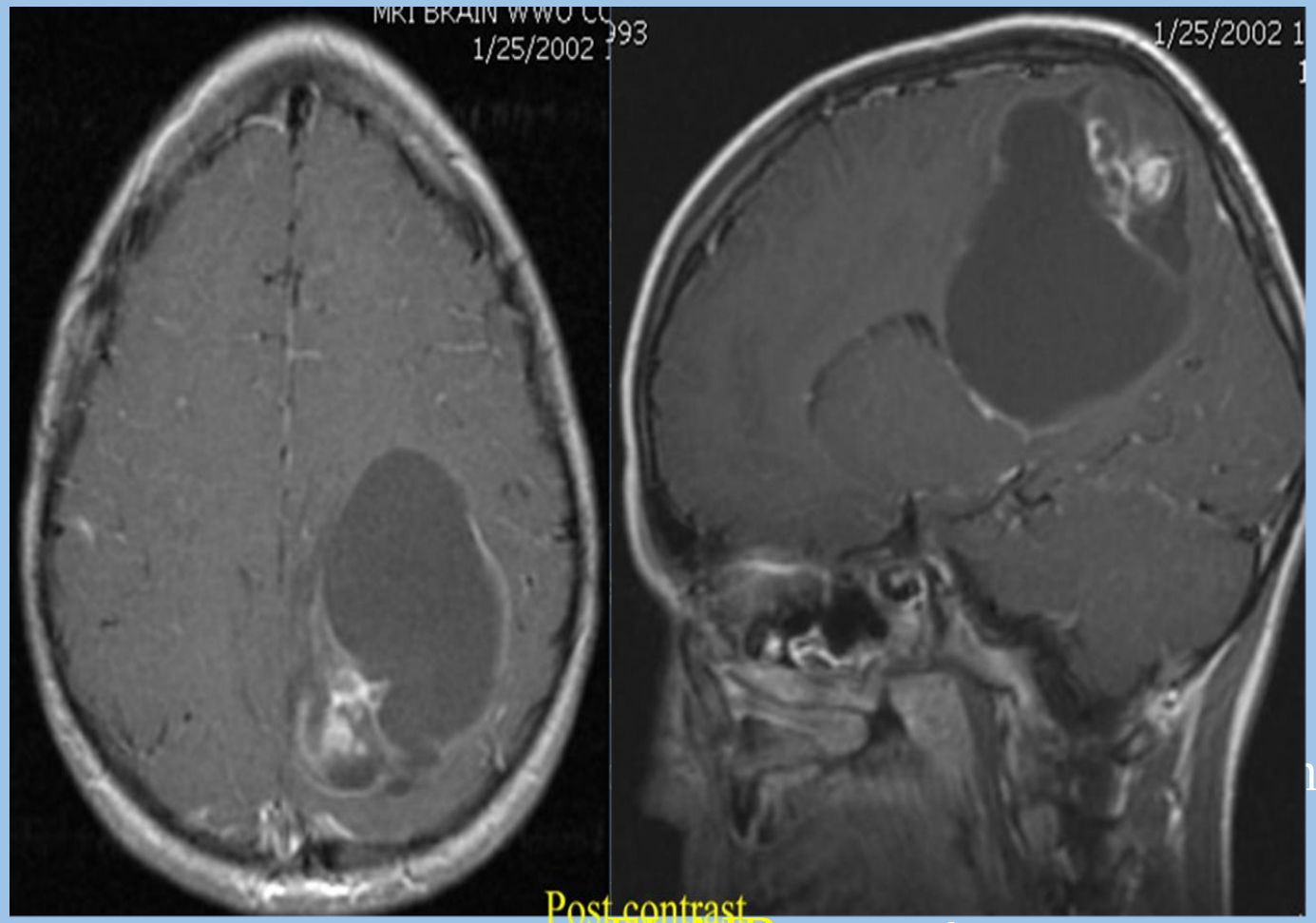
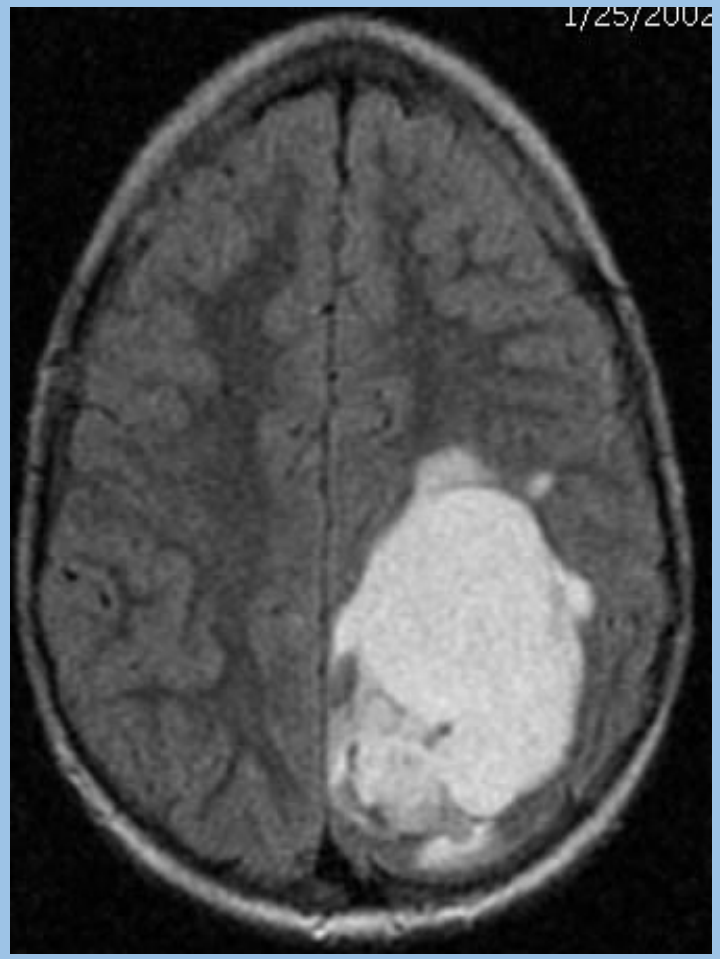


Supratentorial brain tumor; Cerebral Astrocytoma



Post contrast



FLAIR areas of necrosis

Neuroblastoma

Extracranial solid tumor

Most common malignancy in **infancy**
Embryonal origin so peak age at **first 2 years**
Derived from **neural crest cells in adrenal gland** and **sympathetic nervous system**

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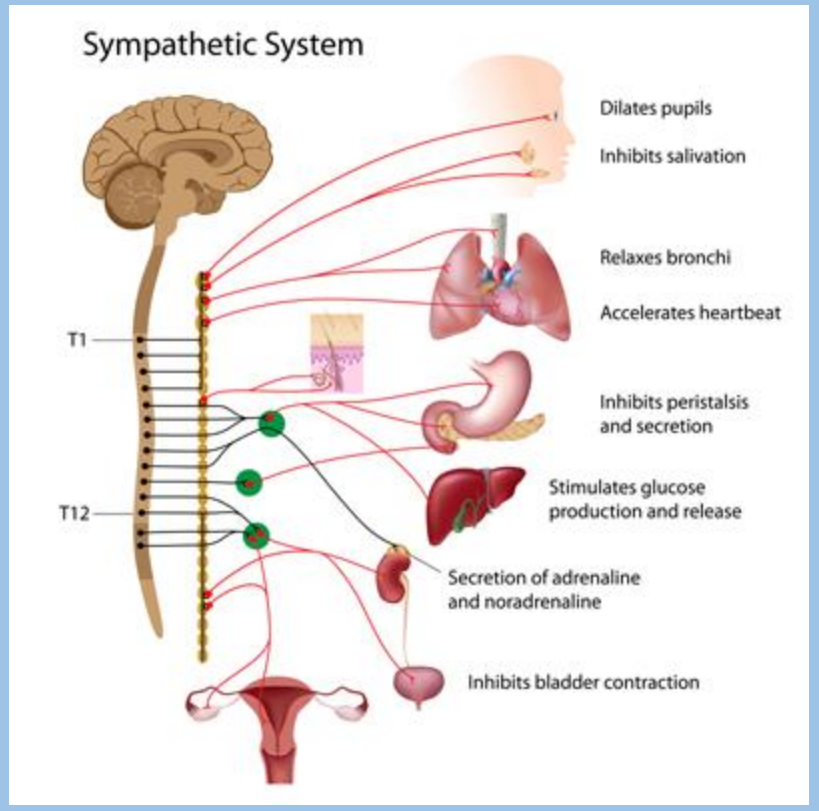
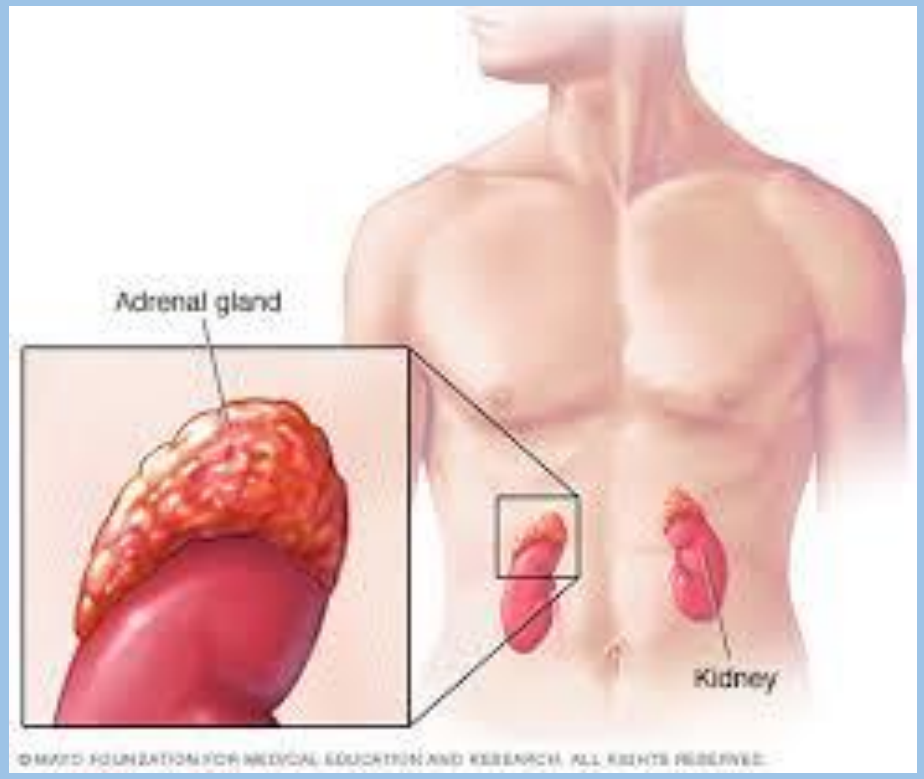

Sympathetic System
Dilates pupils
Inhibits salivation
Relaxes bronchi
Accelerates heartbeat
T1
Inhibits peristalsis
and secretion
Stimulates glucose
production and release
T12
Secretion of adrenaline
and noradrenaline
Inhibits bladder contraction

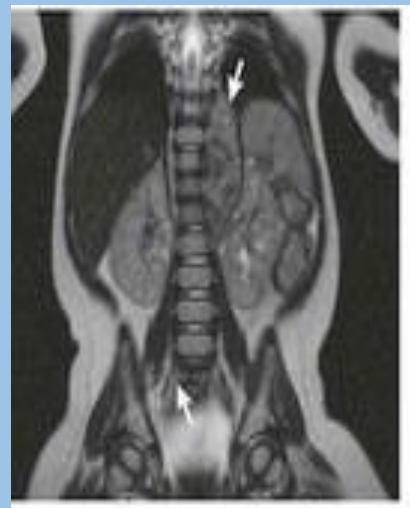

Adrenal gland
Kidney

Clinical features of NB

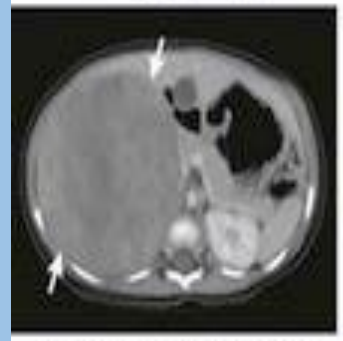
Mass:
Abdominal mass (adrenal gland or sympathetic chain) is the main site involved.
Mass along the sympathetic chain (neck, thoracic, abdomen and pelvis)
Compression of spinal cord if the mass is paraspinal.

Fever, weight loss
Secretory diarrhoea
Horner syndrome
Superior vena cava syndrome
Opsomyoclonus intermittent jerky eye movements and cerebellar ataxia.

Signs of metastasis to liver, bone marrow, bone, skin, lymph nodes
If periorbital bone involved causes ecchymosis and eye proptosis (Raccoon sign)

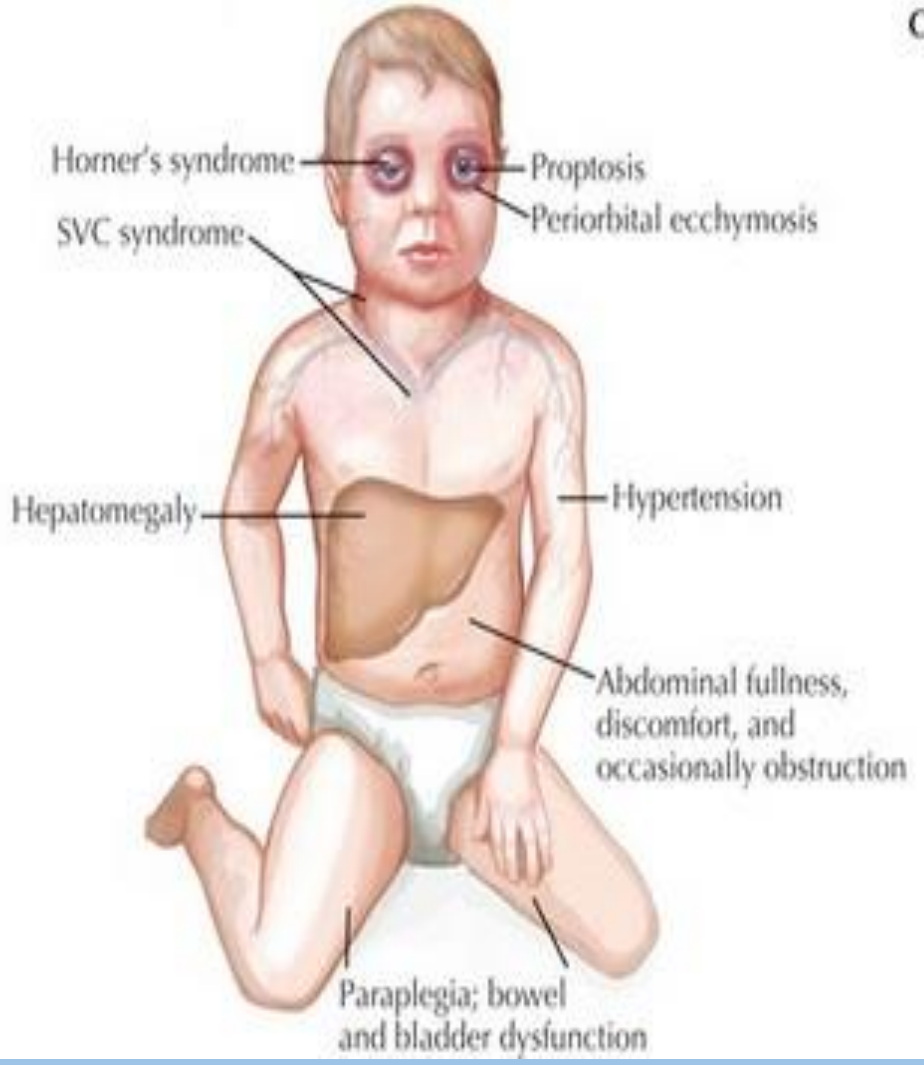


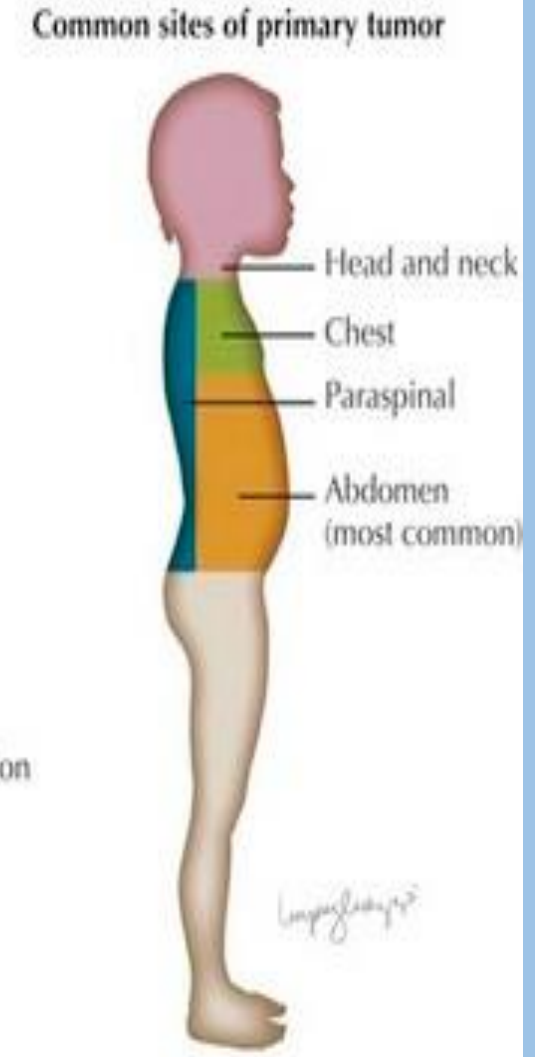
MR image, paraspinal tumor



CT, abdominal tumor

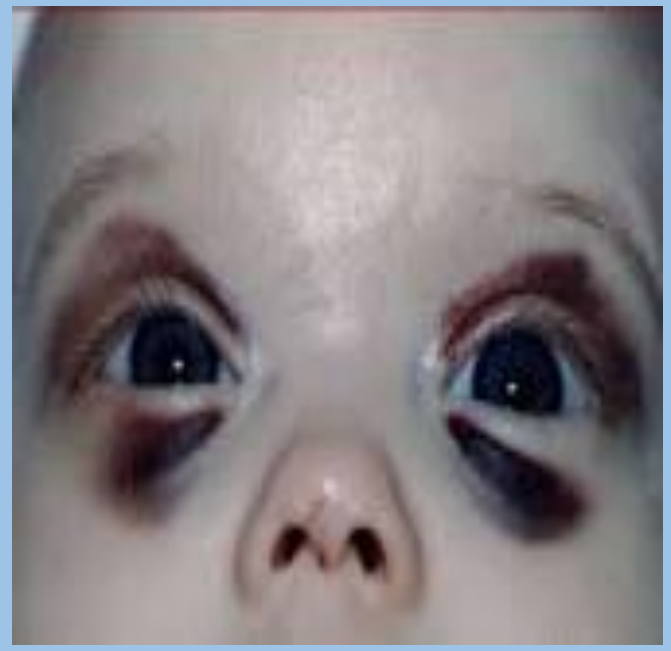
Radiology images courtesy of Lisa States, MD Children's Hospital of Philadelphia





Racoon sign

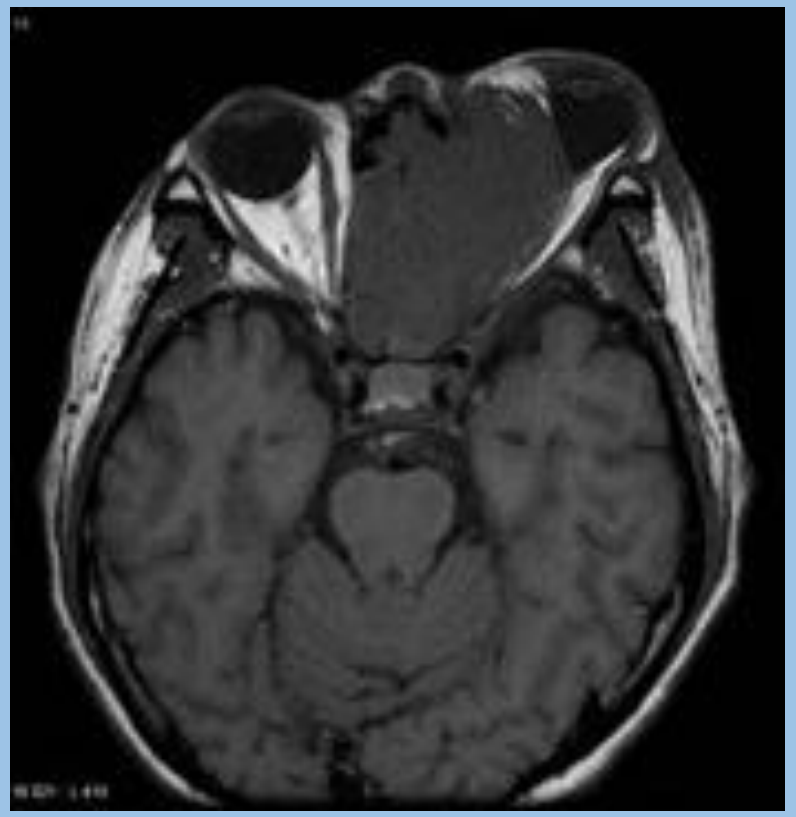
Eye proptosis and ecchymosis around the eye



Panda eyes

Raccoon eyes; Raccoon sign

Neuroblastoma



Horner syndrome

- Small pupil (miosis)
- Drooping of the upper eyelid (ptosis)
- Little or no sweating (anhidrosis)

- **Stage 1:** The tumor can be removed completely during surgery. Lymph nodes attached to the tumor removed during surgery may or may not contain cancer, but other lymph nodes near the tumor do not.
- **Stage 2A:** The tumor is located only in the area it started and cannot be completely removed during surgery. Nearby lymph nodes do not contain cancer.
- **Stage 2B:** The tumor is located only in the area where it started and may or may not be completely removed during surgery, but nearby lymph nodes do contain cancer.
- **Stage 3:** The tumor cannot be removed with surgery. It has spread to regional lymph nodes (lymph nodes near the tumor) or other areas near the tumor, but not to other parts of the body.
- **Stage 4:** The original tumor has spread to distant lymph nodes (lymph nodes in other parts of the body), bones, bone marrow, liver, skin, and/or other organs, except for those listed in stage 4S, below.
- **Stage 4S:** The original tumor is located only where it started (as in stage 1, 2A, or 2B), and it has spread only to the skin, liver, and/or bone marrow, in infants younger than one. The spread to the bone marrow is minimal, usually less than 10% of cells examined show cancer.

Differential diagnosis of NB

Wilms tumor
Child Abuse
Leukemia, if metastasis to bone marrow

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Investigations of NB

CBC

Chest X ray (calcification)

Urinary catecholamine:
Vanilylmandelic acid & Homovanillic acid (VMA & HVA)

Neuron specific endolase

Ultrasound abdomen

CT scan of chest, abdomen, pelvis

Bone isotopic scan
123-MIBG scintscan

Bilateral bone marrow biopsies for histopathology, Immunophenotyping

Tumor markers for NB:

- Catecholamines:

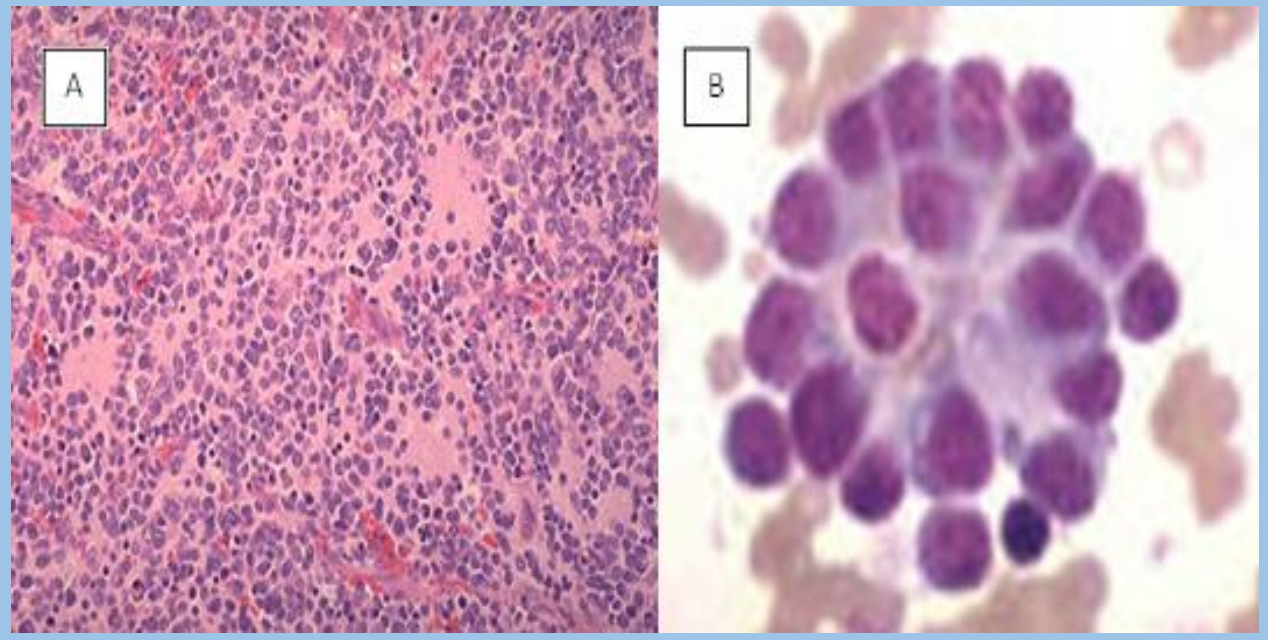
vanillylmandelic acid (VMA), homovanillic acid (HVA)
adrenaline, noradrenaline

- Neuron-specific enolase (NSE)
  (glycolitic enzyme of brain and neuroendocrine tissues)

- Ferritin

- Lactate dehydrogenease (LDH)

Rosette cells (Histopathology)



Treatment of NB

* Surgical resection

* Chemotherapy
(Vincristine, Cyclophosphamide, Doxorubicin, Cisplatin, Etoposide)

* Bone marrow transplantation (autologous)

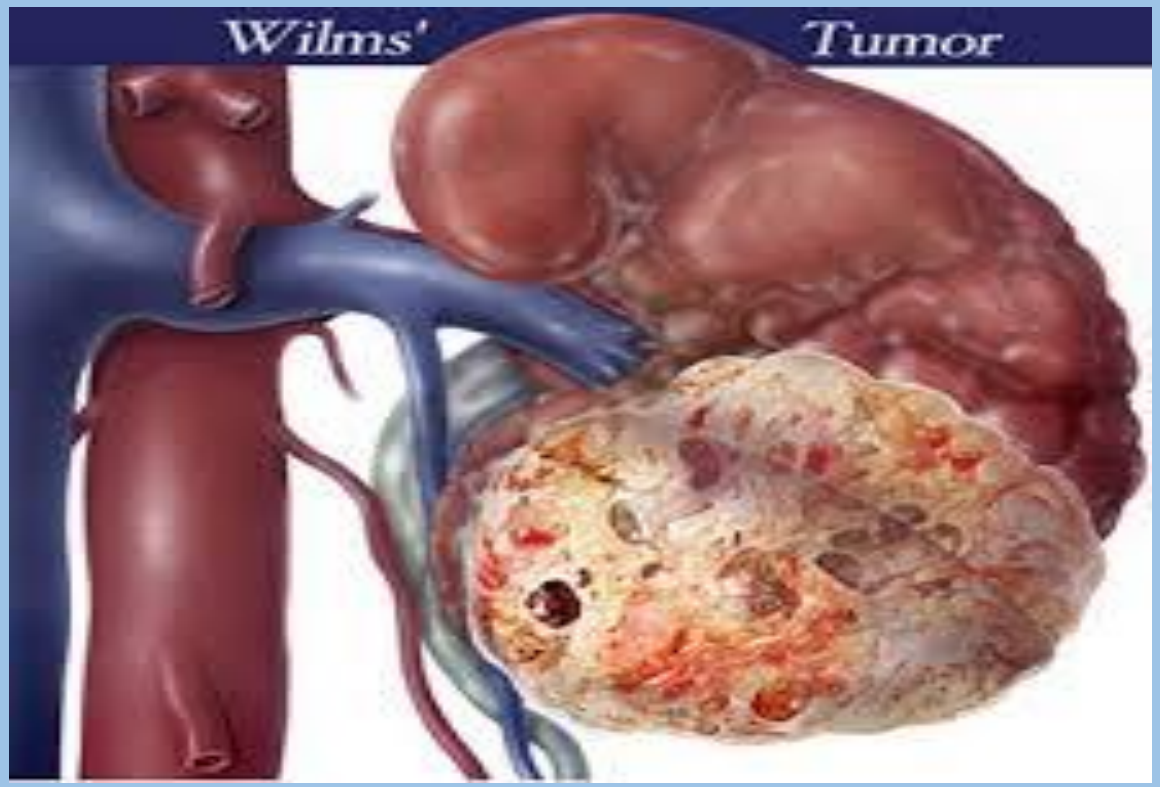
WILM'S TUMOR

Wilms Tumor

Most common renal malignancy in children

It arise from primitive, metanephric blastemal
Has genetic predisposition
Associated with many congenital anomalies

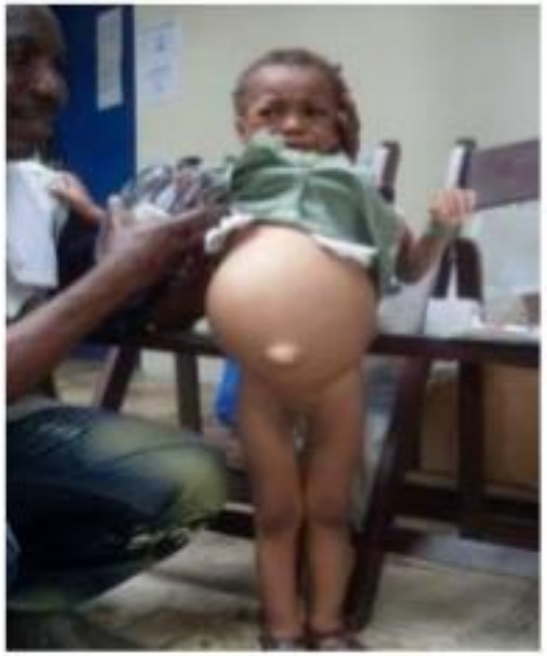
Wilms tumor is intra-renal tumor



Signs & symptoms in delayed diagnosis Wilms tumor

Signs and Symptoms

- Nontender, abdominal mass
- Abdominal swelling
- Abdominal pain
- Fever
- High blood pressure
- Vomiting
- Hematuria
- Loss of appetite
- Constipation



Differential diagnosis of Wilms tumor

Hydronephrosis

Neuroblastoma

Polycystic disease of kidney

Lymphoma

Retroperitoneal Rhabdomyosarcoma

DIAGNOSIS

- Abdominal ultrasound
- Abdominal CT Scan
- Evaluation of IVC
- CBC
- Urinalysis
- Liver and renal function tests
- Chest X-ray
- Biopsy of tumor tissue


Wilms tumor (heterogenous)
Nephroblastic rests (homogenous)

Treatment of Wilms tumor:
Surgery, Chemotherapy, & Radiotherapy according to the stage

MANAGEMENT

NWTS-5 Treatment Recommendations for Wilms' Tumor	
Stage I (FH)	Surgery, no radiotherapy, dactinomycin + vincristine for 18 wk
Stage I focal anaplasia	Surgery, no radiotherapy, dactinomycin + vincristine for 18 wk
Stage II (FH)	Surgery, no radiotherapy, dactinomycin + vincristine for 18 wk
Stage II focal anaplasia	Surgery, 1080 cGy to tumor bed, dactinomycin +vincristine + doxorubicin for 24 wk
Stage III (FH)	Surgery, 1080 cGy to tumor bed, dactinomycin +vincristine + doxorubicin for 24 wk
Stage III focal anaplasia	Surgery, 1080 cGy to tumor bed, dactinomycin +vincristine + doxorubicin for 24 wk

* Infants <11 mo are given half the recommended dose of all drugs. Full doses lead to prohibitive hematologic toxicity in this age group. Full doses of chemotherapeutic agents should be administered to those >12 mo.

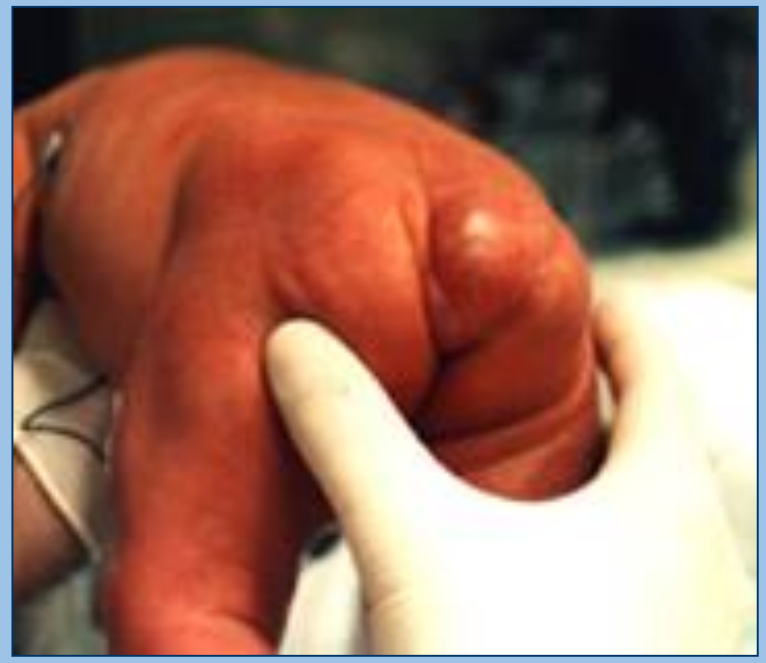
Germ cell tumors

- Develop from embryonal germ cells
- Represent ectodermal, endodermal and mesodermal lineages
- Approximately 3% of childhood malignancies

Sites

- **Testicular GCT** :scrotal enlargement,hydrocele
- **Ovarian tumors**: abdominal pain, acute abdomen, abdominal mass
- **Extragonadal GCT**: main sites of involvement is **sacrococcygeal**

Sacrococcygeal Teratoma



Investigations for Germ Cell Tumor

- **Radiological**
  ultrasound, computed tomography or magnetic resonance imaging

- **Tumor markers**:

  Alpha-fetoprotein (AFP):
  globulin produced in the fetal yolk sac, in embryonal hepatocytes and in gastrointestinal tract. Increase in malignant GCT, hepatoblastoma

  Beta -human chorionic gonadotropin (HCG):
  increase in germinoma/ dysgerminoma, choriocarcinoma

Treatment of Germ Cell Tumor depend on:

stage, location, tumor markers level

- Surgery in stage I
- Advanced stages: chemotherapy, surgery, radiotherapy

Survival

95% - sacrococcygeal teratoma

80% -yolk sac tumor

Retinoblastoma

Most common eye tumor in children

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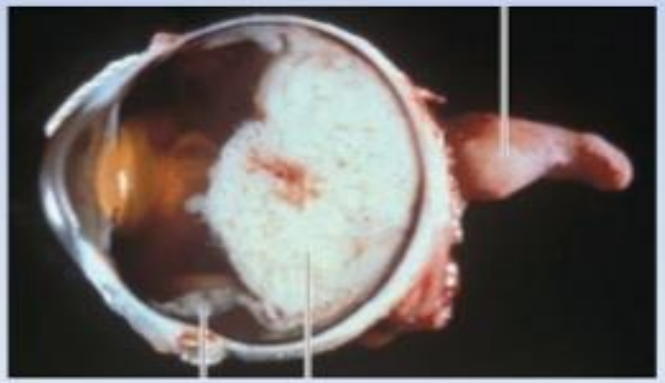
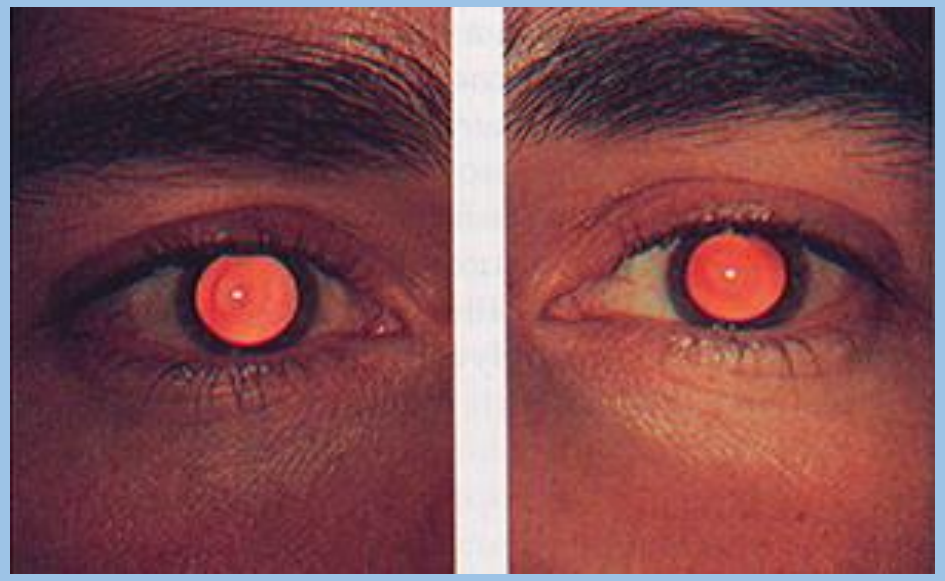
Symptoms of Retinoblastoma

- Problems with eye movements (crossed eyes).
- A persistent red irritation in the eye.
- Differences in pupil size, iris color, abnormal eye movements, bulging forward of the eyes, tearing, and cataract.
- "A white spot on the pupil of the eye."(2)

Retinoblastoma

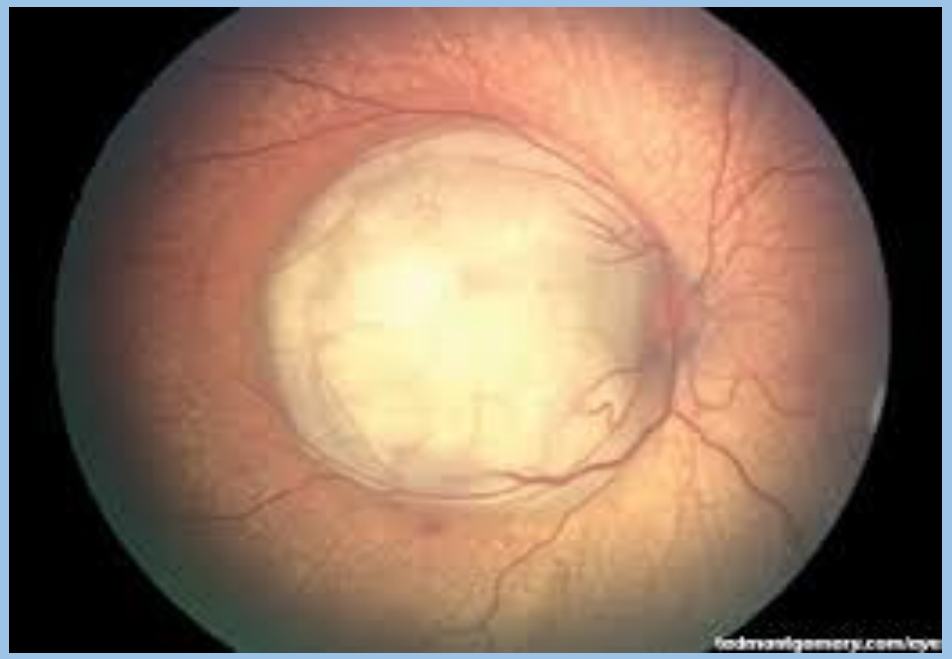


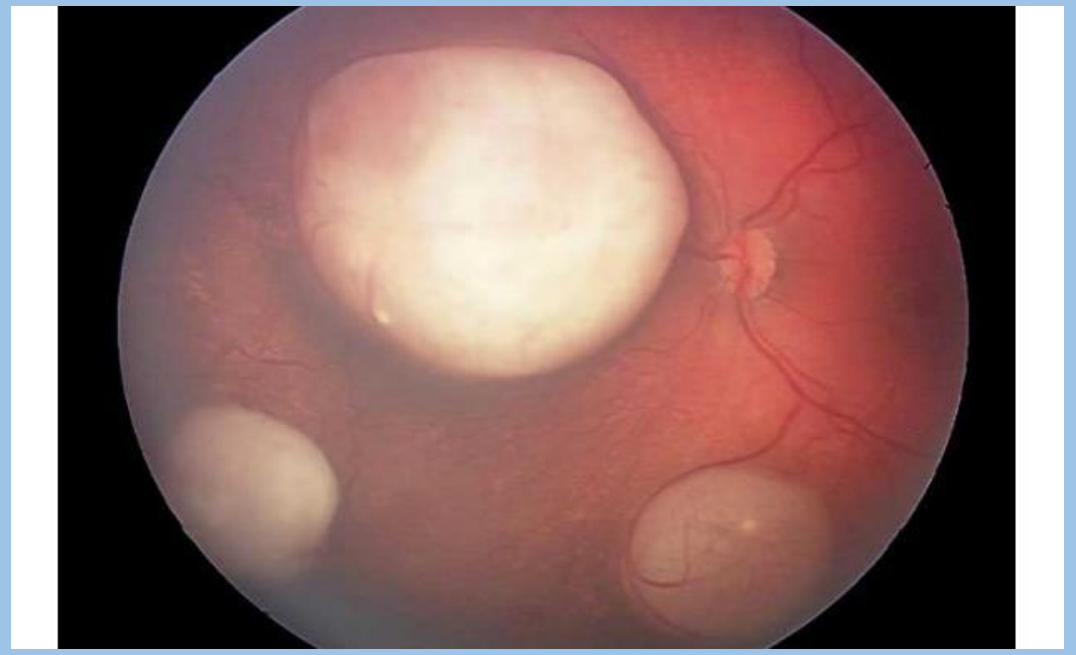


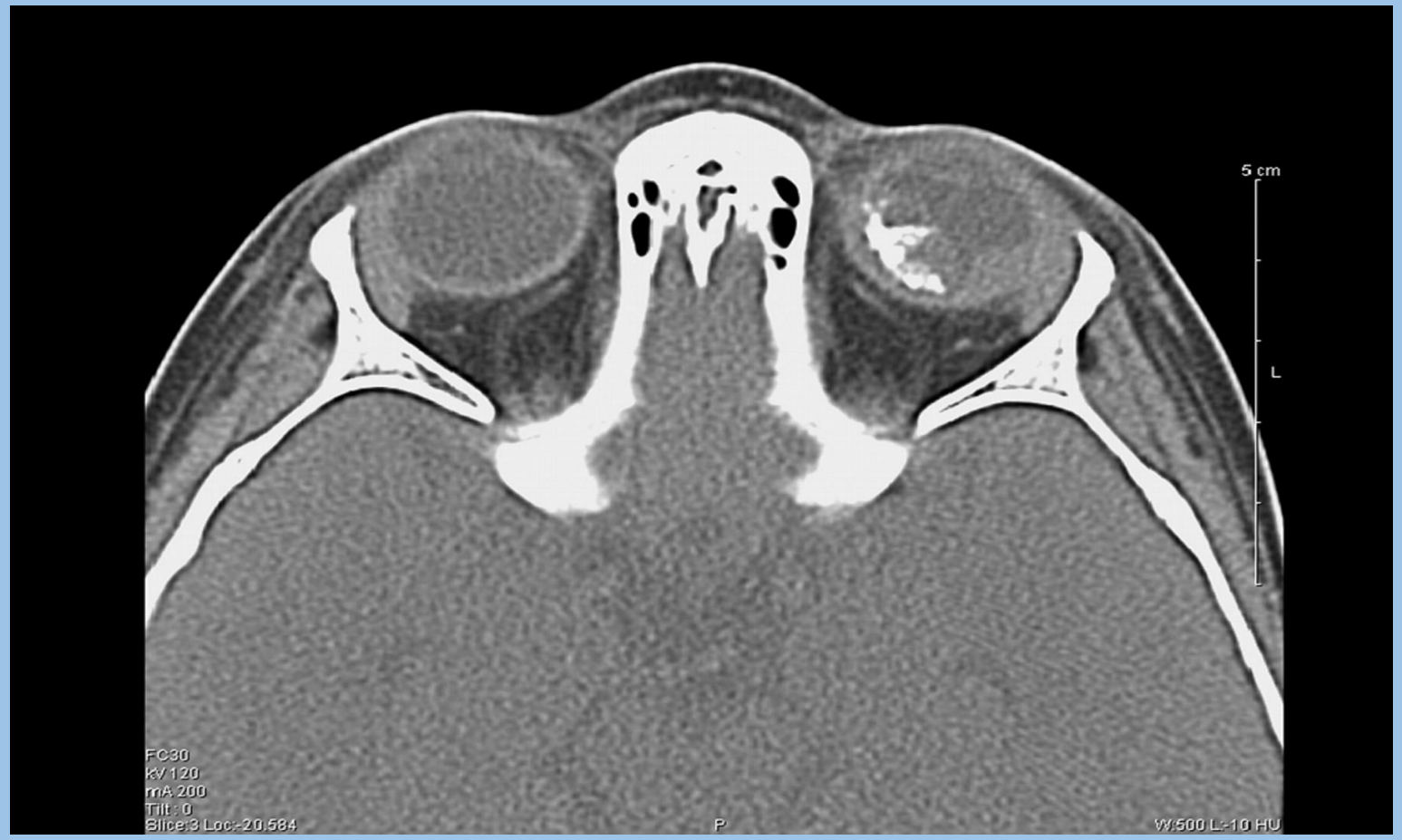
Normal Red Reflex

Abnormal White Reflex

Fundus examination






5 cm
L
FC30
kV 120
mA 200
Tilt: 0
Slice:3 Loc:-20.584
P
W:500 L:-10 HU

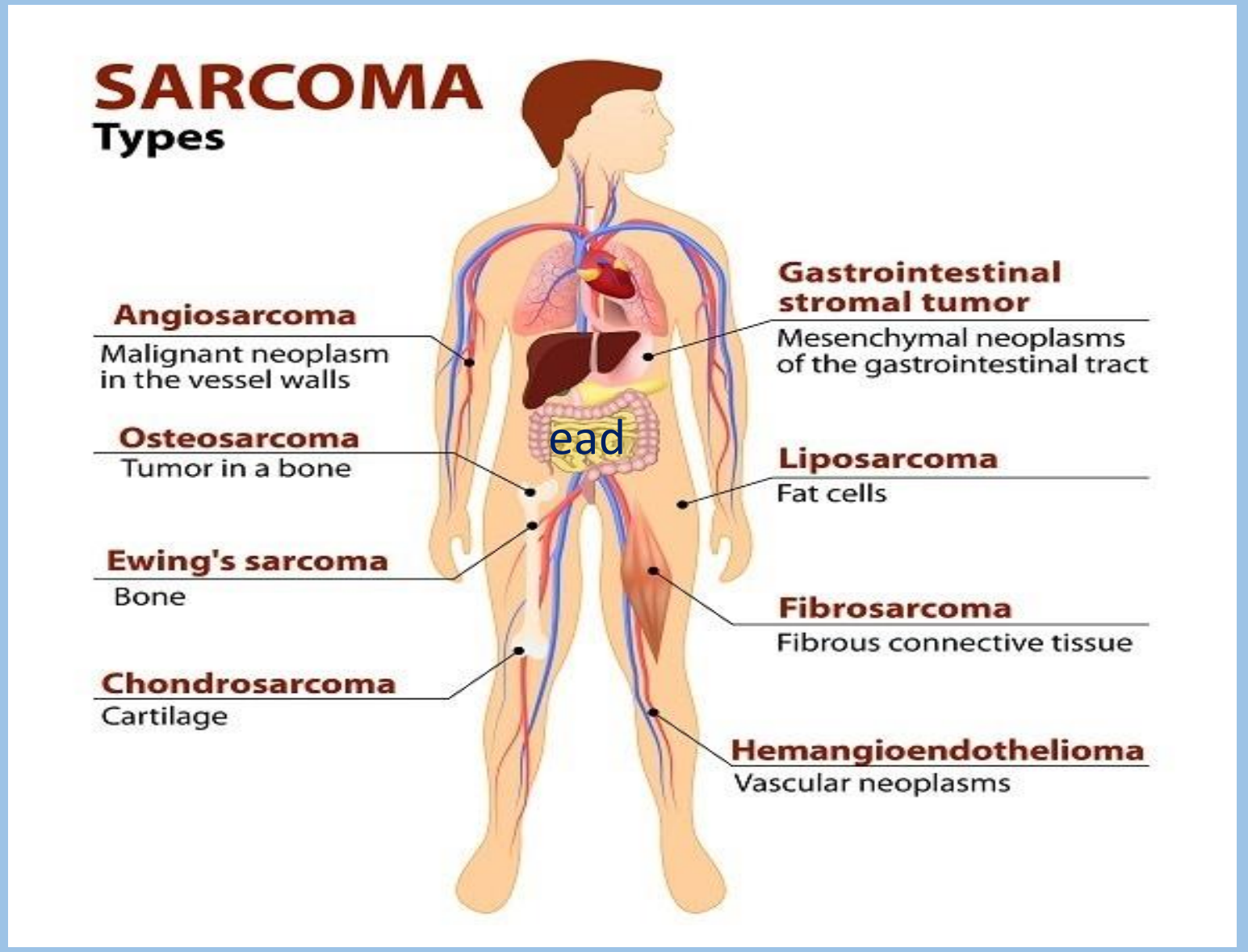
Diagnosis

- Untreated, Retinoblastoma is almost always fatal.
- Early examination is key to survival.

Treatments (4)

- Chemotherapy
- Cryotherapy (freezing treatment)
- Enucleation (removal of the eye)
- External beam radiation therapy (radiation treatment)
- Localized plaque radiation therapy (radiation therapy)
- Photocoagulation (laser treatment)

Sarcomas are rare cancer



ead

Osteosarcoma

Bone tumors represent 2% of all childhood cancers

Osteosarcoma is the most common bone tumor

More common in adolescents (mainly at 10 - 14 years old) can be in adults

Sites:

- Osteosarcoma may arise in any bone
- Most common sites are **long bones of extremities** (near the most proliferative growth plates)
    - Distal end of **femur** 40% near knee joint
    - Proximal end of **tibia** 16% near knee joint
    - Proximal humerus 15%

Osteosarcoma

Clinical presentation:

- Localized bone pain followed by painful enlarging mass
- Pathologic fracture in a minority of cases (5 - 10%)
- Restricted movement in a joint
- Sign & symptoms of metastasis, particularly to bone, lung and regional lymph nodes.

Investigation: Alkaline phosphatase levels often increased, X-ray, CT scan, biopsy for histopathology, immunohistochemical & molecular studies.

Differential diagnosis of OS

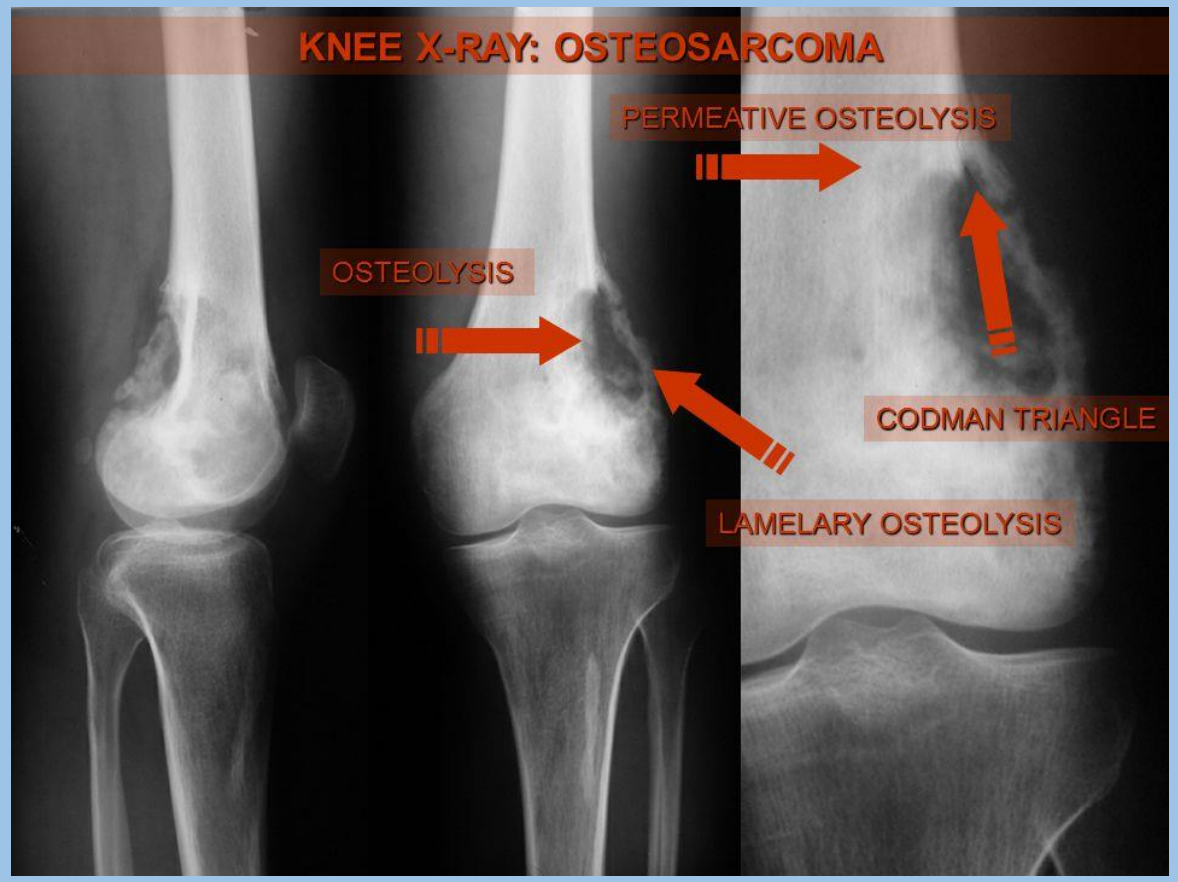
- Osteomyelitis
- Ewing sarcoma
- Metastasis to bone from other cancer
- Aneurysmal bone cyst

Treatment

Orthopaedic Surgical resection often with amputation in advanced stage followed by **chemotherapy.**

Prognosis

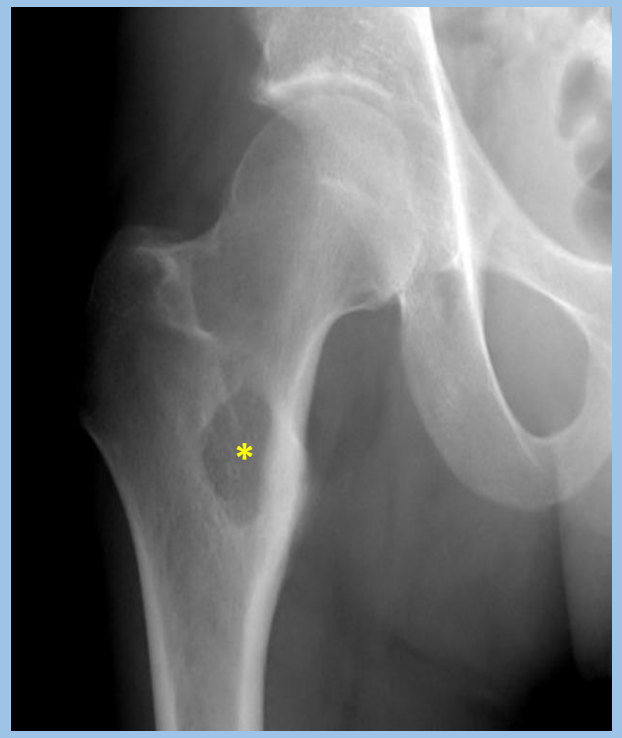
depends on age, sex, site, size, stage, metastasis, histological type, degree of necrosis post induction
Poor prognostic factors: Metastatic tumor to lung & skeletal bone.
Currently, **5-year survival rate** after adequate therapy is approximately **60-80%**



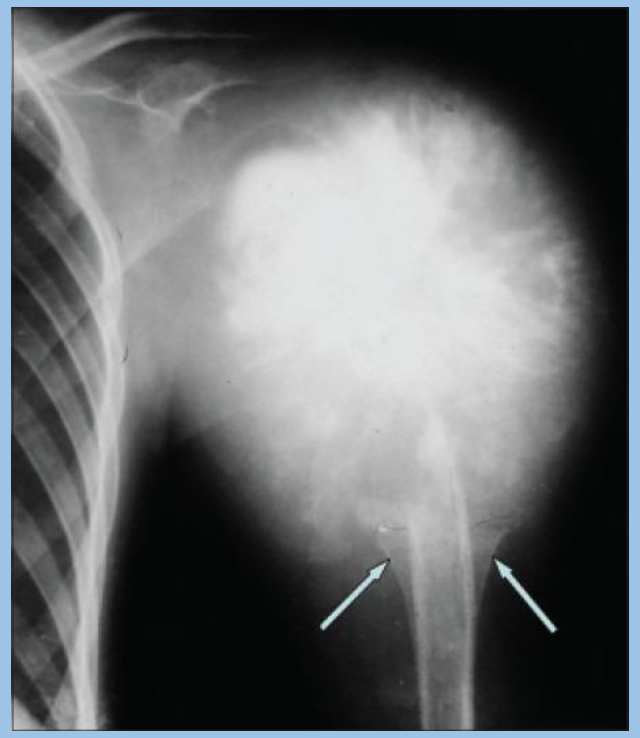
Osteolytic lesions

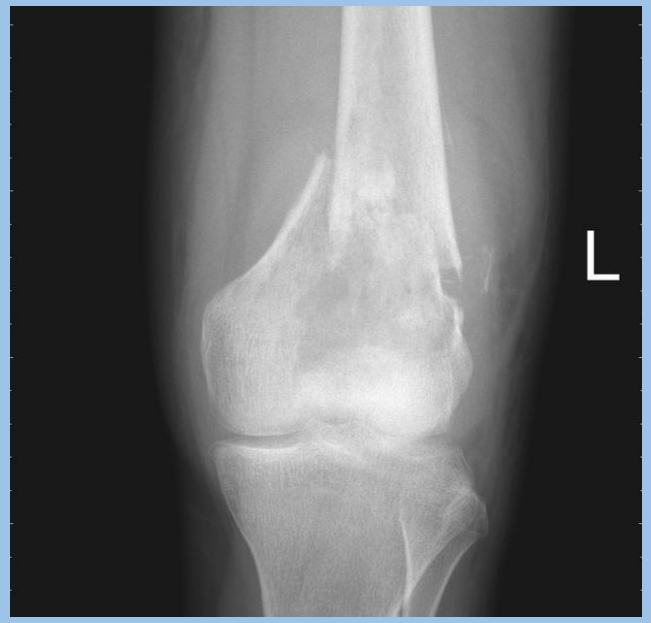
due to invasive, destructive intraosseous mass in osteosarcoma

X ray hip joint shows
Osteolytic lesion at femur
in osteosarcoma

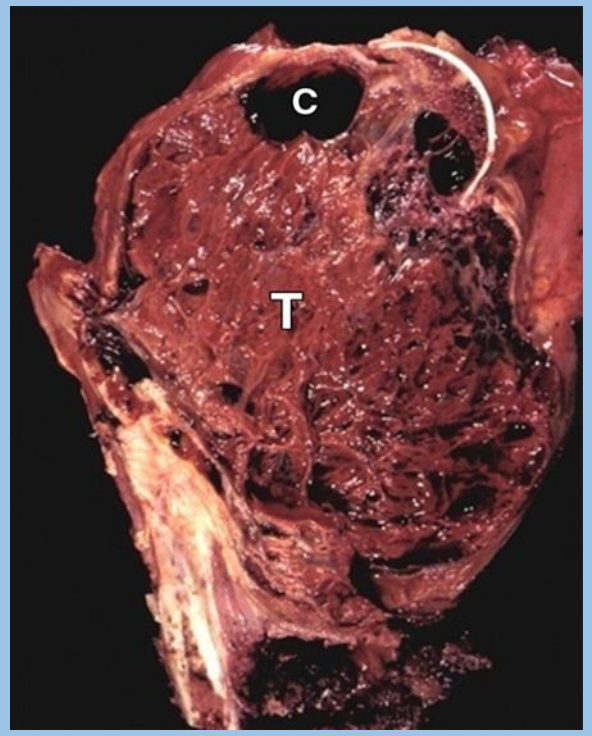


X ray Shoulder joint shows
Sunburst sign (periosteal reactions) at humours
& **Codman triangle** (arrows) tumor permeates cortex and lift up periosteum, then bone deposited in periosteum creating triangle)





Pathological fracture & osteolytic lesion in osteosarcoma



Osteosarcoma

Ewing Sarcoma

It usually affects the bone; however, it develops in the soft tissue around the bone, sometimes called *extra osseous* sarcoma

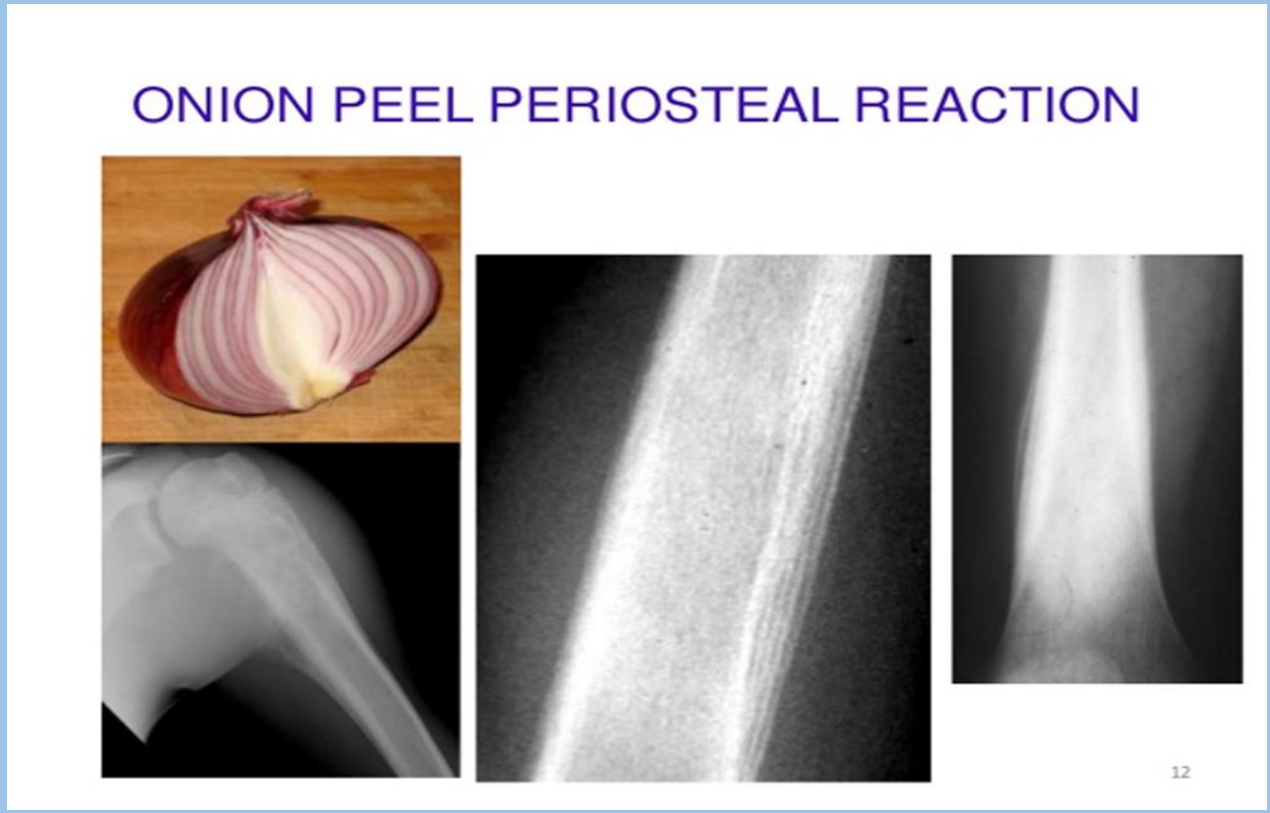
Clinical presentation:

- Bone pain, particularly occurring at night
- Mass or swelling
- Symptoms can sometimes be confused with more common problems such as a **sports injury & growing pain** in children and young people.

Investigation: X-ray (onion sign), CT scan, biopsy for histopathology findings, Immunohistochemical and molecular studies.

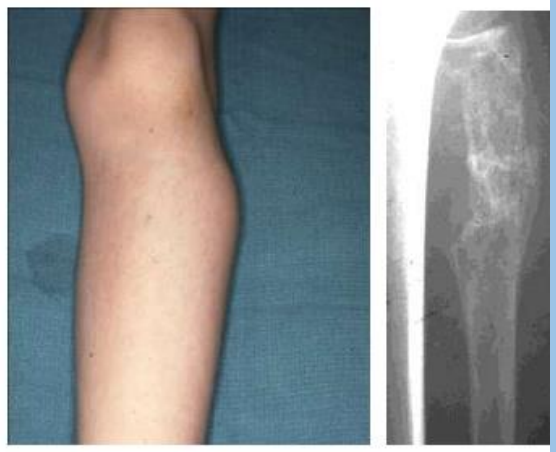
Treatment: Surgery, chemotherapy and radiotherapy

Onion Sign in Ewing sarcoma



Clinical Presentation

- Pain & swelling of affected area
- May also have systemic symptoms:
  - Fever
  - Anemia
  - Weight loss
  - Elevated WBC & ESR,LDH
- Longest lag time in diagnosis for any pediatric solid tumor (mean of 146 days)
- Pathological fracture



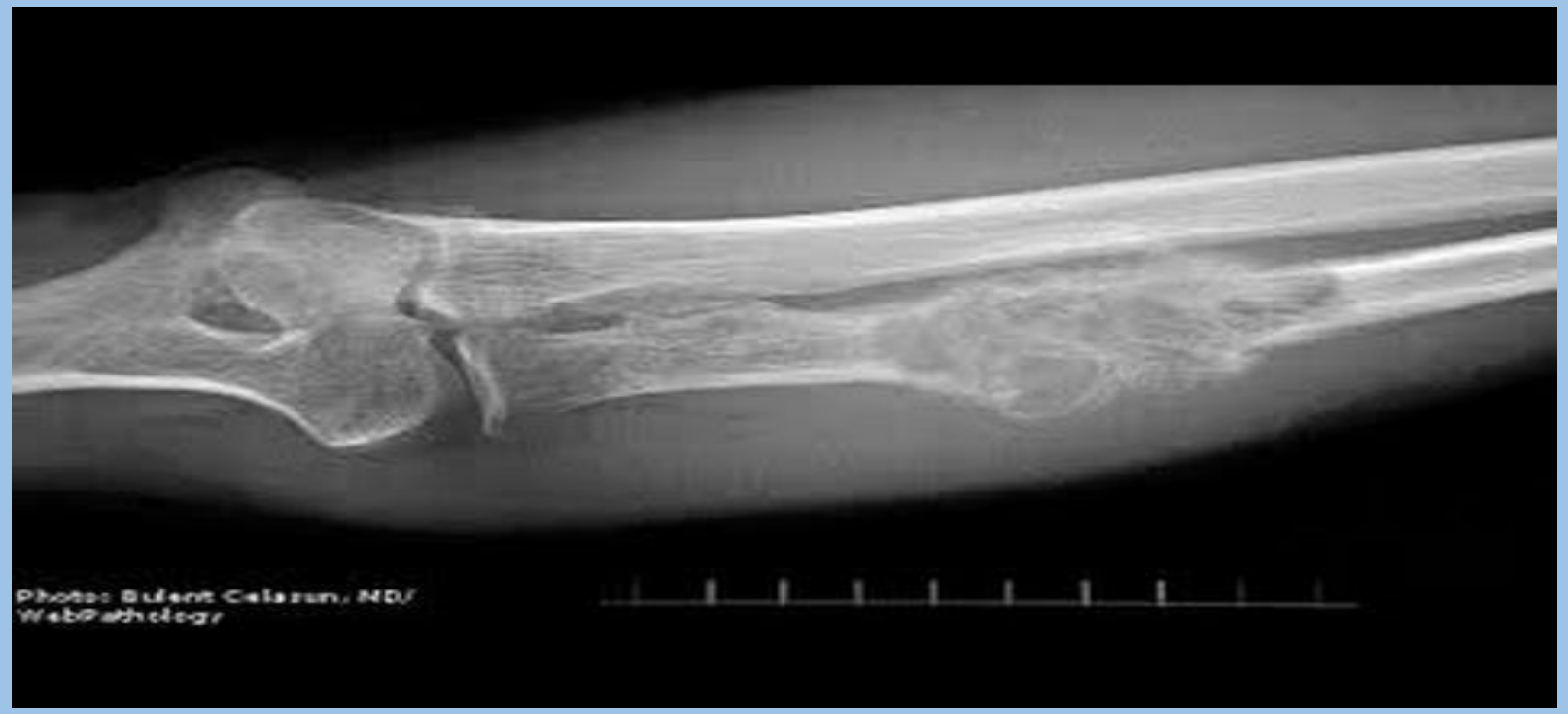
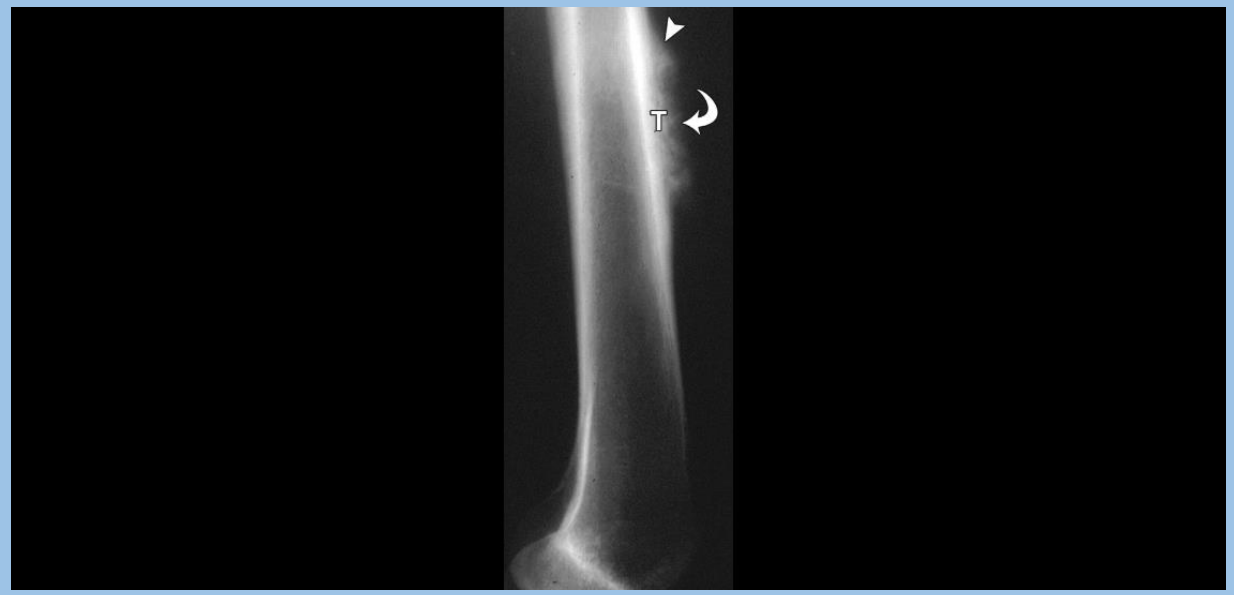


Photo: Bulent Celasun, MD/
WebPathology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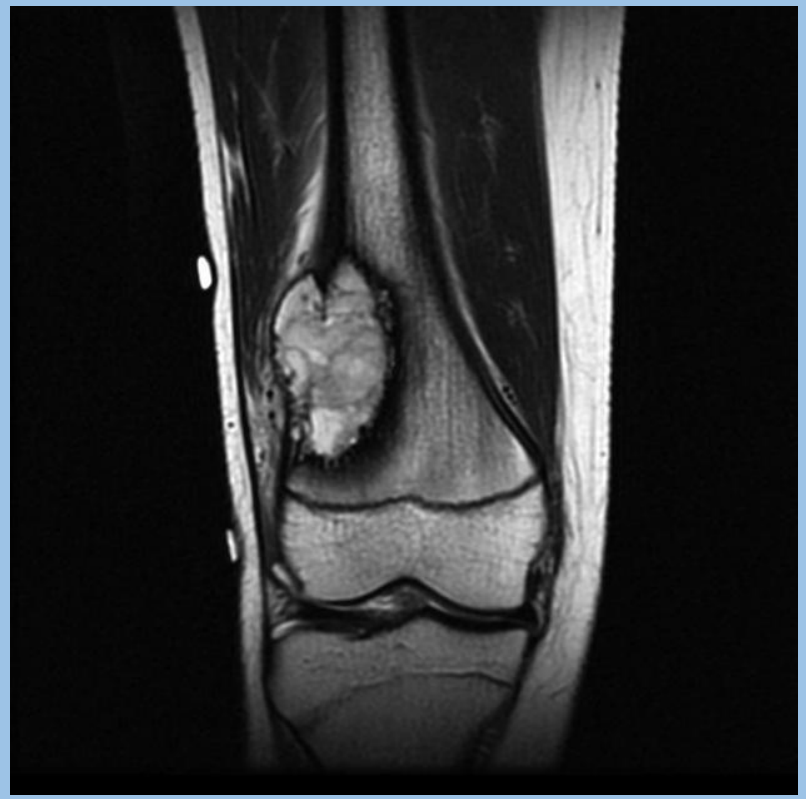

Rhabdomyosarcoma

Tumor of skeletal (striated) muscles cells that have failed to fully differentiate

Sites:

- Head & neck are the most frequent site 35%
- Abdomen & pelvis including abdominal wall and genitourinary muscles 25%
- Extremities 20%
- Other sites 20%

Clinical presentation: varies according to the site of the mass (see next slide)

Investigation for diagnosis: CT scan, Biopsy for histopathology & Immunohistochemical study

Prognosis depends on histological finding (alveolar, Embryonal), stage, site of tumor.

Treatment: Surgery, chemotherapy and radiotherapy


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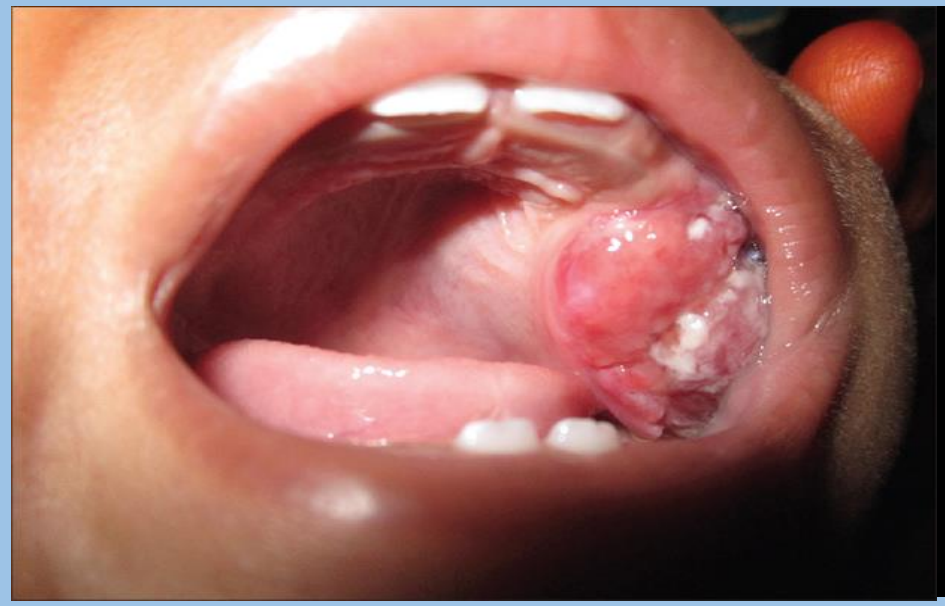
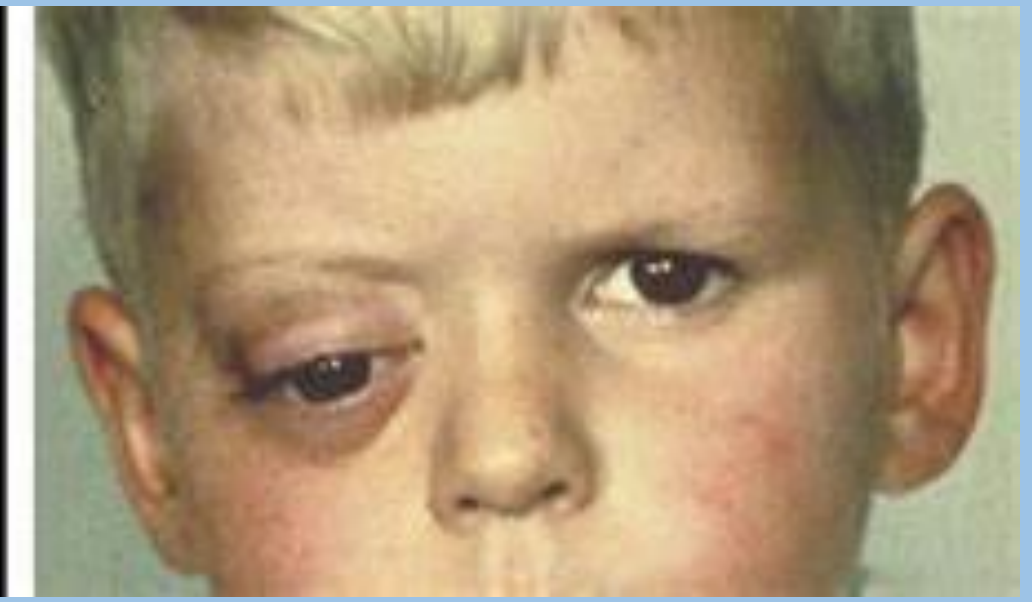
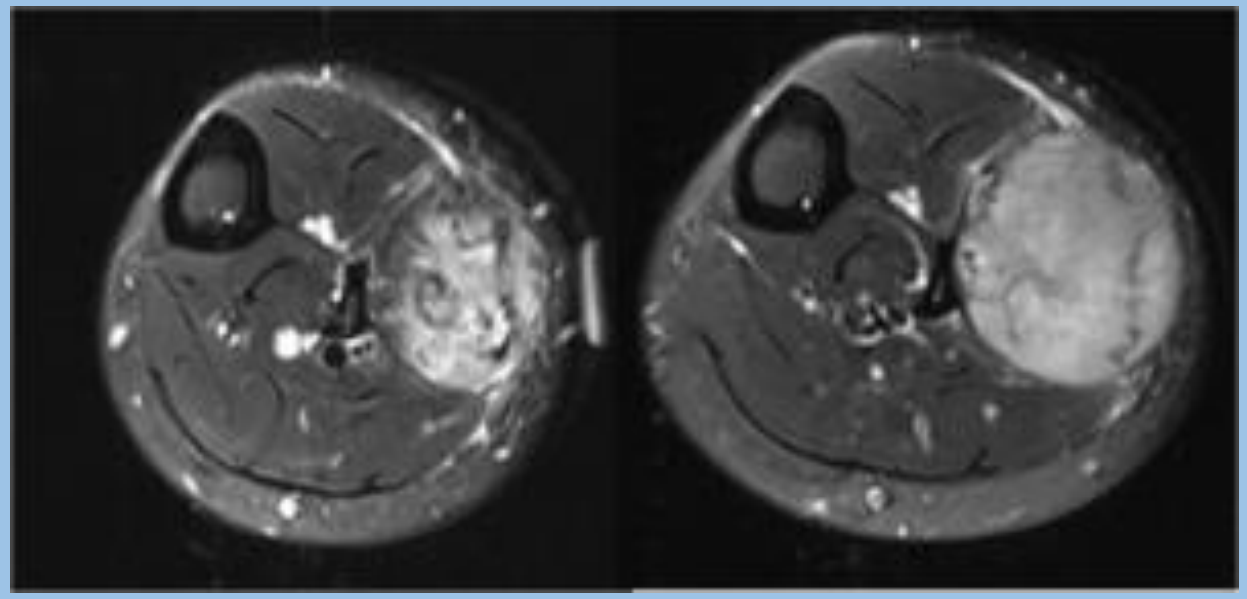
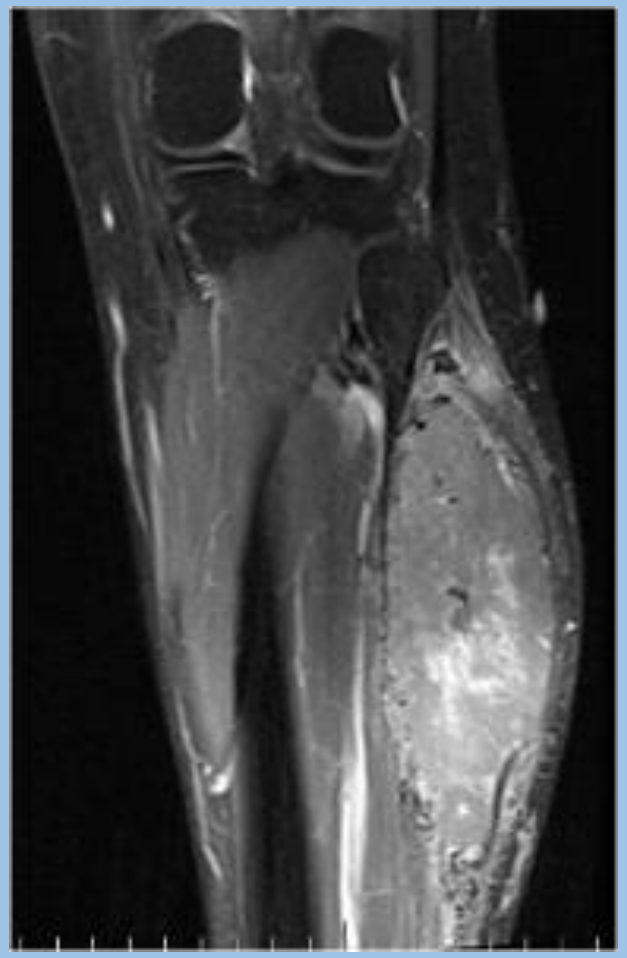




MRI Leg
Rhabdomyosarcoma





Leg swelling differential diagnosis:

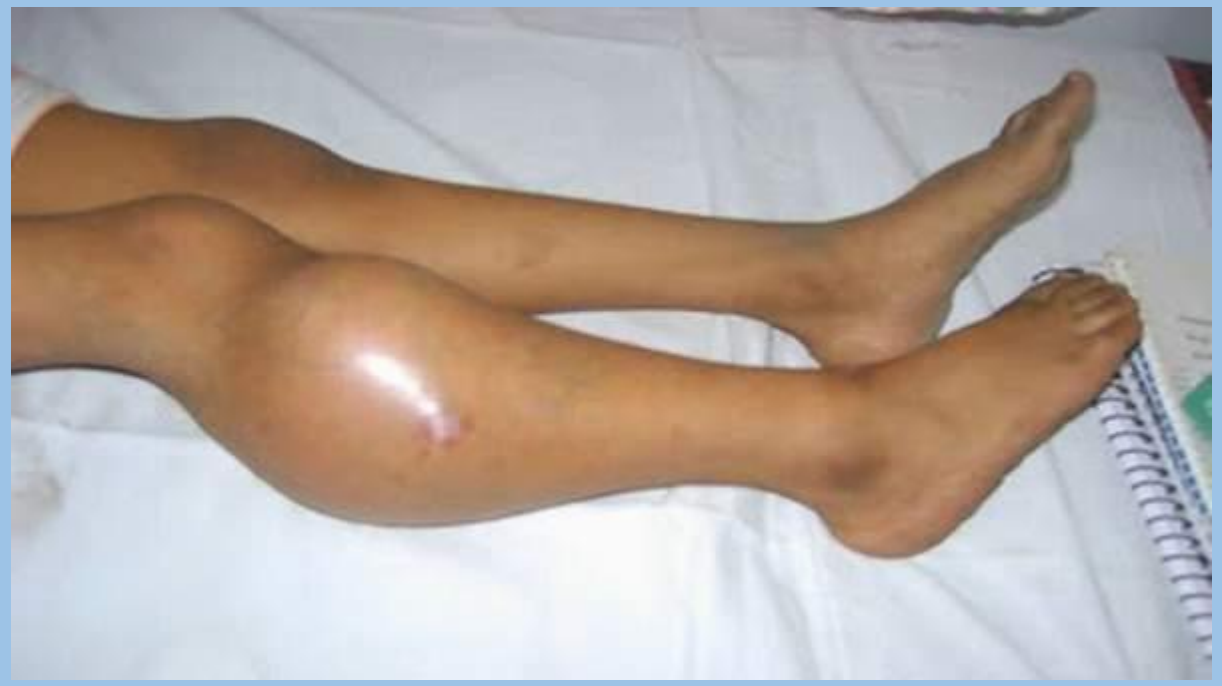
Rhabdomyosarcoma

Osteosarcoma

Ewing sarcoma

Osteomyelitis

etc



THANK YOU

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