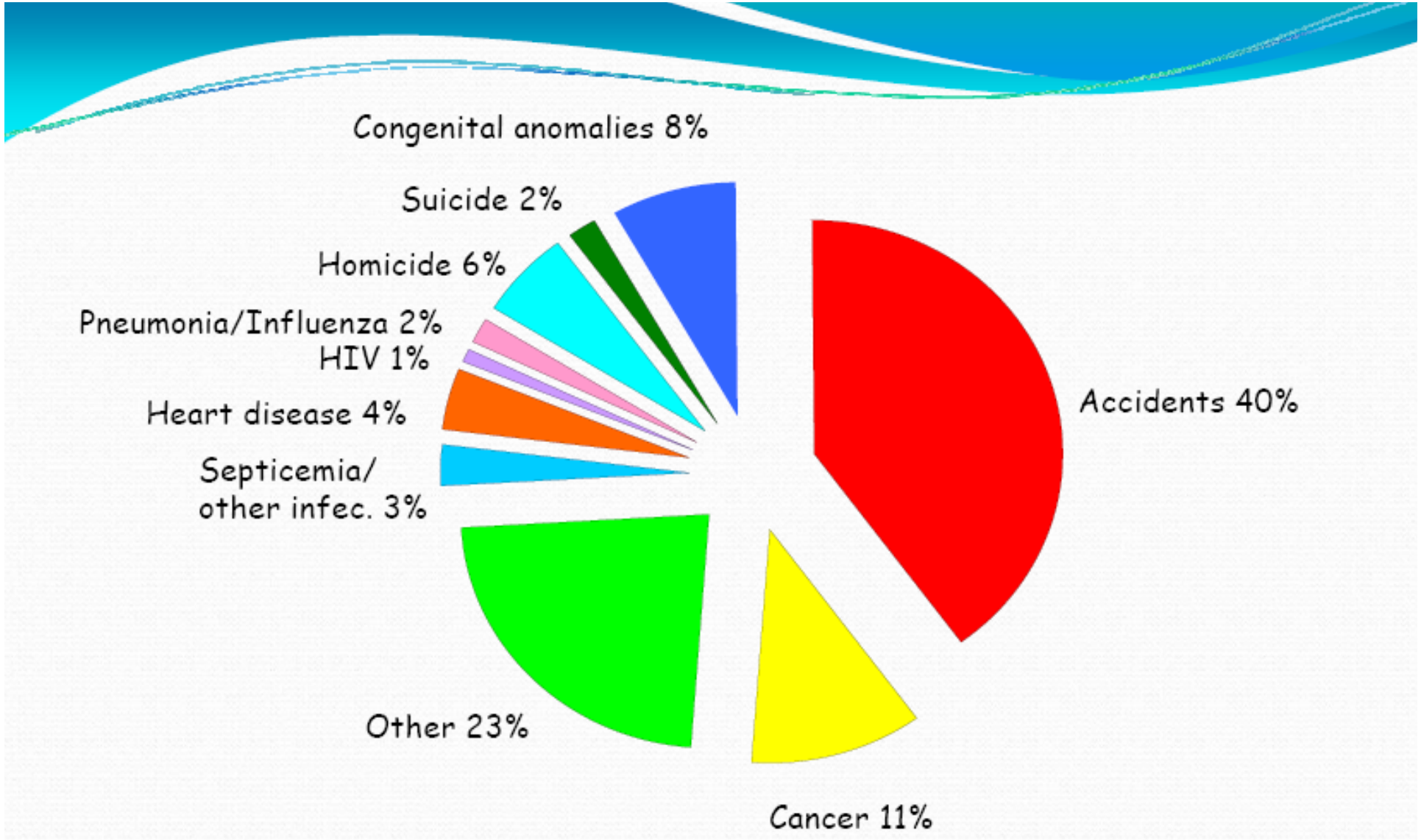
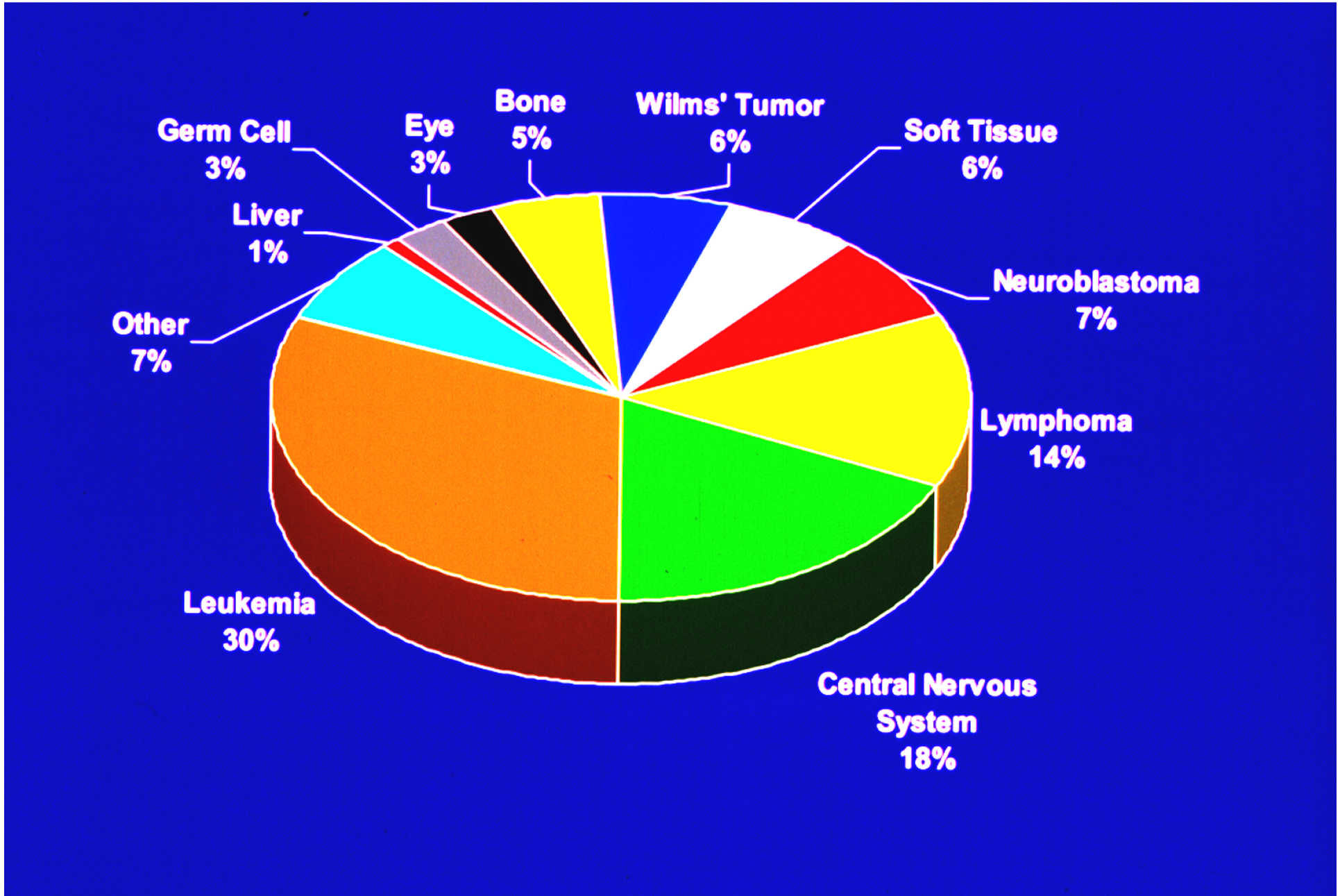
Tumori infantili....



Leading causes of death in children in the United States,. Causes of death among children 1 to 14 years. (Death data are from the National Center for Health Statistics public-use file)

Childhood Cancer

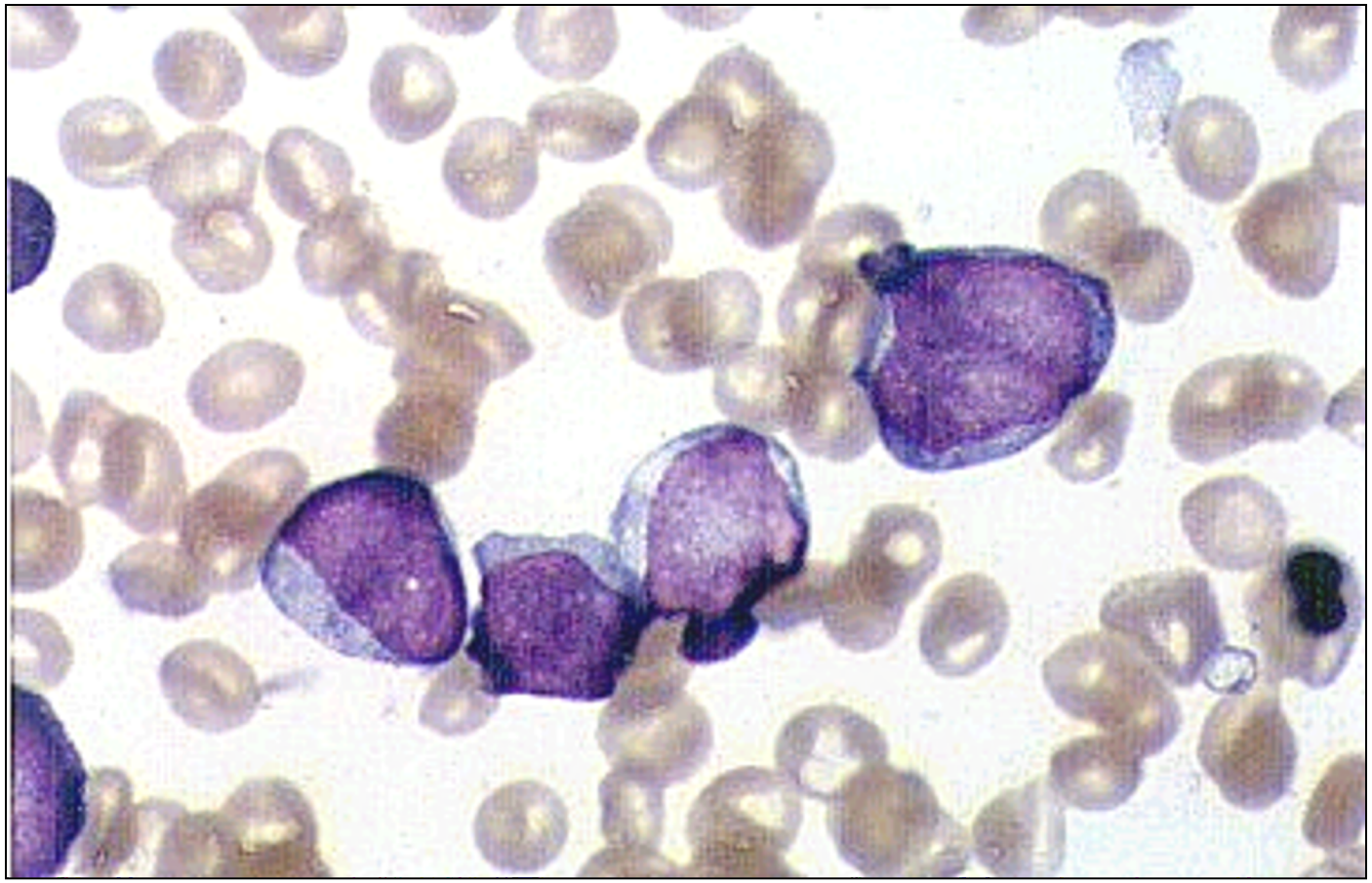


Acute Leukemias

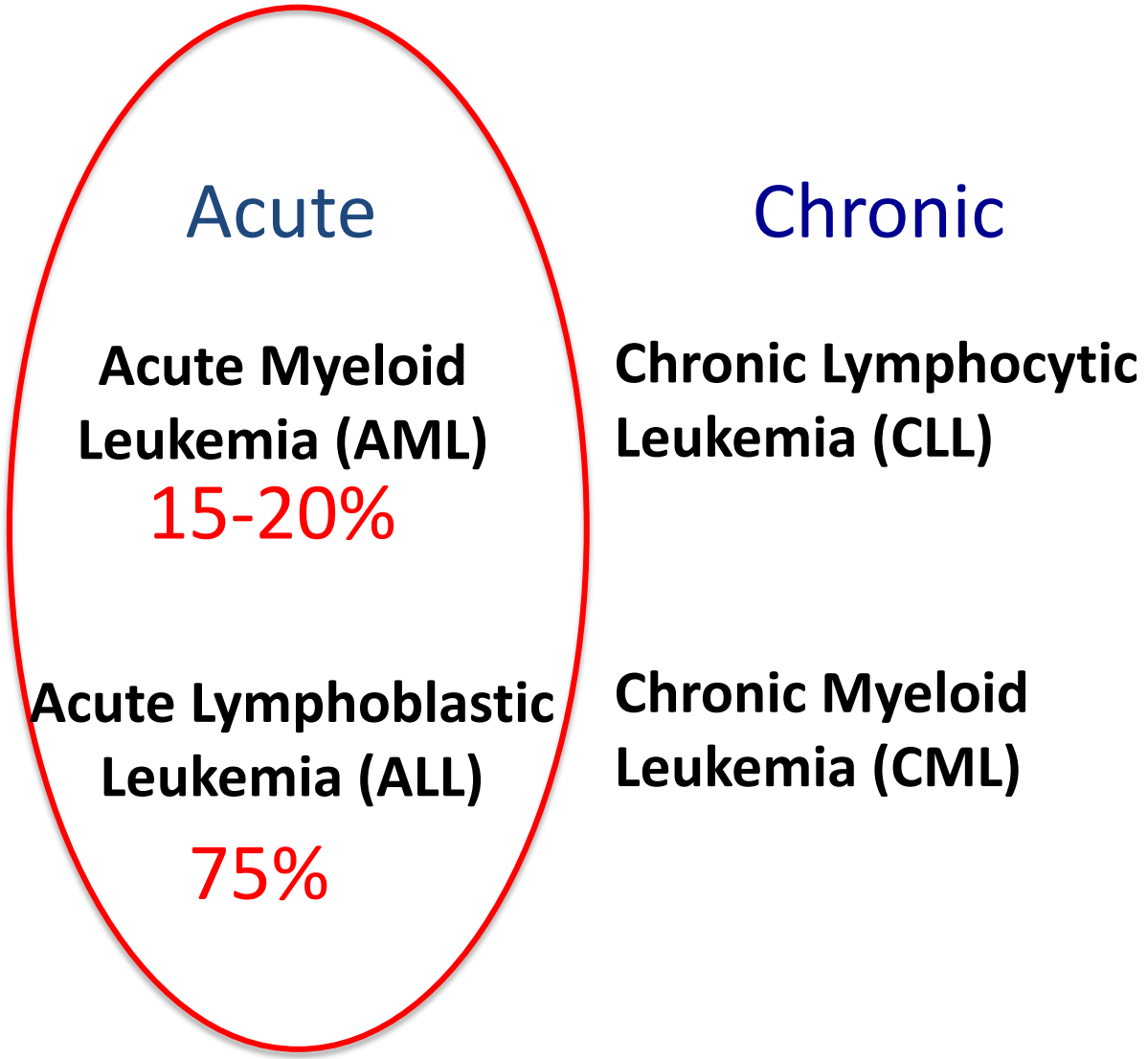
- ✓ Signs of **Lymphoproliferation** (organomegaly, lymphoadenopathy, soft tissue infiltrations, sometime also lungs and CNS...) and **leukostasis** (pulmonary infiltrates/CNS stroke)
- ✓ Signs of systemic inflammation/cytokines imbalance: **fever, bony pain, weight loss, night sweats**
- ✓ Signs of what is "**put aside**" in BM by blasts proliferation:
  - ✓ low red cells: anemia, pallor, asthenia, drowsiness...
  - ✓ Low platelets: bleeding

Acute Leukemia

Accumulation of blasts in the marrow



Classification of Leukemias



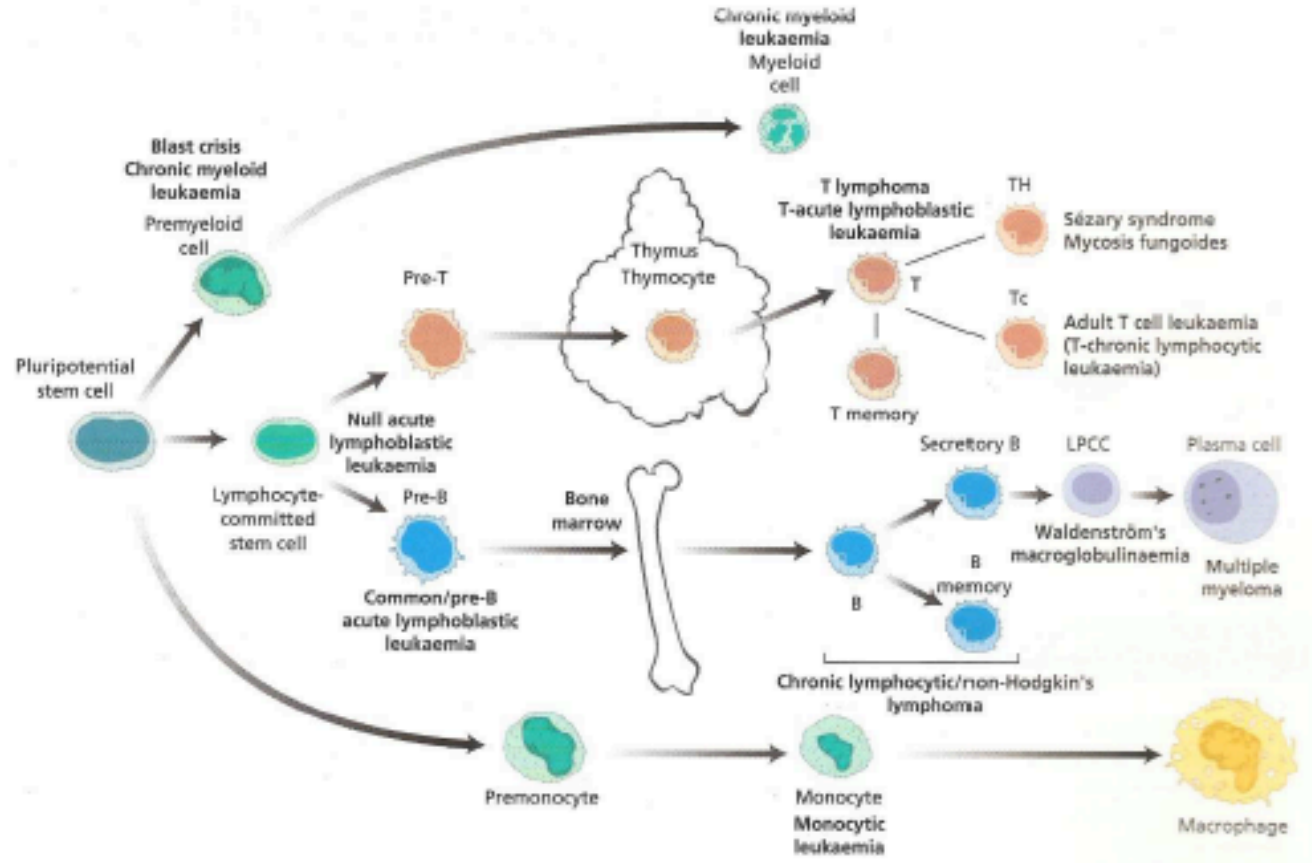
Acute Lymphoid Leukemia

Suspected diagnosis with…

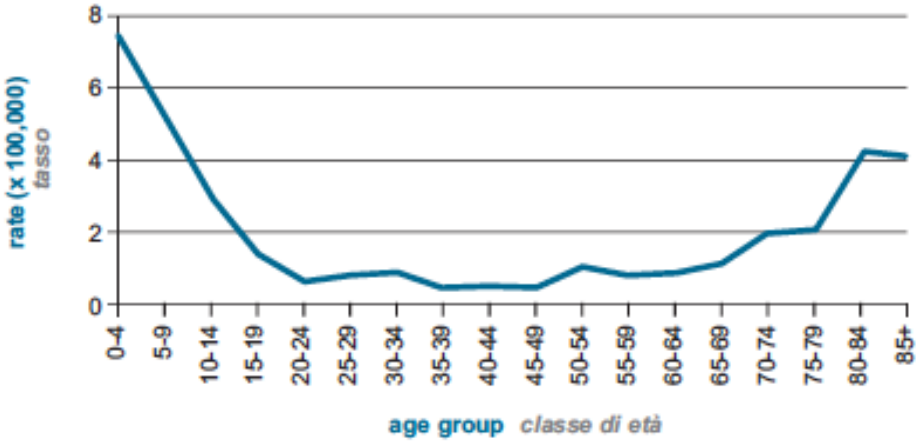
Complete Blood Count

- Leucocytosis/Leucopenia
- Predominant Lymphocytes (ALL)!

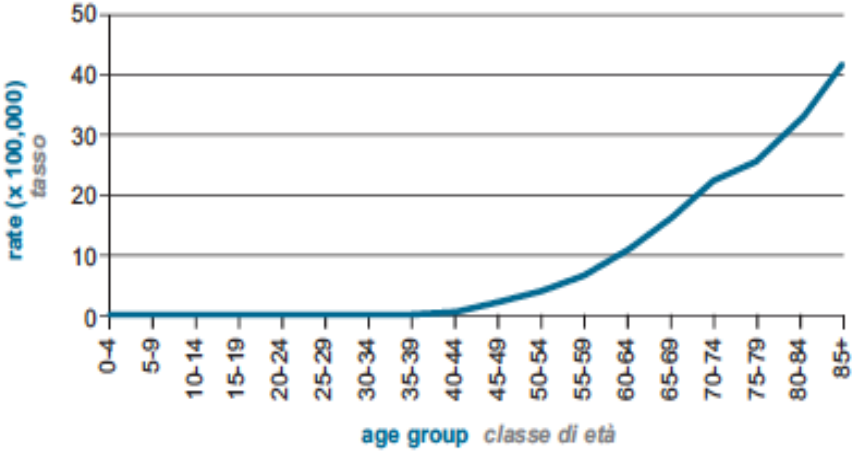
- ✓ **A hematologic urgency/emergency**
- ✓ **Usually fatal within weeks to months without chemotherapy**
- ✓ **Notify Peds H/O promptly if acute leukemia is suspected!**


Chronic myeloid leukaemia
Myeloid cell
Blast crisis Chronic myeloid leukaemia
Premyeloid cell
Pluripotential stem cell
Pro-T
Thymus
Thymocyte
T lymphoma
T-acute lymphoblastic leukaemia
TH
Sézary syndrome
Mycosis fungoides
T
Tc
Adult T cell leukaemia
(T-chronic lymphocytic leukaemia)
T memory
Null acute lymphoblastic leukaemia
Lymphocyte-committed stem cell
Pre-B
Bone marrow
Common/pre-B acute lymphoblastic leukaemia
Secretory B
LPCC
Plasma cell
Waldenström's macroglobulinaemia
Multiple myeloma
B
B memory
Chronic lymphocytic/non-Hodgkin's lymphoma
Premonocyte
Monocyte
Monocytic leukaemia
Macrophage

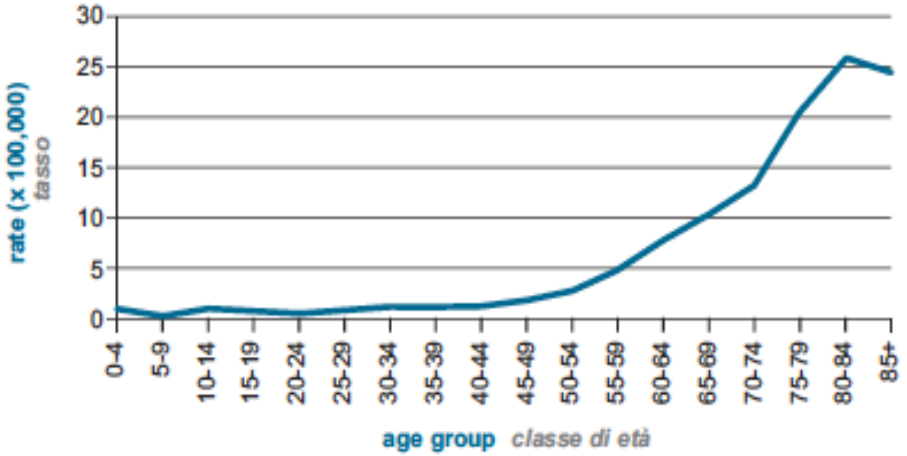
ALL



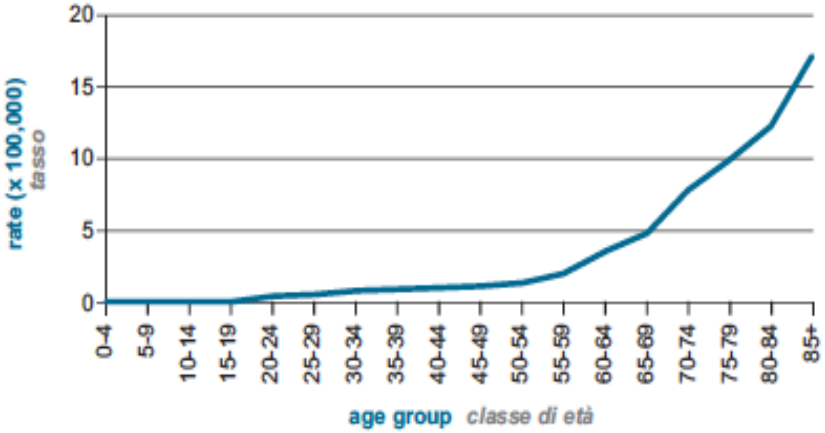
CLL



AML



CML



Clinical Presentation

SIGNs/SYMPTOMs	ALL	AML
Fever	34%	61%
Bleeding	18%	48%
Adenopathy	50%	14%
Bony pain	50%	5%

Laboratory Data

- ✓ White blood cell count: variable (< 10.000 53%; 10,000-49,000 30%; > 50,000 17%)
- ✓ Hemoglobin levels: low
- ✓ Platelet count: low
- ✓ Serum chemical values
  - ✓ Uric Acid and LDH: elevated
  - ✓ Calcium: elevated
- ✓ Chest X-ray: Mediastinal Mass; Preferable to do CXR with initial diagnosis of asthma, especially if you plan to use steroids
- ✓ Coagulation screening: abnormal

Differential Diagnosis

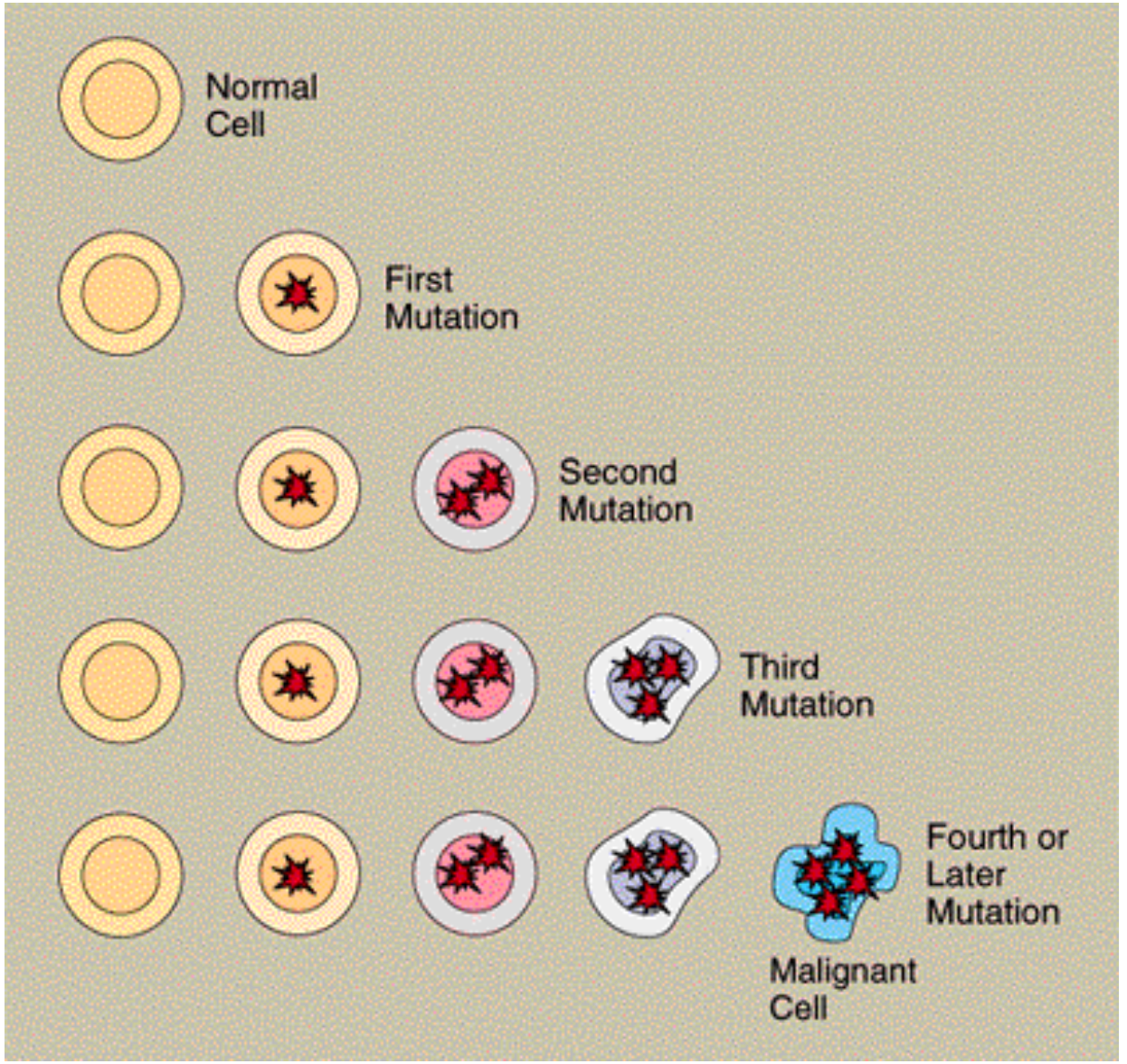
- ✓ Juvenile Rheumatoid Arthritis- caution to use steroids / oral methotrexate before completely ruling out leukemia
- ✓ Mycobacterial infections (TB & non-TB)
- ✓ Infectious mononucleosis
- ✓ Aplastic anemia
- ✓ Neuroblastoma
- ✓ Rhabdomyosarcoma
- ✓ Hypereosinophilic syndrome

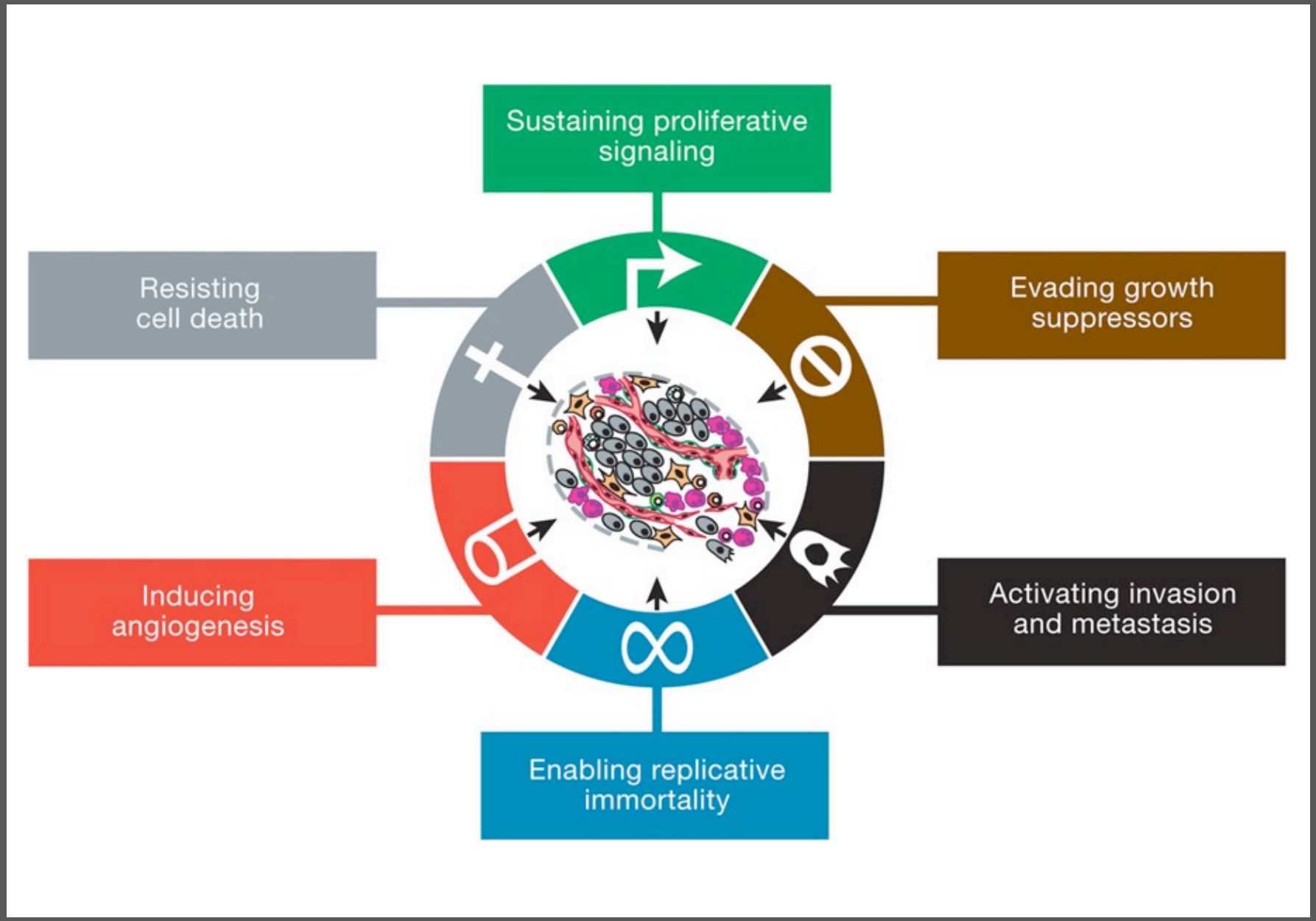
Causes of Acute Leukemias

- ✓ Idiopathic (most)
- ✓ underlying hematologic/immunological disorders
- ✓ chemicals, drugs
- ✓ ionizing radiation
- ✓ viruses (HTLV I)
- ✓ hereditary/genetic conditions

Principles of leukemogenesis

- ✓ A multistep process
- ✓ Neoplastic cell is a hematopoietic pluripotent cell or early myeloid cell
- ✓ Dysregulation of cell growth and differentiation (associated with mutations)
- ✓ Proliferation of the leukemic clone with differentiation blocked at an early stage


Normal
Cell
First
Mutation
Second
Mutation
Third
Mutation
Fourth or
Later
Mutation
Malignant
Cell


Sustaining proliferative signaling
Resisting cell death
Evading growth suppressors
Inducing angiogenesis
Activating invasion and metastasis
Enabling replicative immortality

Newly Diagnosed Patients with Leukemia- Work-up

- ✓ Establish a diagnosis
  - Peripheral blood and bone marrow studies
    - Morphology
    - Immunopathology (cell markers)
    - Cytogenetics
    - Molecular Genetics
  - Liquor studies
- ✓ Risk assessment
- ✓ Protocol enrollment- patients enrolled on clinical trials have better outcome
- ✓ Consent Process

Morphology:
- ✓ PB, BM, Liquor
- ✓ **MPO, esterasi**

Immunopathology (cell markers)
- ✓ Lymphoid: CD3, CD7, CD10, CD19, CD79
- ✓ Myeloid: CD41a, CD61,CD42b, CD33, CD13, CD14, CD15,CD11b,CD36

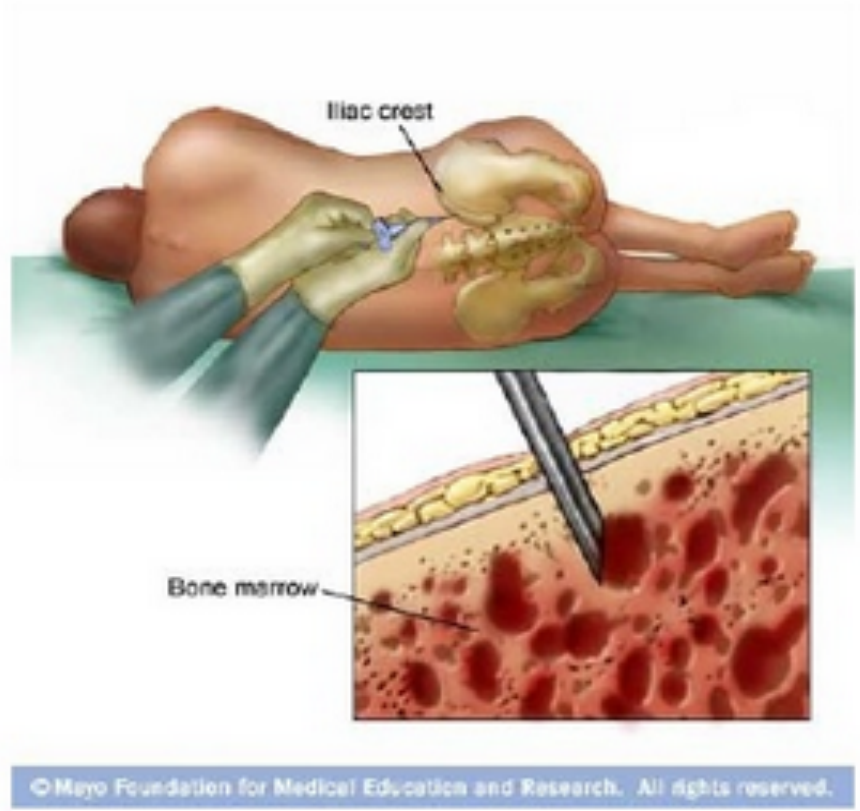
Molecular Genetics
- ✓ traslocations, inversions

Cytogenetics
- ✓ Chromosome abnormalities

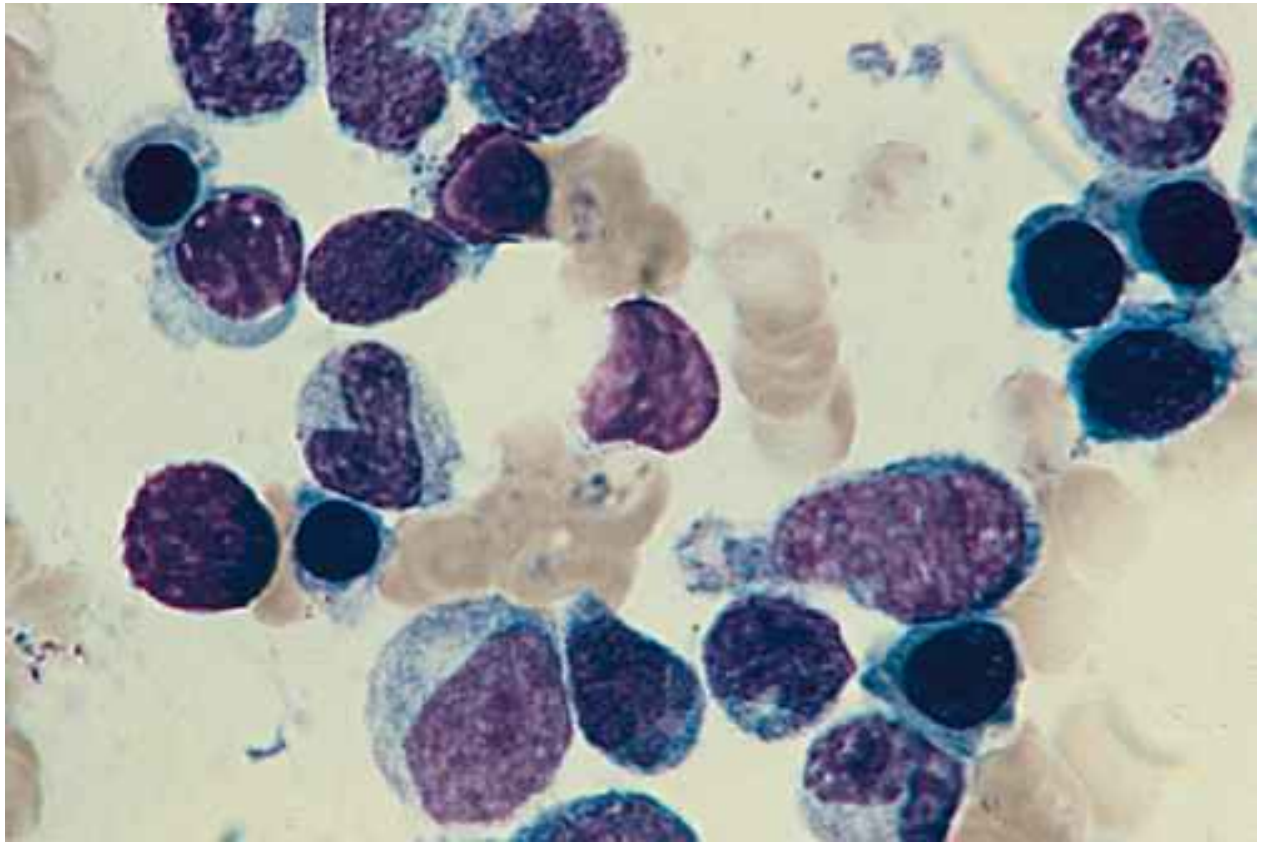
Bone Marrow Aspirate/Biopsy

- ✓ Necessary for diagnosis: Aspirate for ALL; Aspirate/biopsy for AML
- ✓ Useful for determining type
- ✓ Useful for prognosis
- ✓ Acute leukemias are defined by the presence of > 20% blasts (AML) or 25 % blasts (ALL) in bone marrow (% of nucleated marrow cells)

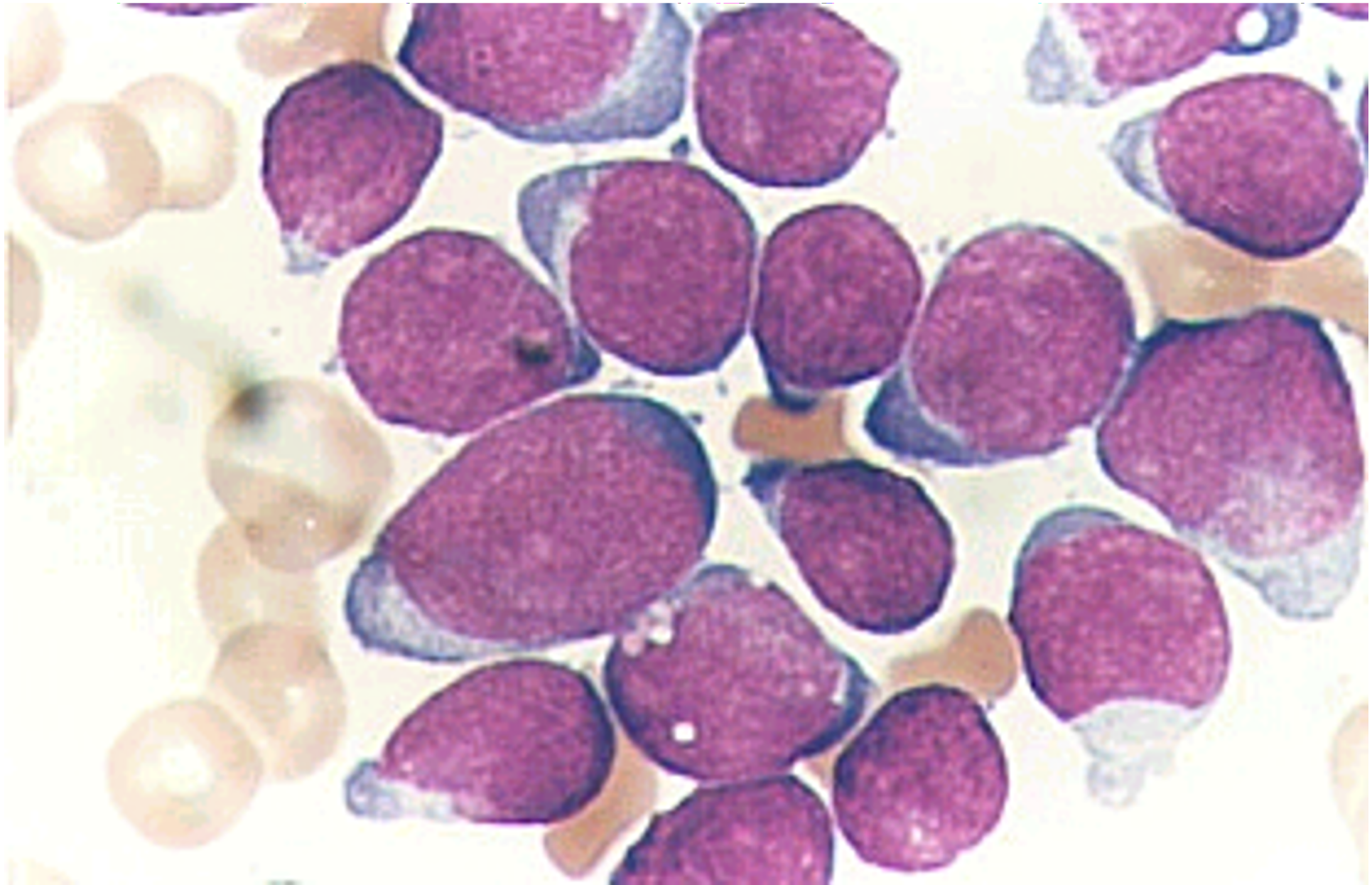
Confirmatory
Bone marrow aspiration/biopsy



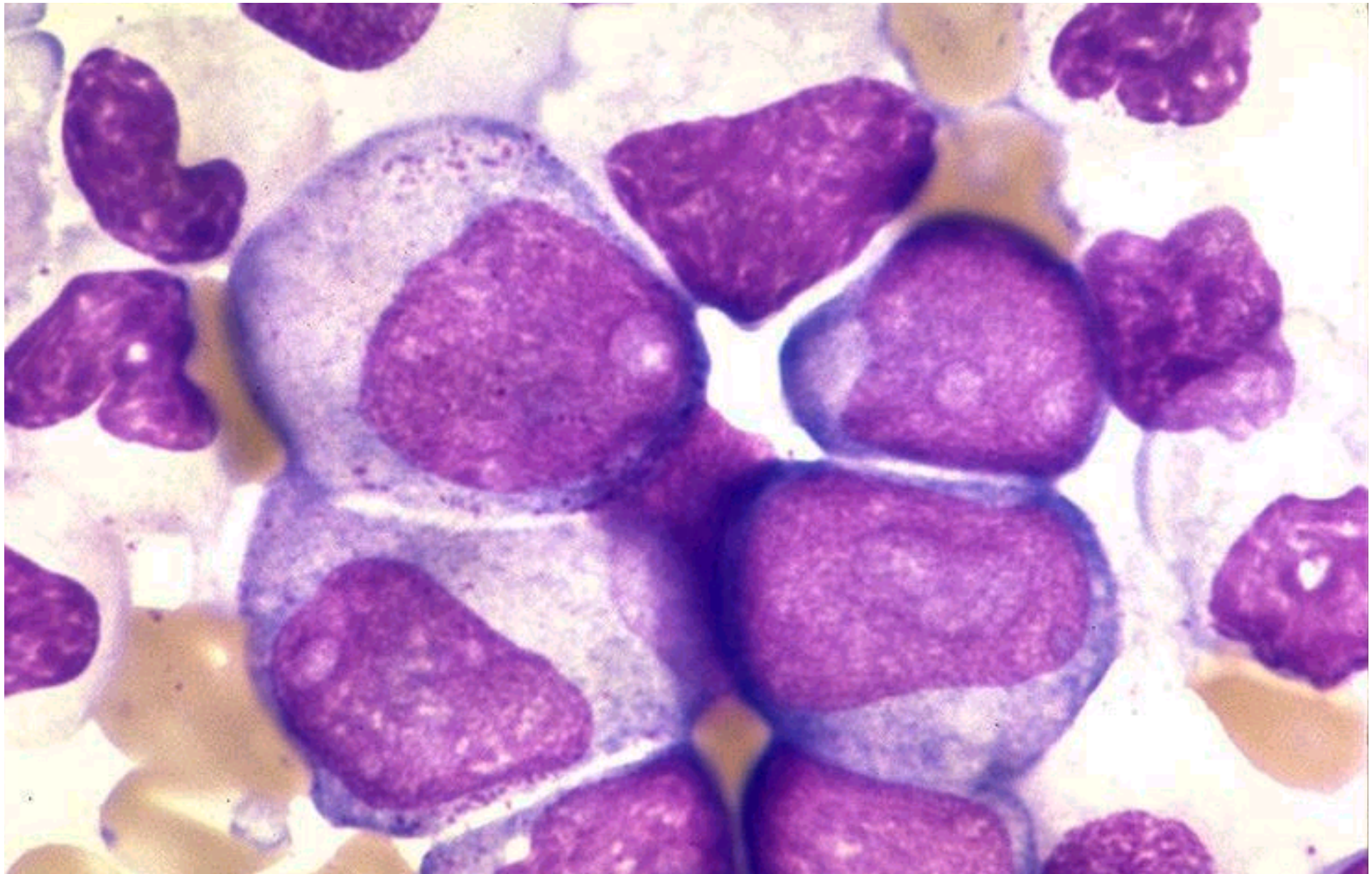
Healthy Bone Marrow



ALL



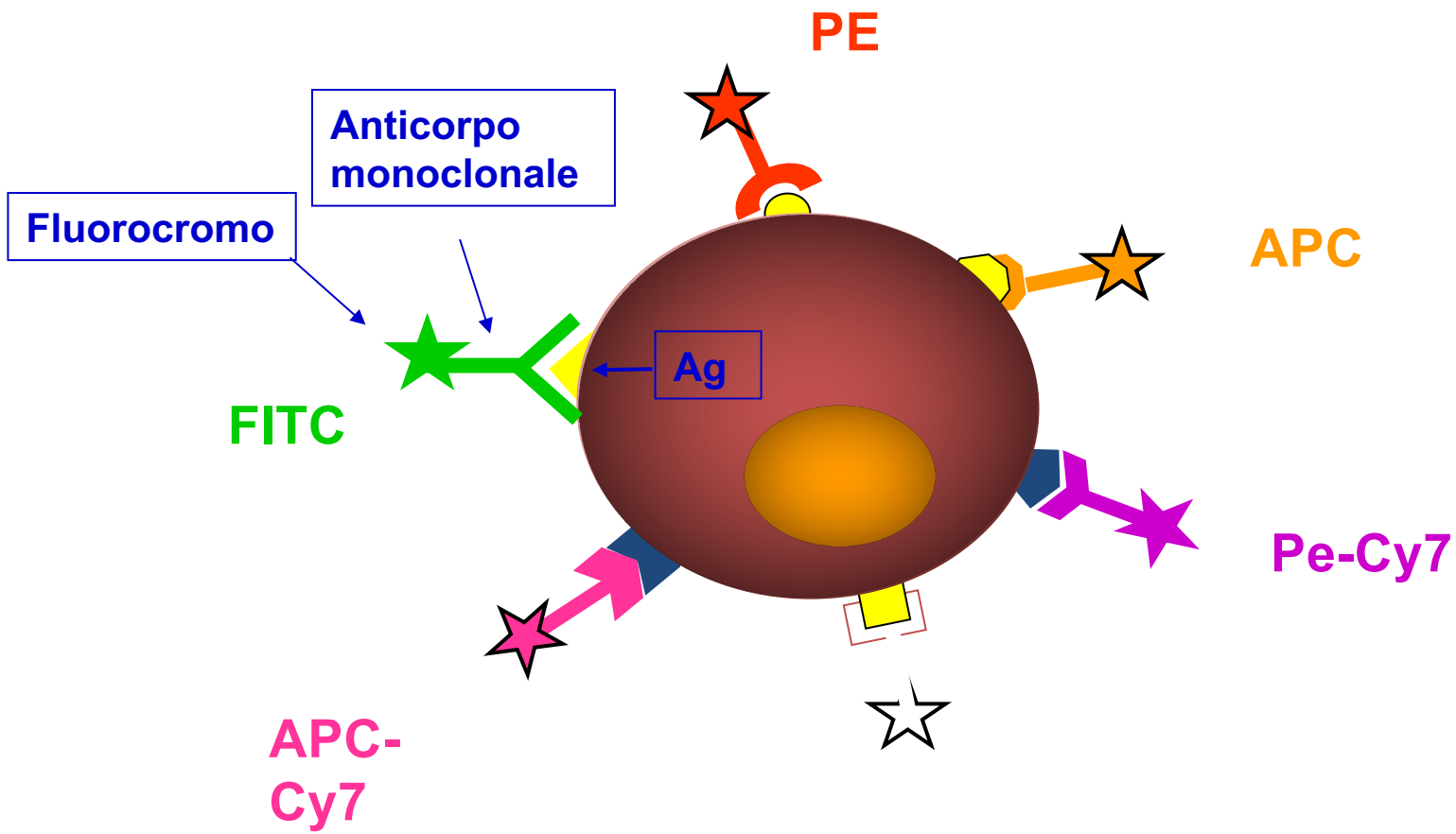
AML



FAB Classification

The French–American–British (FAB) classification systems refers to a series of classifications of hematologic diseases. It is based on the presence of **dysmyelopoiesis** and the quantification of **myeloblasts** and erythroblasts

Immunophenotiping



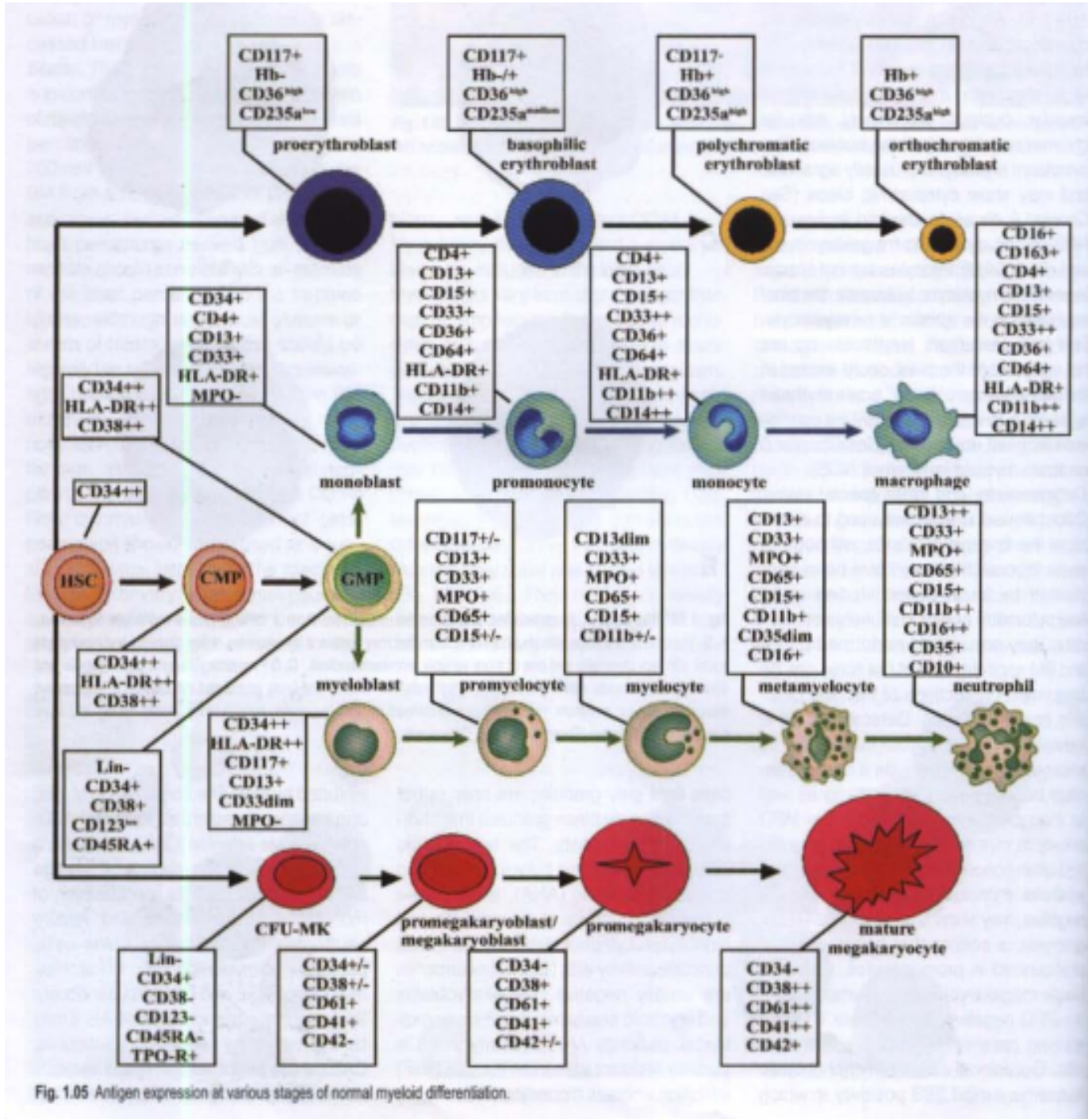
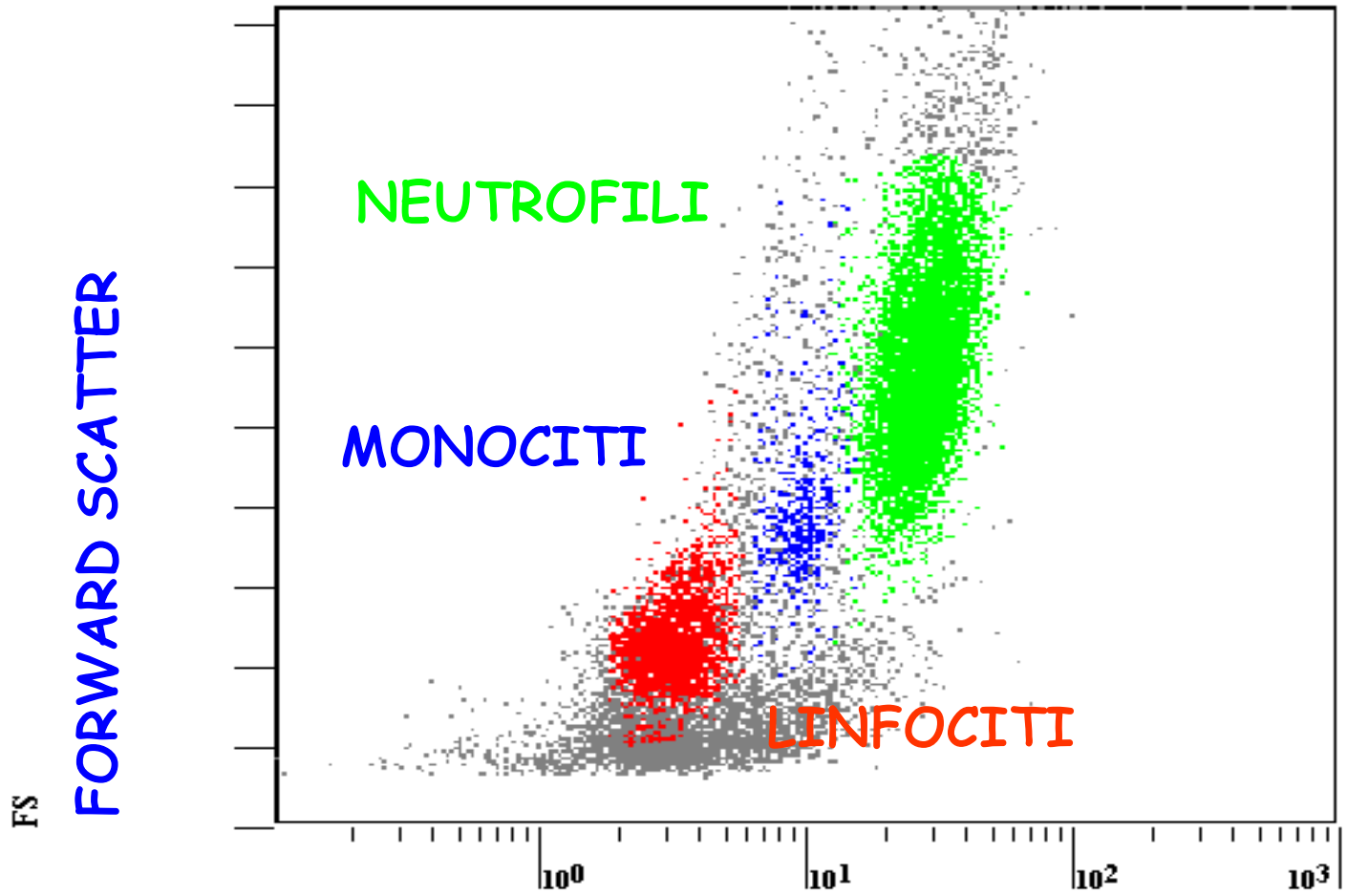
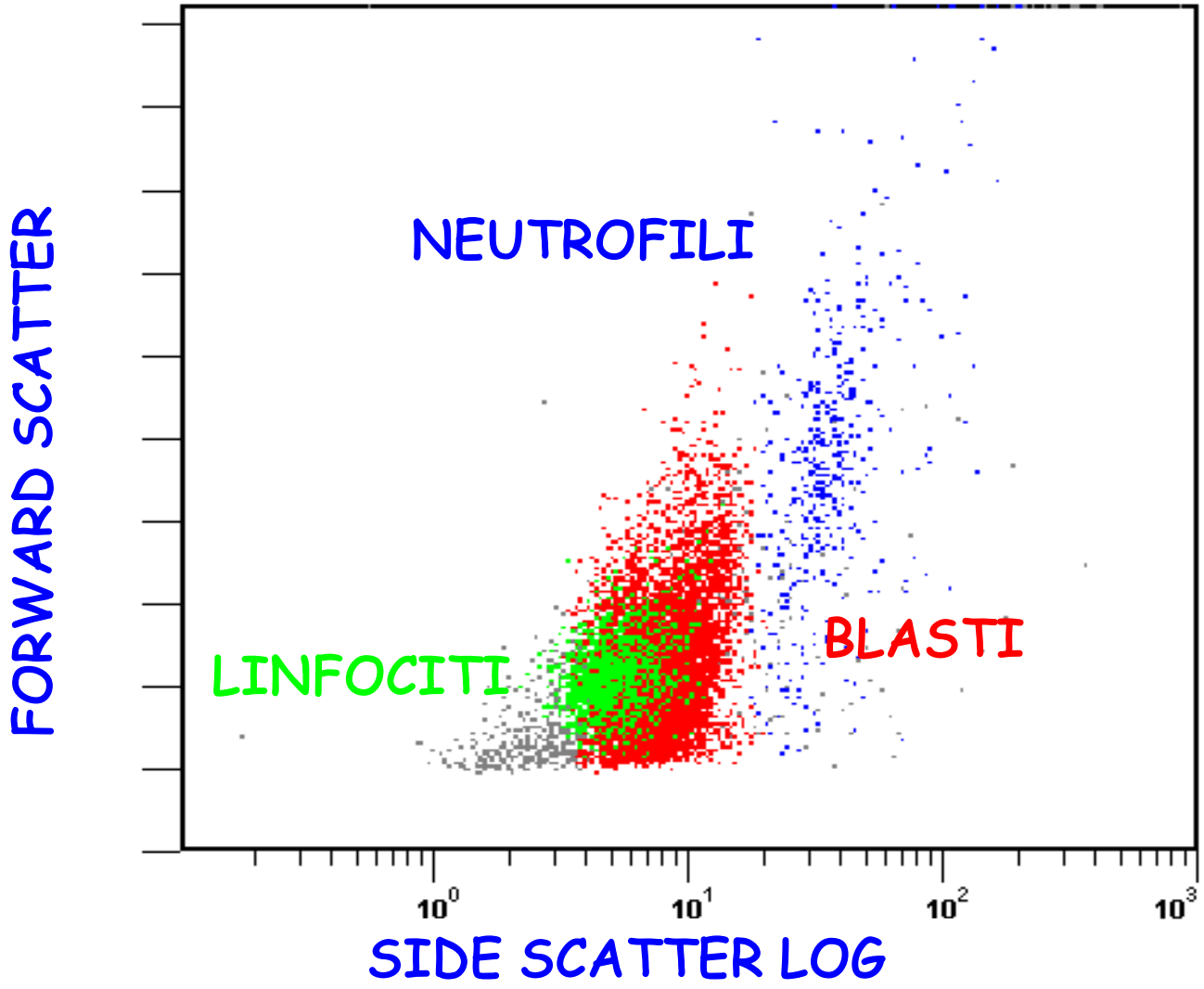


Fig. 1.05 Antigen expression at various stages of normal myeloid differentiation.

PARAMETRI FISICI



PARAMETRI FISICI



Principles of Treatment

- combination chemotherapy
  - first goal is complete remission
  - further Rx to prevent relapse
- supportive medical care
  - transfusions, antibiotics, nutrition, metabolic /electrolyte abnormalities
- psychosocial support
  - patient and family

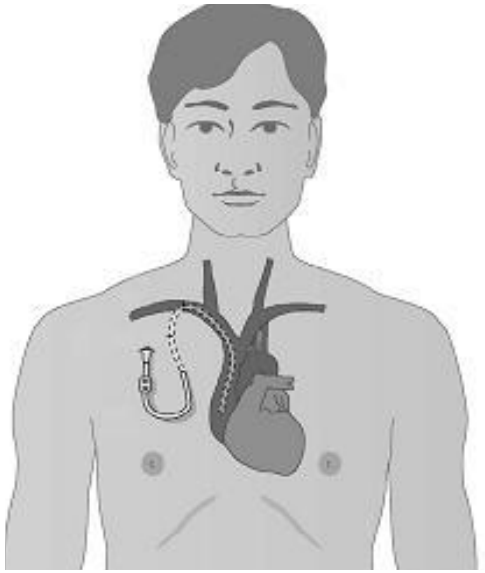
Therapeutic Concepts in ALL

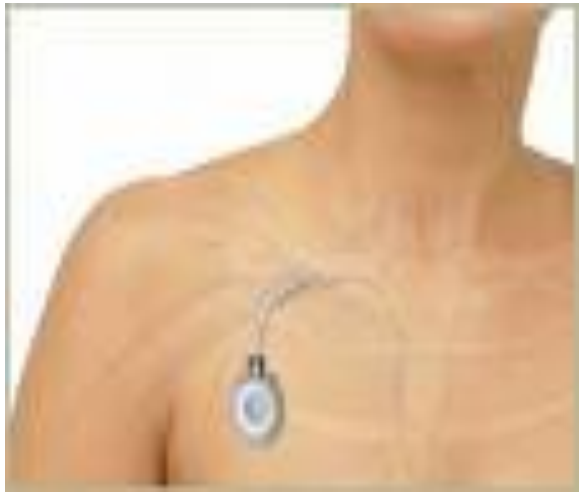
- ✓ Induce a complete remission and restore normal hematopoiesis avoiding excessive toxicity
- ✓ Reduce inapparent leukemia with short-term, high-dosage cytocidal therapy early in remission when the child is well and drug sensitivity is greatest
- ✓ Prevent CNS leukemia (concept of sanctuary)
- ✓ Use prolonged combination chemotherapy to eradicate residual disease when there is no evidence of leukemia

Basic Therapy in Childhood ALL

- ✓ Induction Treatment — 4-8 wk
- ✓ Consolidation treatment (intensification) — 2-10 wk
- ✓ Continuation treatment (maintenance) — 2-3 y
- ✓ Reinduction therapy (delayed intensification) — 2-7 wk
- ✓ CNS-directed therapy — 1-2 y
- ✓ Cessation of therapy — 2.5 y for girls, 3.5 y for boys

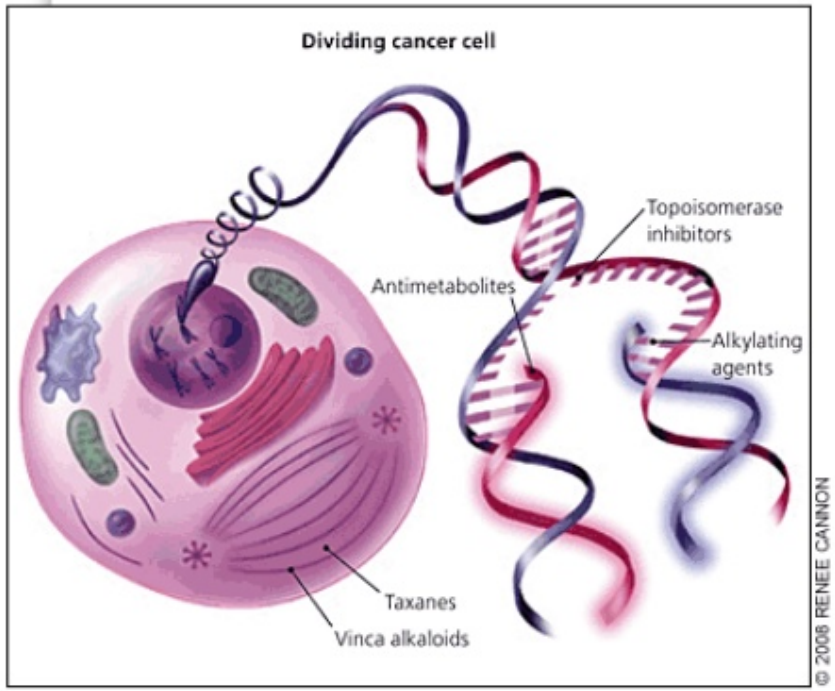
CATETERE VENOSO CENTRALE

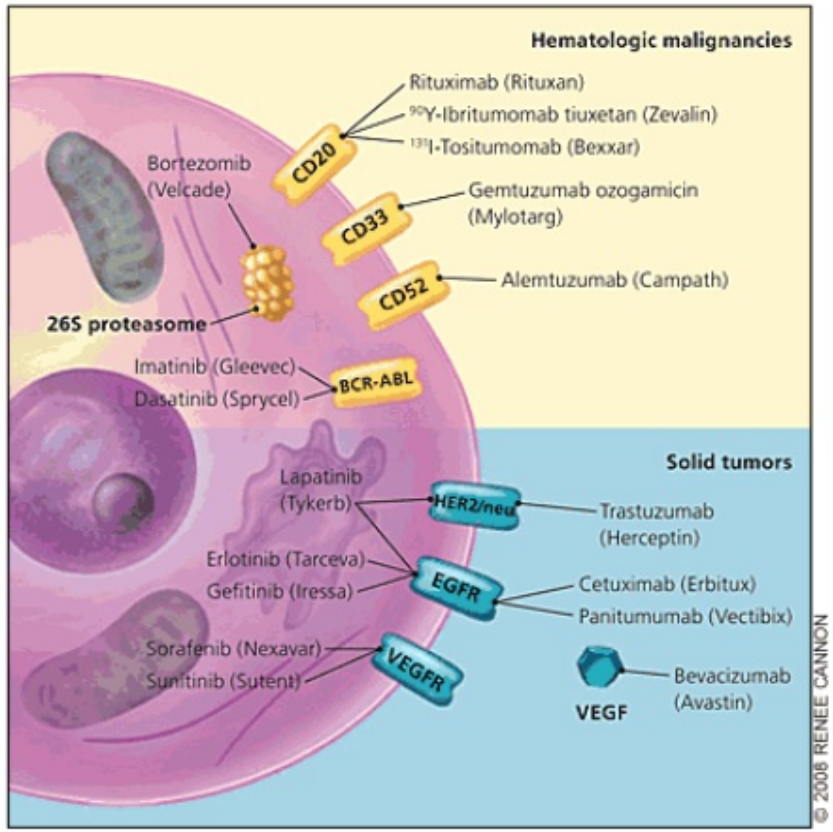




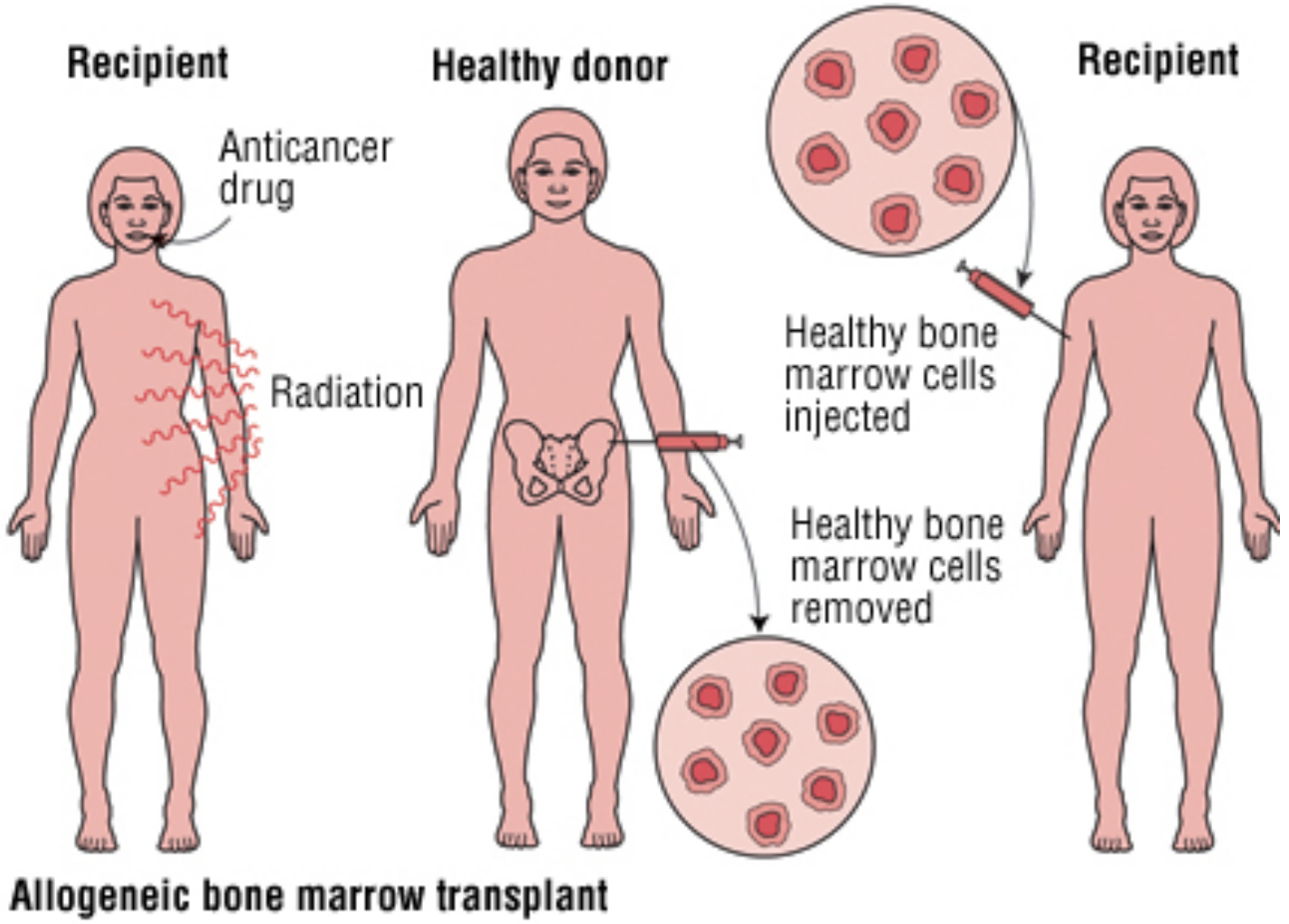
A catheter that is passed through a vein to end up in the thoracic portion of the vena cava or in the right atrium of the heart

Chemotherapy vs Targeted Therapy





Trapianto di cellule staminali emopoietiche

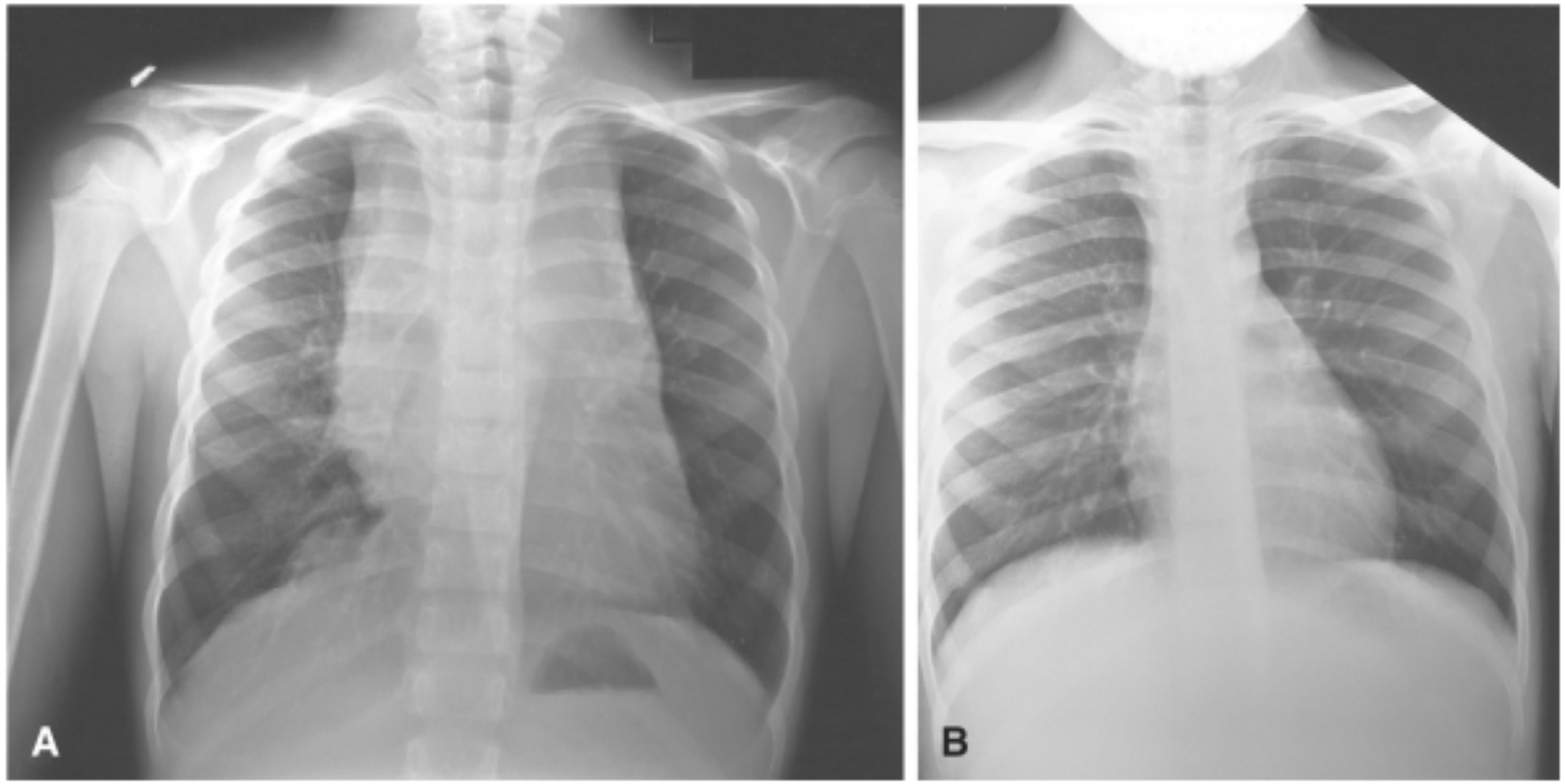


Lymphoma

- Lymphoma is the third most common cancer among children
- The two broad categories of lymphoma, Hodgkin disease (HD) and non-Hodgkin lymphoma (NHL), have different clinical manifestations and treatments

HD clinical manifestations

- Painless, non-tender, firm, rubbery, cervical or supraclavicular lymphadenopathy
- Some degree of mediastinal involvement
- Clinically detectable hepatosplenomegaly rarely is encountered
- Airway obstruction (dyspnea, hypoxia, cough), pleural or pericardial effusion, bone marrow infiltration (anemia, neutropenia, thrombocytopenia)
- Fever of unknown origin


A
B

Diagnosis

- Any patient with persistent, **unexplained lymphadenopathy** unassociated with an obvious underlying inflammatory or infectious process should have a chest radiograph to identify the presence of a mediastinal mass before undergoing node biopsy
- **Evaluation** includes; history, physical examination, and imaging studies, including chest radiograph; CT scans of the chest, abdomen and pelvis; gallium scan; and positron emission tomography (PET) scan
- **Laboratory studies** include a complete blood cell count (CBC) to identify abnormalities that might suggest marrow involvement, erythrocyte sedimentation rate (ESR), which are of some prognostic significance and, if abnormal at diagnosis, serve as a baseline to evaluate the effects of treatment

Treatment

- Treatment is determined largely by;
  - disease stage,
  - age at diagnosis,
  - presence or absence of symptoms,
  - presence of hilar lymphadenopathy or bulky nodal disease
- **MOPP** regimen , **COPP** (cyclophosphamide, vincristine [Oncovin], procarbazine, and prednisone) , **BEACOPP** , **COPP/ABV**

Prognosis

- Most relapses occur within the first 3 yr from diagnosis but relapses as late as 10 yr
- Using current therapeutic regimens, patients with favorable prognostic factors and early-stage disease have an event-free survival (EFS) of 85–90% and an overall survival (OS) at 5 yr of 95%

Non-Hodgkin Lymphoma (NHL)

- NHL accounts for approximately 60% of all lymphomas in children and adolescents
- Survival rates of 90–95% for localized disease and 60–90% with advanced disease

Subgroups

- Burkitt lymphoma (BL),
- Lymphoblastic lymphoma (LL),
- Diffuse large B-cell lymphoma (DLBCL),
- Anaplastic large cell lymphoma (ALCL),

Clinical manifestations

- Depend primarily on pathological subtype and primary and secondary sites of involvement
- NHLs are rapidly growing tumors and can cause symptoms based on size and location

Clinical manifestations

- Site-specific manifestations include;
  - Painless, rapid lymph node enlargement
  - Cough
  - Superior vena cava (SVC) syndrome
  - Dyspnea with thoracic involvement
  - Abdominal (massive and rapidly enlarging) mass
  - Intestinal obstruction
  - Intussusception-like symptoms
  - Ascites with abdominal involvement
  - Nasal stuffiness
  - Earache
  - Hearing loss
  - Tonsil enlargement with Waldeyer ring involvement
  - Localized bone pain (primary or metastatic)

Pretreatment Studies for Staging Pediatric Non-Hodgkin Lymphoma

- Complete blood cell count
- Serum electrolytes, uric acid, lactate dehydrogenase, creatinine, calcium, phosphorus Liver function tests (ALT, AST)
- Chest radiograph
- Neck, chest, abdominal, pelvic CT
- Positive emission tomography scan
- Bilateral bone marrow aspirate and biopsy
- Cerebrospinal fluid cytology, cell count, protein

Treatment

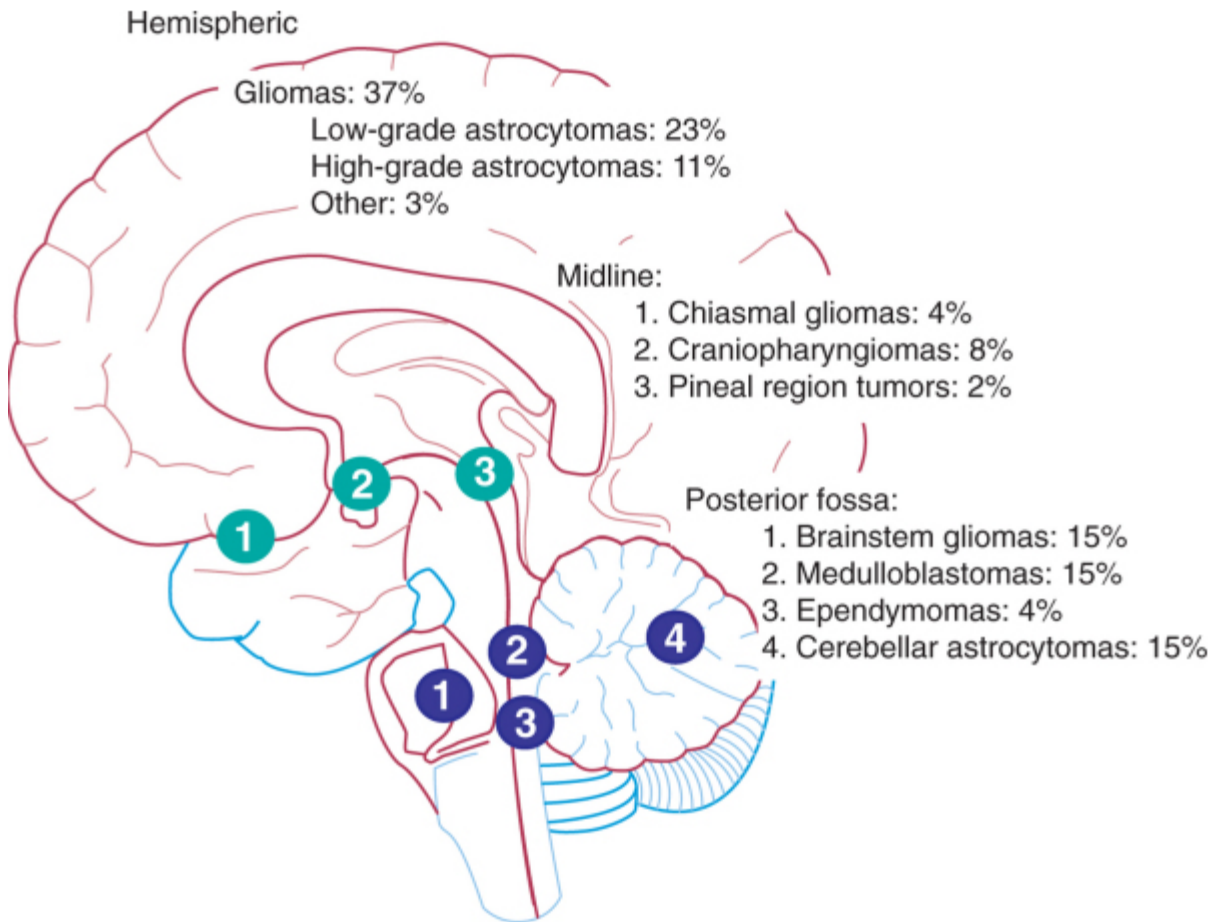
- The primary modality of treatment for childhood and adolescent NHL is multiagent systemic chemotherapy and intrathecal chemotherapy
- Surgery is used mainly for diagnostic and/or biologic specimens and staging but rarely is used for debulking large masses
- **Radiation therapy** is rarely, if ever, used, except in special circumstances such as **CNS involvement** in LL or occasionally BL, acute SVC, and acute paraplegias

Prognosis

- The prognosis is excellent for most forms of childhood and adolescent NHL
- Patients with localized disease have a 90–100% chance of survival, and patients with advanced disease have a 60–95% chance of survival

BRAIN TUMORS

- The overall mortality among this group approaches 45%. These patients have the highest morbidity, primarily neurologic, of all childhood malignancies
- Surgery with complete resection, if feasible, is the foundation, with radiation therapy and chemotherapy used based on the diagnosis, patient age, and other factors

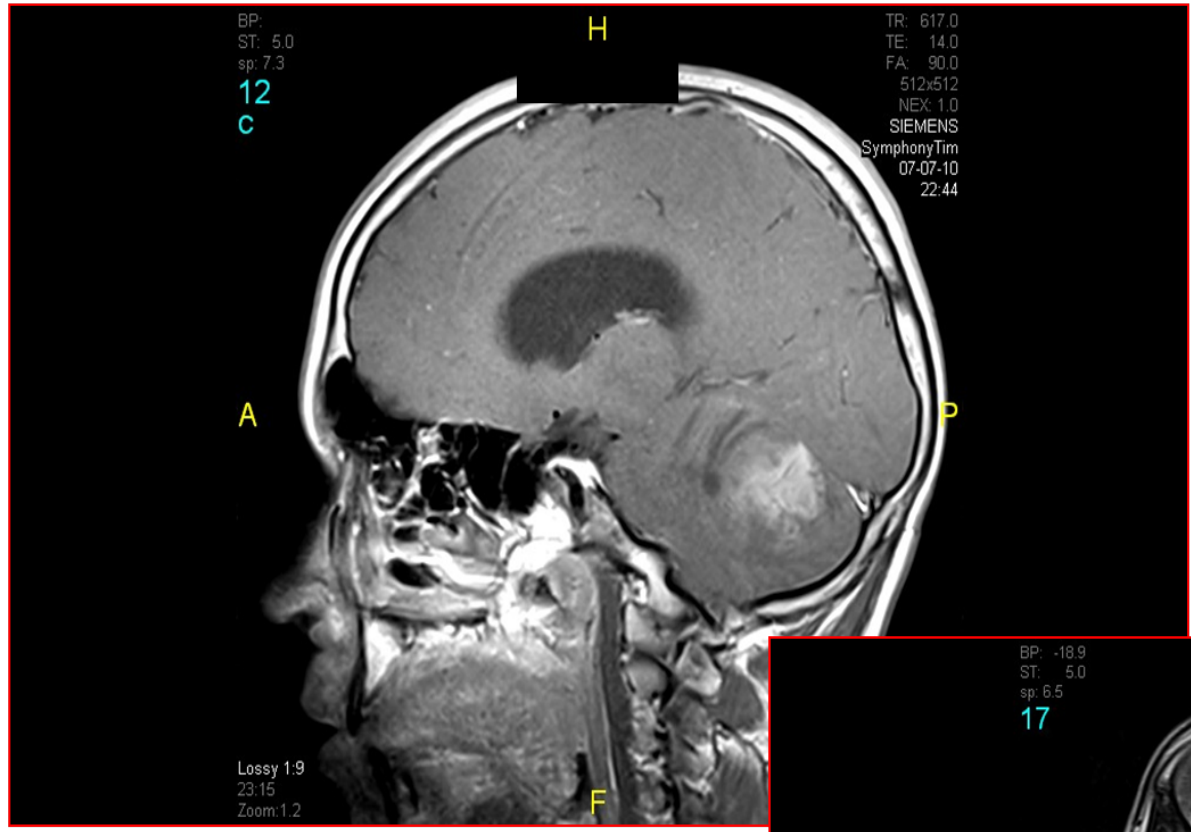

Hemispheric
Gliomas: 37%
Low-grade astrocytomas: 23%
High-grade astrocytomas: 11%
Other: 3%
Midline:
1. Chiasmal gliomas: 4%
2. Craniopharyngiomas: 8%
3. Pineal region tumors: 2%
Posterior fossa:
1. Brainstem gliomas: 15%
2. Medulloblastomas: 15%
3. Ependymomas: 4%
4. Cerebellar astrocytomas: 15%
1
2
3
1
2
3
4

Clinical manifestations

- Increased intracranial pressure (ICP)
- Classic triad of headache, nausea and vomiting
- Torticollis may result in cerebellar tonsil herniation. Blurred vision, diplopia, and nystagmus also are associated with infratentorial tumors
- Supratentorial tumors more commonly are associated with focal disorders such as motor weaknesses, sensory changes, speech disorders, seizures, and reflex abnormalities
- Neuroendocrine deficits such as diabetes insipidus, galactorrhea, precocious puberty, delayed puberty, and hypothyroidism

Diagnosis

- The evaluation of a patient suspected of having a brain tumor is an emergency
- Initial evaluation should include a complete history, physical examination (including ophthalmic), and neurologic assessment with neuroimaging
- For primary brain tumors, **MRI** is the neuroimaging standard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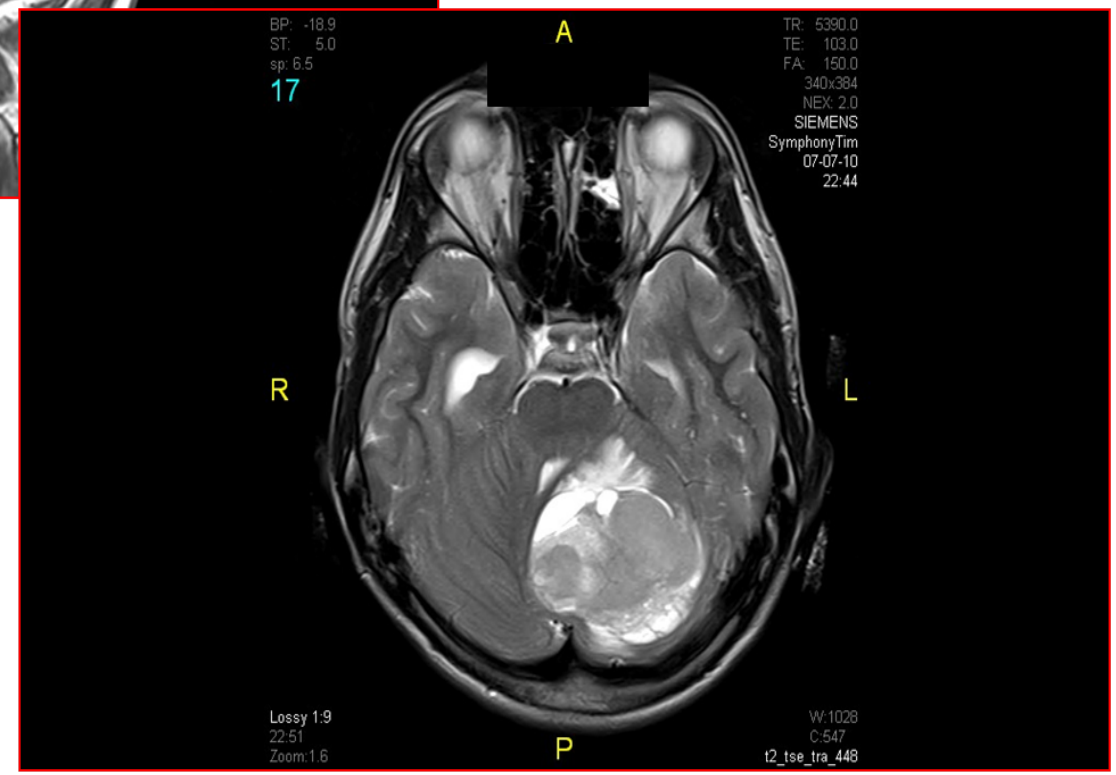
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Neuroblastoma

- Neuroblastoma (NB) is an embryonal cancer of the peripheral sympathetic nervous system with heterogeneous clinical presentation and course
- NB is the third most common pediatric cancer,
- The median age at diagnosis is 2 yr, and 90% of cases are diagnosed by 5 yr of age

Clinical manifestations

- NB may develop at any site of sympathetic nervous system tissue
- The signs and symptoms of NB reflect the tumor site and extent of disease
- Most cases of NB arise in the abdomen, either in the adrenal gland or in retroperitoneal sympathetic ganglia

Diagnosis

- NB usually is discovered as a mass or multiple masses on plain radiographs, CT, or MRI
- Tumor markers, including homovanillic acid (HVA) and vanillylmandelic acid (VMA) in urine, are elevated in 95% of cases and help to confirm the diagnosis
- A pathologic diagnosis is established from tumor tissue obtained by biopsy

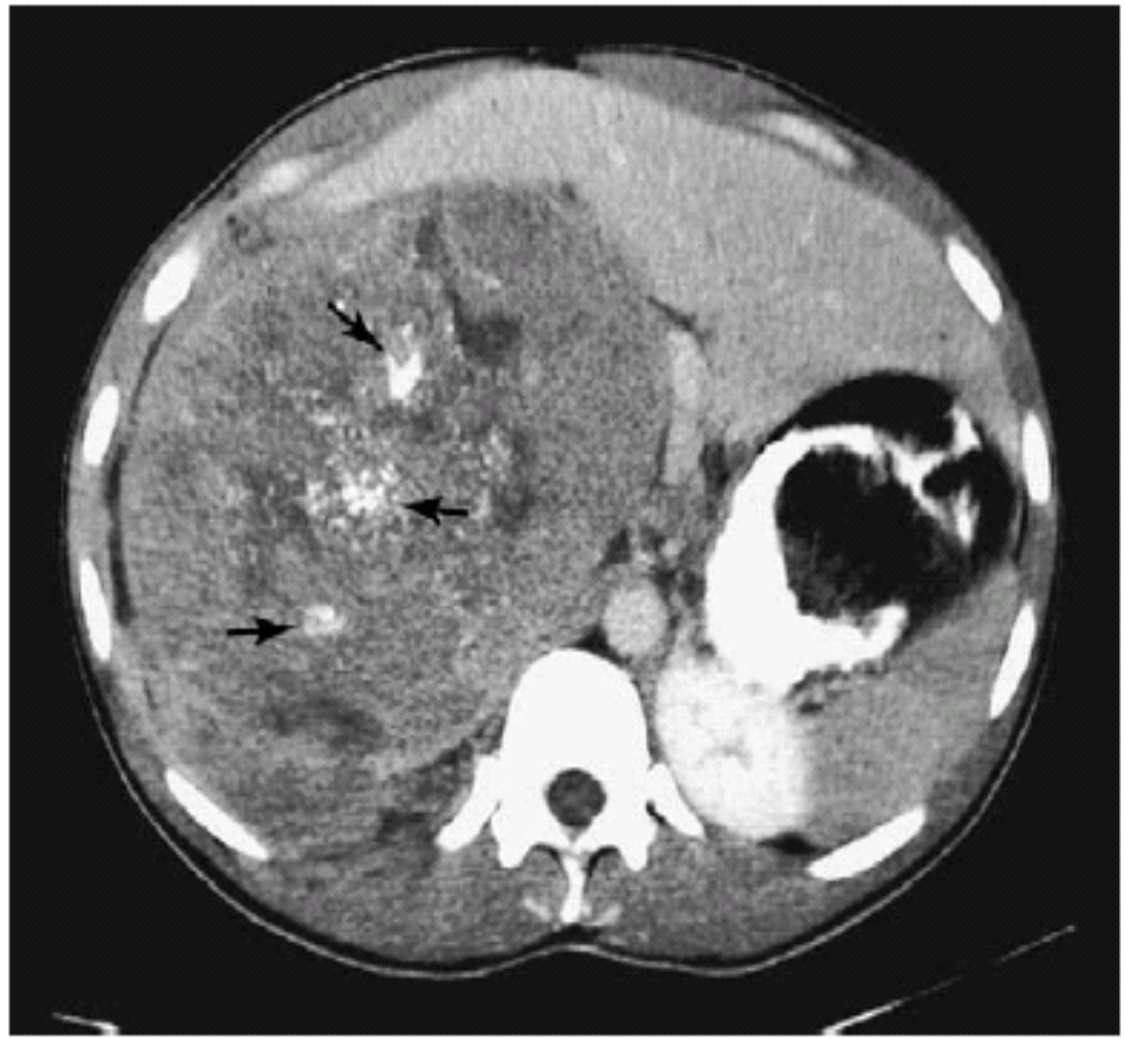
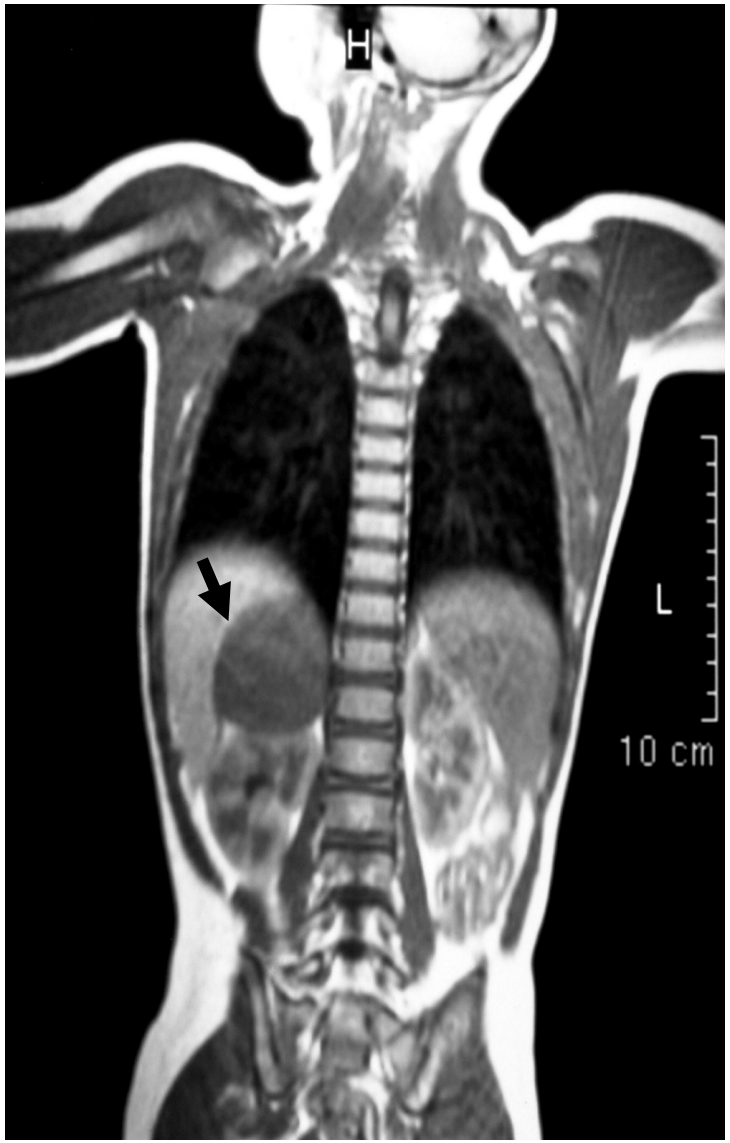


Fig. 1. Neuroblastoma with characteristic calcifications (*arrows*) on CT scan.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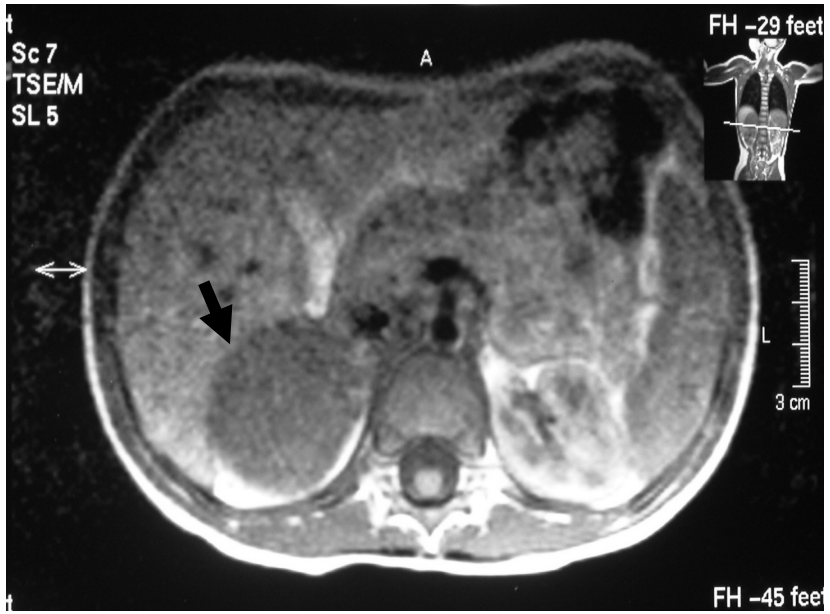
10 cm


Sc 7
TSE/M
SL 5
A
FH -29 feet
L
3 cm
FH -45 feet

Treatment

- The usual treatment for low-risk NB is surgery for stages 1 and 2 (Even in stage 2 with small amounts of residual tumor, the cure rate is >90% without further therapy)
- Treatment of intermediate-risk NB includes surgery, chemotherapy, and, in some cases, radiation therapy

WILMS TUMOR

- Wilms tumor, also known as **nephroblastoma**, is a complex mixed embryonal neoplasm of the kidney composed of three elements: blastema, epithelia, and stroma

Epidemiology

- Usually occurs in children between 2–5 yr of age
- The second most common malignant abdominal tumor in childhood
- It may arise in one or both kidneys

Clinical manifestations, diagnosis

- Wilms tumor usually presents as an abdominal mass
- ****Any abdominal mass in a child must be considered malignant until diagnostic imaging and laboratory findings define its true nature****
- Once an abdominal mass is discovered, a complete physical examination should be performed, followed by a complete blood count, liver and kidney function studies, and a search for specific tumor markers secreted by the suspected tumor
- Imaging studies include a flat plate of the abdomen, ultrasonography, and CT and/or MRI

Treatment

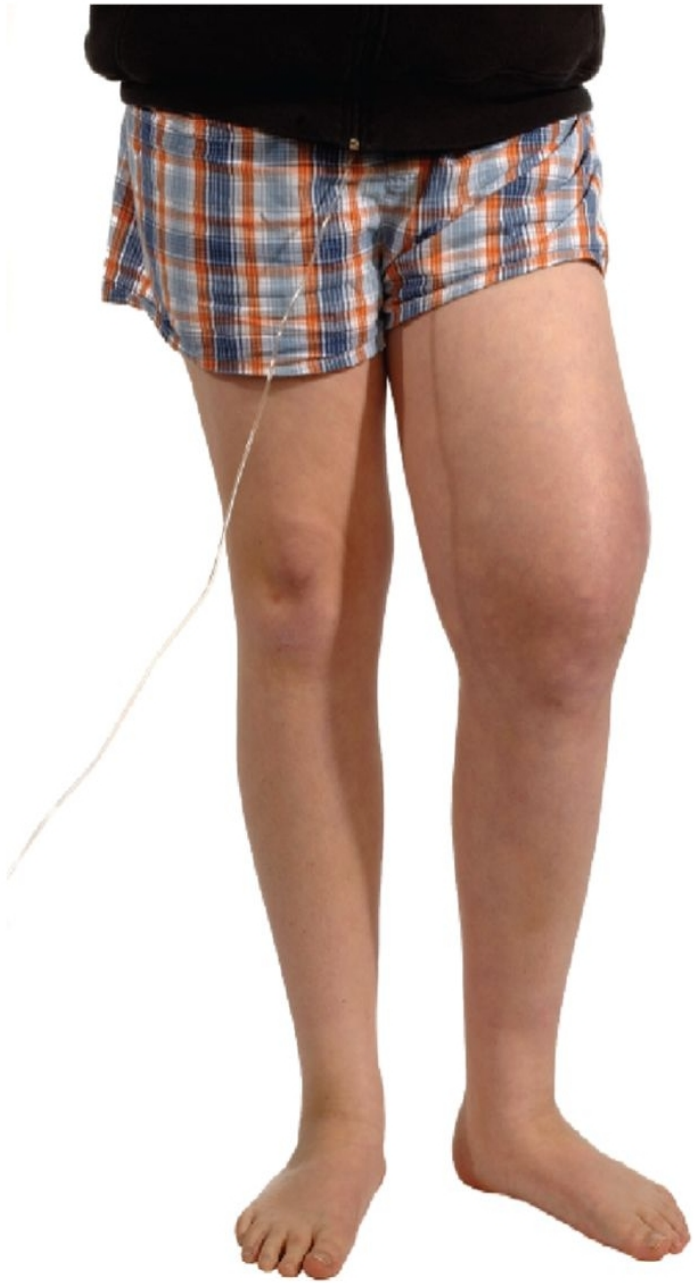
- Surgical extirpation of the tumor should be performed
- During the operation the contralateral kidney should be examined to exclude bilateral Wilms tumor
- Most centers follow chemotherapy guidelines provided by the National Wilms Tumor Study Group

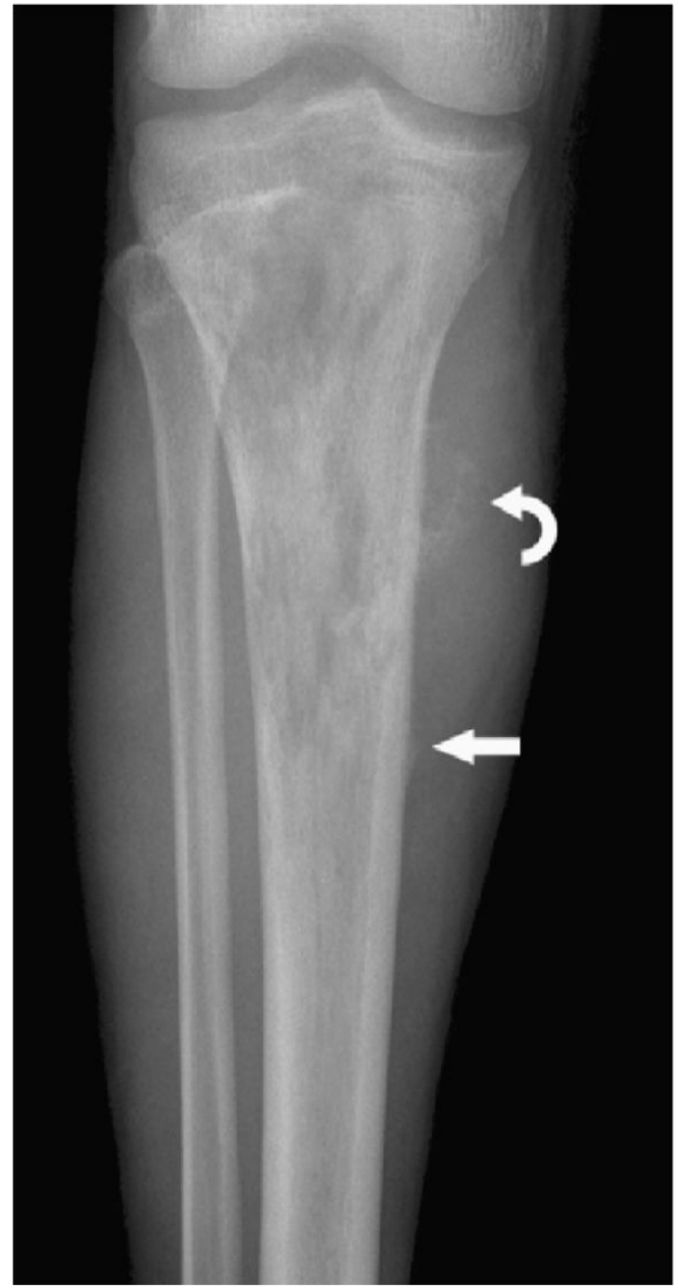
Prognosis

- The prognosis is worse with a larger tumor (>500 g), advanced stage (III and IV), and an unfavorable histologic subtype
- >60% of patients with all stages generally survive
- Stages I through III have a cure rate of >90%

Neoplasms of Bone

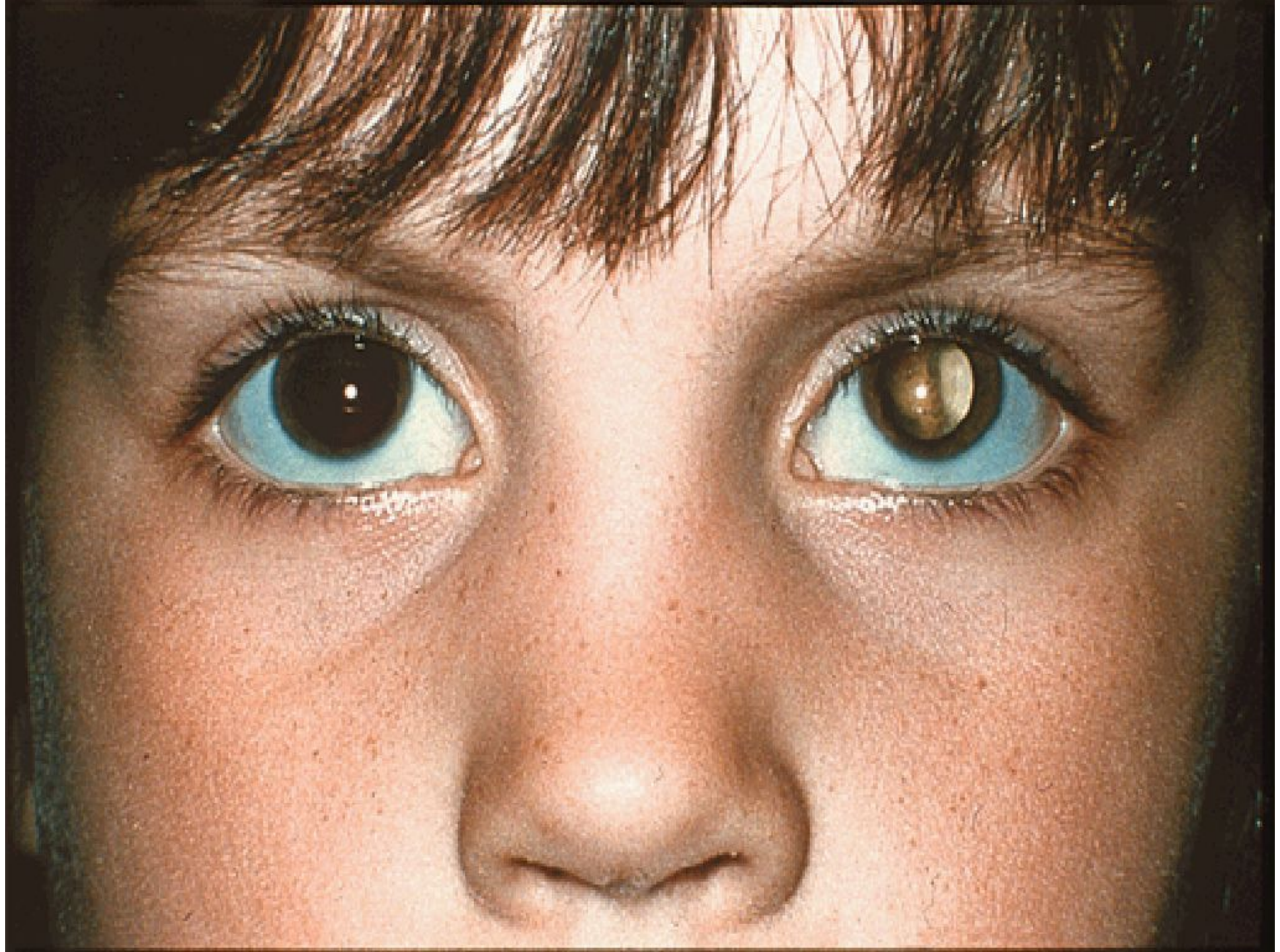
- Osteosarcoma is the most common primary malignant bone tumor in children and adolescents, followed by Ewing sarcoma
- In children <10 yr of age, Ewing sarcoma is more common than osteosarcoma.
- Both tumor types are most likely to occur in the second decade of life





Retinoblastoma

- Only about 10% of retinoblastomas are detected by routine ophthalmologic screening in the context of a positive family history
- Retinoblastoma classically presents with **leukocoria,** a white pupillary reflex , which often is first noticed when a red reflex is not present at routine newborn or well-child examination or in a flash photograph of the child



Diagnosis-treatment

- The diagnosis is established by the characteristic ophthalmologic findings. Biopsy is contraindicated
- The primary goal is cure; the secondary goal is preserving vision
- Enucleation is performed if there is no potential for useful vision
- Chemoreduction in combination with **focal therapy** (laser photocoagulation or cryotherapy) has replaced the traditional approach of enucleation of the more severely affected eye and irradiation of the remaining eye
- Routine ophthalmologic examinations should continue until about 6 yr of age to detect new lesions

In breve….

Tumori del sangue

- Esami sangue
- (Esami strumentali)
- Determinare il tipo del tumore »guardando» le cellule del sangue
- Chemioterapia o nuove immunoterapie

Tumori solidi

- Esami strumentali
- (Esami sangue)
- Determinare il tipo del tumore con biopsia della massa
- Chemioterapia/Radioterapia/Chirurgia

Il paziente oncologico

- E’ a rischio di sepsi fulminante (shock settico) ogni volta che compare la febbre e i valori dei GB sono bassi dopo CT
- Non può mangiare cibi non cotti quando ha GB bassi
- E’ a rischio di complicanze tossiche da CT
  - Mucosite/dermatite…sfaldamento delle mucose/pelle
  - Vomito da CT
  - Insufficienza renale
- Richiede spesso nutrizione artificiale

Come lavarsi le mani?

Lavare le mani quando sono sporche, oppure utilizzare le salviettine monouso

Durata della procedura: 40-60 secondi