

# Tumors of the childhood

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# Children tumors

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Tumor - incorrect, palpable or visible structure

The tumor's etiology

- congenital
- inflammatory
- cancerous

To differentiate

- interview
- physical examination
- knowledge of the tendency to localize tumors in a particular location at a specific population (age, gender, etc)
- additional tests: imaging, histopathological, immunochemical, etc

# Examination

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## Interview

- How long it last
- Allergies, diet, skin changes
- Drugs, vaccinations
- Contact with animals
- Weight loss
- Changes in child character

## Physical examination- the tumor and its:

- localization (local / generalized, symmetrical / asymmetrical)
- size and shape
- consistency, splashing
- soreness, swelling, appearance of the skin
- nodes - single / packages

# Neoplasms

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## BENIGN

- Lipoma
- Fibroma
- Hemangioma
- Nerve tissue tumors (neurofibromas, schwannoma)
- Teratoma

## MALIGNANT

- Leukemia
- Lymphomas
- some CNS tumors
- Sarcomas
- Neuroblastoma
- Retinoblastoma

# Children's oncology

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1. The risk of any individual child developing cancer between birth and 20 years of age is about 1 in 300.
2. Childhood cancer comprise 2% of all malignant tumours but they are the leading cause of death in this age group
3. Both benign and malignant tumors occur in childhood.
4. Benign tumors are more common than malignant tumors but they are generally of little immediate consequence
5. Most malignant tumors in children arise from hematopoietic, nervous and soft tissues.
6. The 5-year survival of children with all forms of cancer is about 75%, most of whom can be considered cured, although cure rates vary considerably for different diagnosis.

# Differences between pediatric and adults cancers

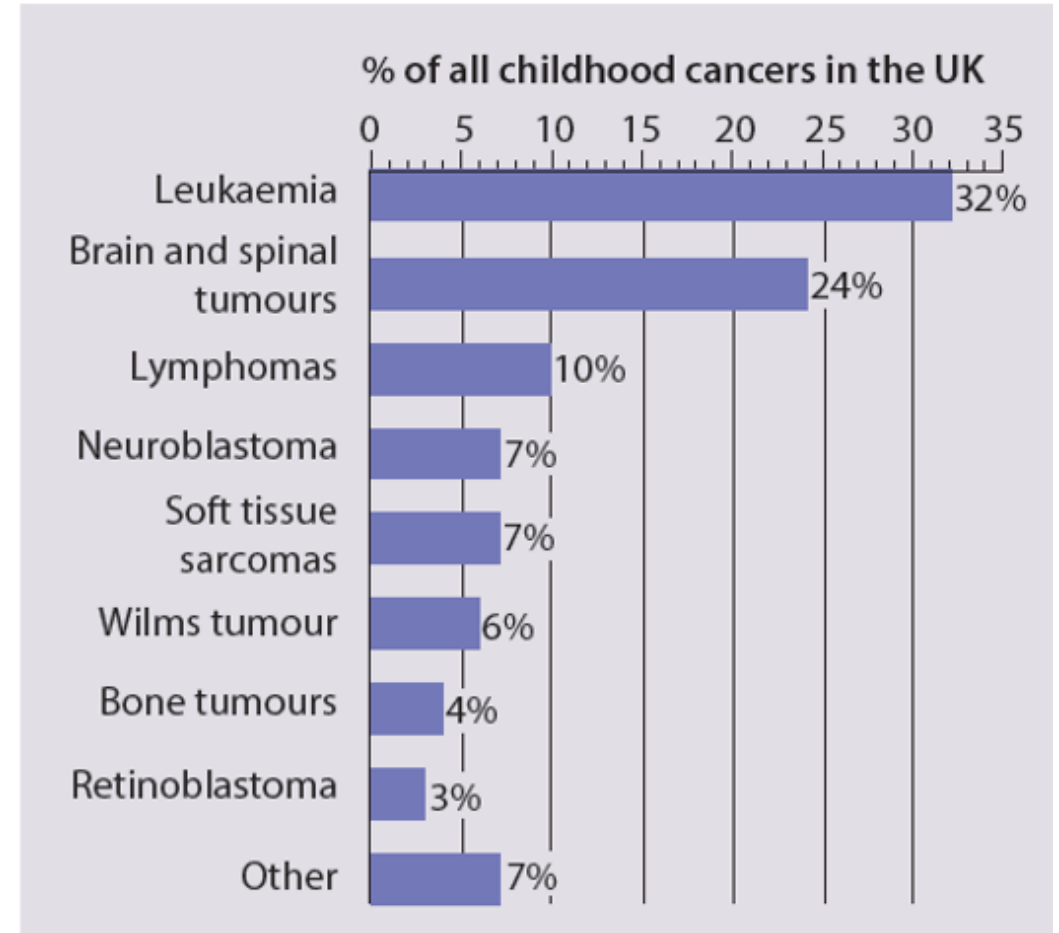
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	Pediatric cancers	Adult cancers
Incidence	<ul style="list-style-type: none"><li>• Rare</li><li>• Depends on age</li></ul>	<ul style="list-style-type: none"><li>• Relatively common</li><li>• Increased incidence with increasing age</li></ul>
Localization	<ul style="list-style-type: none"><li>• Hematopoietic system</li><li>• Neural tissue</li><li>• Soft tissue</li></ul>	<ul style="list-style-type: none"><li>• Epithelial origin - carcinomas (lung cancer, colon cancer, skin cancer)</li></ul>
Regression	<ul style="list-style-type: none"><li>• Tendency to regress spontaneously/ mature</li></ul>	
Histology	<ul style="list-style-type: none"><li>• Primitive / embryonal appearance</li></ul>	<ul style="list-style-type: none"><li>• Pleomorphic- anaplastic appearance</li></ul>
Genetics	<ul style="list-style-type: none"><li>• Simple karyotype</li></ul>	<ul style="list-style-type: none"><li>• Complex karyotypes</li></ul>
Management	<ul style="list-style-type: none"><li>• Curable - chemotherapy/ radiotherapy</li><li>• Even resectable may need chemo</li><li>• May develop second malignancy</li></ul>	<ul style="list-style-type: none"><li>• Often chemo-insensitive</li><li>• Low stage - surgically curable</li></ul>

# Frequency of different kind of cancer

Some types of cancer – including embryonal tumours (such as neuroblastoma, retinoblastoma and Wilms' tumour) and acute lymphoblastic leukaemia (ALL) – occur most commonly in the under 5 years of age.

Other cancers, such as bone tumours, are very rare in younger children, increasing in incidence with age and peaking in adolescence.



# Predisposing factors

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- Genetic- mutations (protooncogens, suppressor genes), some neurocutaneous disorders, chromosomal abnormalities
- Immunodeficiencies
- Infections – EBV, HIV
- Environmental
- Chemotherapy
- Ionising radiation
- Electromagnetic radiation
- In utero infections, toxins etc.

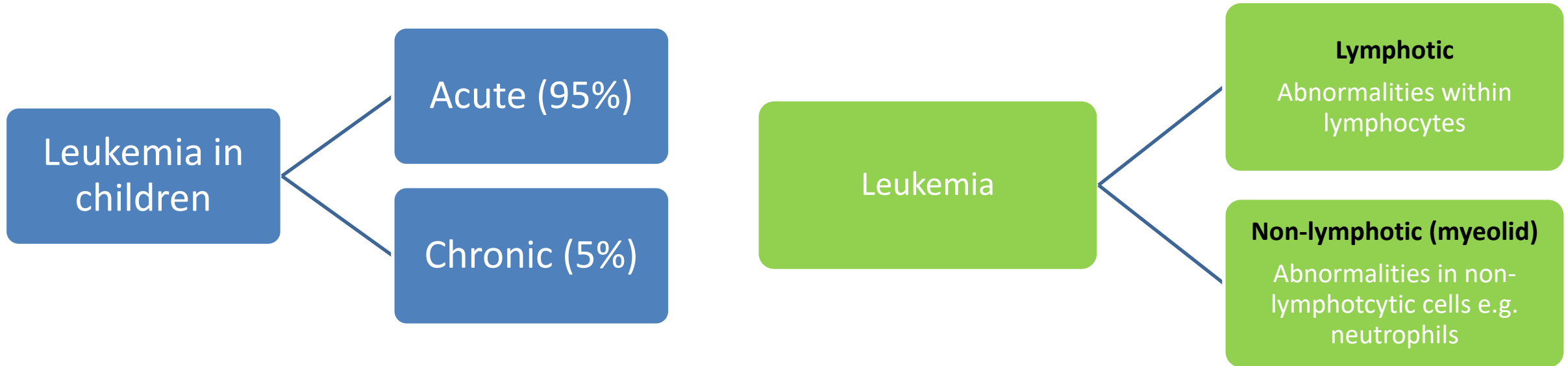
But in most cases the cause of cancer remains unknown



# Leukemia

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- The most common childhood cancer (about 25%)



<https://www.youtube.com/watch?v=KOMGMZeqqgA&t=16s>

# Leukemia

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## ACUTE (95%)

### **ALL – acute lymphocytic/ lymphoblastic leukemia**

- about 80-85% of all childhood leukemia
- Overproduction of immature lymphocytes
- The peak incidence between 2 - 6 years of age, mostly boys
- Estimated survival 79% at 5 years

### **ANLL – acute nonlymphocytic leukemia (mostly acute myeloid anemia, AML)**

- The same incidence in both sexes
- All ages
- 8 types with different clinical course and response for treatment (M0- M7)
- Poorer prognosis – a 5-year survival rate of 41%

## CHRONIC (5%)

### **CML – chronic myeloid leukemia**

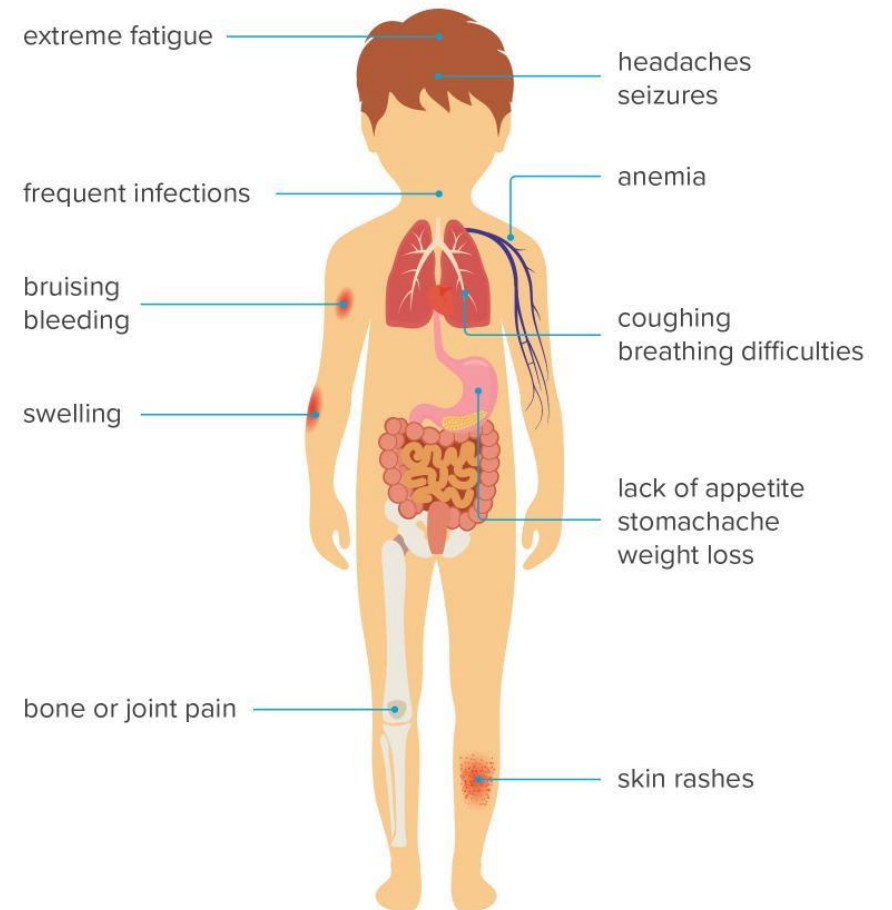
- Rare incidence in children population
- Possibility to transform to ALL within 3-5 years
- Classify to myelodysplastic disorders

# ALL - symptoms

Quick progression of symptoms, usually within 2 – 6 weeks

- Initially nonspecific - anorexia, irritability, lethargy, loss of appetite, loss of weight
- Pallor
- Bleeding
- Petechiae
- Fever
- Night sweating
- Lymphadenopathy, splenomegaly, hepatomegaly
- Bone pain and arthralgia
- Rarely headache and vomiting

## Effects on the Body Childhood Leukemia



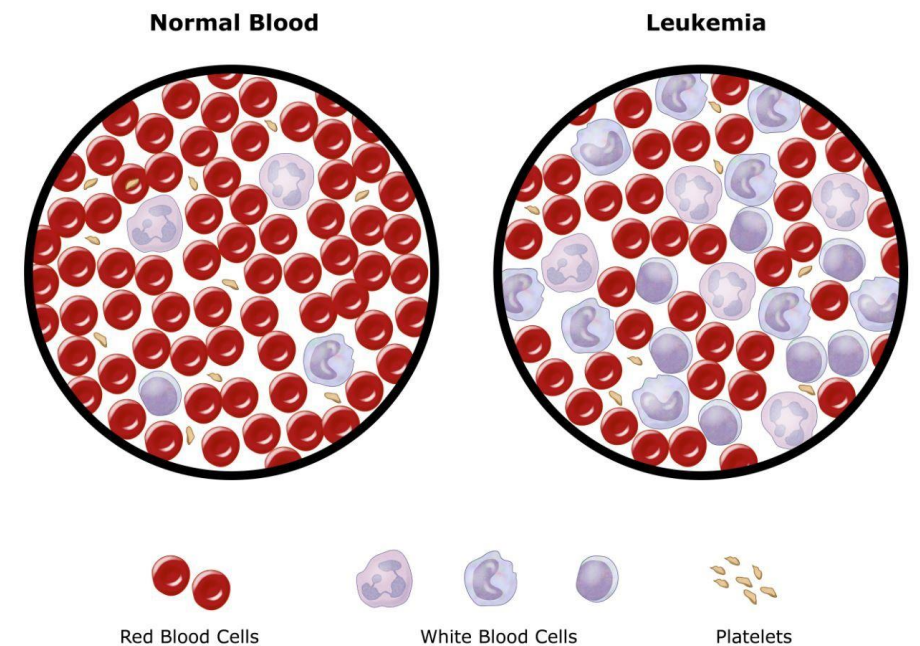
# ALL – diagnosis

## Laboratory studies:

- Cell blood count
  - Anemia,
  - Thrombocytopenia,
  - Increased WBC
- Blood smear
  - Presence of blast cells on peripheral smear
- Increases erythrocyte sedimentation rate (ESR)
- Bone marrow biopsy – leukemic lymphoblasts

## Differential diagnosis

- Aplastic anemia
- Myelofibrosis
- Infections: mononucleosis



# Treatment ALL

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The aim is to induce a lasting remission, defined as the absence of detectable cancer cells

- Chemotherapy
- Steroids
- Radiation therapy
- Bone marrow or stem cell transplants

Prognosis overall cure rate 80%. It is assumed that the 5-year disease-free survival (counted from the end of therapy) is synonymous with cure the child. After this period ALL relapse are very rare.

# ALL- prognosis

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## Worse prognosis

1. Age child below 12 months
2. WBC count more than 50 000/ul
3. Chromosomal transactions t(22:9), t (4:10), Down syndrome
4. Gender - male
5. Cancer spread into the central nervous system
6. Some morphological, immunological, and genetic subtypes
7. No response to initial treatment

# Acute myeloid leukemia - AML

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## Symptoms:

- Pallor, fatigue, petichae,
- Enlarged nodes and hepatosplenomegaly
- **Gingival hyperplasia** in AML M4 i M5

## Investigation:

Anemia, trombotythopenia, neutropenia

WBC count in most cases enlarged

Presence of blast cells on peripheral smear

Diagnosis: 25% myeloblasts in bone marrow

# Treatment

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Chemotherapy

Radiotherapy

Bone marrow transplantation

Worse prognosis:

- no response to induction therapy
- M5 type

Generally, prognosis is poorer compared to ALL



# Lymphomas

- Cancers of the lymphatic system (peripheral to the bone marrow)
- The risk rises throughout childhood
- Mostly: Hodgkin's disease and non-Hodgkin lymphoma

# Non Hodgkin lymphoma (NHL)

- **A**bdominal form (B) and mediast**i**nal form (T)
- asymmetrical enlargement of lymph nodes, mainly supraclavicular (figure mediastinal), sometimes extranodal site
- rare in infants, increasing incidence after 3 years
- Burkitt's lymphoma virus (EBV)
- a high rate of change (days!) and large malignancy (invasion of CNS and bone marrow)

DIAGNOSIS e.g.

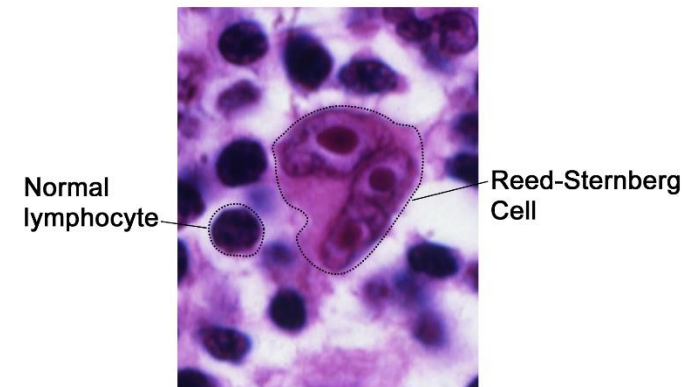
- Cell blood count
- LDH activity (increased) - reflects the size of the tumor
- uric acid levels
- Imaging studies: usg, chest X-ray
- Lymph node biopsy

TREATMENT

mainly chemotherapy (few indications for radiotherapy )

# Hodgkin lymphoma- Hodgkin disease

- Symptoms:
  - painless, firm, cervical or supraclavicular lymphadenopathy
  - rarely hepatosplenomegaly
  - less common: Pruritus, lethargy and anorexia
- Additional tests: mild anemia, reduced number of eosinophilic cells, elevated ESR
- Histopathologically: Reed-Sternberg cells
- Treatment: The association of chemotherapy and radiotherapy



# Oral lesions in the hematopoetic and lymphatic diseases

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Cause of the occurrence of the changes in the oral cavity:

- the presence of neoplastic lesions
- peripheral blood cytopenia
- immune deficiency

The changes in the oral cavity:

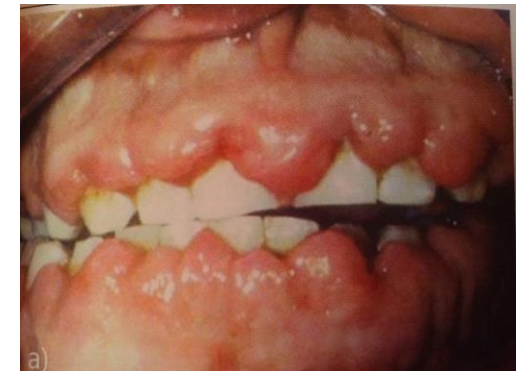
- gingivitis
- periodontitis
- bleeding
- gingival hyperplasia
- petechiae
- erosions
- ulcers of the mucous membranes

# Changes in oral cavity

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Gingival hyperplasia- cause:

- leukemic infiltrates (patients with chronic myelomonocytic leukemia ( CML) or acute leukemia nonlymphocytic (ANLL - M4 and M5))
  - primary neoplastic proliferation originating from the lymphatic system (rare)
  - drug-induced gingival hyperplasia (phenytoin , cyclosporin A, calcium channel blockers )
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- agranulocytosis can cause inflammatory changes and / or fungal infections of tonsils and oral mucosa
  - thrombocytopenia -> development of thrombocytopenic bleedings with symptoms of bleeding gums and petechiae of the oral mucosa
  - anemia ->pale mucous membranes



# Changes in oral cavity

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Patients with NHL (usually from mature B cells)-> increase bacterial and fungal infections in the oral cavity, dry mucous membranes, decreased saliva secretion, viral vesicular lesions on the mucous membranes of the mouth, on the hard palate, soa posterior wall of the pharynx.

EBV - development of post-transplant lymphoproliferative syndrome (PTLD) - local or generalized in patient with immune deficiency

- varying degrees of severity (from reactive hyperplasia, to the development of lymphoma); the cause of hairy leukoplakia, erosions, ulcers

HPV – oncogenic virus

- clinical picture may be asymptomatic, or may be the cause of change of squamous papilloma (7-8% of tumors in children)

# Brain tumors

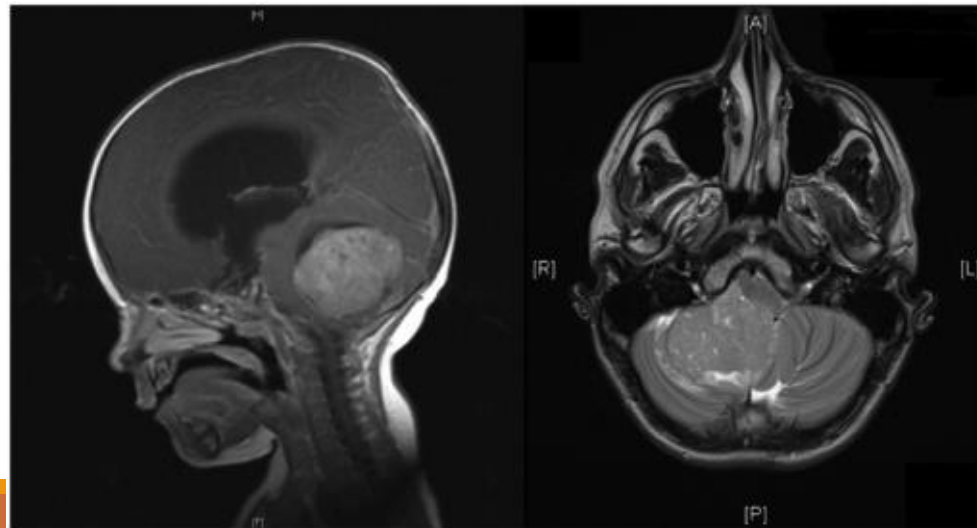
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The most common solid tumors ( 20-25 % of all cancers )

The average age of 7 years 10 months .

Etiology:

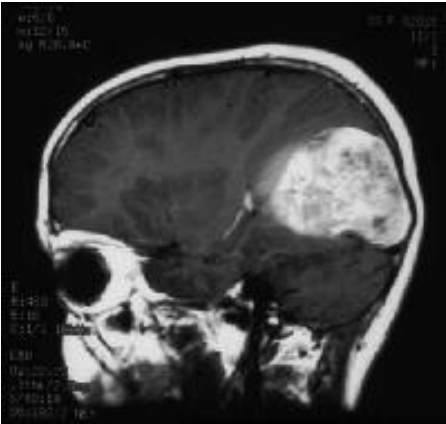
- Hereditary: neurofibromatosis type I and II , tuberous sclerosis , Li - Fraumeni syndrome , Gardener , Turcot , von Hippel -Lindau
- Environmental factor : pesticides , nitrosamines , exposure to ionizing radiation , electromagnetic
- Primary and secondary immune deficiencies



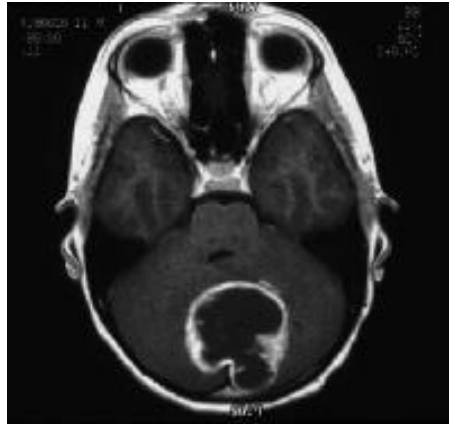
# Brain tumors classification

## Localisation

- Supratentorial (gliomas, ependymomas , PNET tumors, midline - germ cell tumors , pineal tumors)
- Infratentorial (45-60%) -> the cerebellum (medulloblastoma), brainstem (gliomas)



The supratentorial glioblastoma multiforme



The juvenile pilocytic astrocytoma of the cerebellum

- Astrocytoma (~40%) – varies from benign to highly malignant (*glioblastoma multiforme*)
- Medulloblastoma (~20%) – arises in the midline of the posterior fossa. May seed through the CNS via the CSF and up to 20% have spinal metastases at diagnosis – poor prognosis
- Ependymoma (~8%) – mostly in posterior fossa where it behaves like medulloblastoma – moderate/poor prognosis
- Brainstem glioma (6%)
- Craniopharyngioma (4%) – a developmental tumour arising from the squamous remnant of Rathke pouch. It is not truly malignant but is locally invasive and grows slowly in the suprasellar region.



# Brain tumors- symptoms

## Posterior fossa tumors

- the increase intracranial pressure
  - Headaches, especially in the morning
  - Vomiting
  - Consciousness disturbances - sleepiness
- Ataxia and other cerebellar symptoms

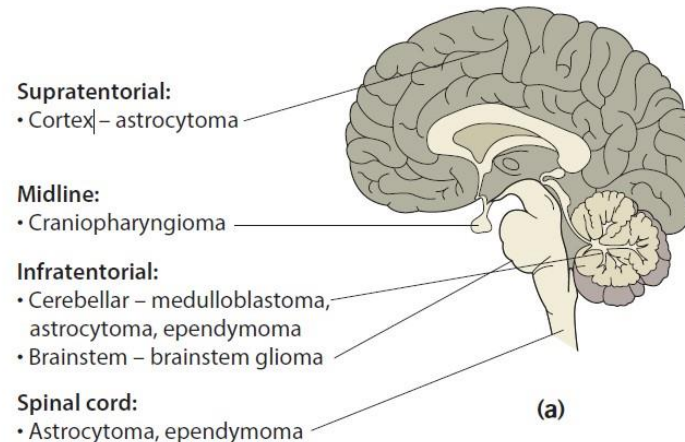
## Supratentorial tumors

- Seizures
- hemiparesis
- focal symptoms
- Behavioral changes

## Tumors midline

- Visual field defect
- visual acuity,
- diabetes insipidus
- Endocrinological abnormalities

## Brain tumours – clinical features



### Raised intracranial pressure

#### Children and adolescents

Headache – worse in the morning  
Vomiting – especially on waking in the morning  
Behaviour/personality change  
Visual disturbance  
Papilloedema

#### Infants

Vomiting  
Separation of sutures/tense fontanelle  
Increased head circumference  
Head tilt/posturing  
Developmental delay/regression



**Headaches and behaviour changes – is there raised intracranial pressure?**

# Brain tumors - diagnosis and treatment

## Diagnosis:

- neuroimaging – preferably MRI
- Cerebrospinal fluid studies (rare)
- Biochemical tests ( AFP , hCG) – embryonal tumors

Treatment- **surgery**, radio and chemotherapy

# Neuroblastoma (NBL)

Second most common solid tumor of infants (up to 2 years)

Derives from neuroblasts

Metastasis to bone marrow

In 2/3 of the cases, the diagnosis of <5 years of age (mean age of onset 2.5 years )  
the most common malignant tumor in neonatal age (34-54 %)

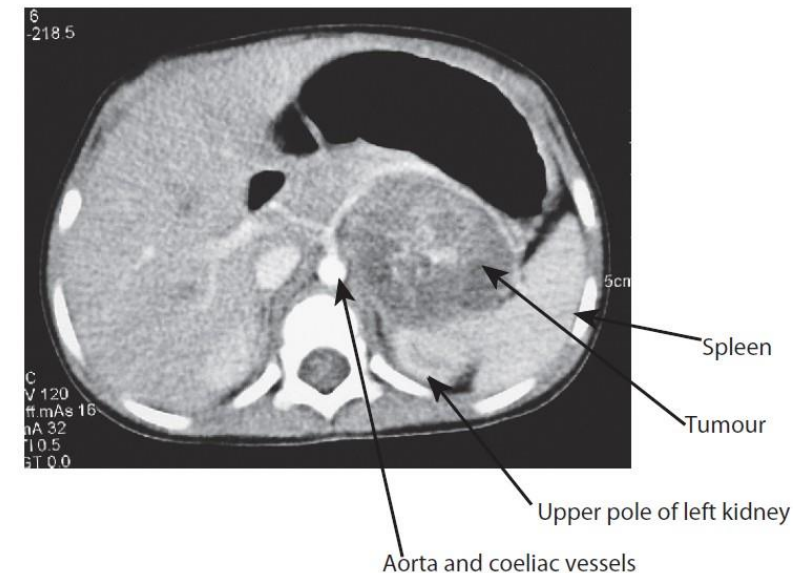
Location:

- retroperitoneal space ( 70-75 %)
- Rear mediastinum (20%)
- neck (5%)

In the time of diagnosis 70% of patients have a metastatic form

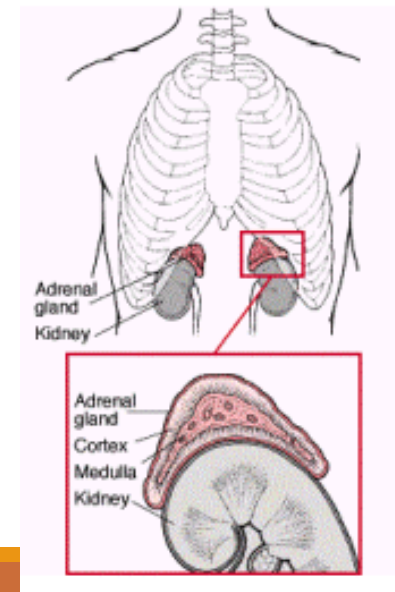
Diagnosis - CT, MRI  $\square$  tumor mass; tumor markers  $\square$  catecholamine metabolites in urine and serum (HVA, VMA), tumor biopsy

Treatment: surgical, chemotherapy and radiotherapy



# NBL symptoms

- abdominal mass -> enlargement of abdomen
- loss of appetite, weight loss
- fever
- abdominal pain, bone pain
- multiple subcutaneous nodules
- exophthalmos
- Horner's syndrome (not characteristic )
  - Myosis
  - Ptosis
  - Enophthalmos
- Overproduction of catecholamines:
  - Diarrhea (escape potassium <- overproduction VIP)
  - episodes of sweating
  - skin redness
  - hypertension



# Wilms tumor- nephroblastoma

derived from renal tissue with low differentiation

the peak incidence of 3-4 years of age

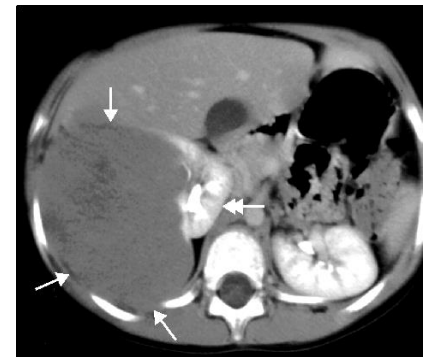
7-10% of childhood cancers

can coexist with other congenital defects

bilateral Wilms tumor

Genetic predisposition:

- WAGR syndrome - Wilms , aniridia , genito - urinary malformations , mental retardation , del 11p13
- Beckwith - Wiedemann syndrome - omphalocele, macroglossia , gigantism , hepatoblastoma, nephroblastoma, gonadoblastoma , del 11p15
- Denys - Drash syndrome - nephropatia, nephroblastoma, pseudohermaphroditism , point mutations in the WT1 gene



# Wilms tumor- symptoms

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- recurrent symptoms of urinary tract infection
- hematuria
- hypertension ( renin secretion )

Symptoms of a tumor in the abdomen:

- Abdominal distension
- abdominal pain, nausea , vomiting, abnormal intestinal transit
- bulge of abdominal wall

**Diagnosis-** USG, CT, Chest X-ray, CT

**Treatment-** surgery, chemotherapy, radiotherapy

# Retinoblasoma

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Symptoms: leukocoria, strabismus, orbital inflammation, pain

- Monocular form, unifocal occurs sporadically, diagnosed between 3-4 years of age, 60% of all cases
- Multifocal form, predominantly in the form of a binocular, hereditary, recognized in most cases in 1 year of life, consists of 25% of all cases

Tumor develops intraocularly, then invades the surrounding tissues and penetrates into the cranial cavity

Potential for metastases

Diagnosis -> characteristic age and symptoms (leukocoria), orbital usg and brain MRI

Treatment: enucleation, photocoagulation, radiotherapy

There is a significant risk of second malignancy (especially sarcoma) in hereditary retinoblastoma – hereditary mutation of protooncogenes



# Rhabdomyosarcoma

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The most common form of soft tissue sarcoma in childhood

Head and neck are the most common localization (40%),

Clinical symptoms :

- Exophthalmos, strabismus, narrowing of the eyelid
- nasal speech, difficulty swallowing
- occupation of the middle ear with the leak and polyps in the external auditory canal
- Increased intracranial pressure, cranial nerve palsies

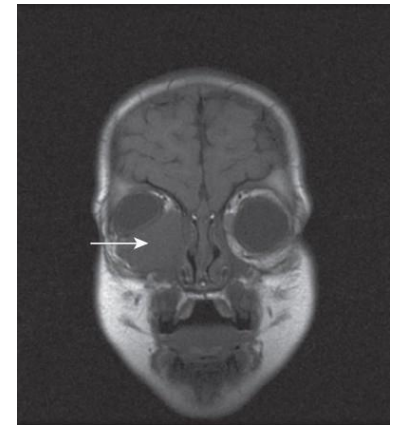
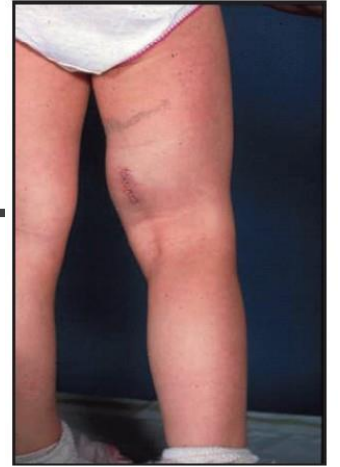
Genitourinary tumours may involve the bladder, paratesticular structures or the female genitourinary tract.

Symptoms include

- dysuria and urinary obstruction,
- scrotal mass
- bloodstained vaginal discharge.

Metastatic disease (lung, liver, bone or bone marrow) is present in approximately 15% of patients at the time of diagnosis and is associated with a vary poor prognosis.

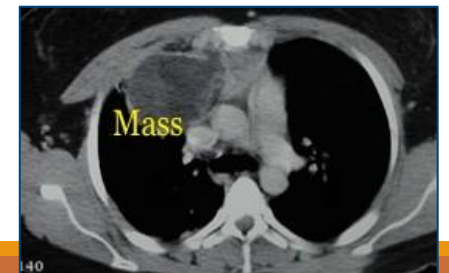
Multimodality treatment (chemotherapy, surgery and radiotherapy)





# Germ cell tumours

- 3-3.7 % of all malignancies in children
- benign or malignant
- Male : Female - 1 : 2-4
- They arise from the primitive germ cells which migrate from yolk sac endoderm to form gonads in the embryo.
- Benign tumours are most common in the sacrococcygeal region, and most malignant germ cell tumours are found in the gonads.
- Serum markers ( $\alpha$ FP and  $\beta$ -HCG) are important in confirming the diagnosis and in monitoring response to treatment.
- Two incidence peaks:
  1. 0-3 yr ( mainly tumors of sacrococcygeal region, testinal tumors)
  2. > 12 years of age (mainly ovary tumors)
- Good response to chemotherapy



# Liver tumors

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0.5-2 % of cancers developmental age

Primary malignant liver tumours are:

1. hepatoblastoma (65%), the peak incidence 1 yrs, genetic factors- Beckwith- Wiedeman syndrome, WAGR, neurofibromatosis
2. hepatocellular carcinoma (25%), the peak incidence 12 years of age, HBV infection, tyrosinemia, biliary atresia

Symptoms: loss of appetite, weight loss, vomiting, abdominal tumor, hepatomegaly

Elevated serum  $\alpha$ -fetoprotein ( $\alpha$ FP) is detected in nearly all cases of hepatoblastoma and in some cases of hepatocellular carcinoma.

Diagnosis- USG, CT, MRI, biopsy

Management includes chemotherapy, surgery and, in inoperable cases, liver transplantation.

The majority of children with hepatoblastoma can now be cured, but the prognosis for children with hepatocellular carcinoma is worse.



Computed tomogram of hepatoblastoma



Computed tomogram of hepatocarcinoma

# Bone tumors

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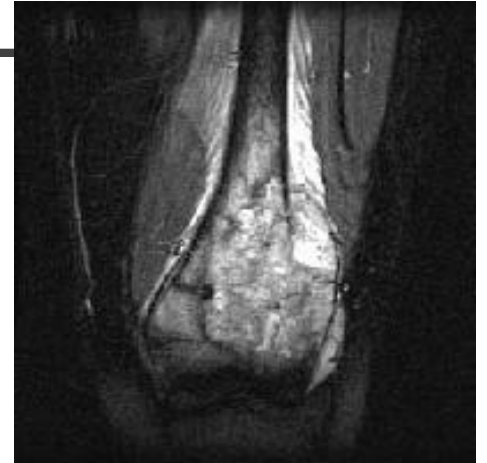
Malignant bone tumours are uncommon before puberty.

Osteogenic sarcoma is more common than Ewing sarcoma, but Ewing sarcoma is seen more often in younger children.

Both have a male predominance

Osteosarcoma:

- The most common malignant bone tumor in children
- The peak incidence 15-19 years of age
- The most common location - metaphyseal distal femur and proximal tibia metaphyseal



# Bone tumors

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## Ewing sarcoma

- It can occur at a younger age
- The most common location - flat bone of the pelvis, shoulder, ribs, long bones- femur, tibia, arrow
- there is often a substantial soft tissue mass
- 1/3 patients at diagnosis is metastatic to the lung

Treatment- combination chemotherapy given before surgery. Whenever possible, amputation is avoided by using *en bloc* resection of tumours with endoprosthetic resection.

In Ewing sarcoma, radiotherapy is also used in the management of local disease, especially when surgical resection is impossible or incomplete, e.g. in the pelvis or axial skeleton.



## Presentation of malignant disease in children

### Brain tumours:

- Raised intracranial pressure
- Neurological signs – depends on anatomical position

### Retinoblastoma:

- Screening if positive family history
- White pupillary reflex or squint

### Lymphomas:

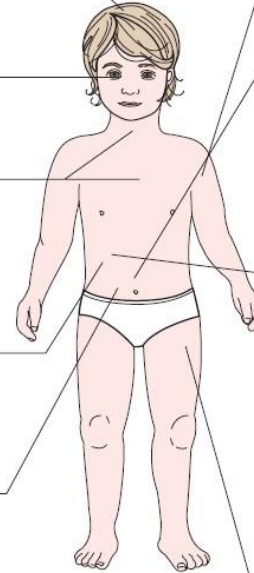
- Enlarged lymph nodes in the head and neck or abdomen
- Mediastinal mass – may cause superior vena caval obstruction.

### Wilms tumour:

- Large abdominal mass in a well child
- Occasionally anorexia, abdominal pain, haematuria

### Langerhans cell histiocytosis:

- Seborrhoeic rash
- Widespread soft tissue infiltration
- Bone pain, swelling or fracture
- Diabetes insipidus



### Soft tissue sarcomas:

- Mass any site

### Neuroblastoma:

- Abdominal mass, crosses the midline
- Spinal cord compression
- Weight loss and malaise
- Pallor, bruising
- Bone pain

### Acute lymphoblastic leukaemia (ALL):

- Malaise, anorexia
- Pallor, lethargy
- Infections
- Bruising, petichiae, nose bleeds
- Lymphadenopathy
- Hepatosplenomegaly
- Bone pain

### Malignant bone tumours:

- Localised bone pain

Pre-school (<5 years old)	School-aged	Adolescence
Acute lymphoblastic leukaemia (ALL) – peak incidence Non-Hodgkin lymphoma	Acute lymphoblastic leukaemia (ALL)	Acute lymphoblastic leukaemia (ALL) Hodgkin lymphoma
Neuroblastoma	Brain tumours	Malignant bone tumours
Wilm tumour		Soft tissue sarcomas
Retinoblastoma		

# Dental care on the oncological patients

As quick as possible!

Chemotherapy : minimum one week earlier

Radiotherapy : a min 2 weeks earlier

Oral hygiene : use a soft toothbrush- toothpaste for children

Liquid to mouth: saline, baking soda, infusions of chamomile ,

Removal of braces

Restrictive diet

# Complications of chemotherapy and radiotherapy

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- A generalized inflammation of the oral mucosa (mouthwashes with pain killers, antifungal, steroids)
- reduced saliva secretion (pilocarpine , Vit. A)
- opportunistic infections (Fluconazole prophylactically)
- tooth caries, necrotic bone inflammation because of radiation
- periodontitis
- dysgeusia, dysphagia
- Secondary tumors and malignancies

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