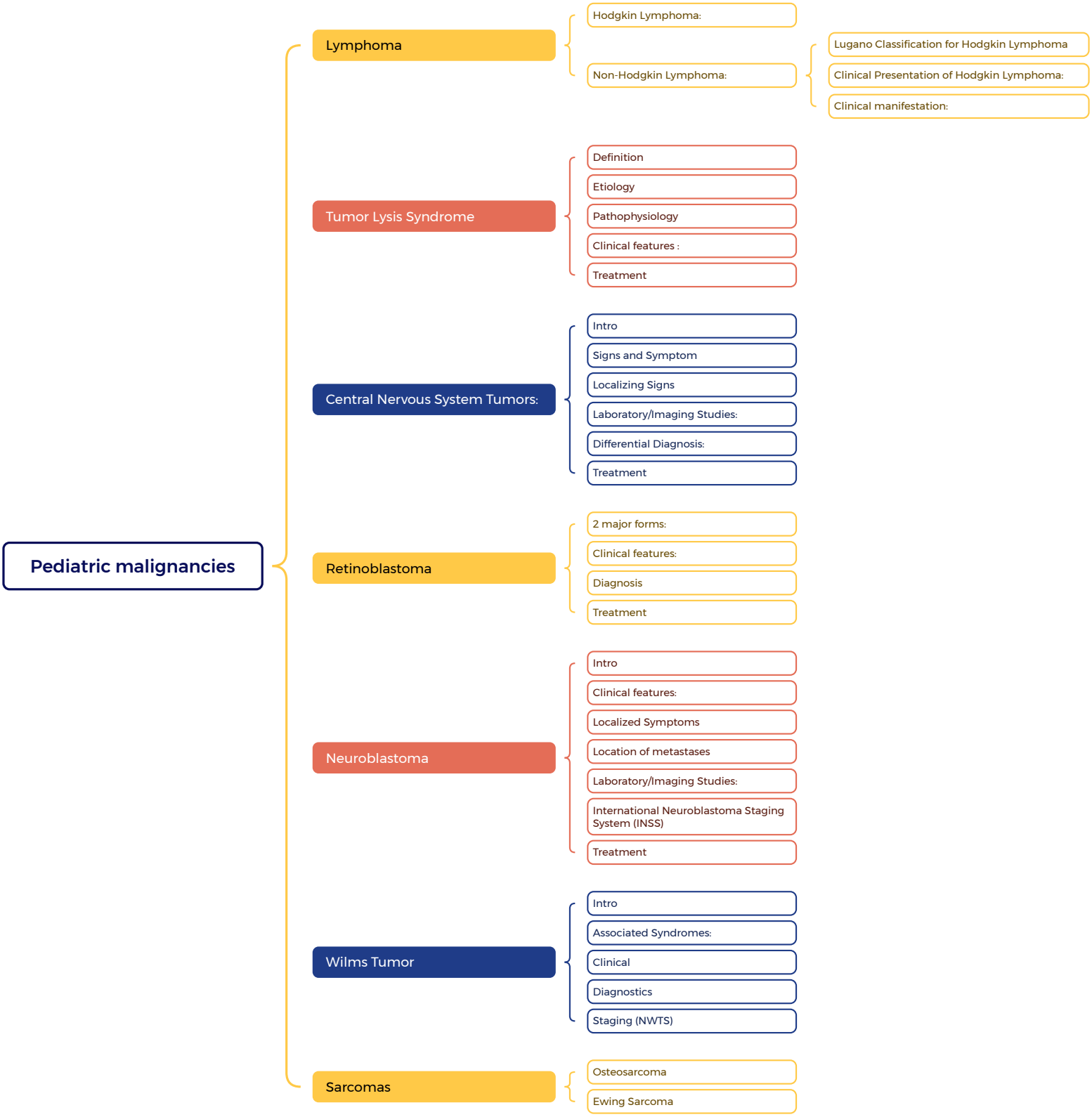
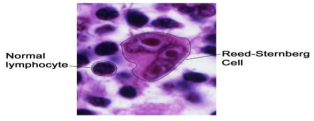
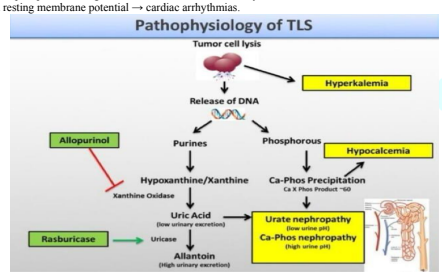
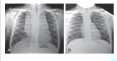
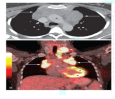
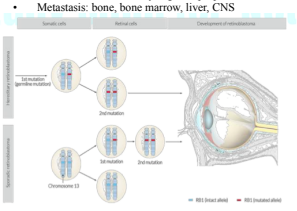


	Lymphoma	Tumor Lysis Syndrome (TLS)
Definition	◦ Neoplastic proliferation of lymphoid cells forming a mass. ◦ Can arise in a lymph node or in extranodal tissue.	• A potentially life-threatening oncologic emergency caused by rapid tumor cell destruction. • Massive release of intracellular contents: potassium (K^+), phosphate (PO_4^{3-}), nucleic acids → uric acid. • Can lead to renal failure and other serious metabolic complications.
Etiology	◦ Third most common cancer among U.S. children ≤14 years old, with an annual incidence of 15 cases per 1 million children. ◦ Most common cancer in adolescents 15–19 years old, accounting for over 25% of newly diagnosed cancers.	• Most common: after cytotoxic therapy in hematologic malignancies (ALL, AML, NHL). • Spontaneous TLS: occurs in patients with very high tumor burden, even before treatment.
Pathophysiology	• **Hodgkin Lymphoma (HL)** 1. Classic Hodgkin Lymphoma - Nodular sclerosing - Mixed cellularity - Lymphocyte predominant - Lymphocyte depleted 2. Nodular Lymphocyte Predominant • Pathognomonic Feature: Reed-Sternberg (RS) cell. - Large cell, 15–45 µm in diameter. - Multiple or multilobulated nuclei. - Hallmark of HL, although similar cells may appear in infectious mononucleosis, non-Hodgkin lymphoma, and other conditions. - Clonal origin from germinal center B cells but typically lost most B-cell gene expression and function.  • **Non-Hodgkin Lymphoma (NHL)** • Includes multiple subtypes: - Burkitt lymphoma - Lymphoblastic lymphoma - Diffuse large B-cell lymphoma - Primary mediastinal B-cell lymphoma - Anaplastic large cell lymphoma - Other less common types	1. **Tumor cells lyse** → release K^+, PO_4^{3-}, nucleic acids into blood. 2. **Nucleic acids** → uric acid → hyperuricemia → urate nephropathy → acute kidney injury (AKI). 3. **Hyperphosphatemia** → PO_4^{3-} binds Ca^{2+} → calcium phosphate crystals → renal tubule obstruction → AKI. 4. **Hypocalcemia** secondary to phosphate binding → increased neuronal excitability → risk of seizures. 5. **Hyperkalemia** → altered resting membrane potential → cardiac arrhythmias. 6. 
	Clinical Presentation of Hodgkin Lymphoma: ◦ Painless lymphadenopathy. ◦ Mediastinal mass (~2/3 of patients). ◦ Constitutional symptoms. ◦ B symptoms (prognostic): • Weight loss of 10% within 6 months. • Drenching night sweats. • Unexplained fevers >38°C for 3 consecutive days. ◦ Other symptoms (not prognostic): • Fatigue, anorexia, mild weight loss. • Pain immediately after alcohol consumption. • Generalized pruritus, often severe in advanced disease. ◦ Laboratory findings: • Markers of inflammation and reticuloendothelial system activation (↑CRP, ESR, ferritin, copper). • Anemia of chronic inflammation. ◦ Immune dysregulation: • Autoimmune neutropenia. • Autoimmune hemolytic anemia (AIHA). • Immune thrombocytopenia (ITP). • Nephrotic syndrome.	• Age-specific Notes: ◦ Non-Hodgkin lymphoma: presentation may vary between 0–14 years and 15–19 years adolescents.	• Directly related to electrolyte disturbances and kidney injury. • Renal: edema, oliguria, decreased urine output • Cardiac: palpitations, arrhythmias, syncope (hyperkalemia) • Neuromuscular: tetany, muscle cramps, seizures (hypocalcemia) • GI: nausea, vomiting, diarrhea **Table 2.10** Criteria for laboratory and clinical diagnosis **The Cairo–Bishop definition (2004)** Uric acid: ≥476µmol/L (8mg/dL) or 25% increase Potassium: ≥6.0mmol/L or 25% increase Phosphate: ≥1.45mmol/L or 25% increase Calcium: <1.75mmol/L or 25% decrease ≥2 of these features between 3 days pre- and 7 days post-tumour treatment encompasses the *laboratory* definition. A *clinical* diagnosis of TLS can be made if AKI, arrhythmias, or seizures occur in conjunction with the laboratory features. Cairo MS, Bishop M (2004). *British Journal of Haematology*, **127**(1), 3–11.
Clinical Features	◦ Very high proliferation rate; early diagnosis and treatment are critical. ◦ High risk for tumor lysis syndrome (TLS). ◦ Can invade CNS and bone marrow. ◦ Mediastinal lymphadenopathy may produce cough or shortness of breath. ◦ B symptoms (fever, night sweats, weight loss). ◦ Burkitt lymphoma may present with abdominal mass or jaw mass, especially in children.	
Treatment	• Imaging Examples (for context): ◦ Anterior mediastinal mass in Hodgkin lymphoma before therapy. ◦ PET/CT may show marked FDG uptake and associated neck masses. ◦ Post-chemotherapy imaging shows reduction of mediastinal masses.	1. IV isotonic fluids: correct electrolytes and maintain urine output 2. Hyperkalemia: cardiac monitoring + IV insulin + dextrose 3. Hyperphosphatemia: hydration, phosphate binders (e.g., sevelamer) 4. Hypocalcemia: usually resolves with phosphate management 5. Hyperuricemia: ◦ Allopurinol → inhibits uric acid production ◦ Rasburicase → converts uric acid → allantoin 6. Severe cases: urgent hemodialysis if K^+, phosphate, or uric acid are critically high
Prevention	**Lugano Classification for Hodgkin Lymphoma** Stage I: Involvement: - **One node** or group of adjacent nodes; Extranodular atatus: - **Single** extranodal lesions without nodal involvement Stage II: Involvement: - **Two or more** nodal groups on the same side of the diaphragm; Extranodular atatus: - Stage I or II by nodal extent with **limited contiguous extranodal** involvement Stage II bulky: Involvement: - II **as above** with "bulky" disease; Extranodular atatus: - Not applicable Stage III: Involvement: - Nodes **on both sides** of the diaphragm - Nodes above the diaphragm with spleen involvement; Extranodular atatus: - Not applicable Stage IV: Involvement: - Additional **noncontiguous** extralymphatic involvement; Extranodular atatus: - Not applicable  **A:** Anterior mediastinal mass in a patient with Hodgkin disease before therapy. **B:** After 2 mo of chemotherapy  Hodgkin lymphoma in a young woman A.CT show a homogeneous anterior mediastinal mass (arrows), The arrowhead points to the SVC., **A.** Ascending acrta B. PET/CT in the coronal plane. The mass shows marked FDG activity (arrows). Note the associated left neck mass (arrowhead)	• Aggressive IV hydration before chemotherapy • Medications to prevent hyperuricemia (allopurinol or rasburicase)

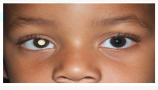
	Pediatric Central Nervous System (CNS) Tumors	Retinoblastoma	Pediatric Sarcomas	
			1. Osteosarcoma (OS)	2. Ewing Sarcoma (ES)

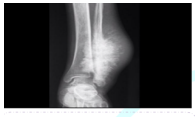
Epidemiology & Etiology	• Annual incidence: ~47 cases per 1 million children <20 yrs.
	• Highest in infants and children ≤5 yrs: ~52 cases per 1 million; mortality ~30%.
	• Highest morbidity among pediatric malignancies, primarily neurological.
	• Most common solid tumors in children.
	
	• Mostly primary tumors:
	  ◦ Low-grade astrocytomas
	  ◦ Embryonic neoplasms: medulloblastoma, ependymoma, germ cell tumors
	
	• Etiology often unknown
	• Risk increased with inherited syndromes:
	  ◦ Neurofibromatosis types 1 & 2 (NF1, NF2)
	  ◦ Li-Fraumeni syndrome
	  ◦ von Hippel-Lindau syndrome
		• Rare retinal tumor; most present by age 5 years
		• Hereditary (25%): bilateral, multifocal; germline RB1 mutations, median age ~15 months
		• Non-hereditary (majority): unilateral/unifocal; somatic RB1 mutations, median age ~30 months
			• Can occur de novo or as a late effect of radiation therapy
			• Associated with Li-Fraumeni syndrome (TP53 mutation)
				• Primitive neuroectodermal tumor (PNET family)
				• Often affects axial skeleton more than OS
				• Common sites: pelvis, femur, ribs

Clinical Approach	• Imaging: MRI brain & spine (study of choice)
	• CSF analysis: histology essential for metastasis
	• LP: contraindicated if increased ICP
	
	Signs and Symptoms
	General and Nonlocalizing Symptoms / **Increased Intracranial Pressure**
	- Headache . / - Headache, irritability.
	- Vomiting . / - lethargy and vomiting .
	- **Behavioral changes** (listlessness) / - Bulging fontanelle/separation of sutures .
	- Developmental delay . / - Papilledema
	- Weight gain/loss. / - **Parinaud syndrome**, upward gaze palsy.
	- Others : endocrine or autonomic dysfunction, failure to thrive). / - Others : anisocoria (unequal pupil size), ataxia, head tilt.
	
	Localizing Signs
	Anatomic Location / **Common signs and symptoms**
	1. Frontal lobe / - Personality changes, decreased speech (Broca's), seizures.
	2. Temporal lobe / - Seizures, poor memory, language comprehension (Wernicke's).
	3. Parietal lobe / - Decreased sense of touch,pain, poor spatial and visual perception, poor interpretation of language
	4. Occipital lobe / - Poor or Loss of Vision.
	5. Cerebellum / - Ataxia, muscle movement, posture.
	6. Brain stem / - Weakness, cranial neuropathies (III-XII), autonomic fxn.
	7. Thalamus / - Weakness/motor control, consciousness, sleep/wake cycle
	8. Hypothalamus / - Autonomic function as temp regulation, thirst, hunger.
	- Endocrinopathies
		• Leukocoria (most common presenting sign)
		• Strabismus
		• Painful, red eye
		• Loss of vision
		• Retinal detachment (later stages)
		• Rare: orbital cellulitis, nystagmus, proptosis
		• Metastasis: bone, bone marrow, liver, CNS
		
		 
			• Pain and mass at the primary site
			• Typically involves metaphysis of long bones
			• Most common sites: distal femur > proximal tibia > proximal humerus
			• Spread:
			  ◦ Skip lesions
			  ◦ Hematogenous → lungs and other bones
				• Local pain and mass
				• Systemic symptoms: fever, weight loss
				• Metastasis: lungs, bone, bone marrow

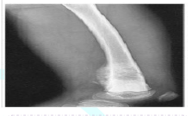
Differential Diagnosis	• Malignant, metastatic, or benign tumors
	• AV malformation, aneurysm
	• Brain abscess, intracranial hemorrhage
	• Pseudotumor cerebri
	• Vasculitis
		• Examination under anesthesia for tumor visualization and intraocular pressure
		• Imaging: ocular ultrasound, orbit & brain MRI, bone scan, bone marrow studies
		• Avoid CT scan: radiation risk in RB1 mutation
		• Biopsy contraindicated: risk of tumor seeding
			• Plain X-ray: osteoblastic, osteolytic, or mixed
			  ◦ Classical signs: Codman triangle (periosteal elevation), sunburst pattern (tumor extension through periosteum)
			• Chest CT: rule out pulmonary metastasis
			• Biopsy: confirm diagnosis
				• Bilateral bone marrow biopsies: detect marrow metastases
				• Plain X-ray:
				  ◦ Characteristic onion skin appearance
				  ◦ Can also show Codman triangle or sunburst pattern

Treatment	• Multimodal: surgery, chemotherapy, radiation • Surgery: complete excision or maximal debulking • Dexamethasone: high-dose for tumor-associated edema • 5-year overall survival: ~50–60%	• Surgery, chemotherapy, radiation, laser photocoagulation Note: Leukocoria = white reflex in pupil instead of normal red reflex.	• Surgery + chemotherapy • Radiation therapy: NOT used	• Surgery + chemotherapy + radiation

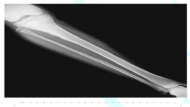
	Tumor Location (NCI SEER Data)
	o Infratentorial tumor location (43.2%).
	o Supratentorial region (40.9%).
	o Spinal cord (4.9%).
	o Multiple sites (11%).
	
	1. Infratentorial : Make up the majority of pediatric brain tumor
	- Most common malignant : medalloblastoma (originate from embryoic stem cells)
	
	2. Supratentorial :
	- Most common is craniopharyngioma, remenant of rathkes pouch of anterior pituitary gland.
		 	1. Soft tissue sarcomas
			  ◦ Most common: Rhabdomyosarcoma
			2. Bone sarcomas
			  ◦ Osteosarcoma (OS)
			  ◦ Ewing Sarcoma (ES)	



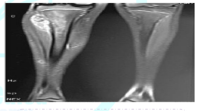
An ill-defined sclerotic area affecting the metaphysic of distal fibula with an aggressive periosteal reaction (Sunburst type)



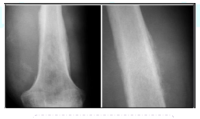
Radiograph of an osteosarcoma of the femur with typical "Sunburst appearance" of bone formation.



Radiograph of tibial Ewing sarcoma showing periosteal elevation or "onion-skinning"



MR image of tibial Ewing sarcoma showing a large associated soft tissue mass.



Ewing sarcoma onion skin

Comparison of Features of Osteosarcoma and the Ewing Family tumor

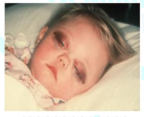
FEATURE	OSTEOSARCOMA	EWING FAMILY OF TUMORS
Age	2nd decade	2nd decade
Race	All races	Primarily whites
Sex (M:F)	1.5 : 1	1.5 : 1
Predisposition	Retinoblastoma, Li-Fraumeni syndrome, Paget disease, radiotherapy	None known
Site	Metaphyses of long bones	Diaphyses of long bones, flat bones
Presentation	Local pain and swelling; often history of injury	Local pain and swelling; fever
Radiographic findings	Sclerotic destruction (less often lytic); sunburst pattern	Primarily lytic, multilaminar periosteal reaction ("onion-skinning")
Differential diagnosis	Ewing sarcoma, osteomyelitis	Osteomyelitis, eosinophilic granuloma, lymphoma, neuroblastoma, rhabdomyosarcoma
Metastasis	Lungs, bones	Lungs, bones
Treatment	Chemotherapy	Chemotherapy
	Ablative surgery of primary tumor	Radiotherapy and/or surgery of primary tumor
Outcome	Without metastases, 70% cured; with metastases at diagnosis, ≤20% survival	Without metastases, 65–75% cured; with metastases at diagnosis, 20–30% survival

	Neuroblastoma	Wilms Tumor (Nephroblastoma)
• Definition:	◦ Embryonal malignancy. ◦ Malignant neuroendocrine tumor of the sympathetic nervous system. ◦ Originates from neural crest cells and may secrete catecholamines.	◦ Most common primary malignant renal tumor in childhood. ◦ Second most common malignant abdominal tumor after neuroblastoma. ◦ Pathology: Arises from primitive metanephric blastema (precursor of normal kidney).
• Epidemiology	◦ Most common malignancy in infancy. ◦ Fourth most common childhood malignancy. ◦ Median age: 22 months (mostly <5 years). ◦ Most common extracranial solid tumor of childhood (8–10%).	◦ Mean age: 3–3.5 years. ◦ Mostly unilateral; up to 10% bilateral. ◦ Median age unilateral: 44 months. ◦ Median age bilateral: 31 months.
• Location	◦ Adrenal glands: 45% ◦ Retroperitoneal sympathetic ganglia: 25% ◦ Paravertebral chest ganglia: 15% ◦ Neck: 5% ◦ Pelvic sympathetic tissue: 5% ◦ Can occur wherever sympathetic nervous tissue exists.	• Etiology: ◦ Exact cause unknown. ◦ Associated with genetic syndromes and mutations.
• Clinical Features:	◦ General Symptoms: Failure to thrive, weight loss, fever, nausea, vomiting, loss of appetite, hypertension. ◦ Local Symptoms: Abdominal suprarenal mass (classic presentation), chest or neck mass depending on site. ◦ Paraneoplastic Effects: Vasoactive intestinal peptide (VIP) secretion, opsoclonus-myoclonus syndrome. ◦ Metastatic Symptoms: Bone pain, anemia (bone marrow involvement), subcutaneous nodules, periorbital ecchymoses ("raccoon eyes").	◦ Palpable abdominal mass: smooth, non-tender, unilateral, does not cross midline. ◦ Other symptoms: abdominal pain (20–40%), fever, hypertension, hematuria. ◦ Most common presentation: incidentally discovered by parents. • Associated Syndromes: ◦ WAGR Syndrome: ▪ Deletion of WT1 gene on chromosome 11. ▪ Components: Wilms tumor (50%), aniridia, genitourinary anomalies, mental retardation.

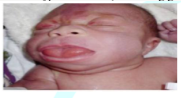
Localized Symptoms

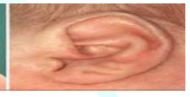
Location of primary tumors	Associated signs and symptoms
Abdomen	- Palpable, firm, irregular abdominal mass that may cross the midline, in contrast to nephroblastoma, which is smooth and usually does not cross the midline. - Abdominal distension and pain, Hepatomegaly ,Constipation
Chest (paravertebral ganglia)	- Spinal cord compression : back pain, weakness, numbness, ataxia, loss of bowel or bladder control. - Dyspnea, cough, Inspiratory stridor.
Neck	- Horner syndrome, if the stellate ganglion is involved - Symptoms due to spinal cord compressions.

Location of metastases	Associated signs and symptoms
Skin	- Subcutaneous nodules
Bones	- Bone pain - Anemia (bone marrow suppression)
Orbit of the eye	- Periorbital ecchymoses (raccoon eyes) , Proptosis.



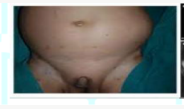
Raccoon eyes

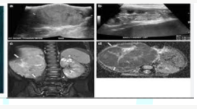




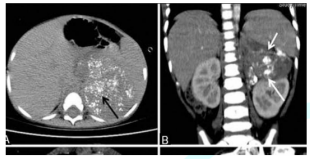
◦ Beckwith-Wiedemann Syndrome:
▪ WT2 gene mutations on chromosome 11.
▪ IGF-2 overactivity.
▪ Features: hyperinsulinism, neonatal gigantism, macrosomia, macroglossia, omphalocele, visceromegaly, earlobe creases, hemihyperplasia.

◦ Denys-Drash Syndrome:
▪ Diffuse mesangial sclerosis.
▪ Wilms tumor.
▪ Male pseudohermaphroditism.

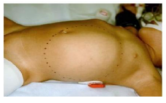


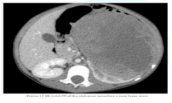


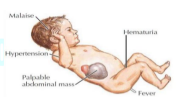
• Laboratory and Imaging Studies:	◦ CBC and X-ray (calcifications may be present). ◦ Urinary catecholamines (VMA, HVA) elevated in ~90%. ◦ CT scan: chest, abdomen, pelvis; may show calcification and hemorrhage. ◦ MIBG scan for localization and metastasis. ◦ Bilateral bone marrow aspiration and biopsy for marrow involvement. ◦ Tissue biopsy required for definitive diagnosis.	◦ History: pre-existing conditions, family history of cancer or congenital defects. ◦ Physical Examination: BP, weight, height, abdominal masses, congenital anomalies. ◦ Laboratory Workup: CBC, platelets, urine analysis, kidney and liver function tests, electrolytes. ◦ Imaging Studies: ▪ Ultrasound: evaluates necrosis, hemorrhage, hydronephrosis, differentiates solid vs cystic masses. ▪ Doppler US: evaluates collecting system, detects tumor thrombi in renal veins/IVC. ▪ CT scan: defines tumor extent, contralateral kidney, metastasis; chest CT screens pulmonary metastasis. ▪ MRI: used if extensive tumor thrombus or differentiation from nephrogenic rests is needed.

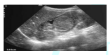


- A left **supra-renal mass** with typical stippled calcifications (arrow in A) and a mass with calcifications (arrow in B) displacing the left kidney inferiorly.

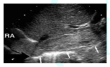




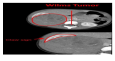




- Rounded solid appearing mass is seen in the interpolar region of the right kidney.
- The mass shows no obvious calcifications



- IVC thrombosis in a child with Wilms' tumor. Longitudinal sonogram of the IVC shows echogenic tumor thrombus (arrows) filling and expanding the IVC lumen and extending into the right atrium (RA)



- CT is useful to define the extent of disease, integrity of contralateral kidney and metastasis.
- Chest CT to screen for pulmonary metastasis

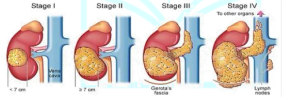
• Treatment	◦ Determined by patient age and clinical stage. ◦ Spontaneous remission possible even in metastatic disease.	◦ Stage-dependent. ◦ Neoadjuvant chemotherapy → nephrectomy → adjuvant chemotherapy.

International Neuroblastoma Staging System (INSS)

Stage	Definition
1	- **Localized** tumor - **Complete** gross excision with or without microscopic residuals - **Negative** ipsilateral lymph nodes
2A	- **Localized** tumor - **Incomplete** gross excision - **Negative** ipsilateral lymph nodes
2B	- **Localized** tumor - **Complete or incomplete** gross excision - **Positive** ipsilateral lymph nodes
3	- **Unresectable unilateral** tumor that crosses the midline with or without lymph node involvement - Any tumor with **positive** contralateral lymph nodes - **Midline tumor** with bilateral tumor or lymph node involvement
4	- Any tumor with dissemination to distant **lymph nodes or other organs** (bone, liver, skin), with the exception of Stage 4S disease
4s	- Localized primary tumor with **dissemination to skin**, liver, or bone marrow, occurring in infants < 12 months

National Wilms Tumor Study (NWTS) staging

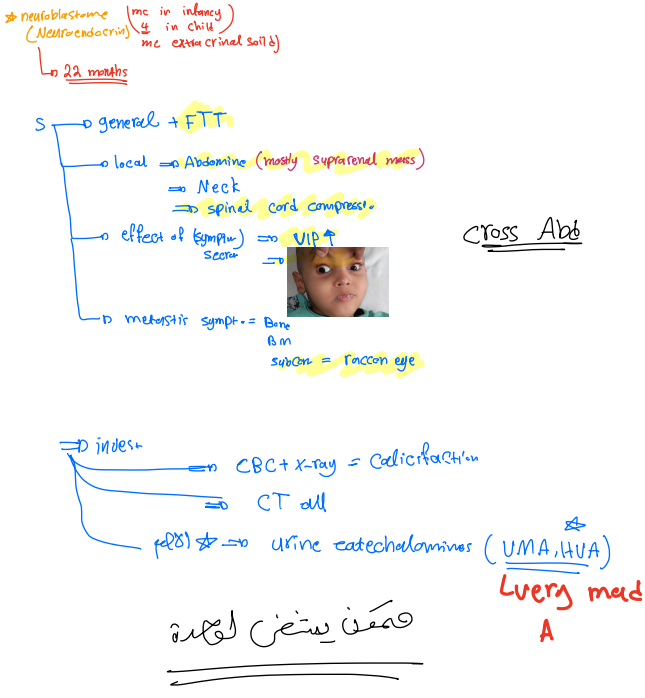
Stage I	- Tumor **confined** to the kidney & completely excised
Stage II	- Tumor **outside** the kidney but completely excised - **Local tumor** spillage during surgery - Lymph nodes negative
Stage III	- **Non hematogenous** disease confined to the abdomen - Perioperative rupture of renal capsule - **Diffuse tumor** spillage during surgery - **Peritoneal** implants - Positive lymph nodes
Stage IV	- **Hematogenous metastases** to lungs or liver
Stage V	- **Bilateral** Wilms' tumor



Differential Diagnosis of Abdominal and Pelvic Tumors in Children			
Tumor	**Age**	**Clinical signs**	**Laboratory finding**
Wilms tumor	Preschool	- **Unilateral** flank mass, aniridia, hemihypertrophy	- Hematuria, polycythemia, thrombocytosis, elevated PTT
Neuroblastoma	Preschool	- **GIT and GUT** obstruction, raccoon eyes, myoclonus-opsoclonus, diarrhea, skin nodules	- Increased urinary **vanillylmandelic acid, homovanillic acid**, or ferritin - Stippled calcification in the mass
Non-Hodgkin lymphoma	>1 yr	- **Intussusception in >2 Yo**	- Increased **lactate dehydrogenase** - Blood cytopenia caused by bone marrow involvement

Differential Diagnosis of Abdominal and Pelvic Tumors in Children			
Tumor	**Age**	**Clinical signs**	**Laboratory finding**
Rhabdomyosarcoma	All	- **GIT and GUT** obstruction - Abdominal pain, vaginal bleeding, paratesticular mass	- Hypercalcemia, blood cytopenia caused by bone marrow involvement
Germ cell tumor/teratoma	Preschool, teenage	- **Females:** Abdominal pain, vaginal bleeding - **Males:** Testicular mass, new-onset hydrocele, sacrococcygeal mass/dimple	- Increased **ß-human chorionic gonadotropin, increased a-fetoprotein**
Hepatoblastoma	Birth-3 yr	- RUQ mass, jaundice - Early puberty in males	- Increased a-fetoprotein
Hepatocellular carcinoma	School age	- RUQ mass, jaundice - Hepatitis B, cirrhosis	- Increased a-fetoprotein

	Wilms Tumor	**Neuroblastoma**
Abdominal mass	- yes	- yes
Primary origin	- intarenal	- Extrarenal, from adrenal gland or paravertebal sympathetic ganglia
Physical examination	- Displacing mass, mainly confined to the flank	- Non-mobile mass, more likely to cross the midline
Pattern of spread	- Direct expansion with displacement of adjacent structures	- Encasement of vessels and aortic elevation
Other	- Intrinsically displaces urinary collecting systems, Asymptomatic, marcoglossia,HTN, hematuria	- Externally displaces kidney, Neural extension, Often calcified, Irritabel child, tender, Raccoon eyes



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