HELLENIC REPUBLIC
National and Kapodistrian University of Athens
EST. 1837

Children' s Hospital "Agia Sofia"

Solid Tumors

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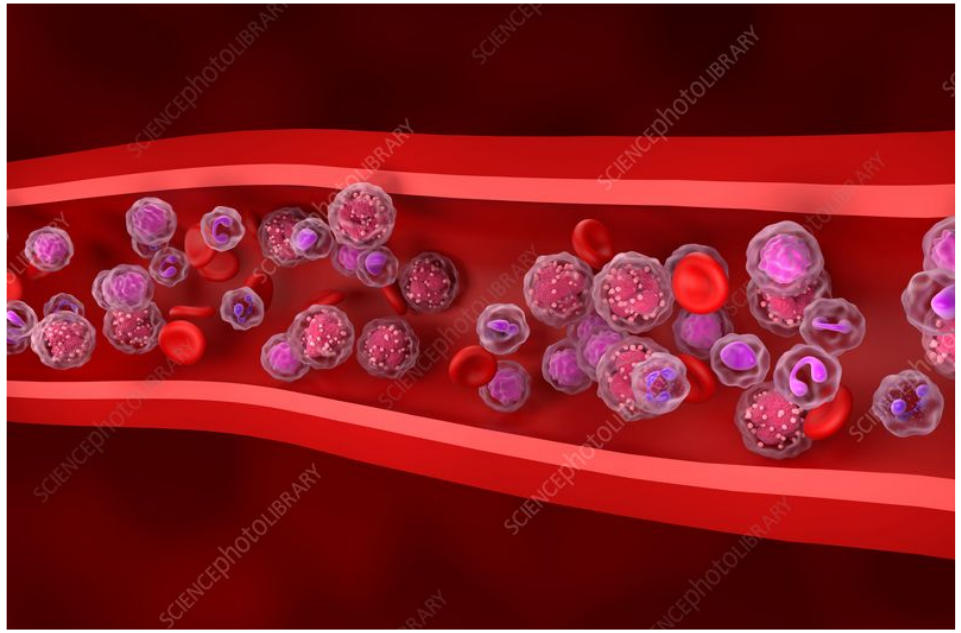
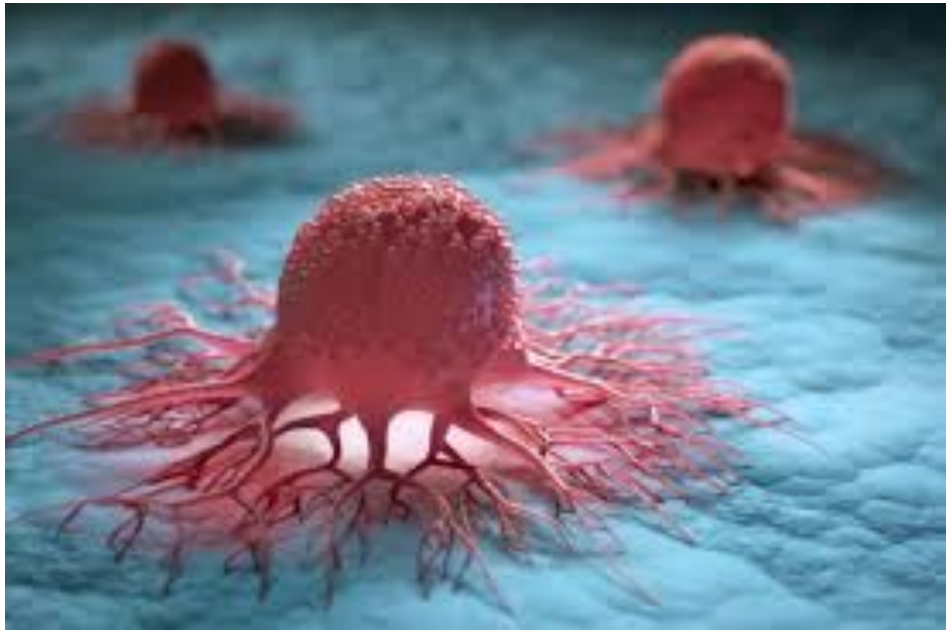
Scope of this lecture

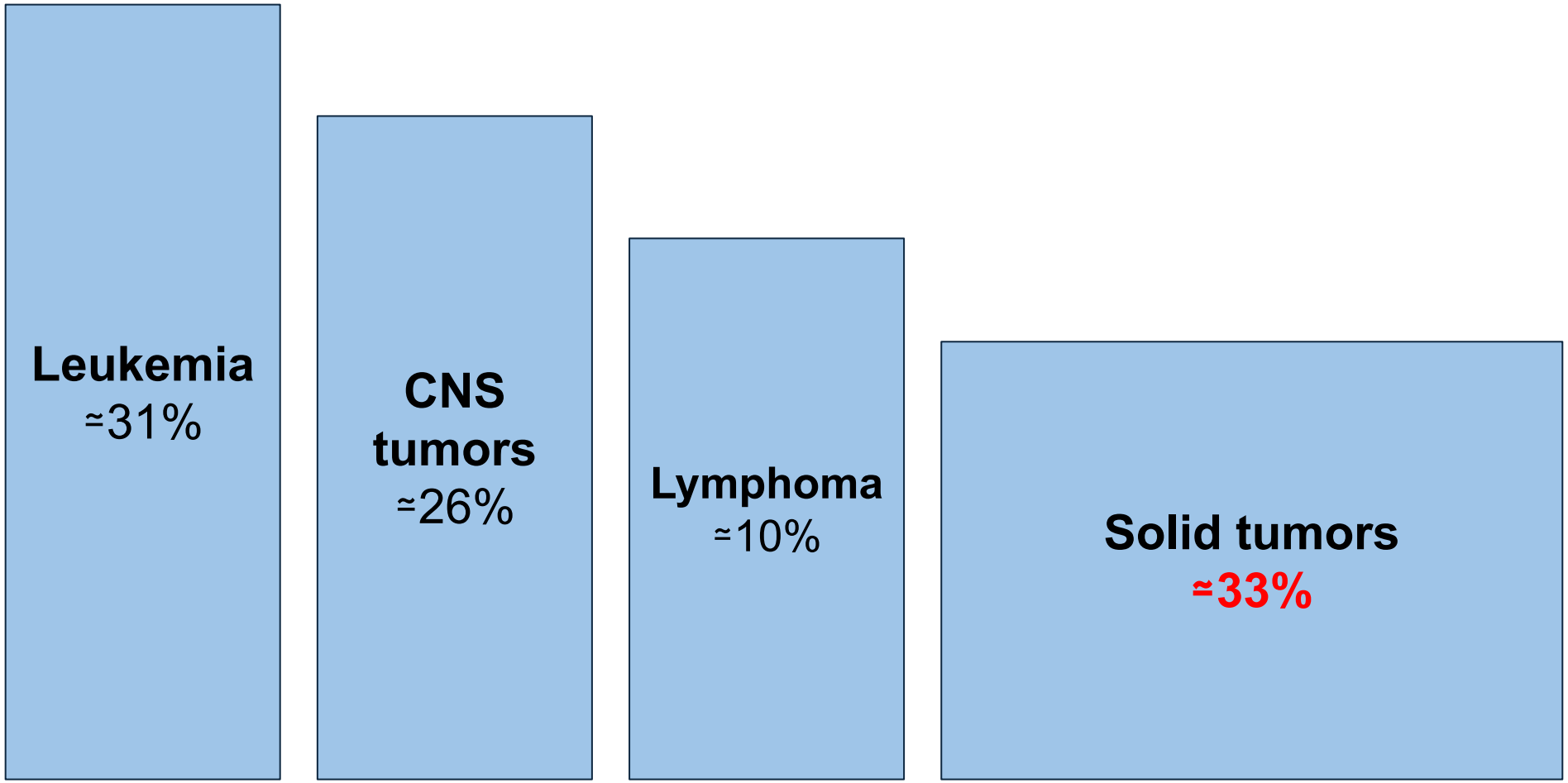
- Introduction to pediatric solid tumors
- Basic epidemiology
- Case-based presentation of
  - Renal tumors
  - Bone tumors
  - Soft-tissue tumors
  - Germ-cell tumors
  - Liver tumors
  - Retinoblastoma

What is a solid tumor?





Epidemiology of childhood malignancies



- Neuroblastoma
- Renal
- Soft tissue
- Bone
- Germ cell
- Retinoblastoma
- Liver
- Epithelial
- Other

Children are not small adults!

Solid tumors
≈33%

- Neuroblastoma
- Renal
- Soft tissue
- Bone
- Germ cell
- Retinoblastoma
- Liver
- Epithelial
- Other

Solid tumors in children:

- Rarer
- Different
  - Etiology
  - Cellular origin (e.g. embryonal)
  - Biology (e.g. driver mutations, genetic complexity)
  - Histology
  - Treatment considerations

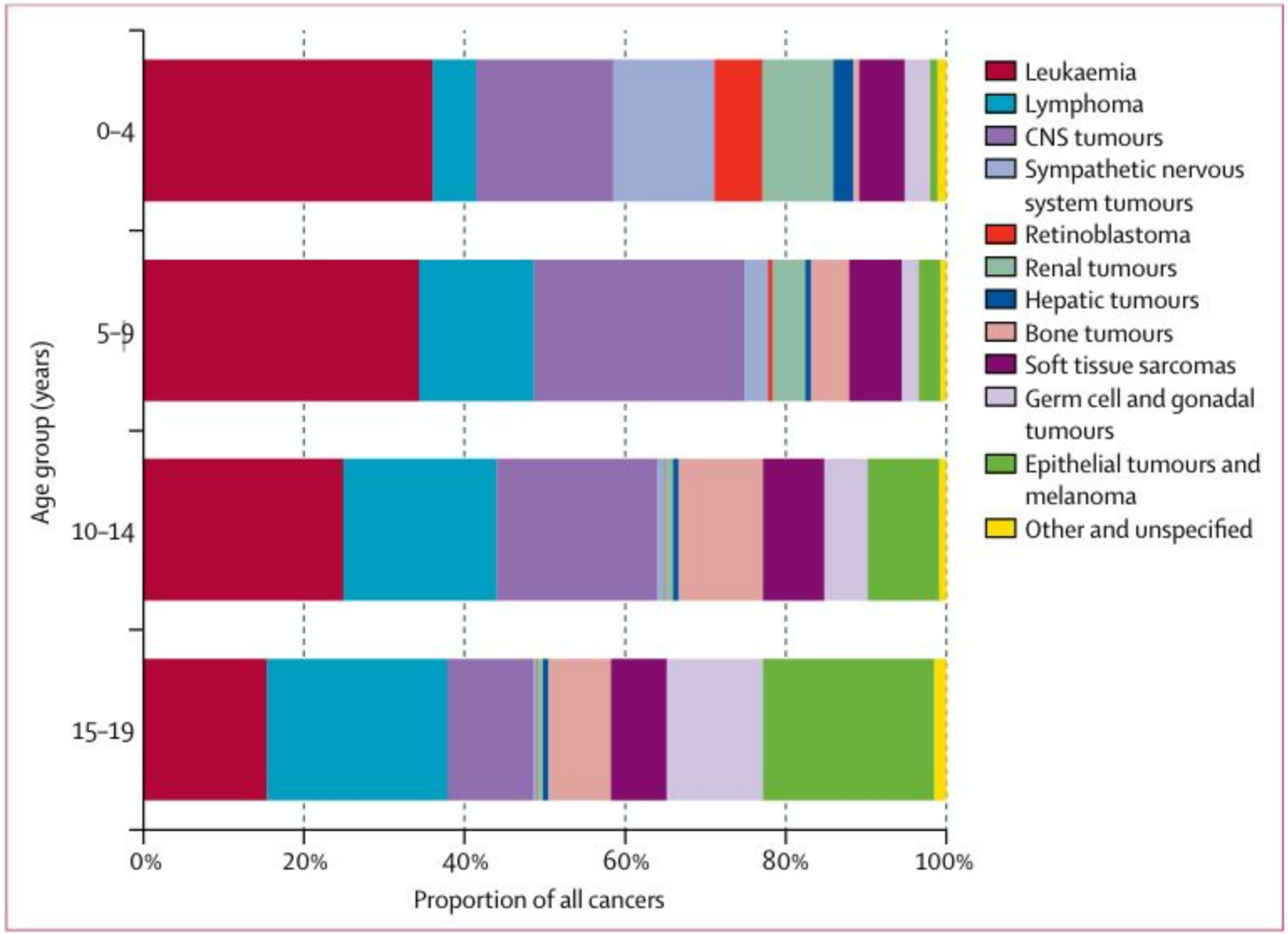
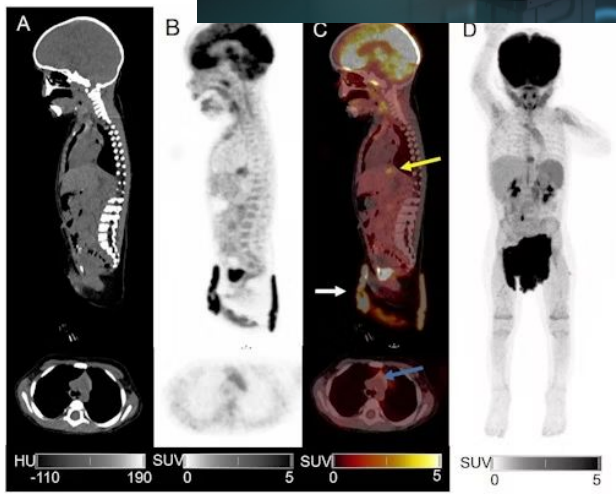


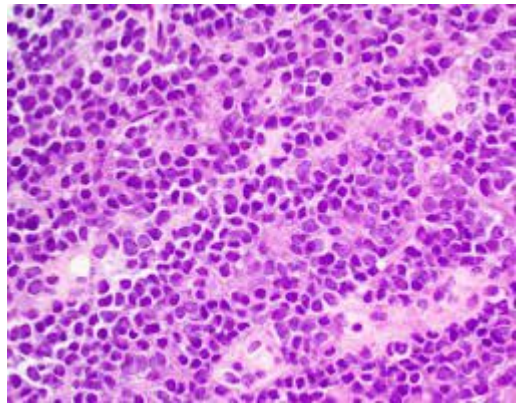
***Figure 2*: Proportional distribution of cancer type by age group, 2001–10, all regions combined**
Tumours classified by *International Classification of Childhood Cancer, volume 3*.[6] Statistics for children younger than 15 years are based on the paediatric dataset and the statistics for those aged 15–19 years are based on the general dataset.

Steliarova-Foucher et al. Lancet Oncology, 2017, Volume 18, Issue 6, 719 - 731

Advances in the diagnosis of solid tumors



Imaging



Histology

Molecular studies

Molecular profiling platforms

- Panel sequencing:
  - SNV and INDEL
  - CNA
  - Germline
  - Fusions (pediatric MATCH)
- WES:
  - SNV and INDEL
  - Germline
  - CNA (MAPPYACTS)
- lcWGS:
  - CNA
- WGS:
  - SNV and INDEL
  - CNA
  - SV and fusions
  - Germline
- RNA-seq:
  - Fusions
  - Gene expression (ZERO)
- Methylation 850K array:
  - Tumour classification
- Gene expression arrays:
  - Gene expression

Nat Rev Cancer. 2019;19(8):420-438

Advances in the management of solid tumors

Surgery

Chemotherapy

Radiotherapy

Immunotherapy

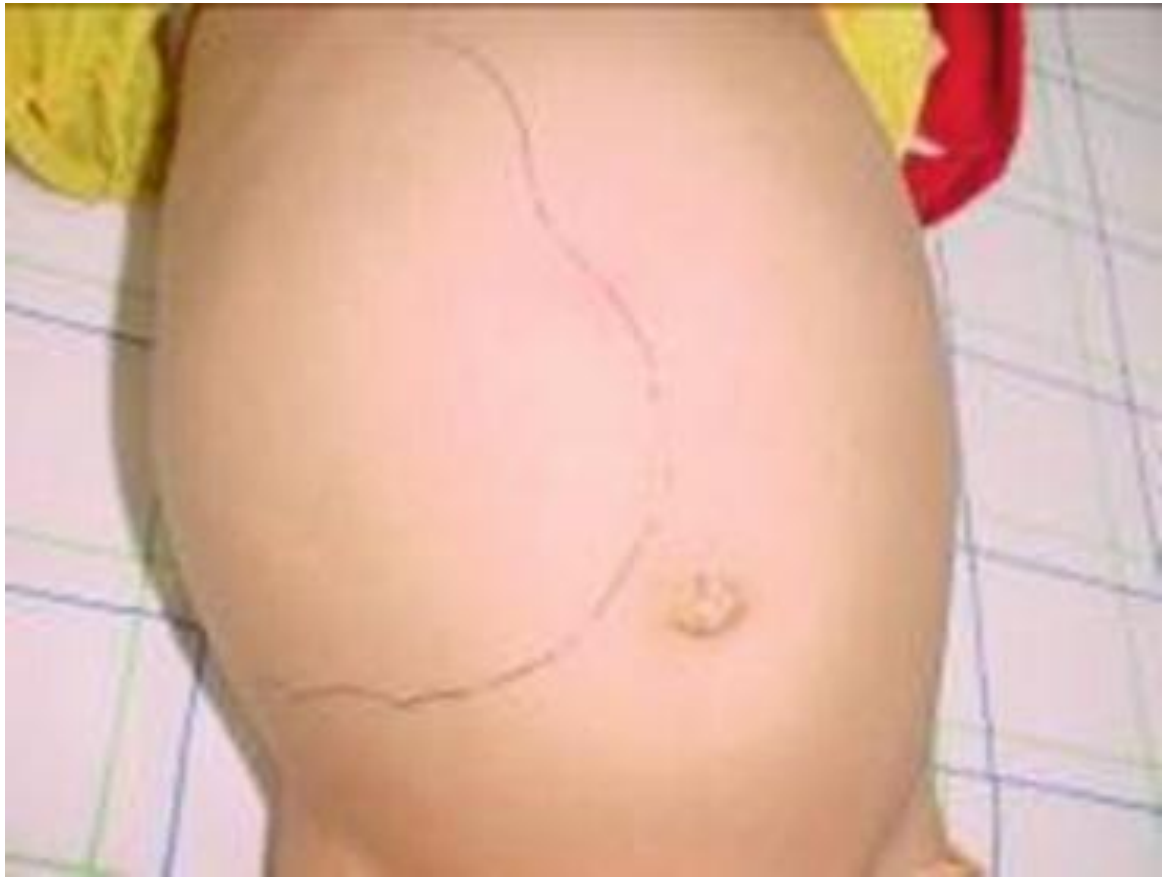
Targeted treatments

18-month-old boy with abdominal distention.

Pediatric examination reveals palpable abdominal mass.

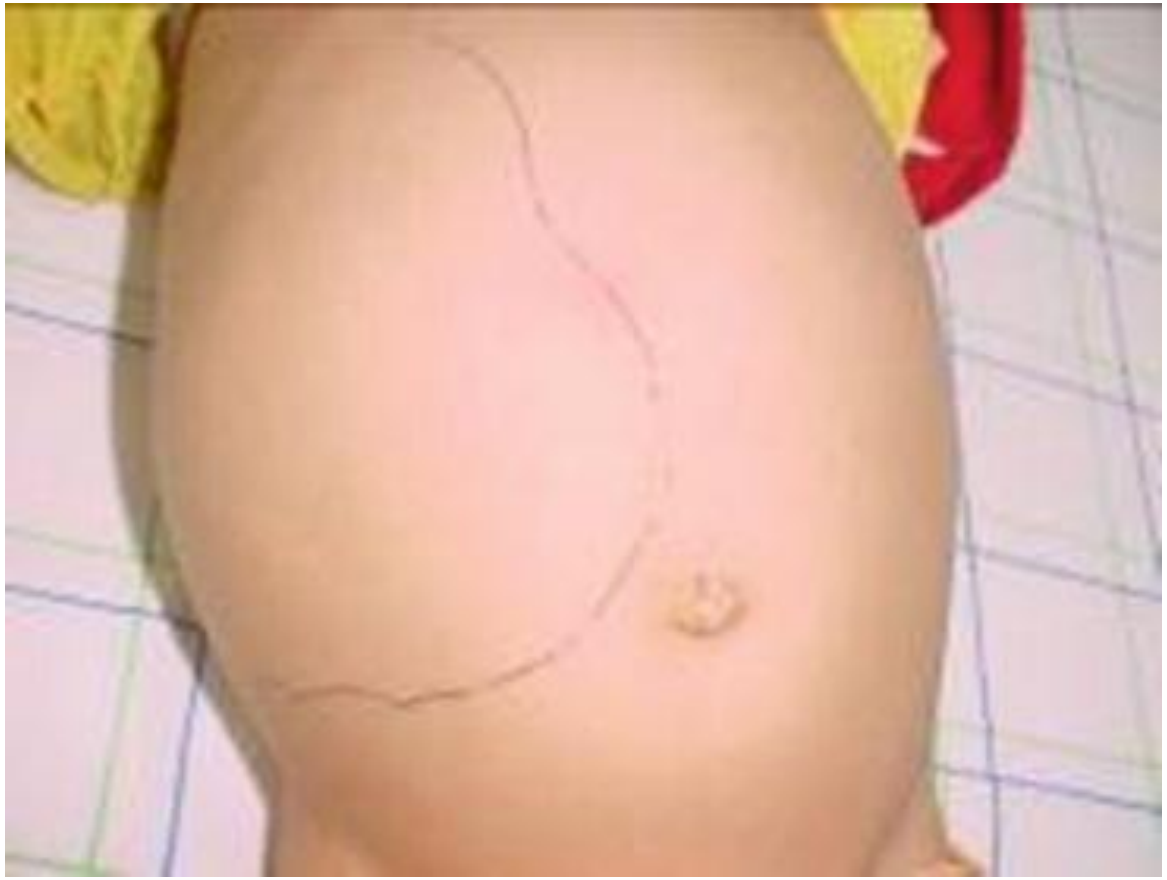
Questions to ask:

1. Any signs of emergency?
2. Most common diagnoses?
3. Where does the mass originate from?



18-month-old boy with abdominal distention.

Pediatric examination reveals palpable abdominal mass.



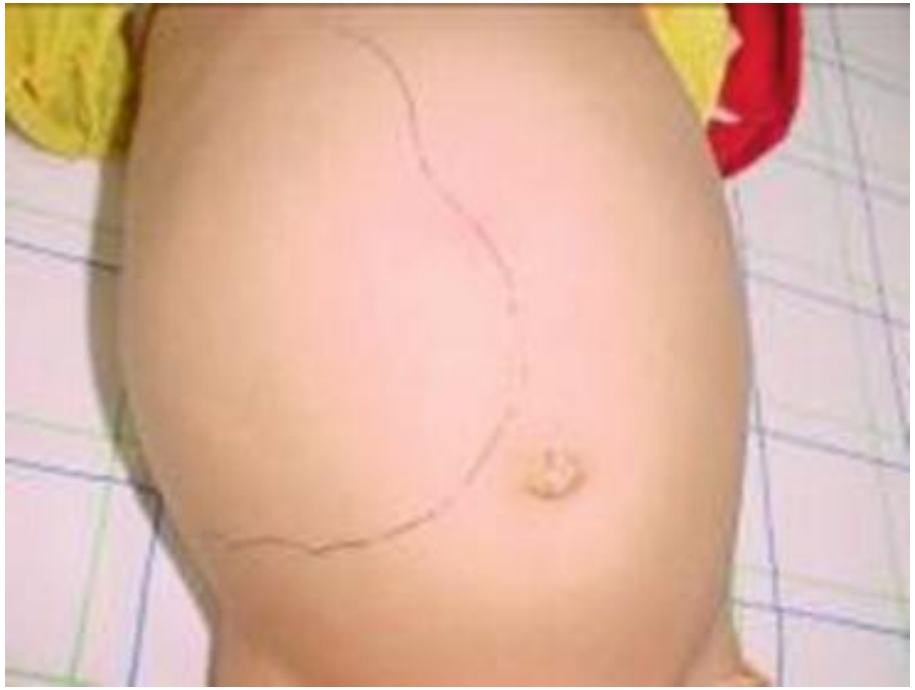
Questions to ask:

1. Any signs of emergency?
2. Most common diagnoses?
3. Where does the mass originate from?

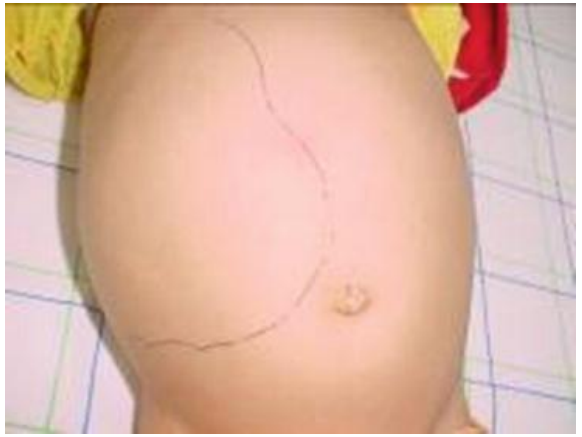
Dyspnea
Arterial hypertension
Urinary obstruction/ hematuria
Constipation/ Billous vomiting
Neurological symptoms

Differential diagnosis of abdominal tumors

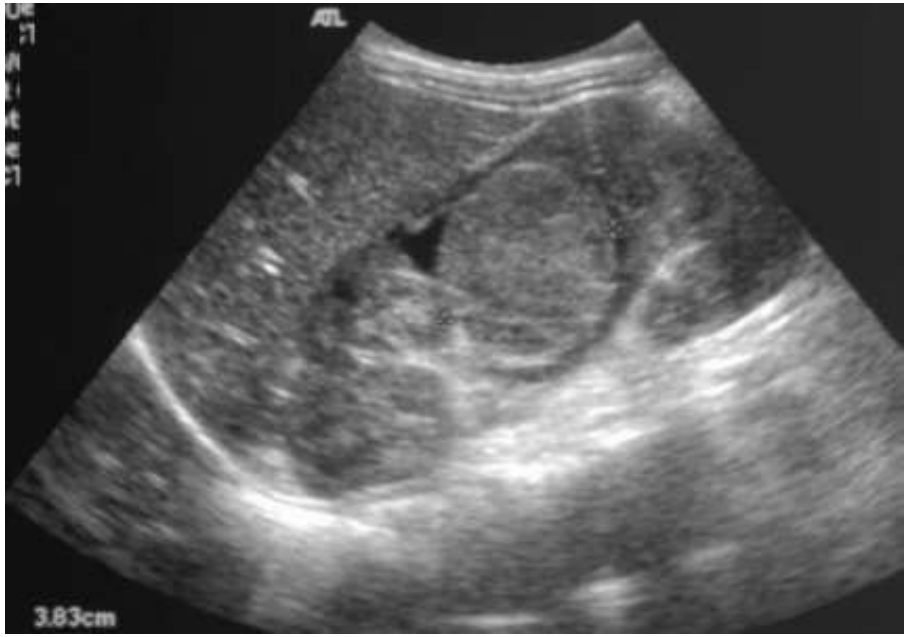
- Leukemia/ Lymphoma
- Neuroblastoma
- Renal tumor (Wilm's)
- Rhabdomyosarcoma
- Hepatoblastoma
- Germ cell tumor
- Other



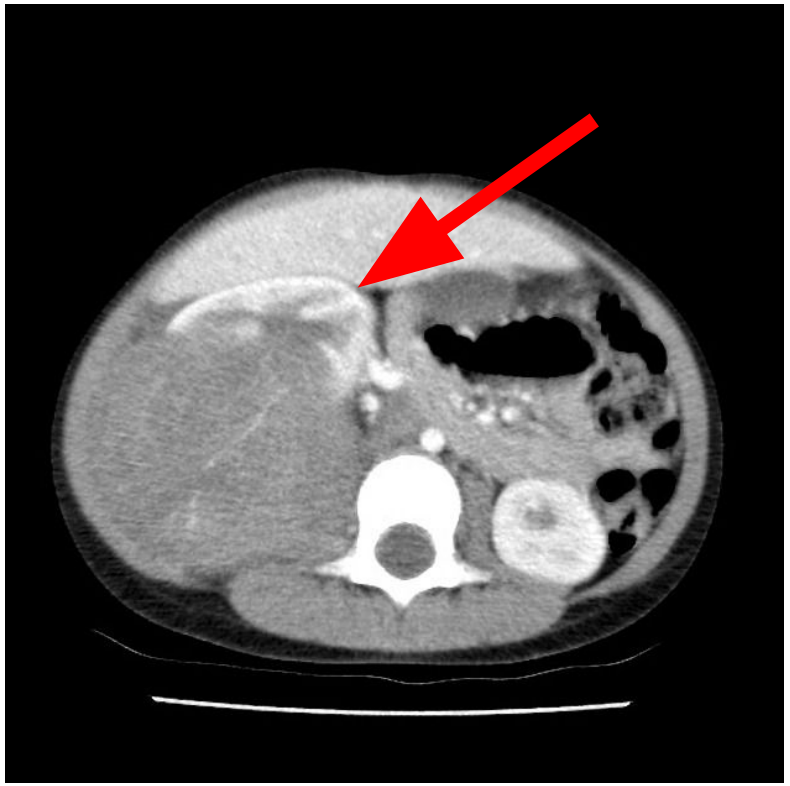
Don't forget the age of the patient!



Abdominal mass, **not crossing the midline**



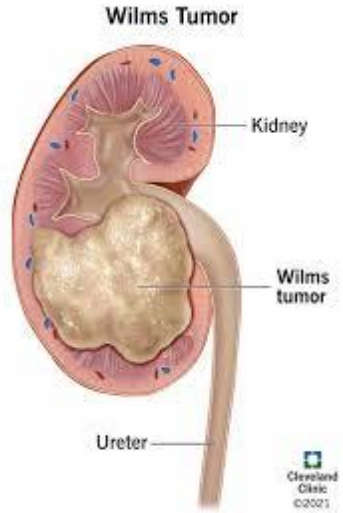
Abdominal U/S:
Solid mass, possibly originating from the right kidney with **no calcifications**

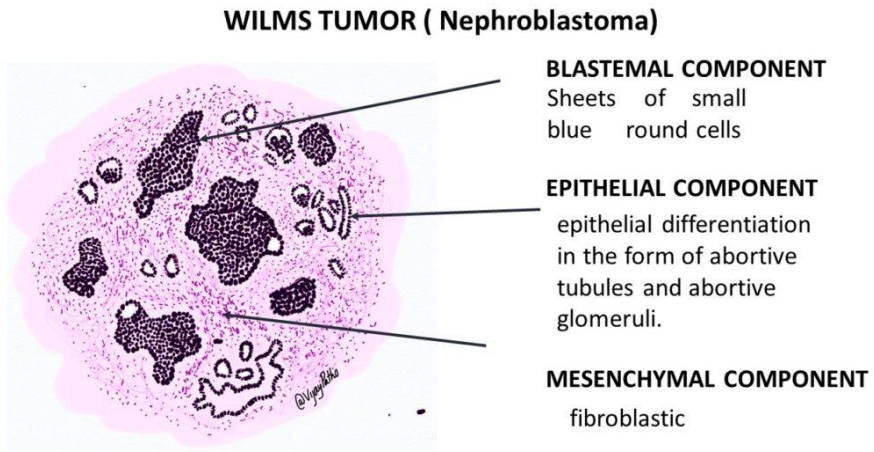


Abdominal MRI:
Solid mass originating from the right kidney (**claw sign**)

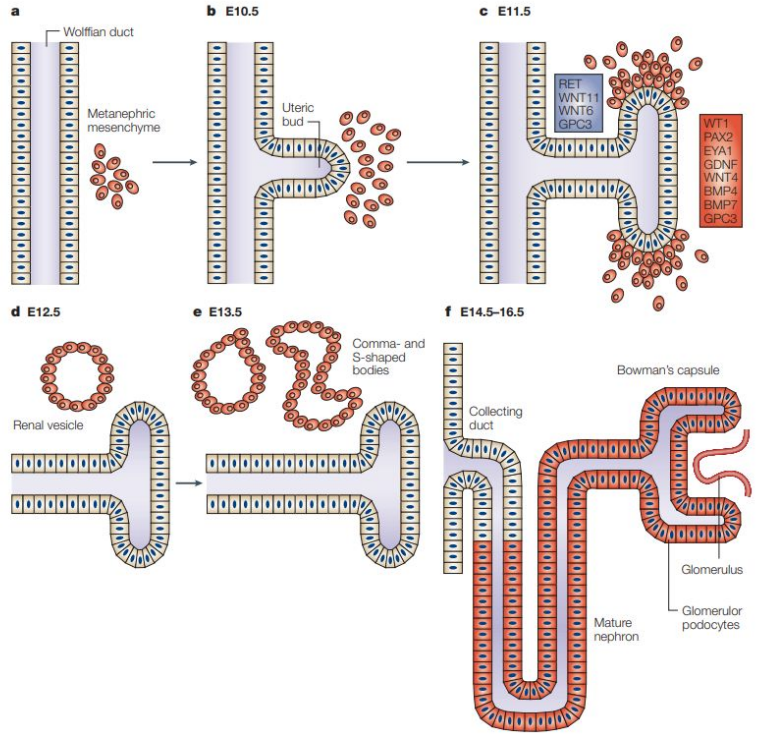
Nephroblastoma (Wilm's tumor)

- The most common pediatric renal tumor
- 6% of all malignancies in childhood
- Embryonal tumor, during the differentiation of glomeruli
- Triphasic histology (stroma, epithelial, blastema)
- Genetic aberrations in developmental genes (e.g. WT1) are involved in Wilm's tumor
- WT1: transcription factor implicated in kidney and gonad differentiation before birth



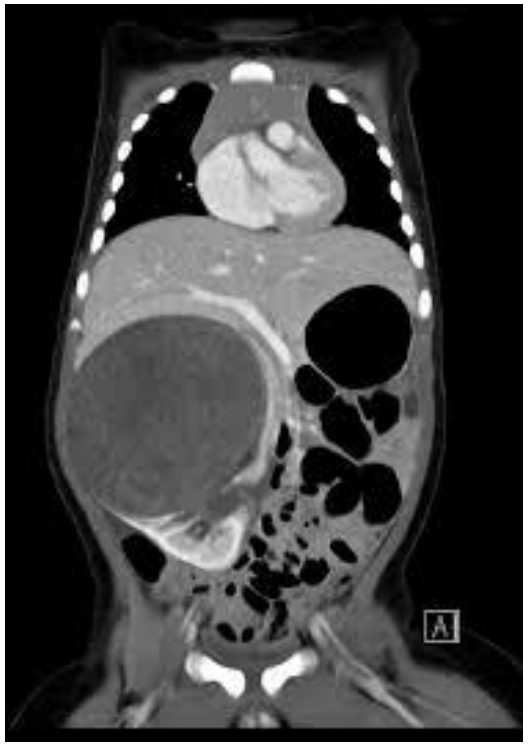


Nat Rev Dis Primers **7**, 75 (2021)



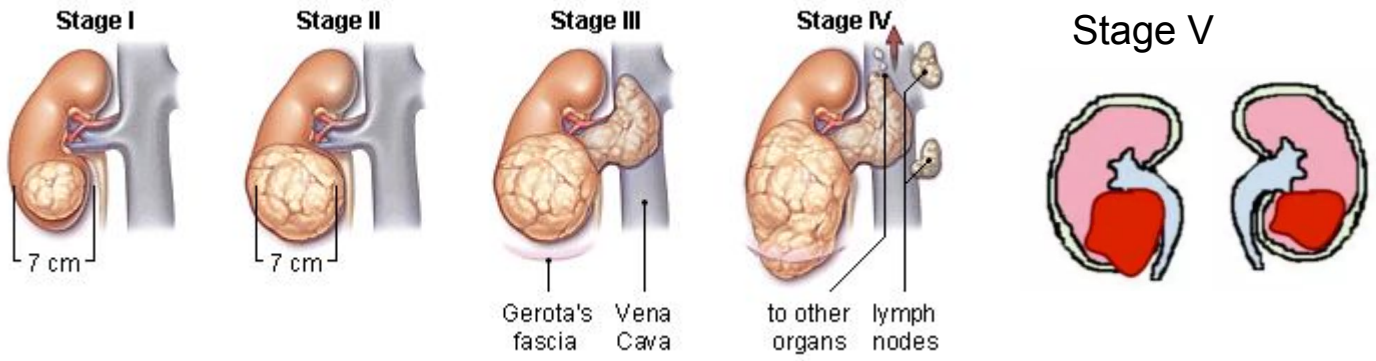
Nat Rev Cancer 5, 699–712 (2005).

- Most common clinical presentation: **palpable abdominal mass**
  - Hematuria (gross/ microscopic)
  - Abdominal pain, arterial hypertension (due to pressure/infiltration of renal vessels
  - General symptoms (malaise, weight loss, anorexia, low grade fever etc.)
  - Can be **asymptomatic, incidental finding**
  - Look for **phenotypical characteristics, family history**



- Imaging
  - Ultrasound (calcifications)
  - Abdominal MRI (**Claw sign, neoplastic thrombi**)
  - CT thorax (nodules)

- Metastasizes in **lungs > bones > brain**



- Diagnosis → US, MRI/CT, **biopsy not always required**

TABLE 1 Summary of recommended indications for diagnostic core needle biopsy of renal neoplasms in children, adolescents and young adults without features of genetic predisposition, under SIOP-RTSG protocols

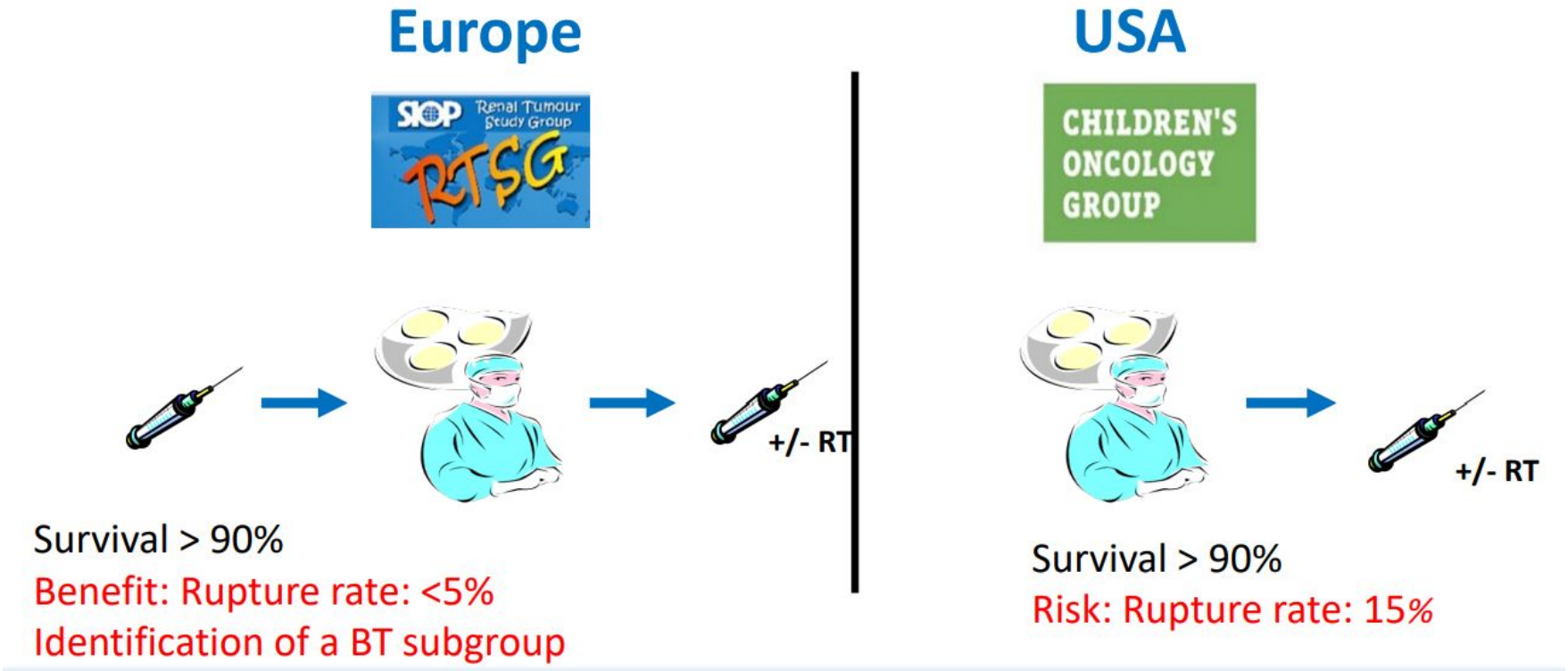
	Features typical of WT (i.e. *not* requiring biopsy) *all* criteria required	Biopsy *not* recommended if *any* of these criteria met	Biopsy recommended if *any* of these criteria met	Indication to be discussed in tumour board meetings if *any* of these criteria met
Clinical criteria	Age ≥6 months but <7 years, No infectious syndrome	Age <3 months (upfront surgery indicated)	Age ≥10 years, Age between 7 and 10 years, Tumour volume[a] <200 ml	Age ≥3 months but <6 months, Infectious syndrome, Urinary tract infection
Radiological criteria	Obvious renal origin, Unilateral tumour with volume over 80 ml, Solid or mixed (solid and cystic) without calcification, Metastases absent or limited to lungs and age >2 years	Totally cystic tumour (primary surgery, if indicated), Bilateral kidney tumours in children ≥6 months but <7 years and/or typical nephroblastomatosis at imaging (presumptive chemotherapy)	Uncertain renal origin, Atypical metastases: bones (any age), central nervous system (any age), pulmonary (<2 years)	Intratumour calcifications, Tumour volume under 80 ml, Large necrotic adenopathy, Bilateral kidney tumours and ≥7 years
Biochemical criteria	Normal urinary catecholamines, Normal serum calcium, LDH less than 4× upper limit of normal		Elevated urinary catecholamines, Hypercalcaemia *and* age <4 years	LDH over 4× upper limit of normal

Note: 6 months = 182 days life.

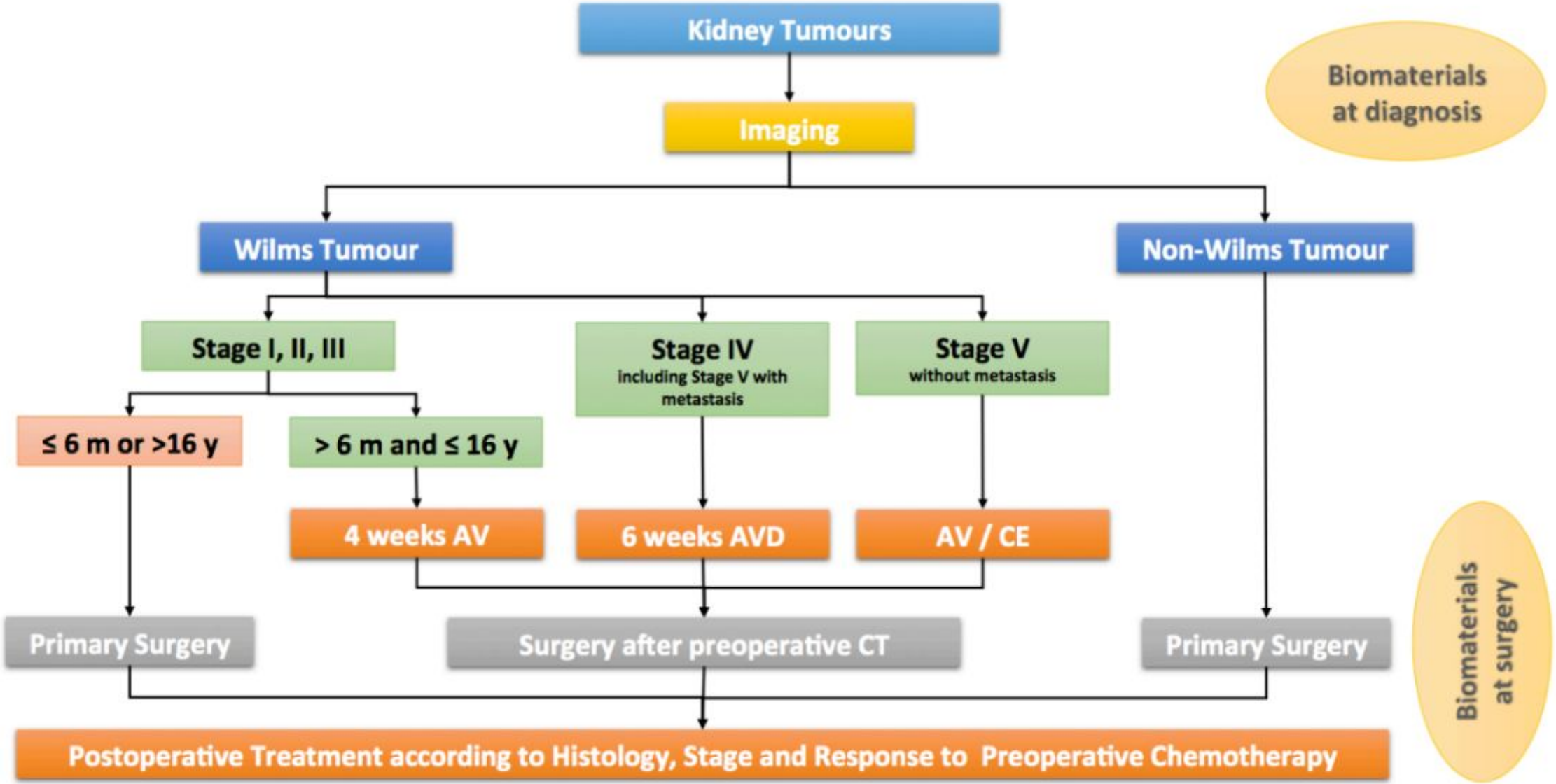
Abbreviations: LDH, lactate dehydrogenase; SIOP-RTSG, International Society of Paediatric Oncology Renal Tumour Study Group; WT, Wilms tumour.

[a]Tumour volume = length (cm) × width (cm) × thickness (cm) × 0.523.

- Management
  - Surgical excision
  - Pre- and post-operative chemotherapy
  - Radiotherapy



19.11 Appendix 10: Flowcharts and treatment schedules



Renal tumor? Look and ask questions!

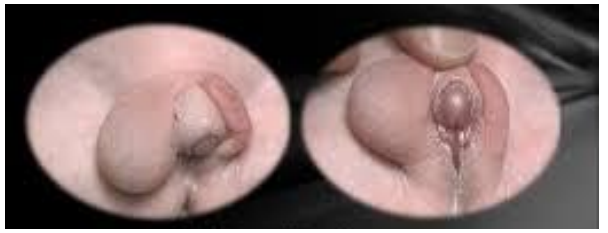
- Phenotypic characteristics
- Gigantism/Semihypertrophy
- Big tongue
- Eyes: aniridia
- Ear clefts
- Skin: cafe au lait spots
- Omphalocele
- Urogenital tract: ambiguous genitalia, hypospadias, other

- Hypoglycemia
- Family history

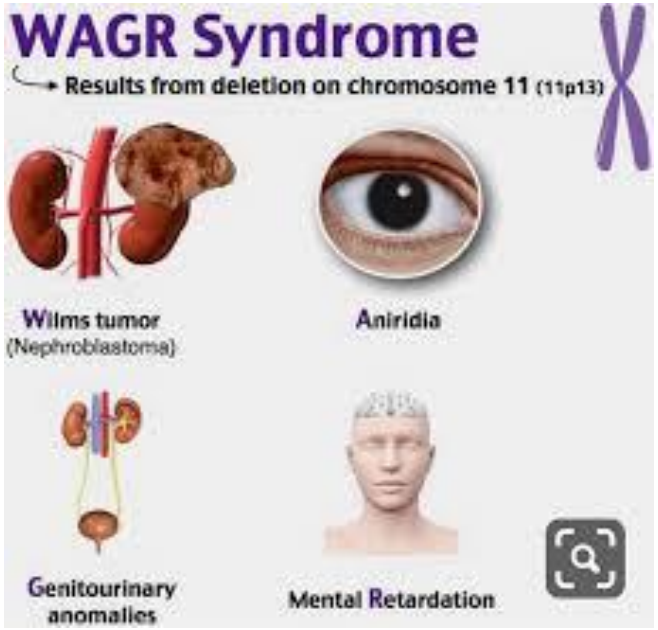
Major Criteria - BWS	Minor Criteria - BWS
Gigantism (Prenatal/postnatal macrosomia)	Pregnancy related findings – placentomegaly, placental mesenchymal dysplasia, polyhydramnios
Hemi hyperplasia	Prematurity
Abdominal wall defect – omphalocele, umbilical hernia	Neonatal hypoglycemia
Ear anomalies – anterior linear lobe creases, posterior helical pits	Cardiomegaly, structural cardiac anomalies
Embryonal tumors	Nevus flammeus, other vascular malformation
Visceromegaly	Diastasis recti
Renal abnormalities	Midface hypoplasia
Positive family history	Coarse facies

Chromosomal deletion syndrome 11p15.5 of maternal origin – abnormal methylation pattern for genes IGF2, CDKNIC, LIT1

Denys - Drash syndrome



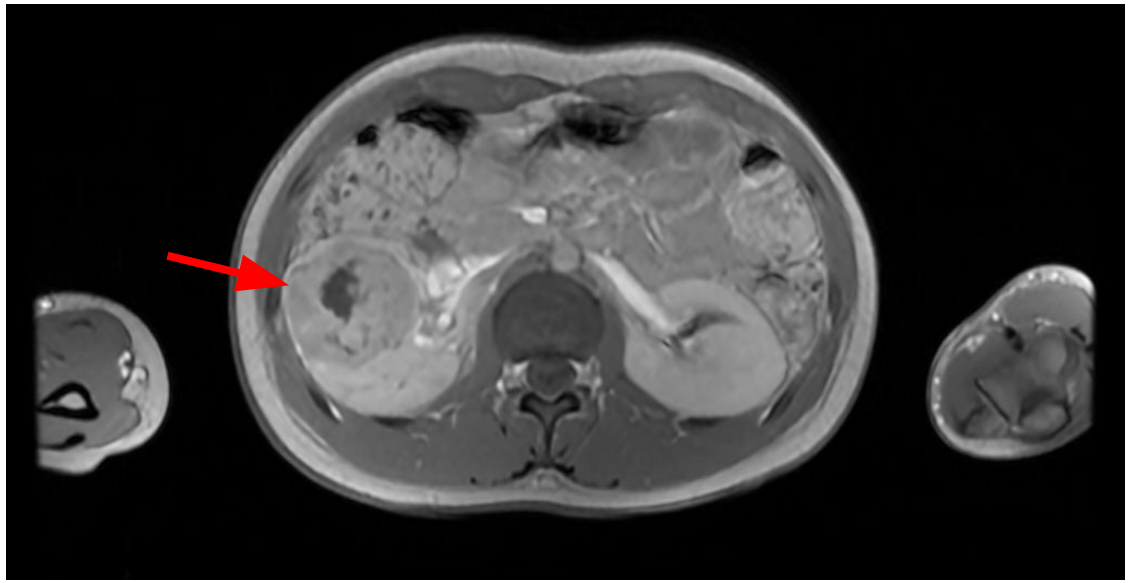
- Ambiguous genitalia
- Glomerulosclerosis – Mesagnial sclerosis
- Predisposition for Wilms Tumor
- Defect in WT1

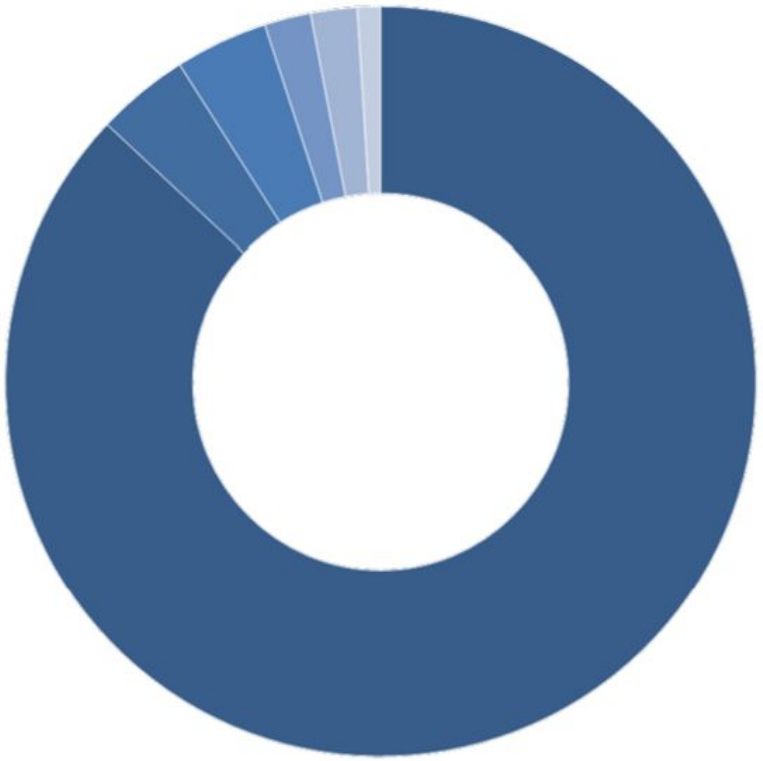


- Associated with WT1, WT2 (11p), WT3 (16q), WTX genes and with cancer predisposition syndromes (e.g. Li-Fraumeni)

Follow-up every 3 months until 5 years old, then yearly
Abdominal US and urine spot for hematuria

15 year-old girl with gross hematuria





Renal tumors:

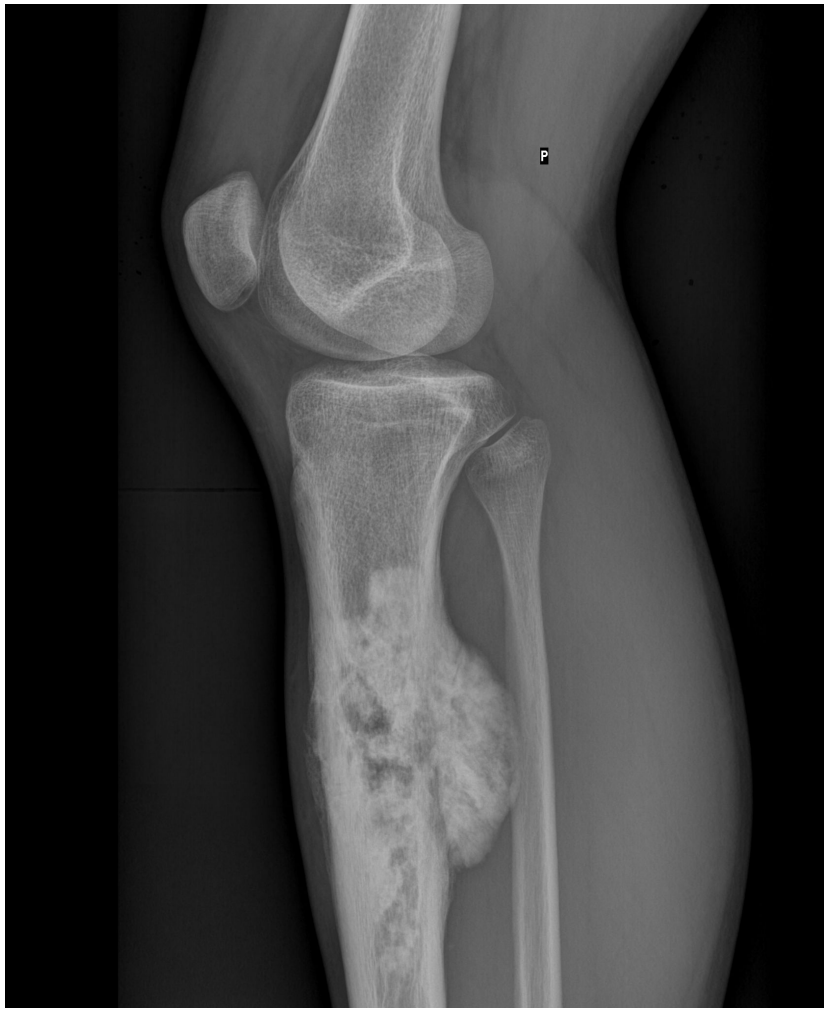
- Wilms Tumor
- Renal Cell Carcinoma
- Clear Cell Sarcoma of the Kidney
- Congenital Mesoblastic Nephroma
- Malignant Rhabdoid Tumor of the Kidney
- Other

Non-WT
(± 10-20%)

SIOP Renal Tumour Study Group
RTSG

11-year-old boy with three-week history of pain in the left leg.

One month ago, reported fall during soccer game.



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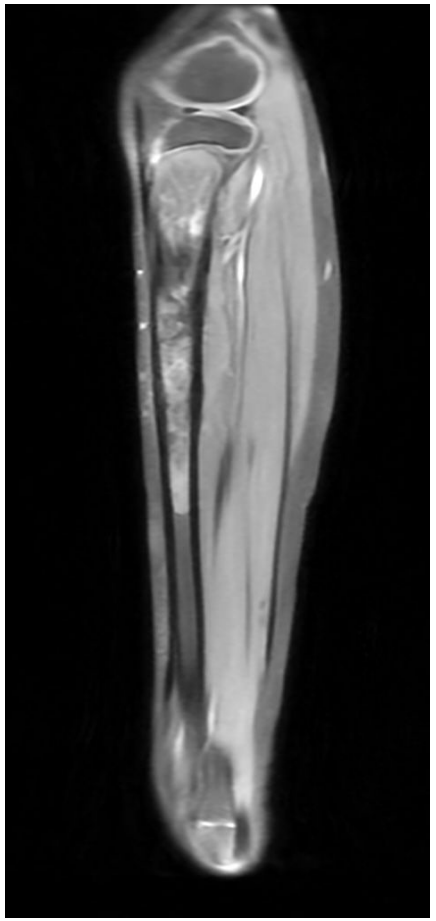
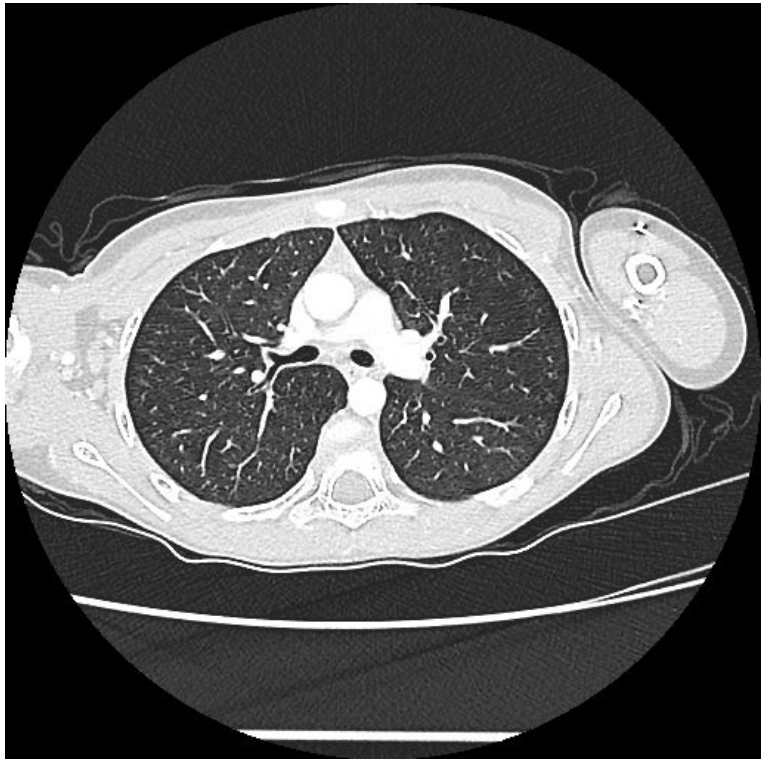
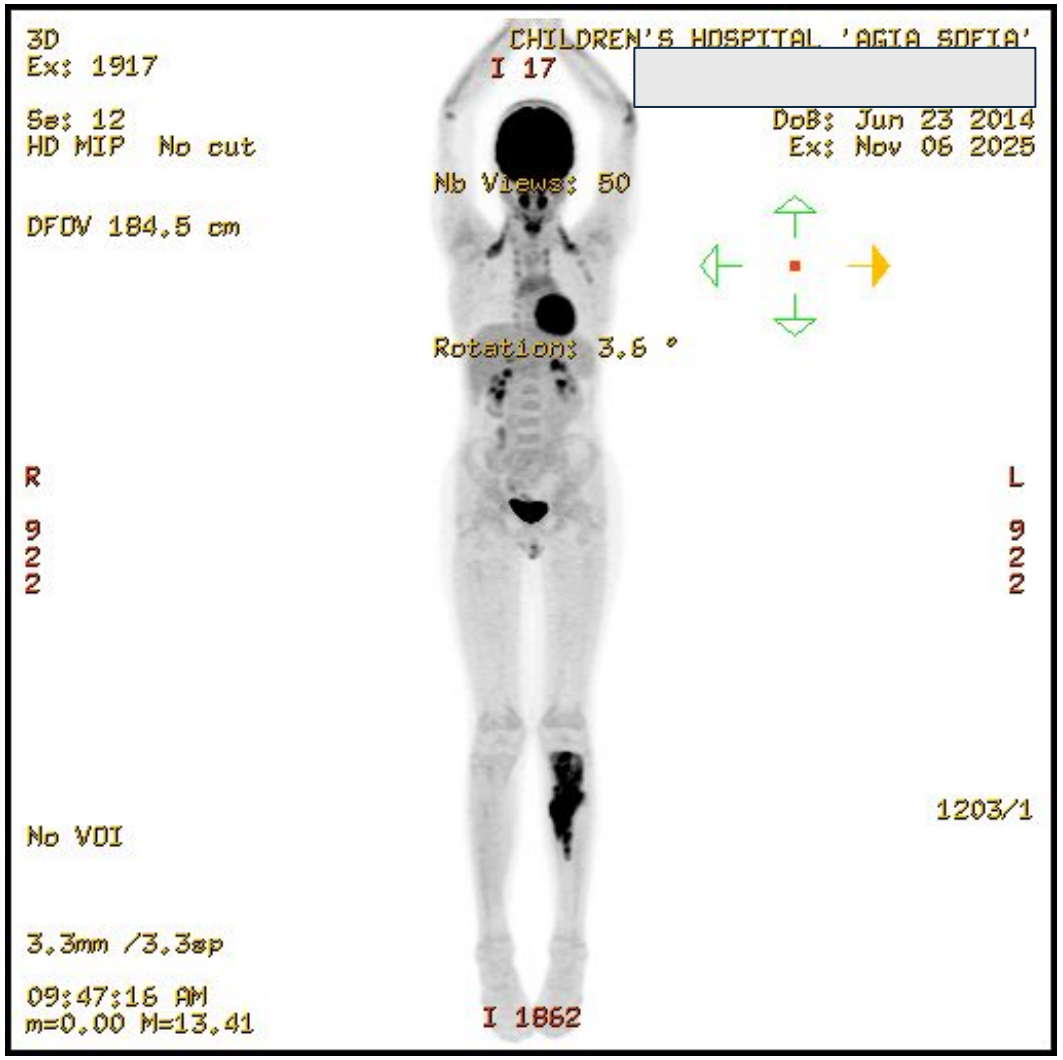






Osteosarcoma

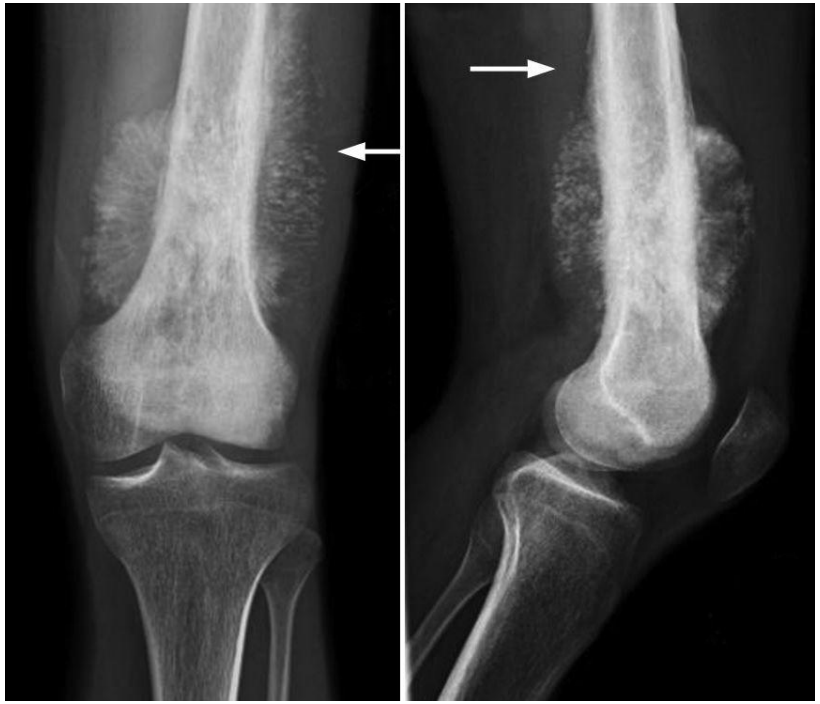
- The most common malignant bone tumor
- The third most common malignancy in adolescents
- Originates from mesenchymal cells, malignant osteoid synthesis
- **Age at first presentation is closely related with osteoblast activity**
  - i.e. when there is rapid tissue formation
  - Pubertal spurt
- Association with cancer predisposition syndromes (Li Fraumeni, Bloom etc.)
- Femur 41%, tibia 41%, humerus 10%
- Prognosis: 70% survival, if metastatic disease: 46%

- Clinical presentation
  - Local pain (90%)
  - Local oedema (50%)
  - Walking difficulty (45%)
  - Pathologic fracture, faster growth of pathologic bone, joint insult
  - 80% of patients has micro-metastases upon diagnosis (difficult to detect) and 15-20% has evident lung metastases

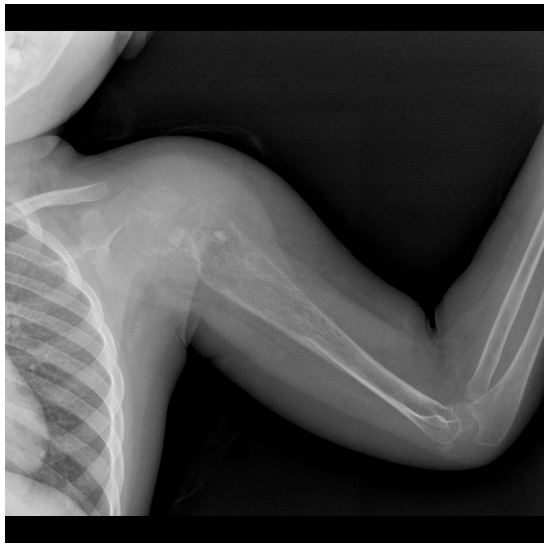
- Diagnosis
  - Bone scan, CT/MRI of the lesion, CT thorax

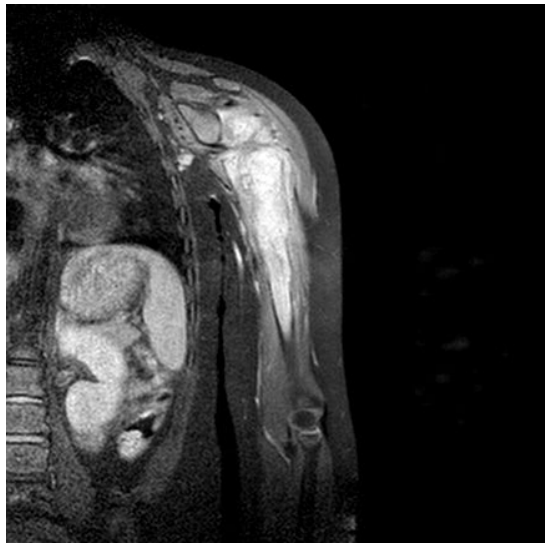
- Management
  - Surgical excision, pre- and post-operative chemotherapy
  - Tumor necrosis >90% after pre-operative chemotherapy good prognostic factor
  - No radiotherapy (**osteosarcoma is not radiosensitive**)

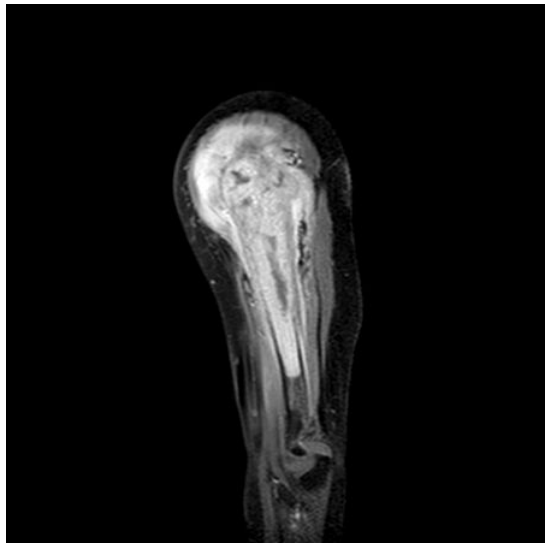
- Prognosis
  - 5-year survival 70%, if metastatic disease 46%

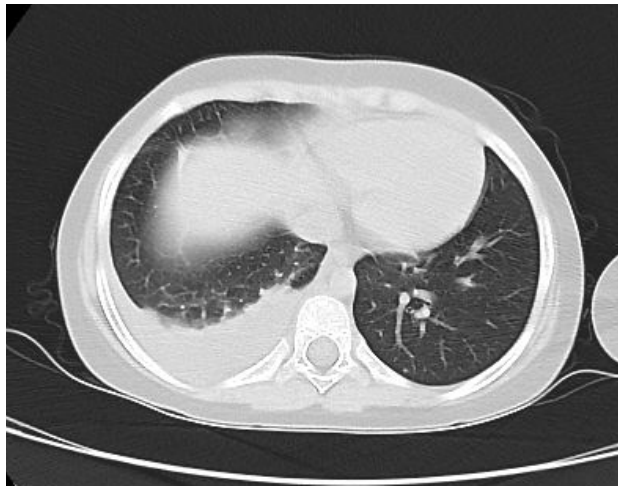


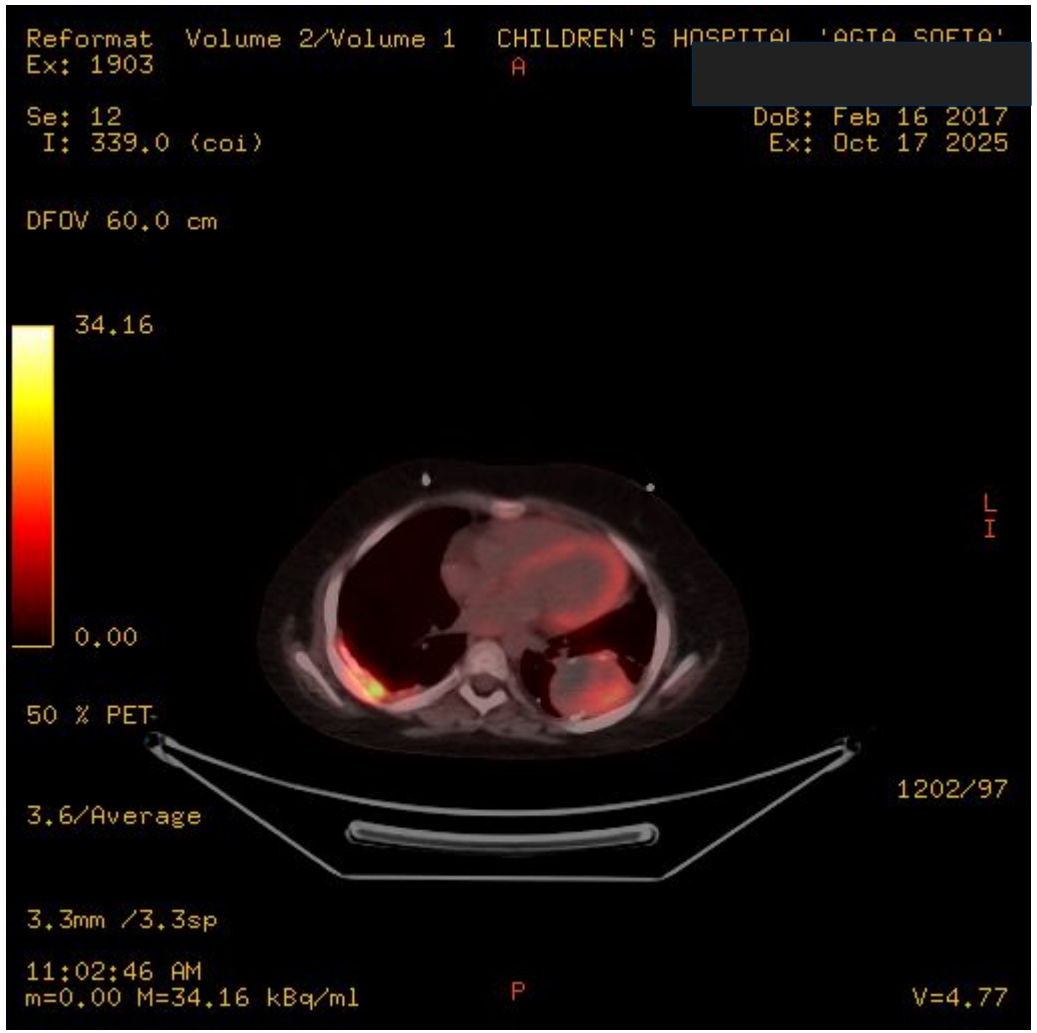
Sunburst pattern occurs when the lesion grows too fast and the periosteum does not have enough time to lay down a new layer and instead the Sharpey's fibers stretch out perpendicular to the bone.







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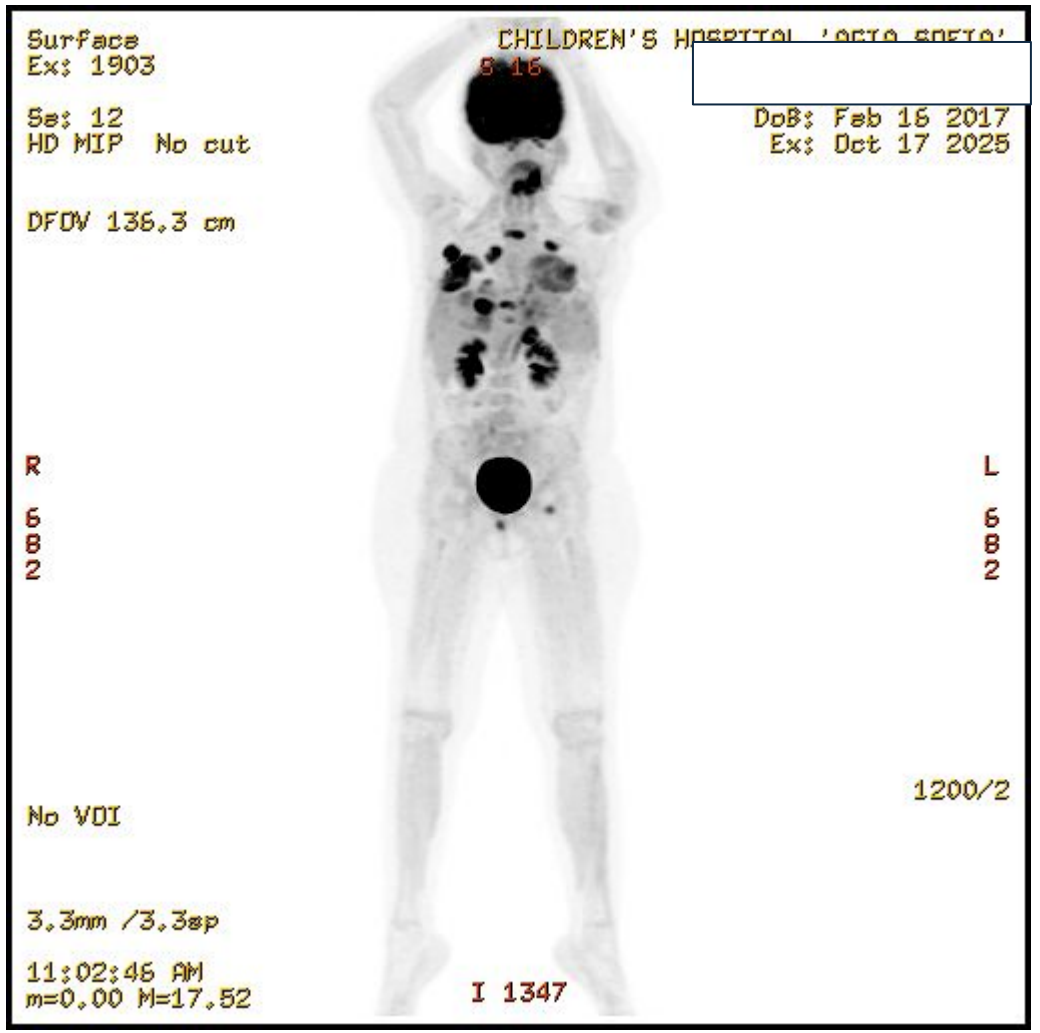
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Se: 12
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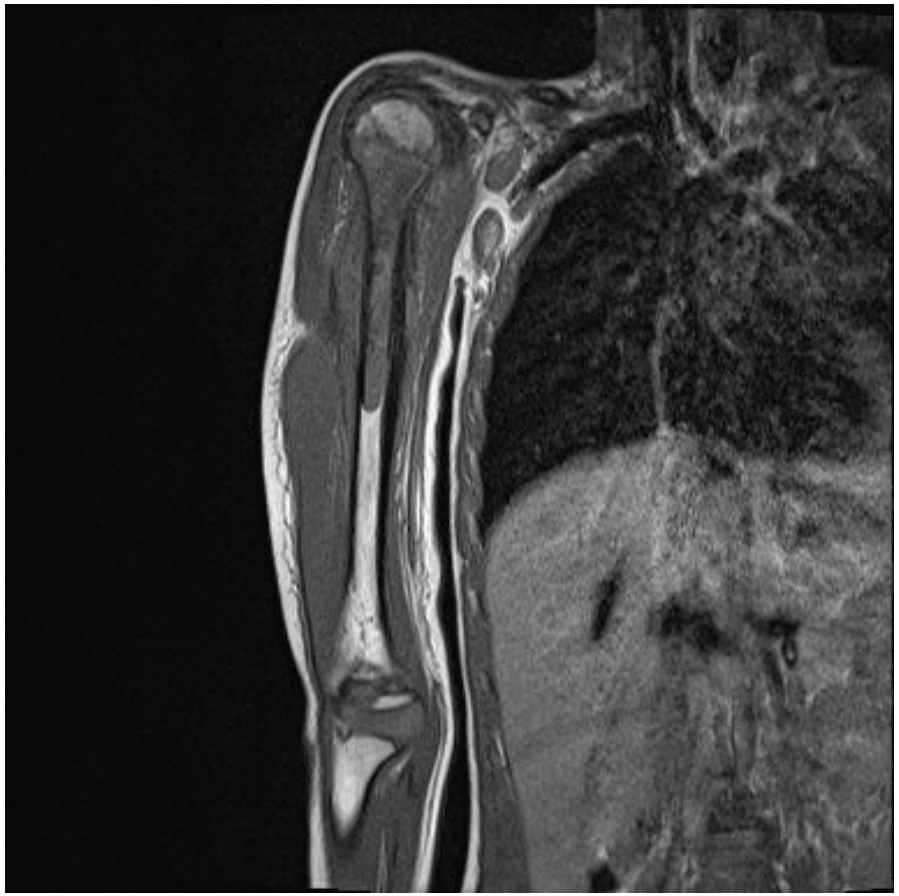
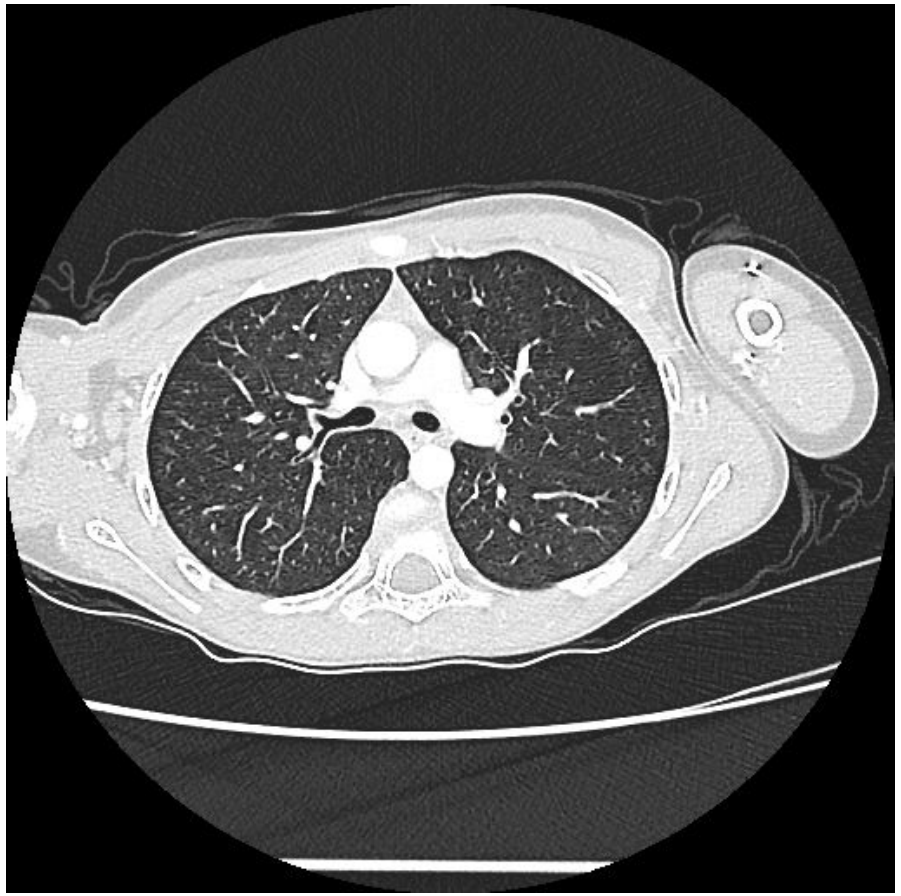
7-year-old boy with four-week history of pain in the arm.

Difficulty in playing sports.





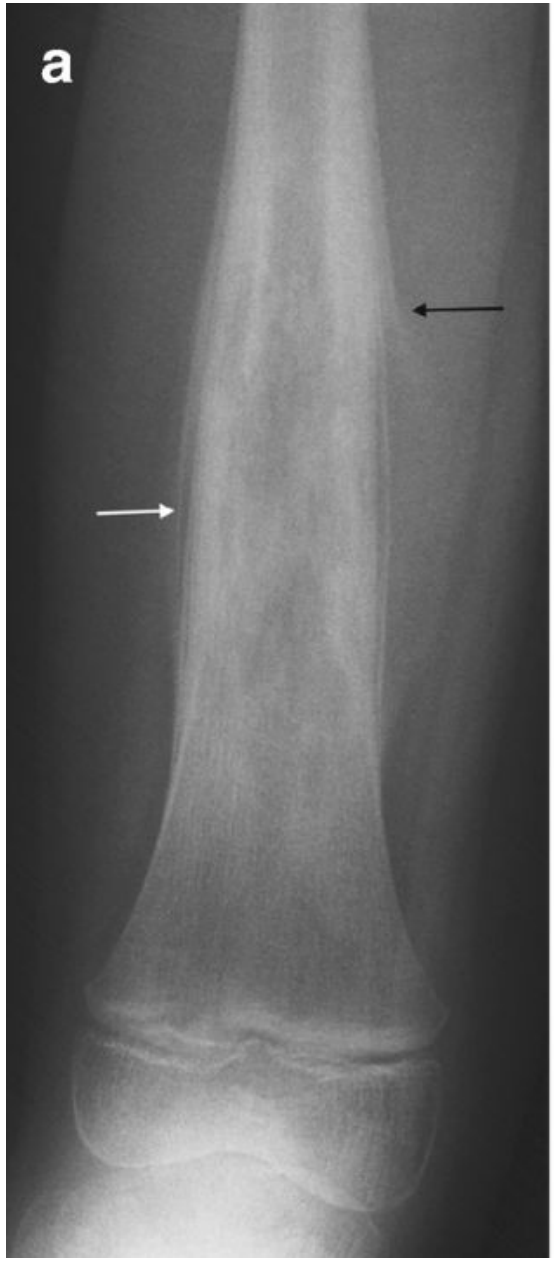
Ewing sarcoma

- Origin from **neural crest cells**, possibly from metaganglionic cholinergic neurons of parasympathetic nervous system

- >90% of patients have the translocation t(11;22)(q24;q12) leading to the production of a chimeric protein, EWS-FLI1
  - **EWS-FLI1**: Transcription factor that has been proven to mutate inoblasts in cell cultures

- Most common locations
  - Lower limbs 35%
  - Pelvis 26%
  - Thoracic wall 10%
  - Spine and upper limbs 8%
  - Head 3%

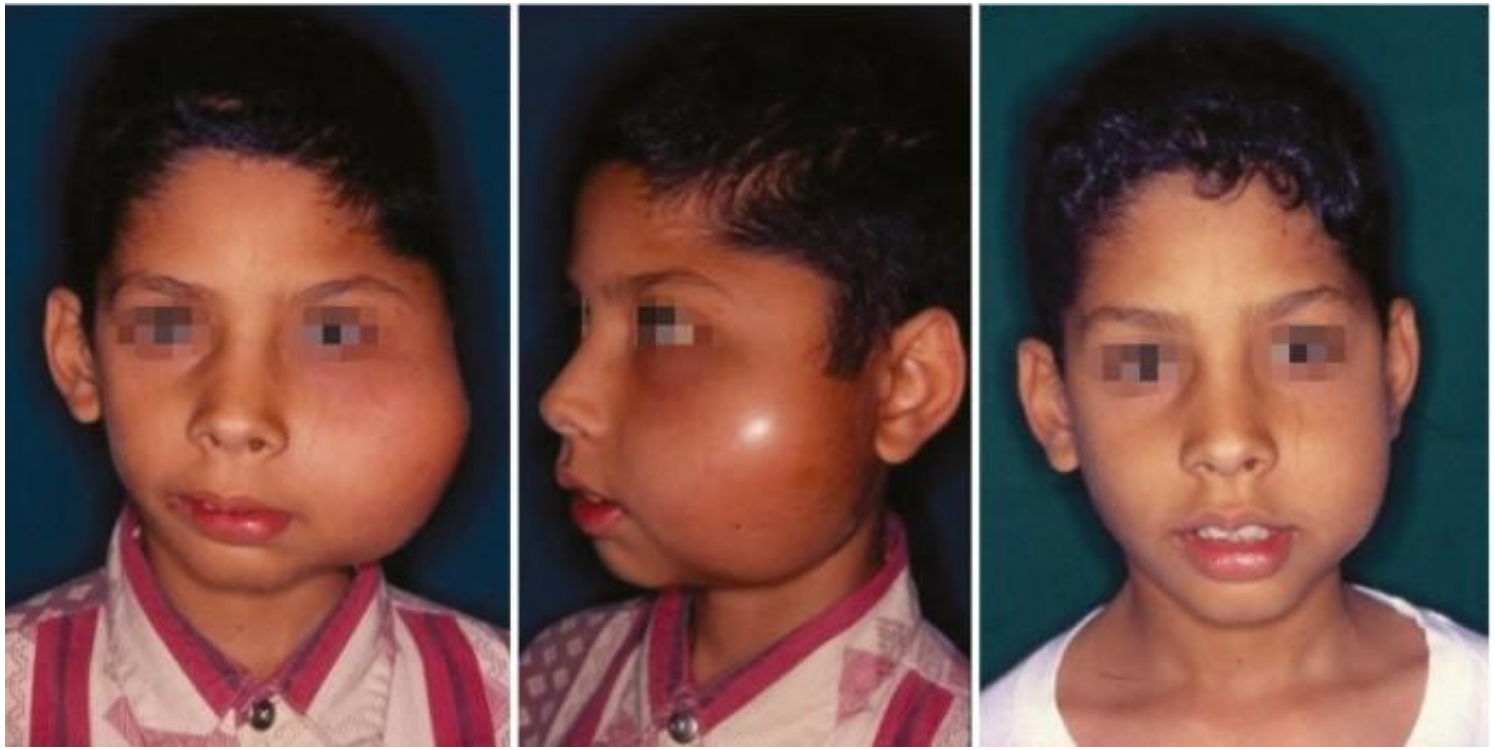
- Clinical presentation
  - Local pain
  - Oedema of limb
  - Fever
  - Inability to walk
- Diagnosis
  - Xray onion peel and periosteal reaction, osteolytic lesions, sclerosis
    - **Note: 5-8% of patients have normal X-rays!**
  - MRI of the lesion
  - Metastatic workup
    - PET/CT scan (**20-30% have metastases at diagnosis),** CT thorax, BM, trephine
- Management
  - Surgical excision
  - Pre- and post-operative chemotherapy
  - Radiotherapy (Ewing sarcoma is radiosensitive)
- Prognosis
  - 3-year survival 70% if no metastases
  - If metastases present upon diagnosis prognosis is <20%



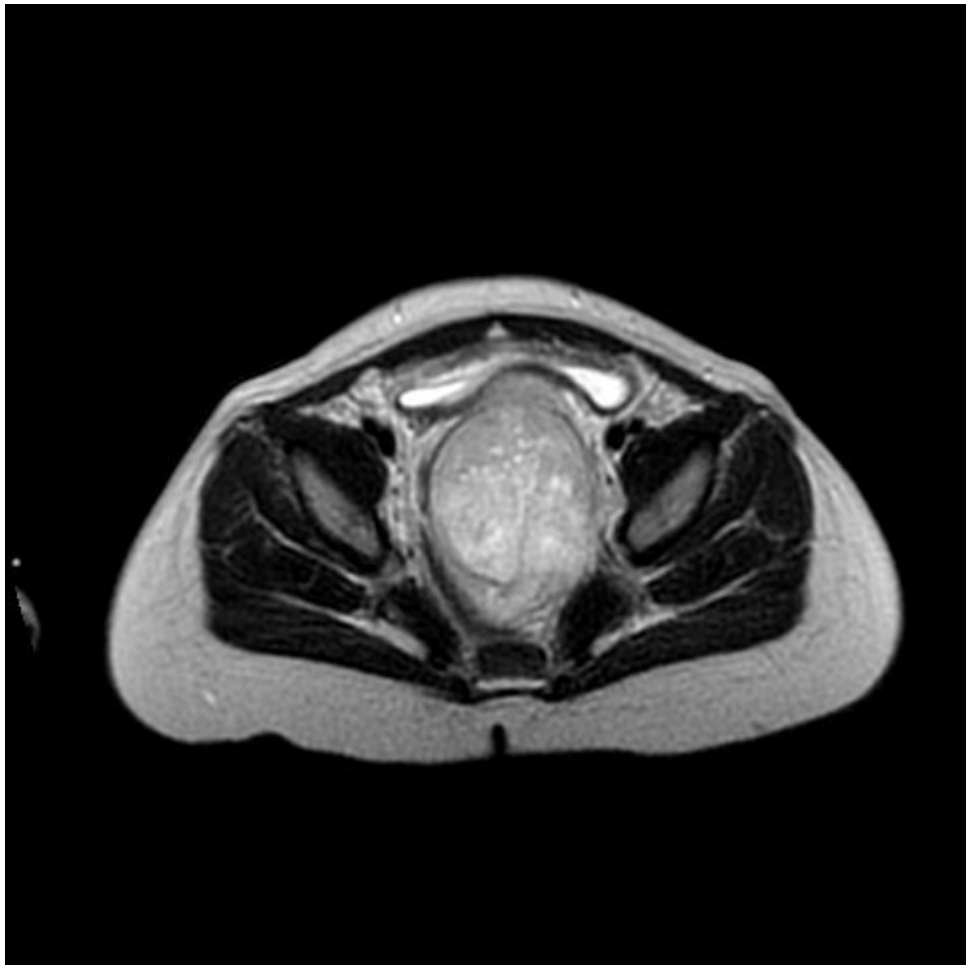
onion skin pattern (white arrow), periosteal reaction

Osteosarcoma vs Ewing sarcoma

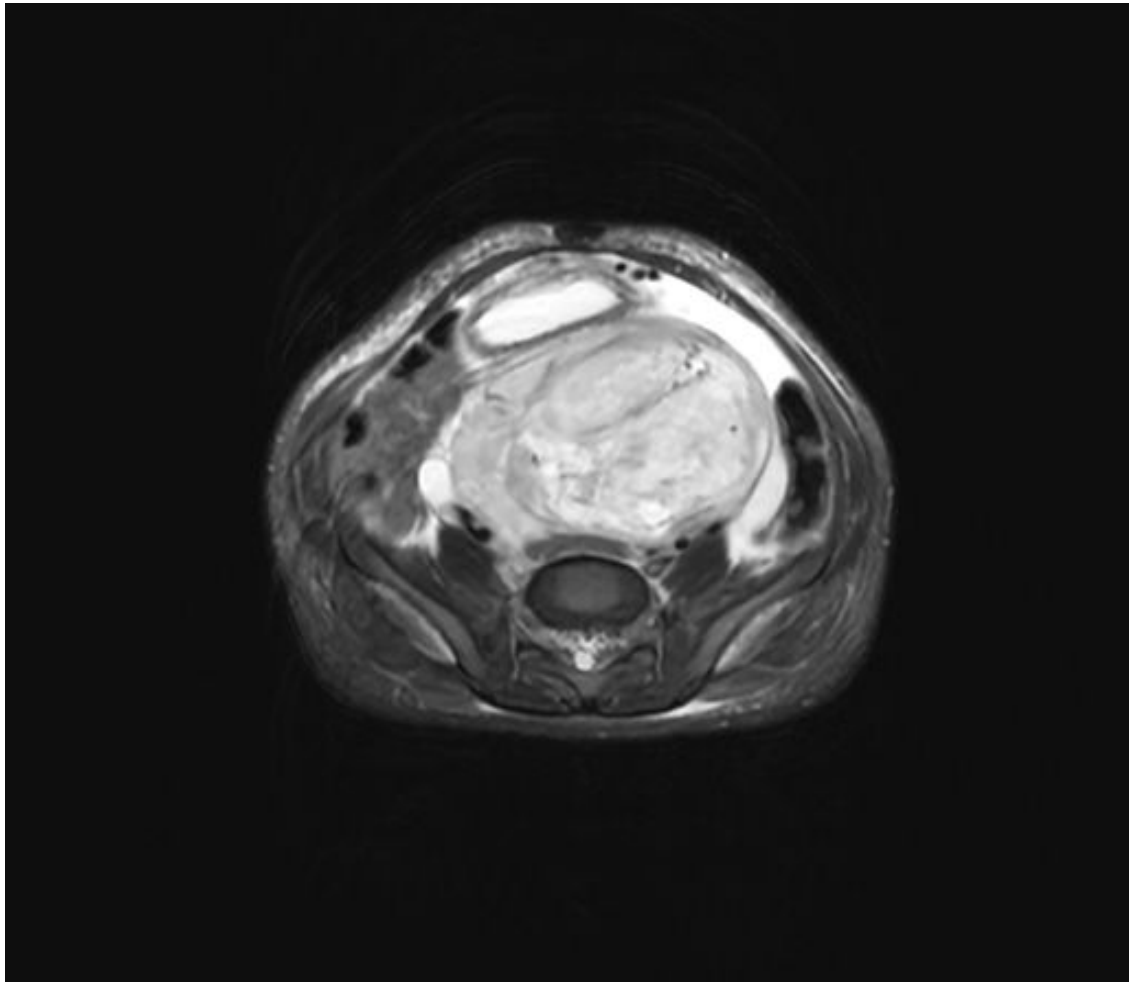
Parameter	Osteosarcoma	Ewing
Origin	Prodromal mesenchymal cells	Neural crest cells
Age	10-14 years (pubertal spurt)	10-20 years
Sex	Boys > girls	Boys > girls
Constitutional symptoms	Rare	More common
Location	Metaphysis	Diaphysis
X-ray	“Sunburst pattern”	“Onion skin”
Management	Radio-resistant	Radio –sensitive
Prognosis in metastatic disease	<20%	20-30%



20-month-old boy with difficulty in urination

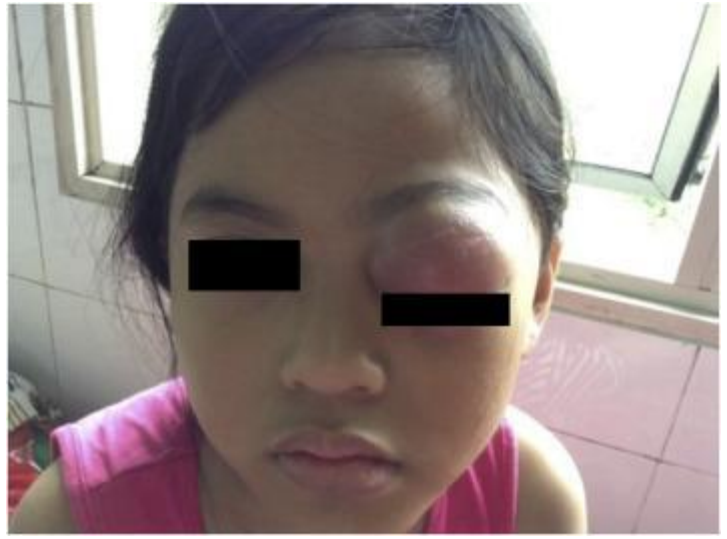


11-month-old boy with restlessness, discomfort



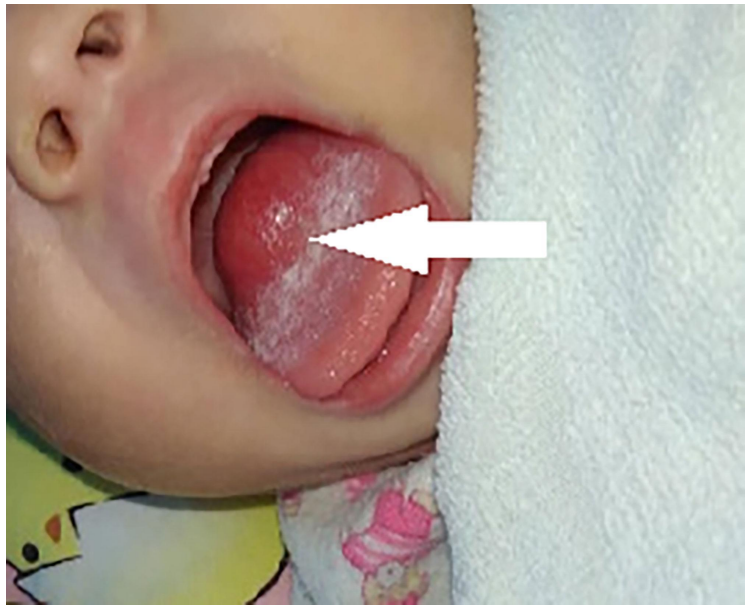
Rhabdomyosarcoma

- Soft tissue sarcoma, affecting striated muscle fibers
- Primitive **mesenchymal** cells that typically differentiate into skeletal tissue
- The most common soft tissue sarcoma diagnosed in children



- 2 age-peaks
  - 2-6 years: Prostate, vagina, bladder, head and neck
  - 15-19 years: limbs, torso, male reproductive system

- Head and neck RMS 35-40% in the cranial orbit, nasopharynx, soft tissue



- May be associated with
  - Anatomic anomalies of CNS, GI or urinary tract
  - NF1
  - Lung adenomatosis
  - Li-Fraumeni, chromosomal anomalies

- Clinical presentation according to the location
  - Soft tissue mass, Head and neck: Dyspnea, dysphagia, eyelid swelling, strabismus
  - Parameningeal: CNS symptoms

- Diagnosis: MRI of the lesion, biopsy
- Staging with CT thorax, 18-FDG PET/CT scan, BM + trephine

- Histopathology
  - Embryonal – associated with aneuploidies of the RAS and TP53 genes
  - Alveolar - two distinguishing chromosomal translocations, t(2;13)(q35;q14), which is more common, and t(1;13)(p36;q14)
  - Genetic fusions **PAX3::FOXO1 and PAX7::FOXO1** associated with these chromosomal translocations.
  - Pleomorphic/ Spindle cell/ Sclerosing subtypes

Table 3: Risk Group Assignment

Risk Group	Subgroup	Fusion Status	IRS Group	Site	Node Stage	Size or Age
Low Risk	**A**	Negative	I	Any	N0	Both Favourable
Standard Risk	***B***	Negative	I	Any	N0	One or both Unfavourable
	C	Negative	II, III	Favourable	N0	Any
High Risk	***D***	Negative	II, III	Unfavourable	N0	Any
	E	Negative	II, III	Any	N1	Any
	F	Positive	I, II, III	Any	N0	Any
Very High Risk	***G***	Positive	II, III	Any	N1	Any
	H	Any	IV	Any	Any	Any

Risk Group assignment is determined at diagnosis

Fusion status: Where fusion gene status is unavailable histopathology will be use. Non-alveolar disease should be defined as fusion gene negative and alveolar disease should be defined as fusion gene positive.

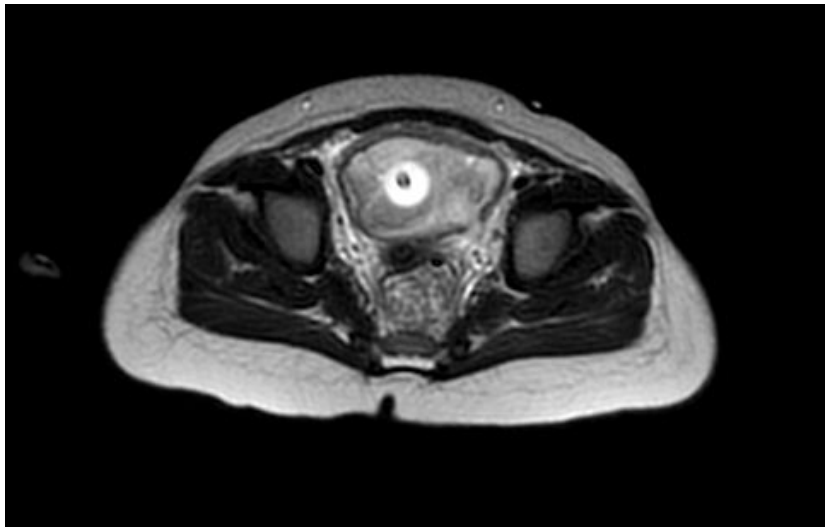
Site: Favourable sites are: GU including bladder-prostate, head & neck non-parameningeal, orbit and biliary primaries . Unfavourable sites are: all other sites

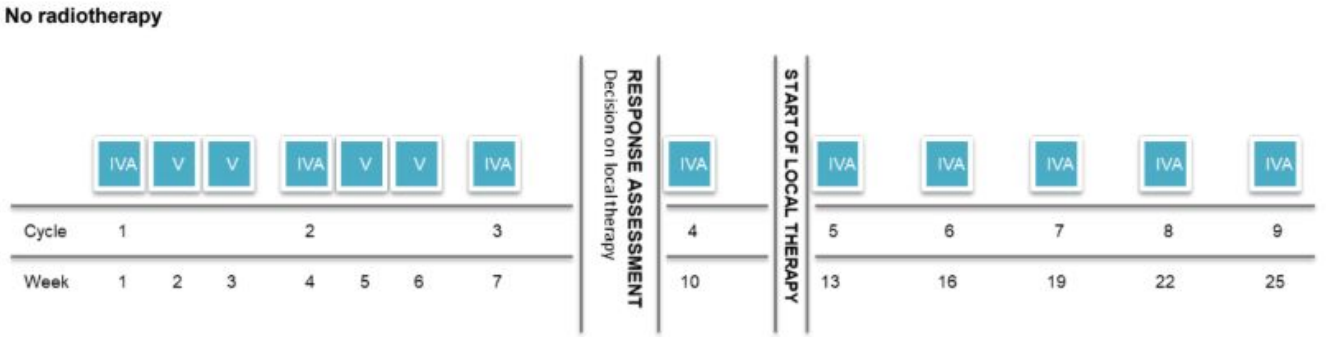
Node Stage: N0 = 0 positive lymph nodes, N1 = ≥ positive lymph nodes

Age: Favourable is defined as age over 1 and under 10 years of age at diagnosis

- Management →Chemotherapy →Surgical excision →Radiotherapy
- Prognosis → Depends on site, histology (embryonal favourable), age, stage, presence of genetic fusions

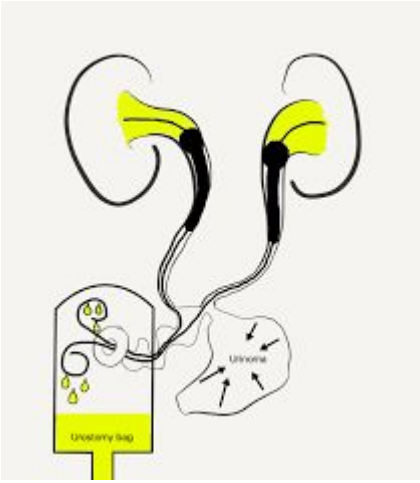
9-month girl with UTI and sepsis (Ps. aeruginosa) → renal U/S→ large bladder lesion





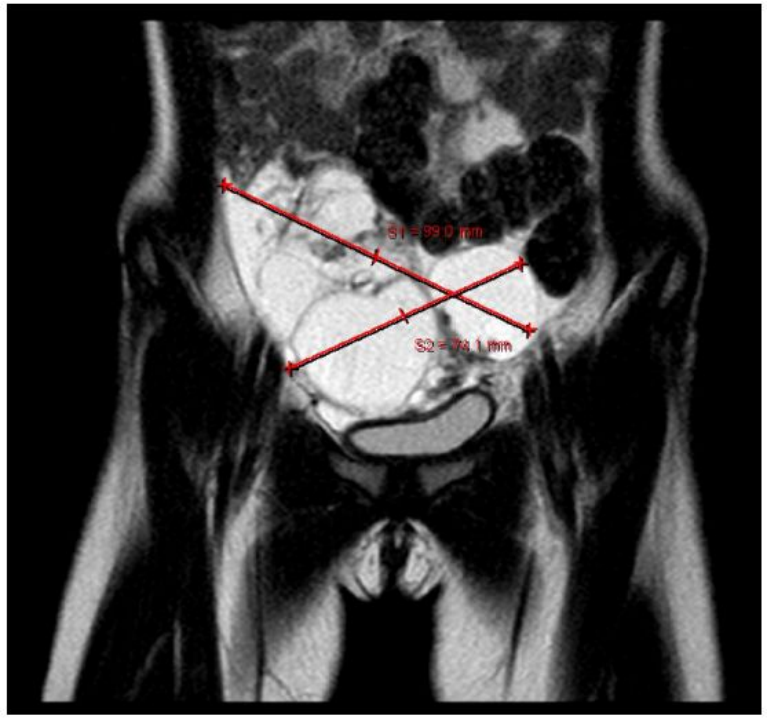
Biopsy → Embryonal RMS
No metastatic sites

Remission! But… significant nephrotoxicity

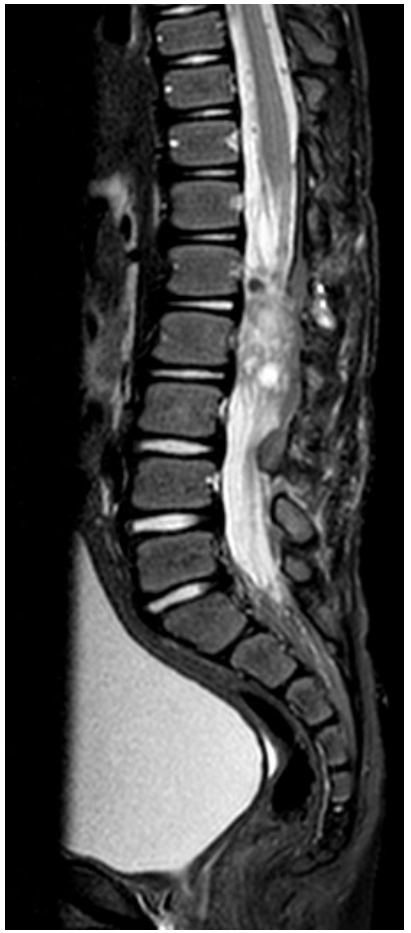


11-year-old boy with asymptomatic scrotal enlargement

5-year-old girl with abdominal pain RLQ



2-year-old boy with bladder and gait disturbances



Germ-cell tumors

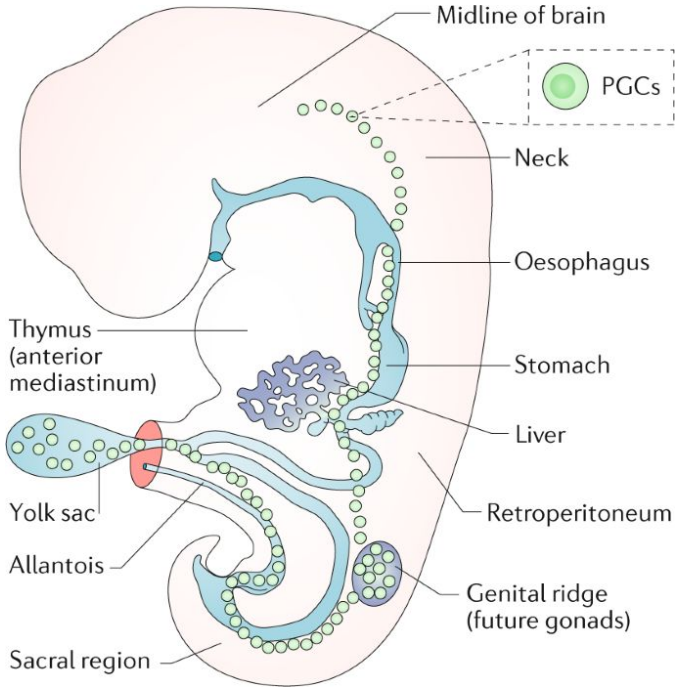
- Embryonal origin from primordial germ cells (endoderm) that would evolve to sperm cells and oocytes

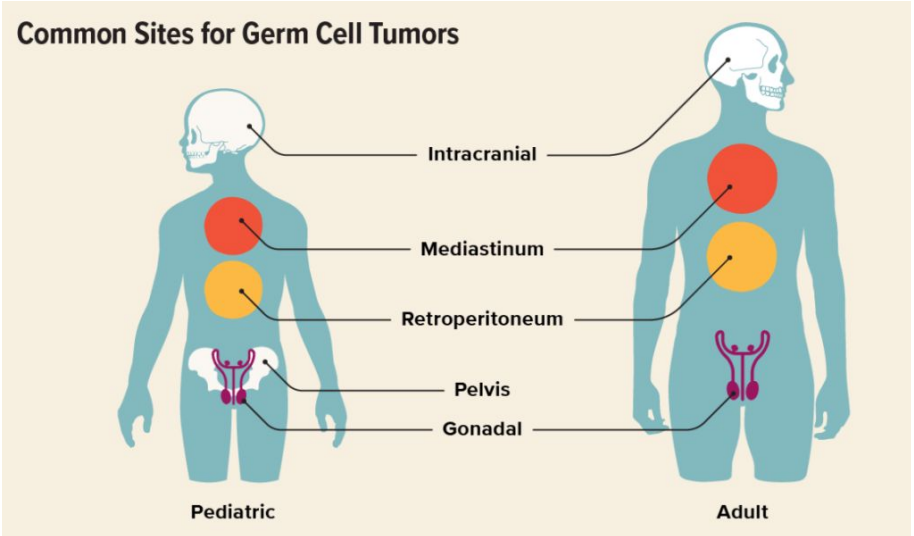
- Remaining germ cells in the migration route may give rise to GCT
  - Midline
  - CNS
  - Mediastinum
  - Retroperitoneal space
  - **Sacrococcygeal space**
  - Gonads

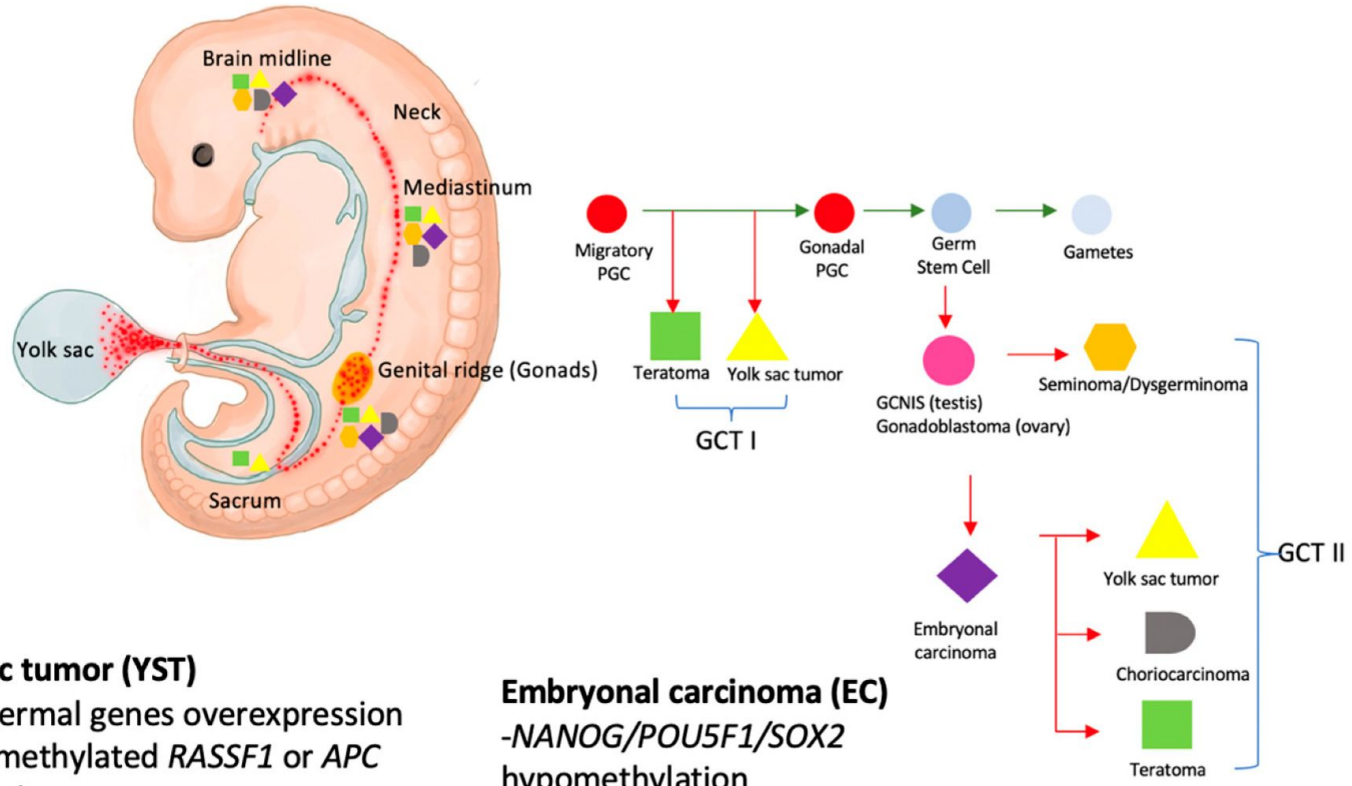
Extragonadal locations: 60%

Gonadal locations: 40%

- Rare <5% of all childhood malignancies
- Can be benign or malignant or indeterminate







Yolk sac tumor (YST)
-Endodermal genes overexpression
-Hypermethylated *RASSF1* or *APC*
-*GATA6/ FOXA2* overexpression
-*ERBB4* upregulated

Teratoma
-higher expression of ectodermal genes

Embryonal carcinoma (EC)
-*NANOG/POU5F1/SOX2* hypomethylation
-*TNFRSF8* overexpression
-isochromosome 12

Mediastinal germ cell tumor
-*TP53* mutation

Seminoma/Dysgerminoma
-12p chromosome overexpression
-12p isochromosome
-*KIT* or *RAS* mutation

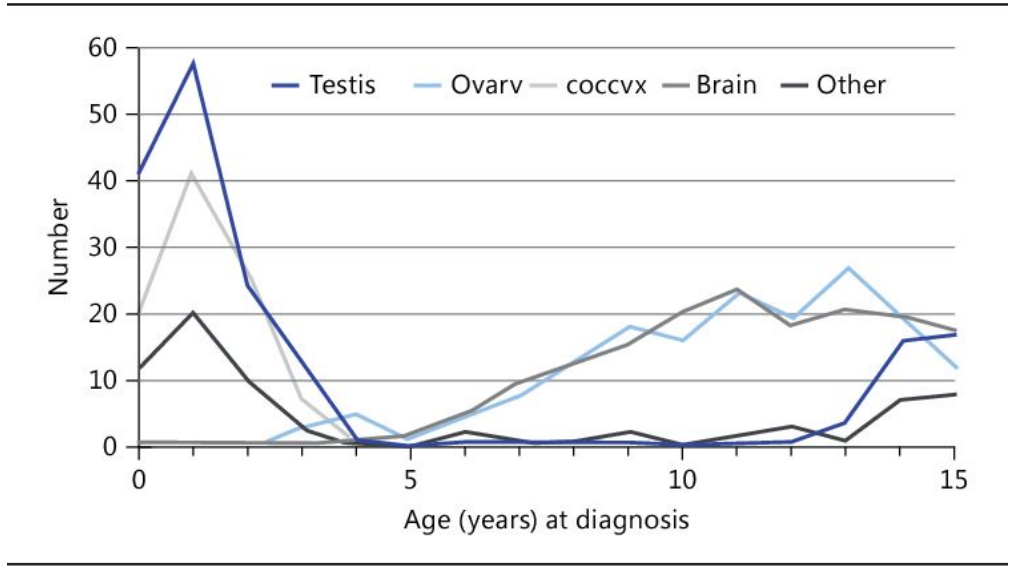
- The type of GCT depends on the stage of differentiation of the PGC

- Variable location, histology (often mixed), age and presentation

- Normal differentiation → normal gonads
- Low differentiation (germinal state) →germinoma
- Embryonic differentiation → embryonal carcinoma
- Extra-embryonic differentiation → yolk sac tumors and choriocarcinoma
- Somatic differentiation → teratoma

Cancers 2023, 15(7), 1998;

- Two-peaked pattern 3 years-old and adolescents (think: hormones)
- Girls>Boys overall
  - but malignant GCTs more common in boys
- Most common site is sacrococcygeal area
- Most common GCTs in children are:
  1. Teratomas
  2. Germinomas
  3. Choriocarcinomas
  4. Yolk sac tumors
  5. Sertoli-Leydig cell tumors
- Most common GCTs in adolescents are
  1. Seminomas



- Germ cell tumors are embryonal tumors!
- **a-fetoprotein**
- **β-chorionic gonadotropin**

- Clinical presentation **depends on location**
  - **Gonadal tumors**
    - Ovarian tumors: enlarged abdomen, acute or chronic pain
    - Testicular tumors: Painless mass in scrotum

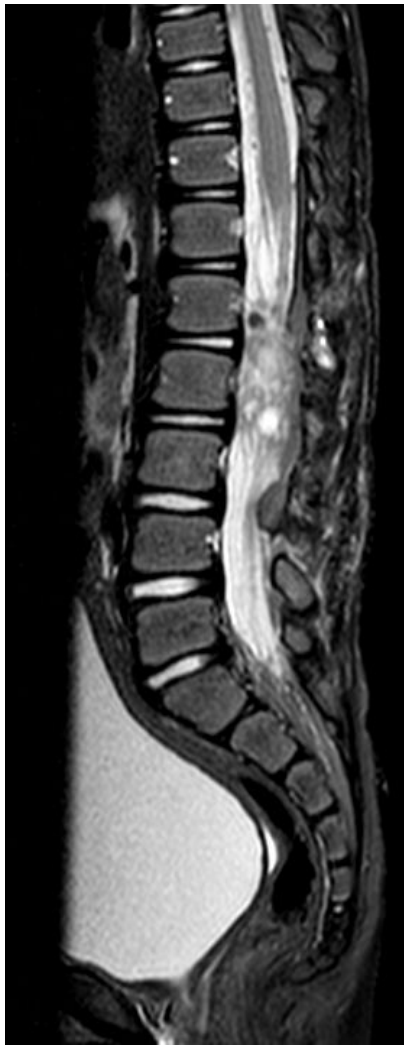
  Always include genitals in clinical examination!

  - **Extragonadal tumors**
    - **Sacrococcygeal**: Obstruction of rectum or urinary tract
    - **Brain**: Increased intracranial pressure, Parinaud syndrome (upgaze palsy mydriasis, nystagmus), failure to thrive, endocrine abnormalities
    - **Mediastinal**: Asymptomatic to dyspnea, superior vena cava syndrome, cardiac tamponade
    - **Retroperitoneal**: Pain, pressure in adjacent organs

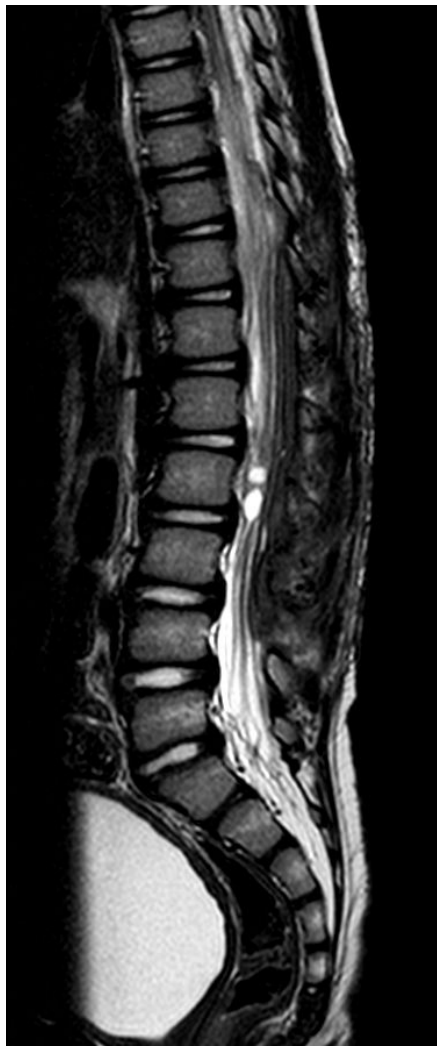
- Management
  - **Surgery**
  - Chemotherapy (cisplatin-based)
  - Radiotherapy (occasionally)

- Outcome
  - Best prognosis mature teratoma
  - Worst prognosis choriocarcinoma
  - **Follow-up aFP, bHCG**

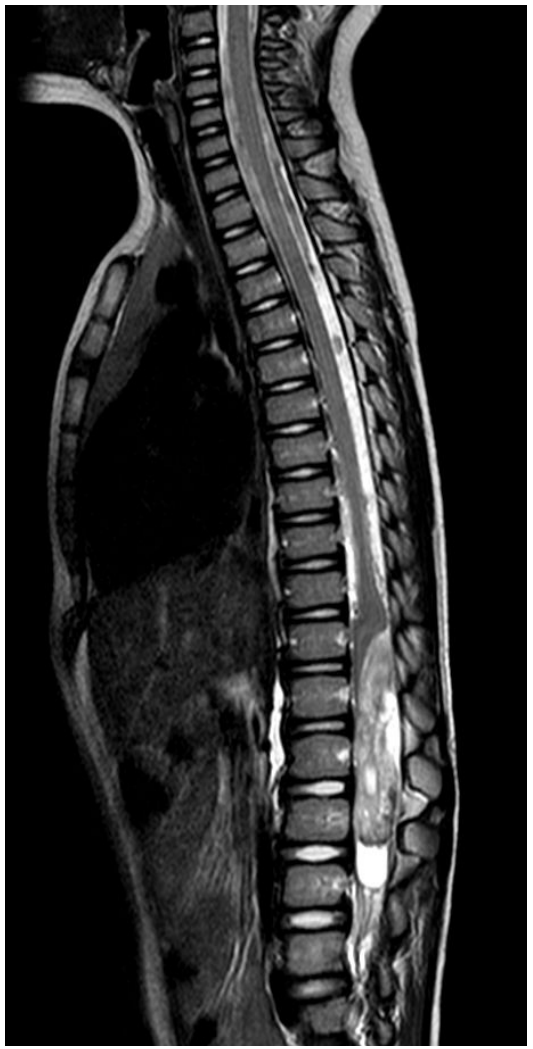
2-year-old boy with bladder and gait difficulties, aFP: 300 ng/ml



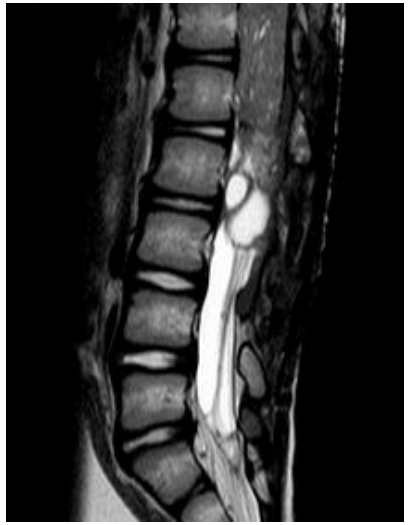
SURGERY



RELAPSE



- **Chemotherapy**
- **2nd surgery**
- **Chemotherapy (other regimen)**
- **HDCT + auto BMT**
- **3rd surgery**

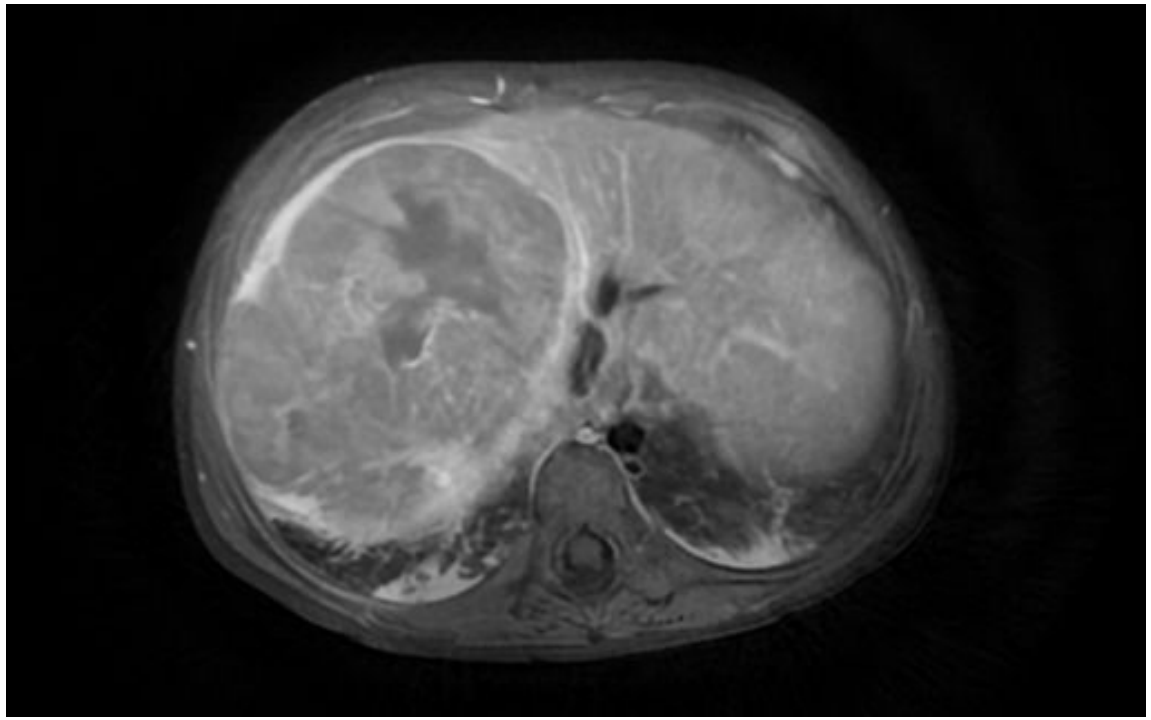


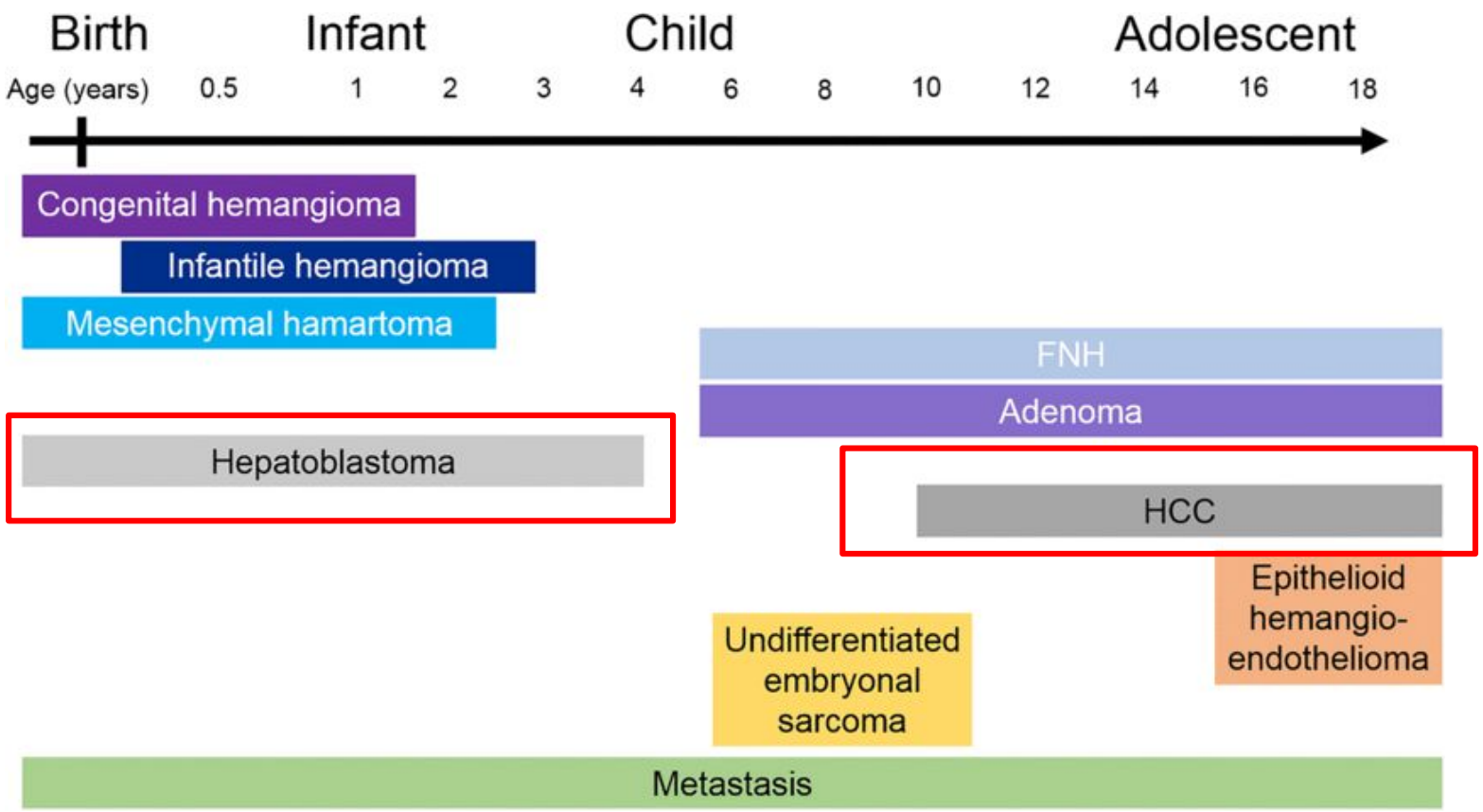
Radiotherapy

*Relapse: increase in aFP values → lesion dimensions

- 2-year-old boy with abdominal distention and jaundice

  - aFP: 80.000 ng/ml





Graphical depiction of liver tumor frequency based on patient age. Benign lesions are demarked by white font, while malignant lesions have black font. FNH focal nodular hyperplasia, HCC hepatocellular carcinoma

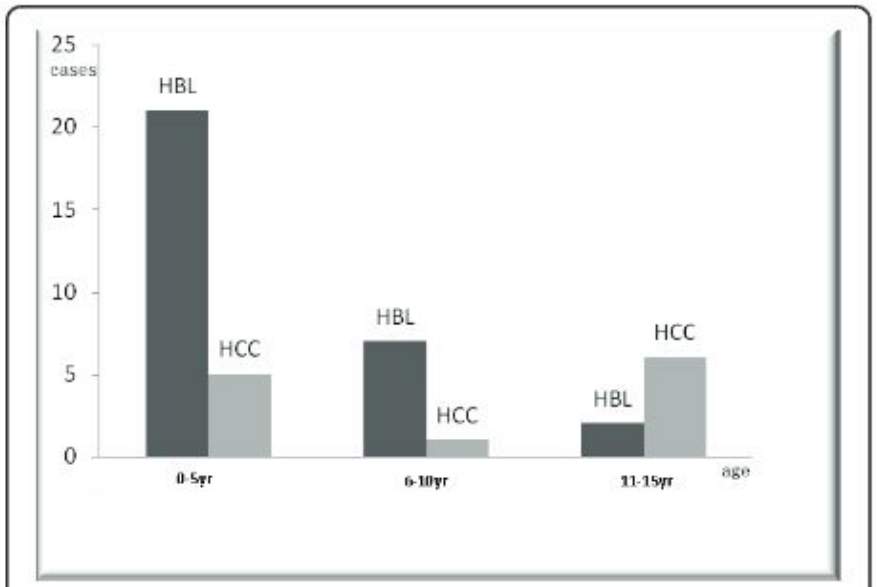
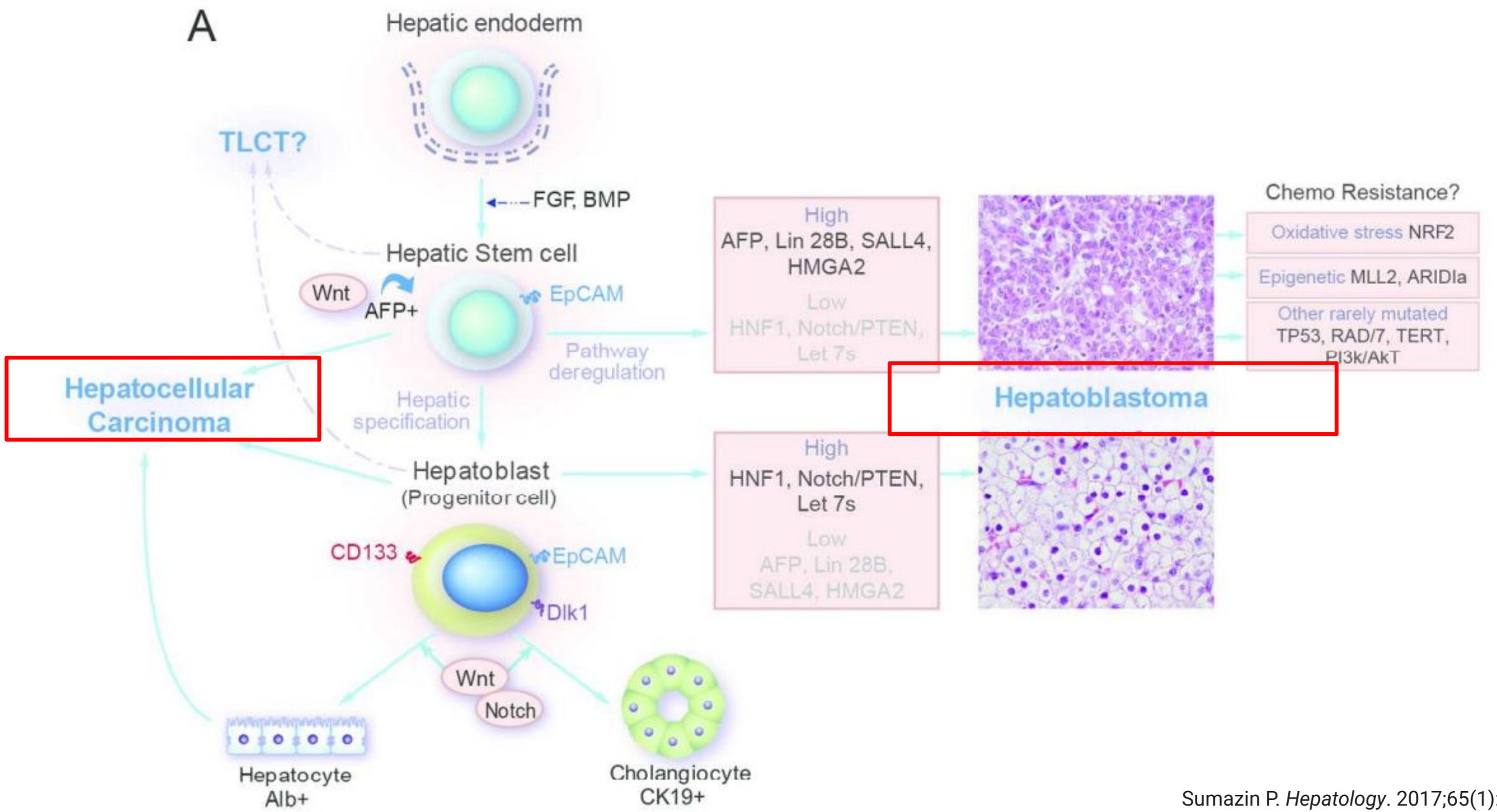


Figure 1 Histogram shows the different distributions of hepatoblastoma (HBL) and hepatocellular carcinoma (HCC) related to the onset age.

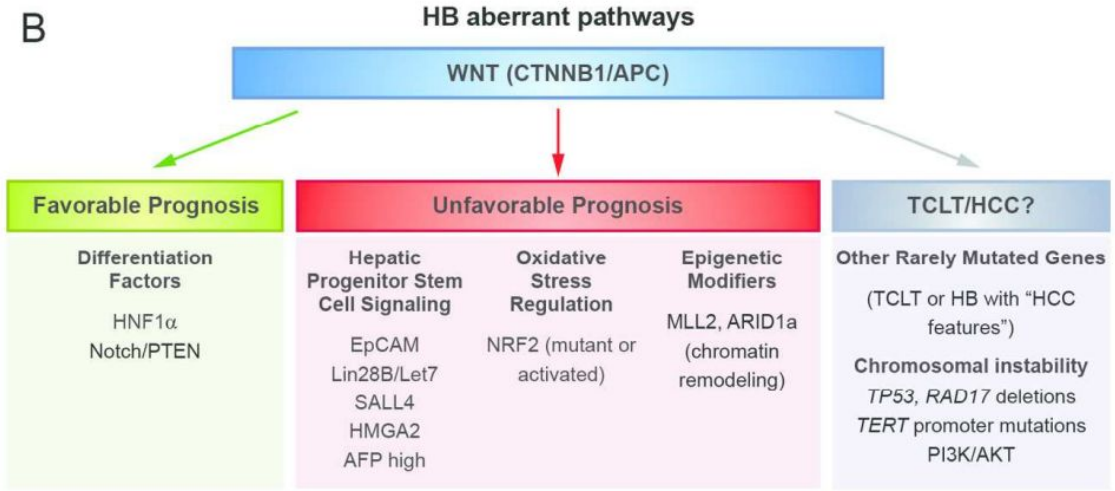
Zhuang *et al. BMC Gastroenterology* 2011, **11**:78
http://www.biomedcentral.com/1471-230X/11/78

Figure 5



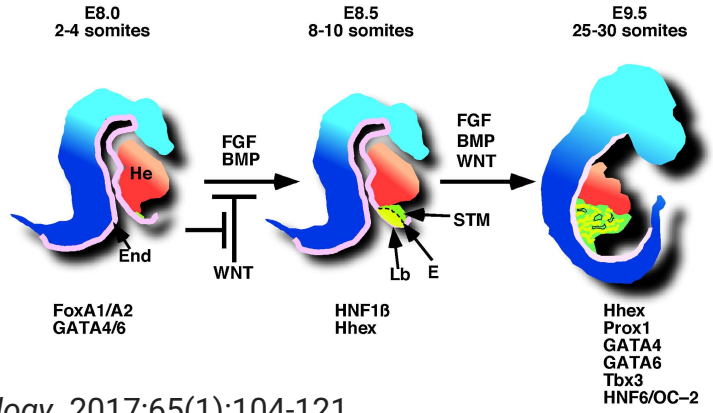
Sumazin P. *Hepatology*. 2017;65(1):104-121.

Hepatoblastoma



- Origin from hepatic stem cells that give rise to the epithelial components of the liver
- 3rd wk of gestation liver appears -Rapid growth until 10th wk
- WNT/β-Catenin signaling pathway
  - induces hepatic progenitor cells proliferation and differentiation into hepatocytes.

- Association with predisposing syndromes
  - Beckwith-Wiedeman
  - Semihypertrophy
  - Aicardi syndrome
  - Familial adenomatous polyposis
  - Glycogen storage disease
  - Prematurity with VLBW
  - Trisomy 18



Sumazin P. *Hepatology*. 2017;65(1):104-121.

Hepatoblastoma

- Clinical presentation
  - Abdominal mass/ distention
  - Abdominal pain
  - Vomiting/ Anorexia/ Weight loss

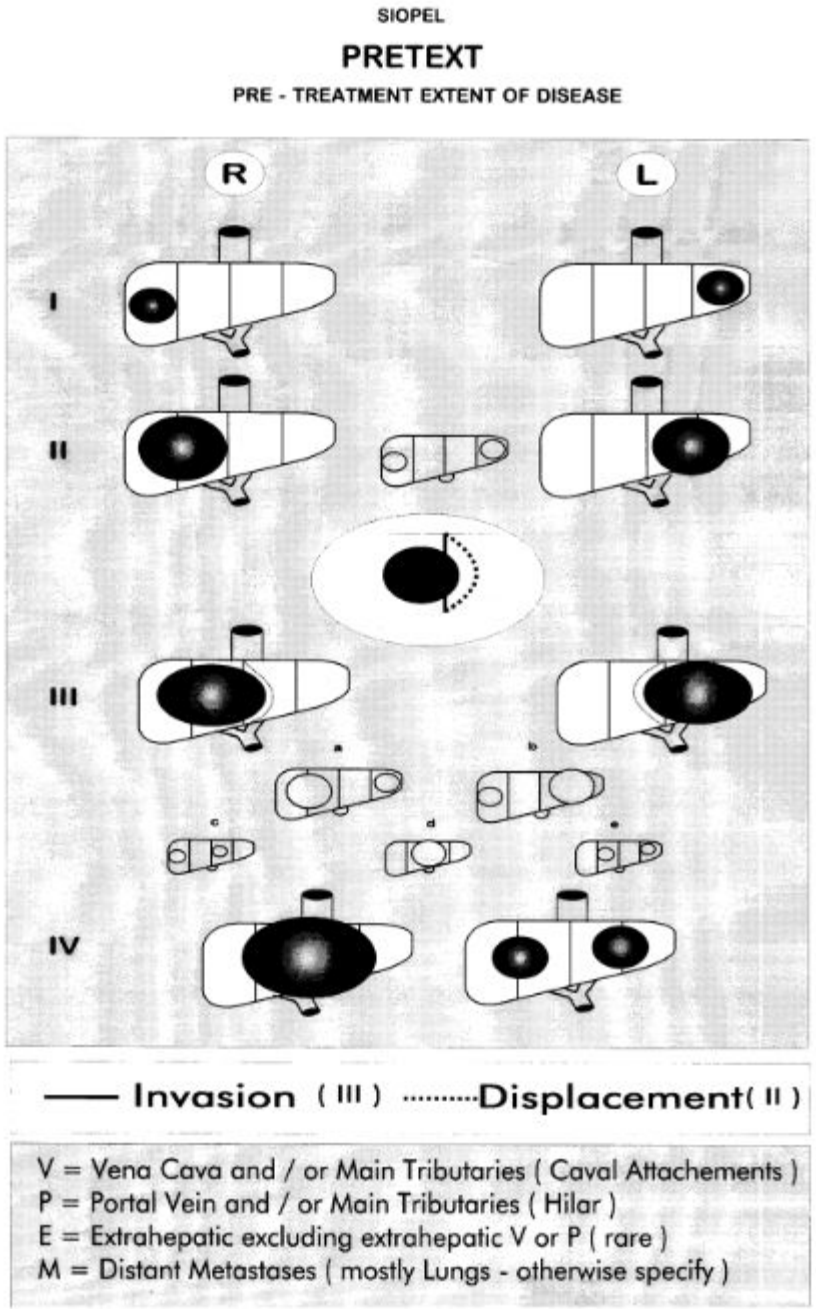
- Management
  - Surgical excision
  - Chemotherapy (pre- and post-operative)
  - Radiotherapy (tumor sensitive to radiotherapy)
  - Liver transplantation (if surgery not possible and no metastases)

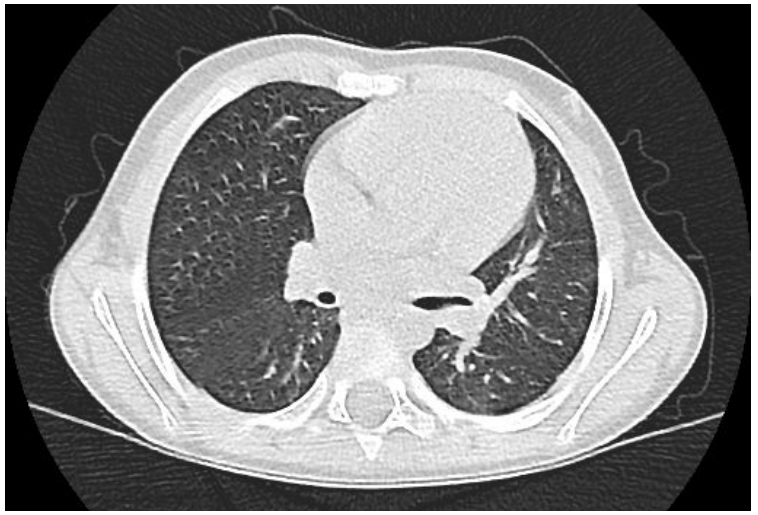
- Prognosis
  - Depends on the stage and type
  - Overall favourable (>90%)

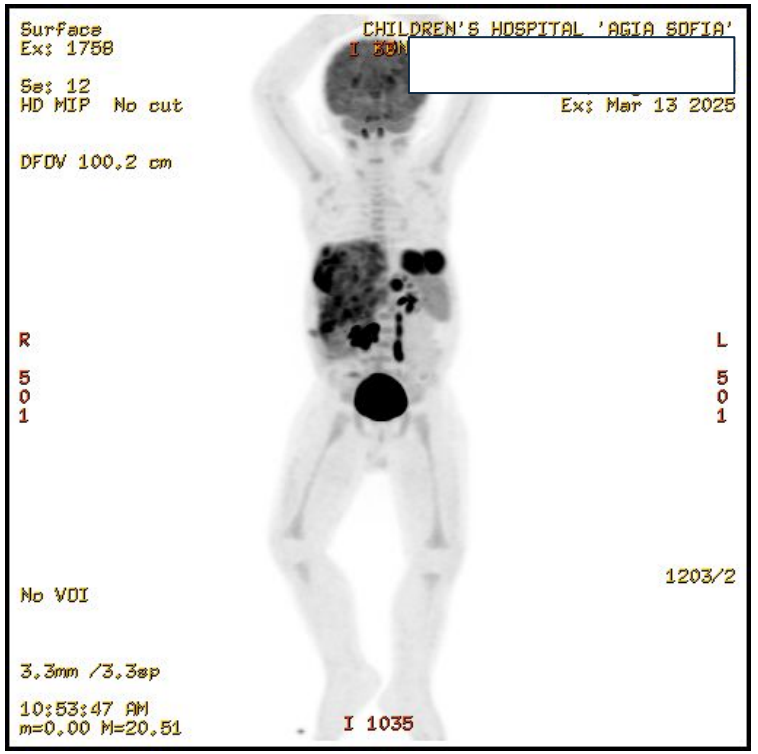
Hepatoblastoma is an embryonal tumor
- **a-fetoprotein**
- **β-chorionic gonadotropin**

However 50% of patients with hepatocellular carcinoma also have elevated aFP levels

Figure 10.1


SIOPEL
PRETEXT
PRE - TREATMENT EXTENT OF DISEASE
R
L
I
II
III
IV
a
b
c
d
e
—— Invasion (III) .....Displacement(II)
V = Vena Cava and / or Main Tributaries (Caval Attachements)
P = Portal Vein and / or Main Tributaries (Hilar)
E = Extrahepatic excluding extrahepatic V or P (rare)
M = Distant Metastases (mostly Lungs - otherwise specify)




Surface
Ex: 1758
Se: 12
HD MIP No cut
DFOV 100.2 cm
CHILDREN'S HOSPITAL 'AGIA SOFIA'
Ex: Mar 13 2025
R
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5
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1203/2
No VOI
3.3mm /3.3sp
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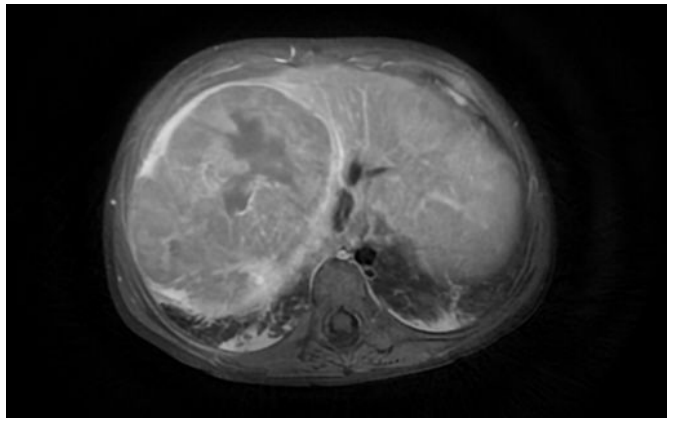
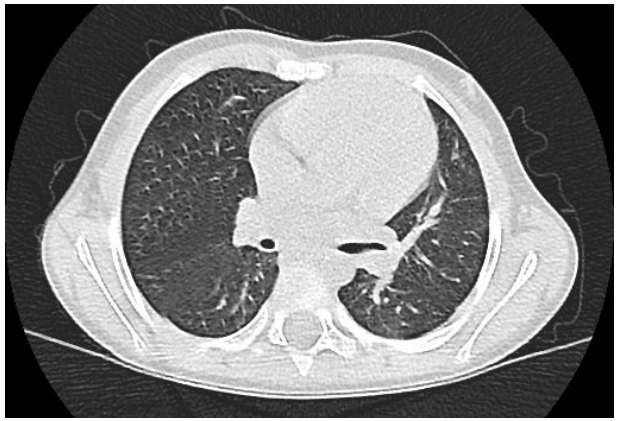
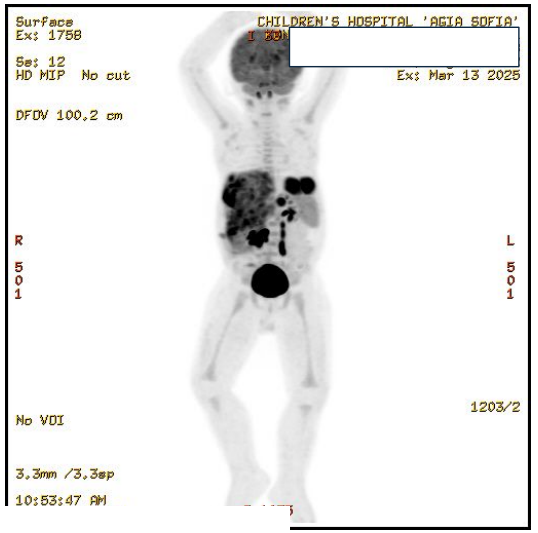
I 1035






Surface
Ex: 1758
Se: 12
HD MIP No cut
DFOV 100.2 cm
CHILDREN'S HOSPITAL 'AGIA SOFIA'
Ex: Mar 13 2025
R
L
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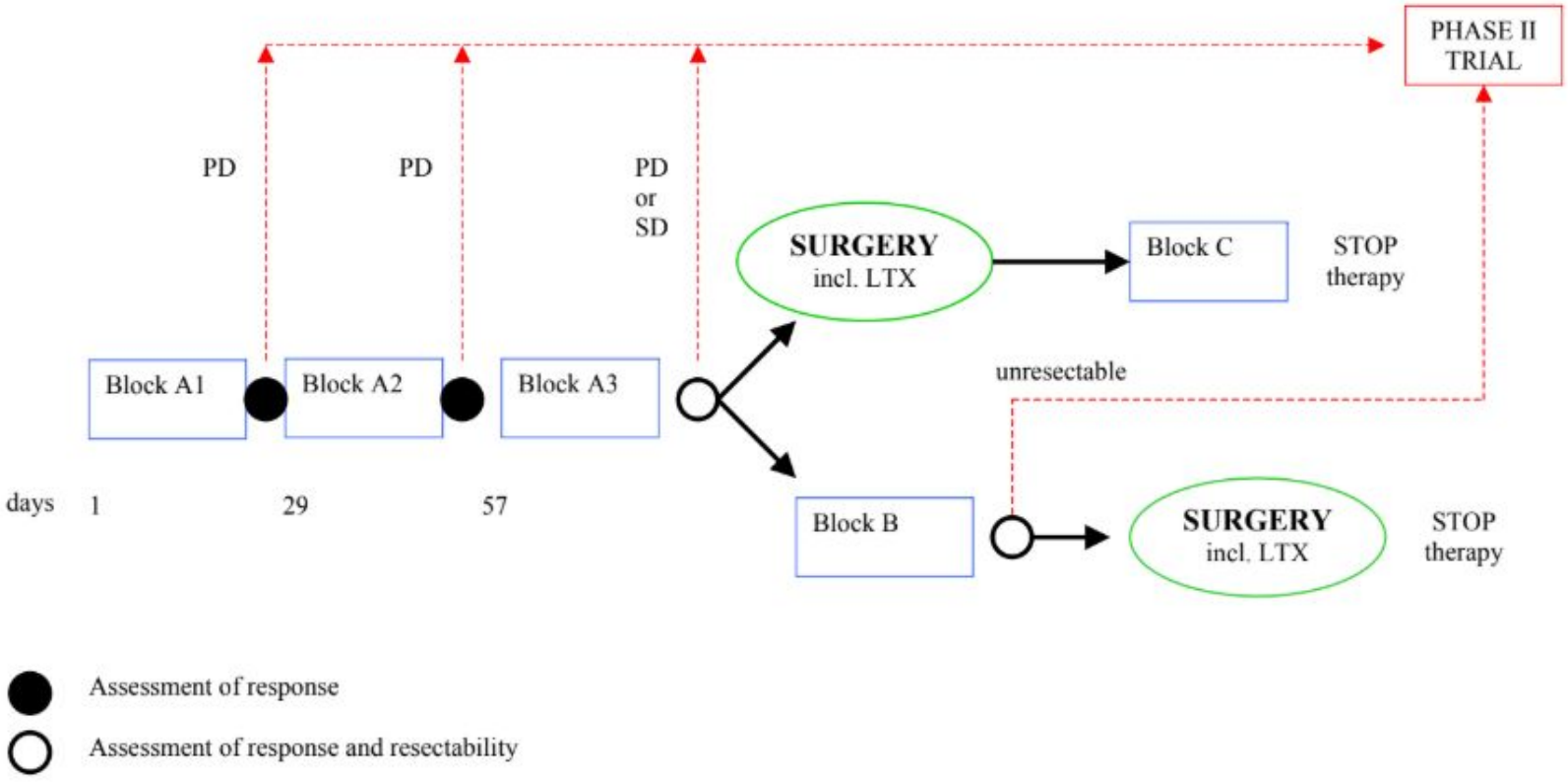
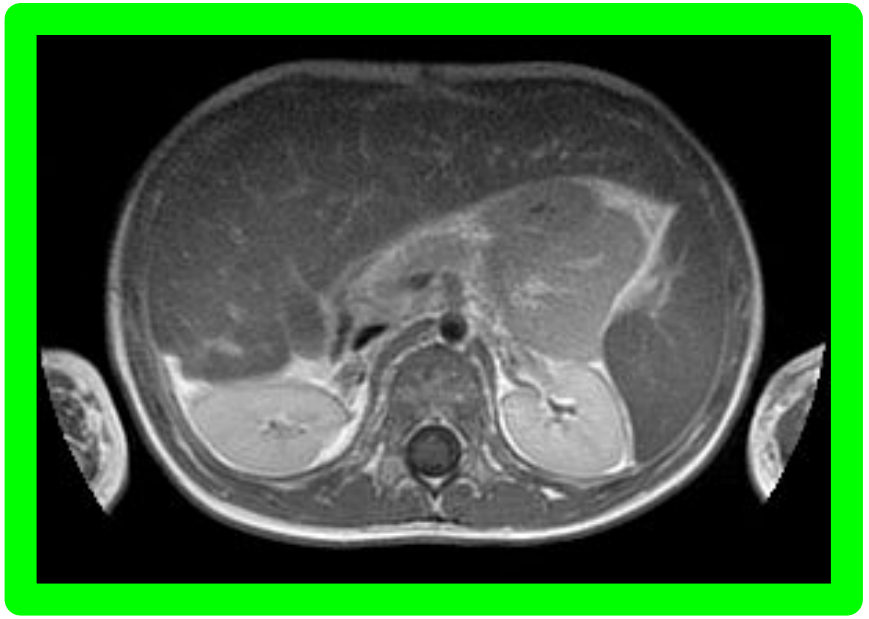
1203/2
3.3mm /3.3sp
10:53:47 AM

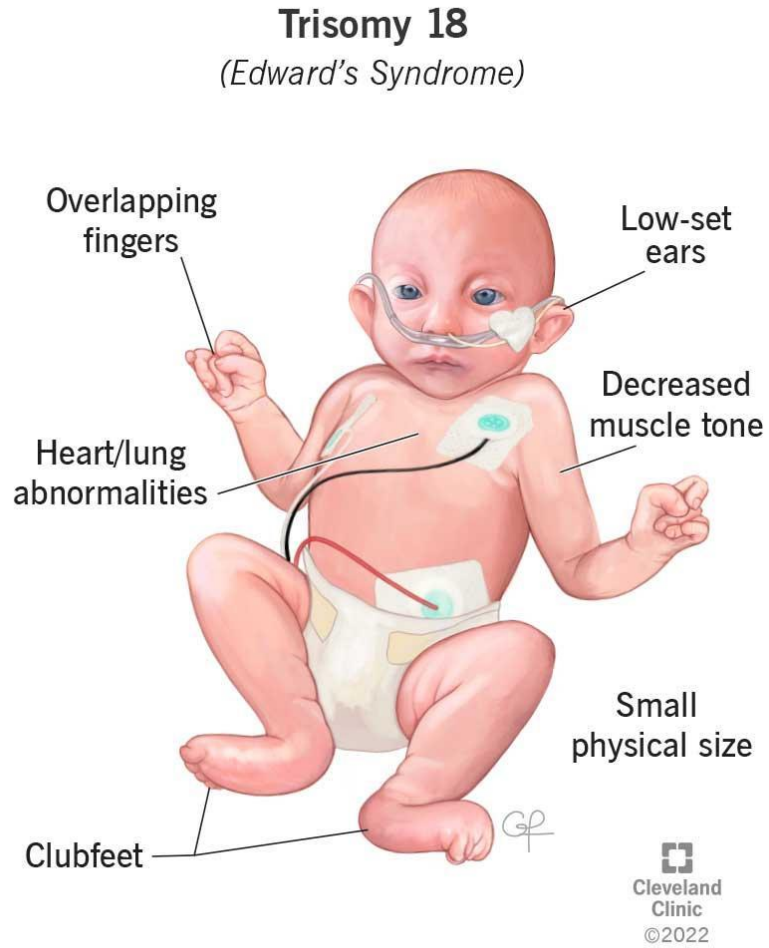

PHASE II TRIAL
PD
PD
PD or SD
SURGERY incl. LTX
Block C
STOP therapy
Block A1
Block A2
Block A3
unresectable
days
1
29
57
Block B
SURGERY incl. LTX
STOP therapy
Assessment of response
Assessment of response and resectability



Major Criteria - BWS	Minor Criteria - BWS
Gigantism (Prenatal/postnatal macrosomia)	Pregnancy related findings – placentomegaly, placental mesenchymal dysplasia, polyhydramnios
Hemi hyperplasia	Prematurity
Abdominal wall defect – omphalocele, umbilical hernia	Neonatal hypoglycemia
Ear anomalies – anterior linear lobe creases, posterior helical pits	Cardiomegaly, structural cardiac anomalies
Embryonal tumors	Nevus flammeus, other vascular malformation
Visceromegaly	Diastasis recti
Renal abnormalities	Midface hypoplasia
Positive family history	Coarse facies

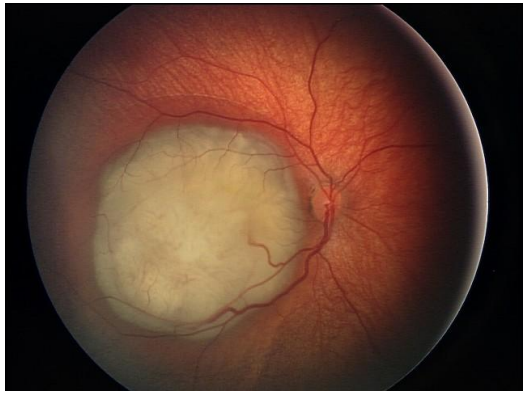
Chromosomal deletion syndrome 11p15.5 of maternal origin – abnormal methylation pattern for genes IGF2, CDKNIC, LIT1

- **Remember appropriate follow-up in known syndromes!**
- **Every 3 months until 5 years old, then yearly**



VSD, ASD, PDA

Retinoblastoma

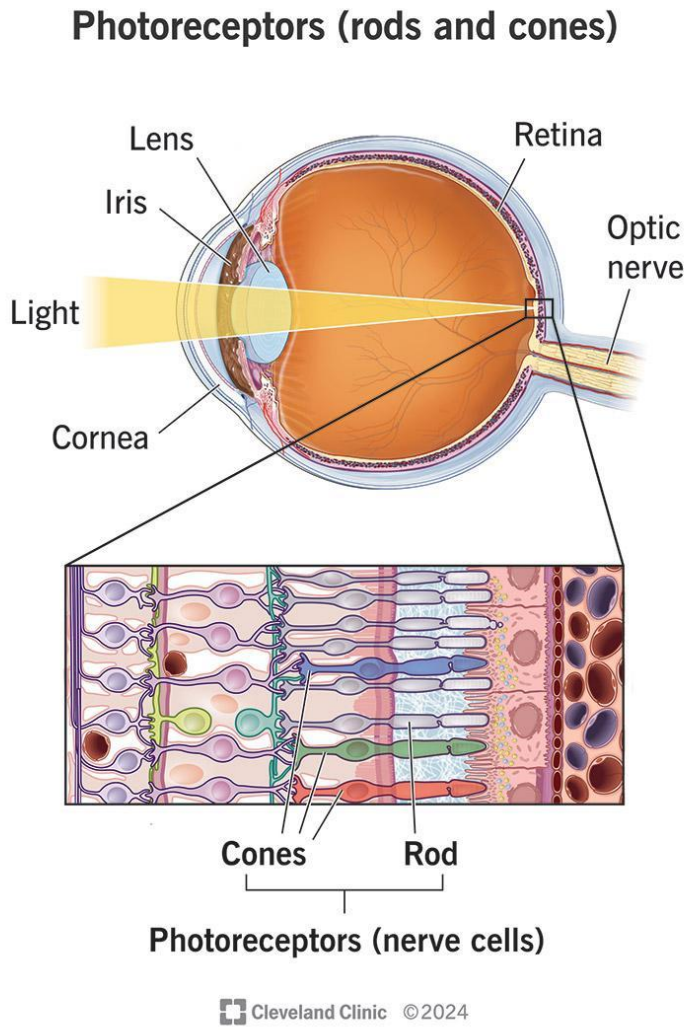


- Rare tumor
  - 4% of childhood malignancies
  - 1:14.000-23.000 live births
  - Embryonal origin -Development in the first three years of life

- Loss-of-function mutation on the RB1 gene (13q)
  - Tumor suppressor gene
  - pRb protein implicated in cell proliferation
  - Affects the developping prodromal cells of the cones
  - 20% of people with partial loss of 13q develop RB

- Unilateral (more common) or bilateral

- Familial/sporadic, hereditary or not
  - All bilateral RB's are inherited in an AD fashion
  - And 20% of unilateral RB's



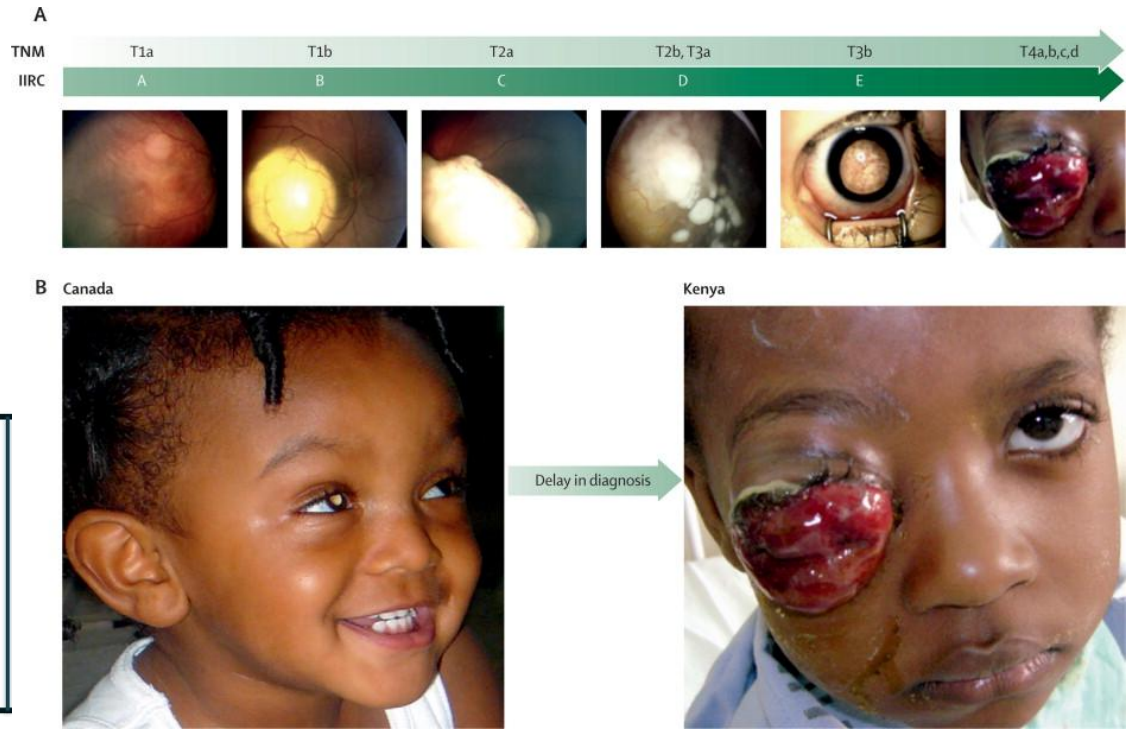
Photoreceptors are light-sensitive nerve cells in your eyes. Rod photoreceptors detect light only, while cones detect colors.

- Symptoms
  - Leukocoria (>50%), mydriasis, inability to focus
  - Strabismus, amblyopia, iris heterochromia
  - Conjunctival redness (newly formed vessels)
  - Pain, possibly glaucoma

- Diagnosis
  - **RED REFLEX from birth and in all pediatrician visits <3y**
  - Ophthalmoscopy – MRI
  - NO BIOPSY (*exception if needed for differential diagnosis*)

- Management
  - **Goals : Preservation of life > eye > vision**
  - Depends on staging (infiltration of adjacent tissues)
  - Topical therapy: Laser, cryotherapy
  - Ocular extraction
  - Chemotherapy
  - Radiotherapy

- Prognosis
  - **Timely recognition is of the essence!**
  - 95% if RB restricted in the retina
  - 70% if metastatic RB (but outside CNS)
  - <10% if CNS metastases



Progression of retinoblastoma (A) from small intraretinal tumours that can be cured by laser treatment and cryotherapy (TNM T1a, IIRC A) to massive orbital retinoblastoma probably extending into the brain (TNM T4a-b). A difference in age at diagnosis recorded between Canada and Kenya could be the difference between possible cure and certain death (B). The Canadian child with leucocoria was diagnosed because of the left-hand image, which was taken by his sister with his mother's mobile phone. TNM=Tumor Node Metastasis Cancer Staging.[22] IIRC=the International Intraocular Retinoblastoma Classification.[23]

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Young child with leukocoria: Think RB until proven otherwise

Old child with leukocoria: Think ocular toxocariasis!

- *Ask for living conditions, pets (cat/dog), water facilities*
- *Peripheral eosinophilia, treatable with albendazole*

- Symptoms
  - Leukocoria (>50%), mydriasis, inability to focus
  - Strabismus, amblyopia, iris heterochromia
  - Conjunctival redness (newly formed vessels)
  - Pain, possibly glaucoma

- Diagnosis
  - **RED REFLEX from birth and in all pediatrician visits <3y**
  - Ophthalmoscopy – MRI
  - NO BIOPSY (*exception if needed for differential diagnosis*)

- Management
  - **Goals : Preservation of life > eye > vision**
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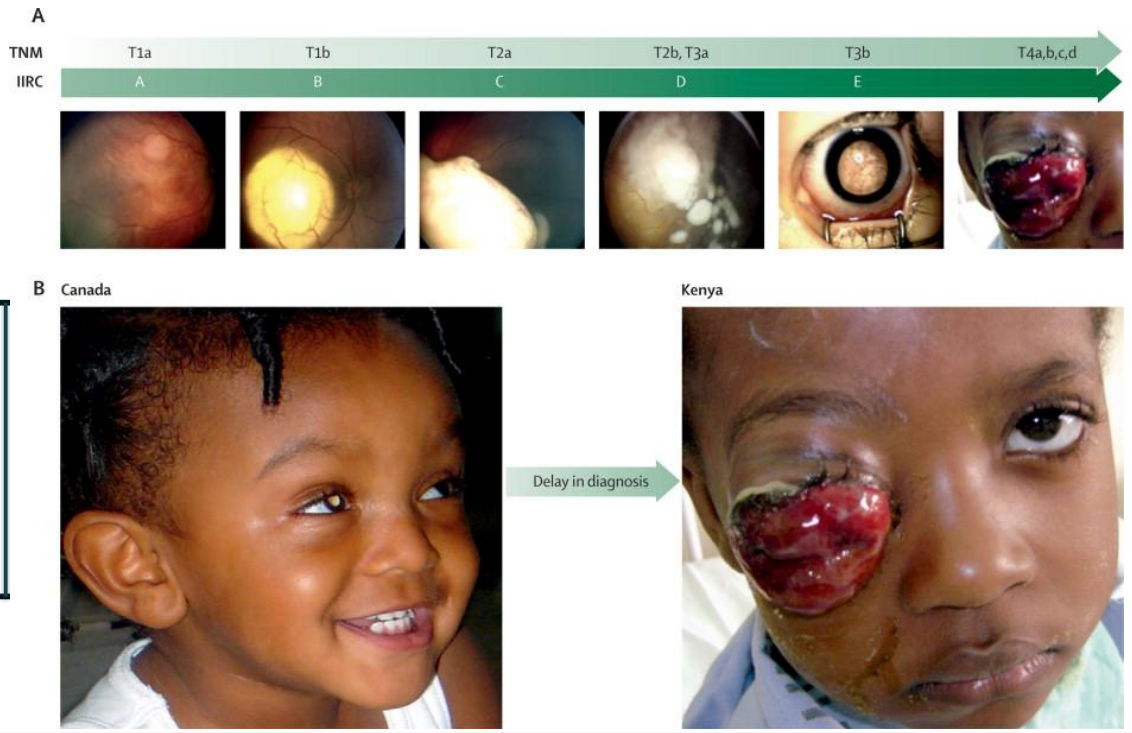

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When suspecting a solid tumor in a child/adolescent, **ask questions!**

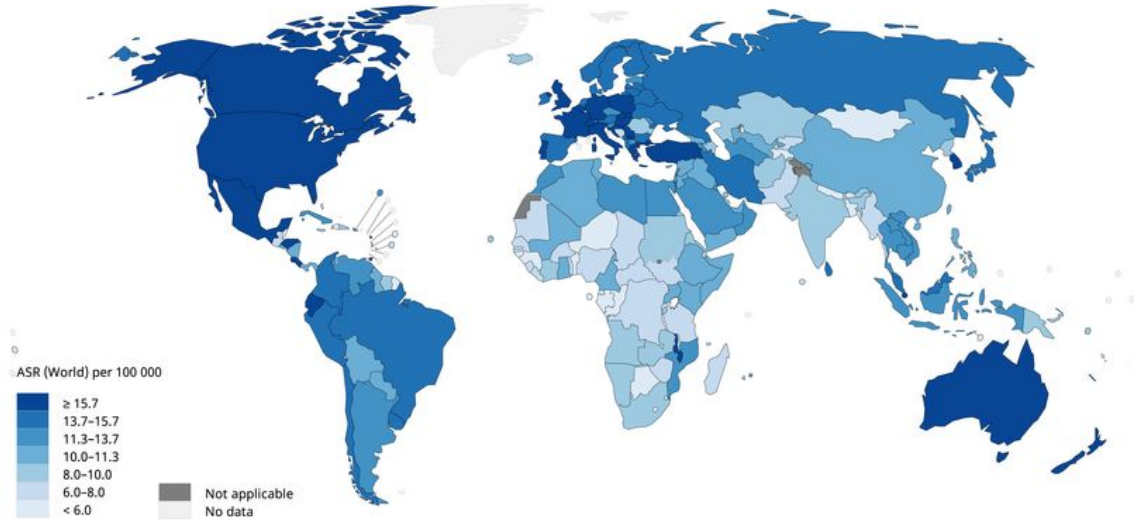
1. Signs of emergency
2. Site of origin (...and cell of origin)
3. Basic epidemiology (age, most common diagnoses)
4. Biomarkers (aFP, bHCG)
5. Metastases
6. Phenotype, family history, associated syndromes

Always seek expert opinion

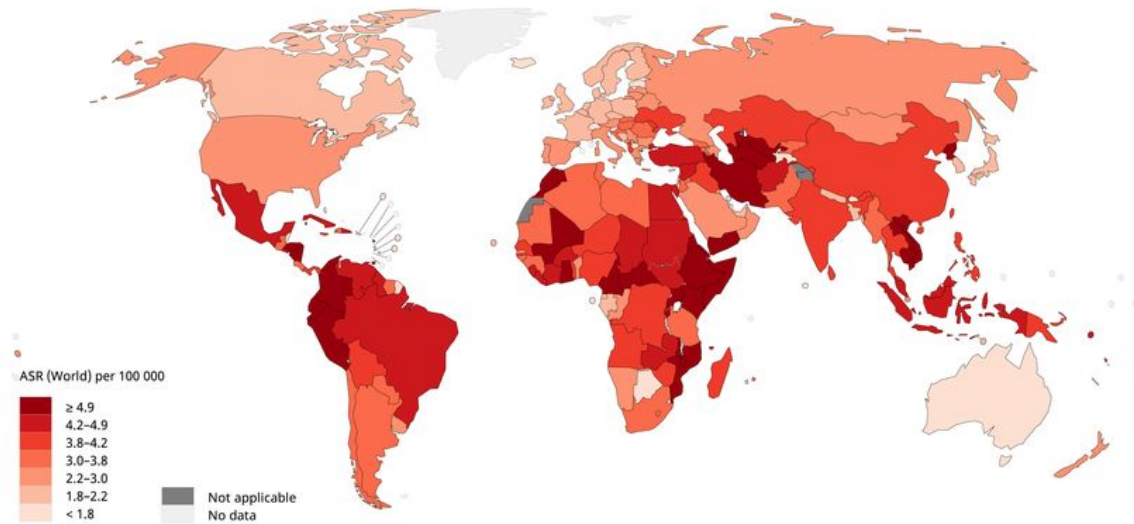
Refer the patient to Ped Hem/Onc

Clinical examination of all patients in routine visits!

incidence



mortality



Data source: GLOBOCAN 2020 Graph production: IARC(http://gco.iarc.fr/today) World Health Organization