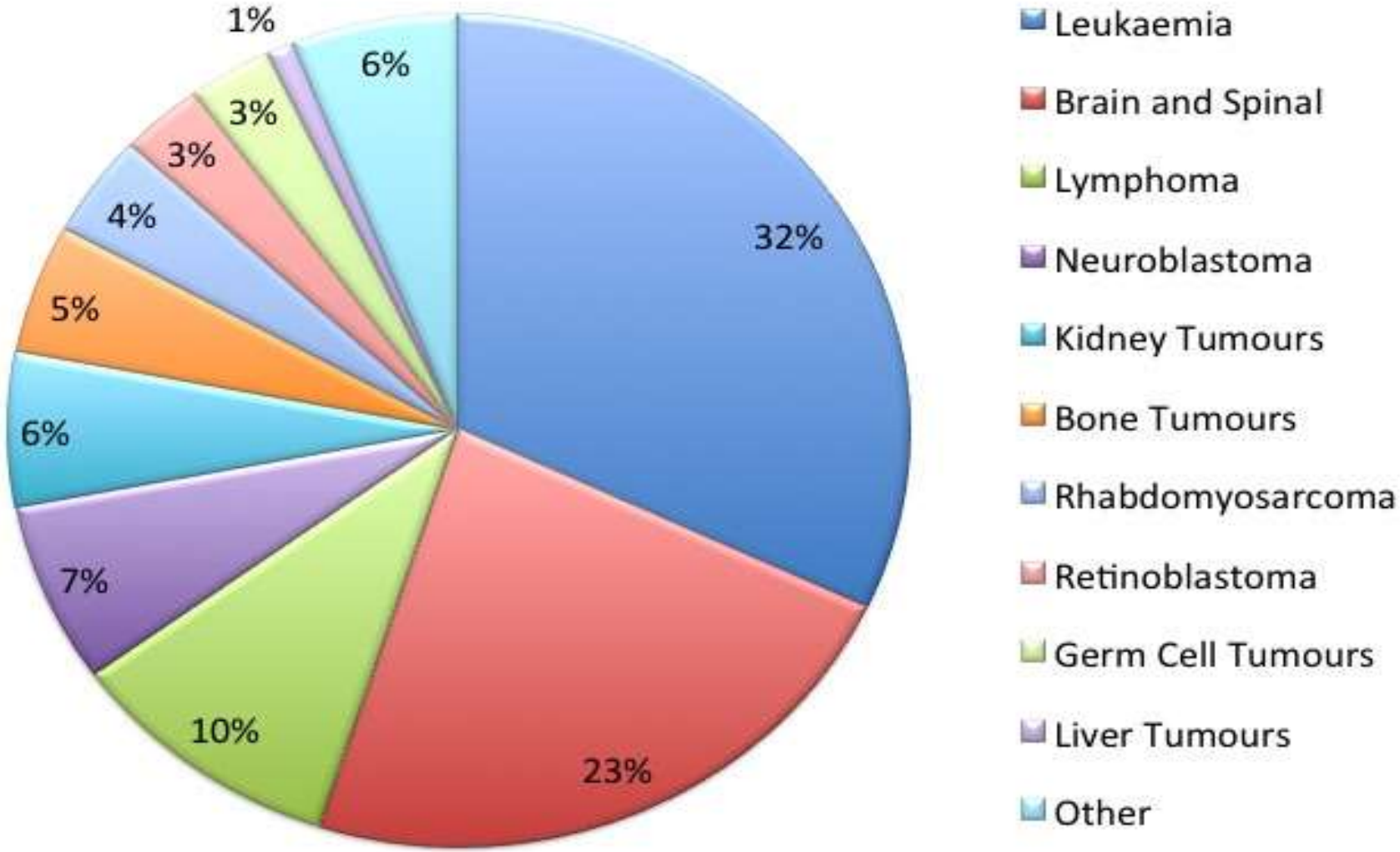
Pediatric neoplasms

Ala’a Almaaiteh, MD

Pediatric neoplasms

- Include malignant tumors “cancers” and nonmalignant tumors
- Pediatric cancers are uncommon
- Less than 1% of all newly diagnosed cancer cases in US
- Differs from adult malignancies in prognosis and distribution by histology and tumor site
- The most common pediatric malignancy is acute leukemia, with survival rate up to 90%

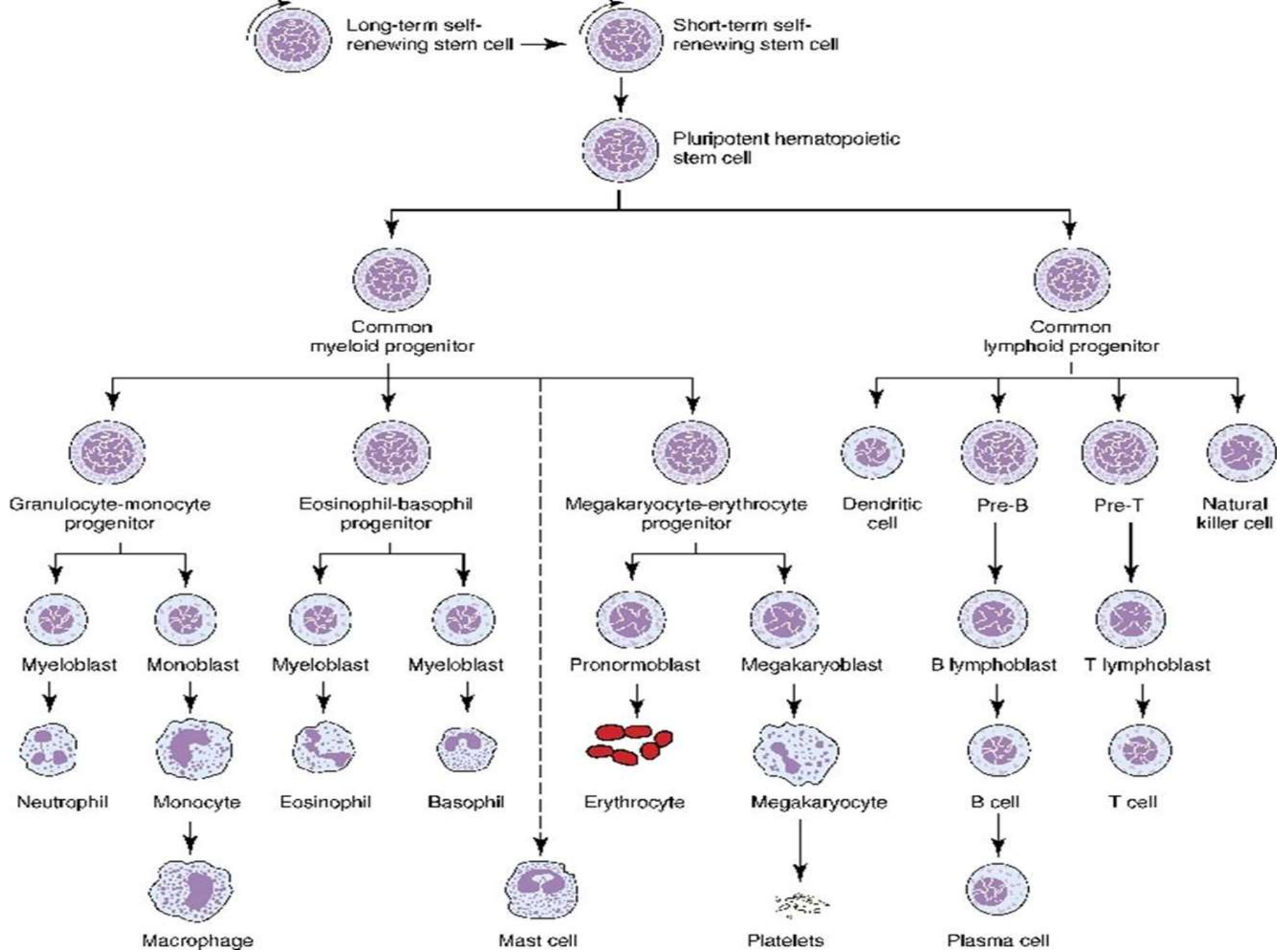
Distribution of Childhood Cancer



Leukemias

The leukemias

- A group of malignant diseases in which genetic abnormalities in a hematopoietic cells give rise to an unregulated clonal proliferation of cells.
- Accounts for 31% of pediatric malignancies
- Acute lymphoblastic leukemia (ALL) accounts for 77% of cases
- Acute myelogenous leukemia (AML) 11%
- Chronic myelogenous leukemia (CML) 2-3%
- Juvenile myelomonocytic leukemia 1-2%


Long-term self-renewing stem cell
Short-term self-renewing stem cell
Pluripotent hematopoietic stem cell
Common myeloid progenitor
Common lymphoid progenitor
Granulocyte-monocyte progenitor
Eosinophil-basophil progenitor
Megakaryocyte-erythrocyte progenitor
Dendritic cell
Pre-B
Pre-T
Natural killer cell
Myeloblast
Monoblast
Myeloblast
Myeloblast
Pronormoblast
Megakaryoblast
B lymphoblast
T lymphoblast
Neutrophil
Monocyte
Eosinophil
Basophil
Erythrocyte
Megakaryocyte
B cell
T cell
Macrophage
Mast cell
Platelets
Plasma cell

ALL

- Incidence: 3-4/100,000
- Peak age group 2-3 years
- Male more than females
- Etiology: unknown, several genetic and environmental factors: Chemical, Drugs, Ionizing Radiation.
- More common with certain chromosomal abnormalities, e.g., down syndrome, bloom syndrome, ataxia-telangectesia, and fanconi anemia

Classification (immunophenotyping)

1. Pre-B ALL 85%
2. T-Cell ALL 15%
3. Mature B (Burkitt) ALL 1%

- Many chromosomal abnormalities in most ALL cases are used as diagnostic and prognostic factors

SUBTYPE	CHROMOSOMAL ABNORMALITY	INFLUENCE ON PROGNOSIS	INCIDENCE
ACUTE LYMPHOBLASTIC LEUKEMIA			
Precursor-B	Trisomy 4,10, and 17	Favorable	25%
Precursor-B	t(12;21)	Favorable	20-25%
Precursor-B	t(1;19)	None	5-6%
Precursor-B	t(4;11)	Unfavorable	2%
Precursor-B	t(9;22)	Unfavorable	3%
Mature B-cell (Burkitt)	t(8;14)	None	1-2%
Precursor-B	Hyperdiploidy	Favorable	20-25%
Precursor-B	Hypodiploidy	Unfavorable	1%
ACUTE MYELOGENOUS LEUKEMIA			
M1*	t(8;21)	Favorable	5-15%
M4*	inv(16)	Favorable	2-11%
M3*	t(5;17)	Favorable	6-15%
General	del(7)	Unfavorable	2-7%
Infant	11q23	Unfavorable	2-10%

*Per the French-American-British classification of acute myelogenous leukemia (see Table 489-4).

Good prognostic factors

1. Age : 1-10 year.

2.WBC: < 50,000

3.Chrom. Abnormalities: presence of TEL/AML1 gene. Philadelphia-negative, hyperdiploidy, absence of MLL rearrangement

4.Immunophenotype: B-cell ALL

5. No CNS involvement

6.Early Response to Chemotherapy

Clinical Manifestations

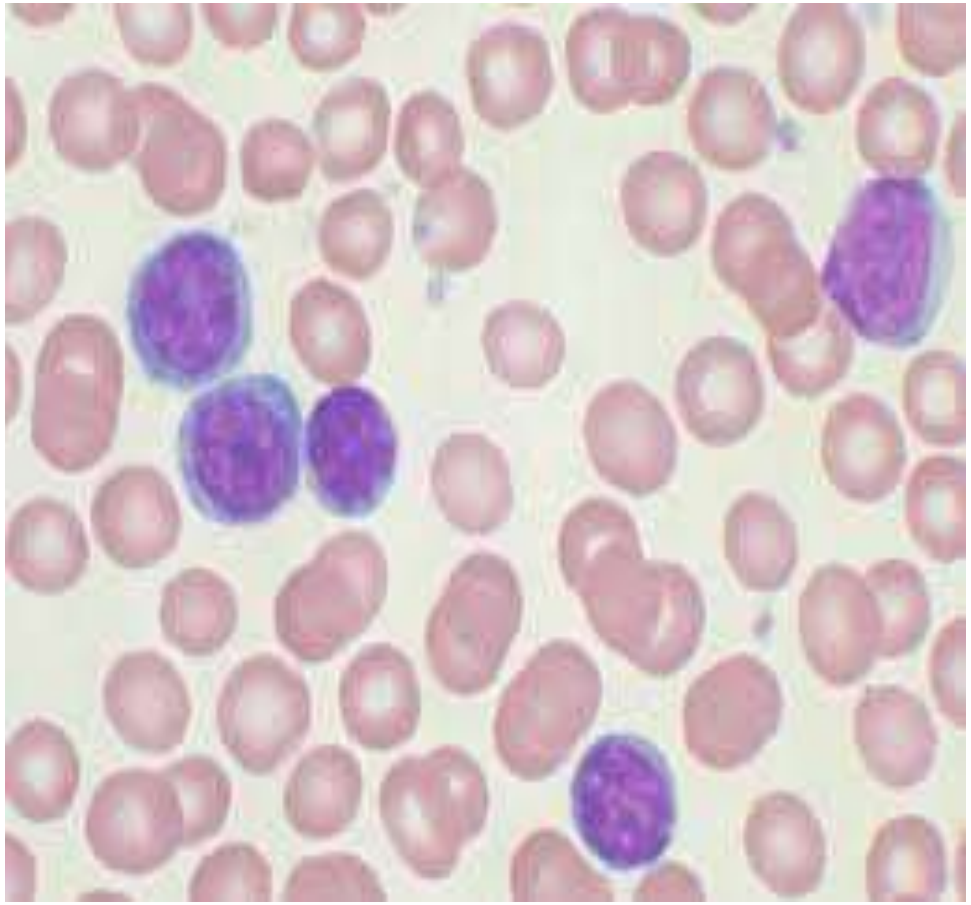
- Initial symptoms are nonspecific and relatively brief:
  - Anorexia, fatigue, malaise, and irritability
  - low-grade fever
  - Sever bone or, less often, joint pain, particularly in the lower extremities
  - history of an upper respiratory tract infection in the preceding 1-2 mo
- Later signs and symptoms of bone marrow failure
- Organ infiltration can cause lymphadenopathy, hepatosplenomegaly, testicular enlargement, or central nervous system (CNS) involvement
- Respiratory distress may be due to severe anemia or mediastinal node comparison of the airways.

Physical examination findings

- pallor, listlessness
- purpuric and petechial skin lesions, or mucous membrane
- lymphadenopathy, splenomegaly, or, less commonly, hepatomegaly.
- In patients with bone pain, there may be exquisite tenderness over the bone
- CNS involvement: papilledema
- Testicular mass: rare
- Respiratory distress: in T-cell with large anterior mediastinal mass

Diagnosis

- CBC: most patients have sever anemia and thrombocytopenia. High WBC (not in all cases)
- Blood film: peripheral blasts
- bone marrow aspiration and biopsy, flow cytometry, cytogenetics, and molecular studies.
- LP and CSF examination for blasts
- CXR: mediastinal mass
- High lactate dehydrogenase (LDH)



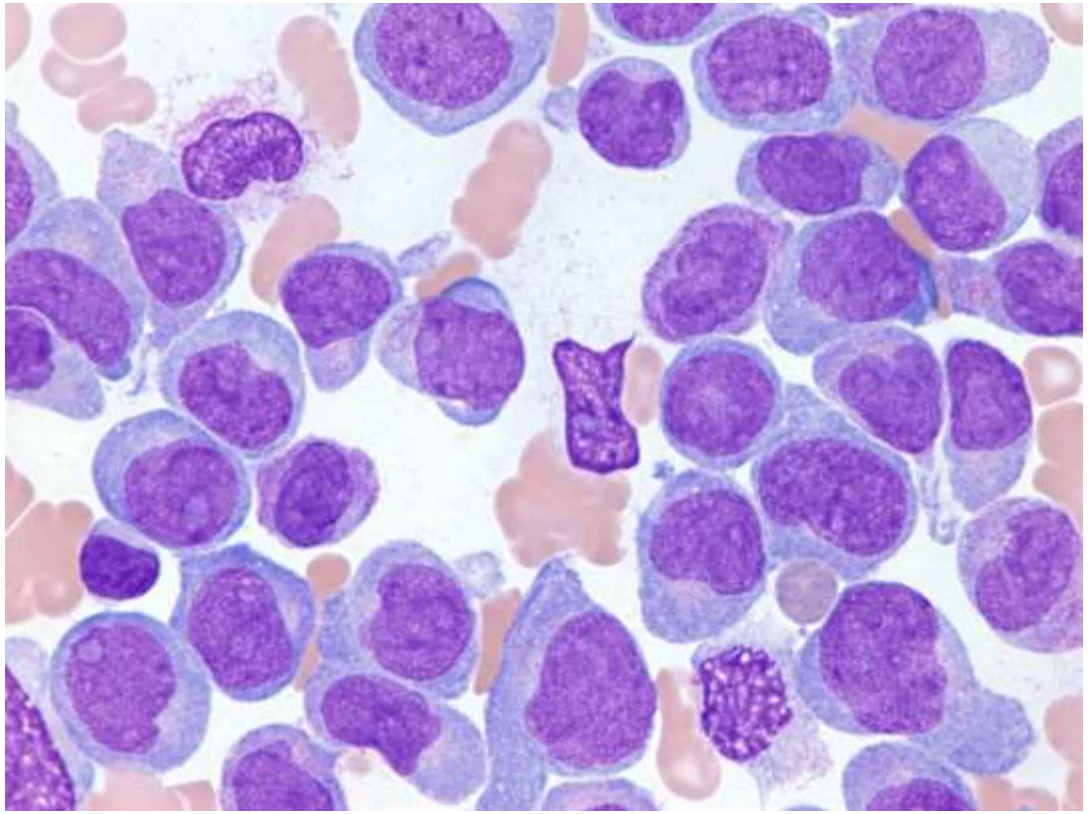
Differential Diagnosis

- aplastic anemia (congenital or acquired) and myelofibrosis
- Failure of a single cell line eg.e, transient erythroblastopenia of childhood, ITP, and congenital or acquired neutropenia.
- Infectious mononucleosis in patients with acute onset of fever and lymphadenopathy and from rheumatoid arthritis in patients with fever, bone pain but often no tenderness, and joint swelling.
- (AML) and other malignant diseases that invade the bone marrow

Treatment

- The single most important prognostic factor in ALL is the treatment
- 5 years survival rate > 80%
- Without effective therapy, the disease is fatal.
- Duration is 2.0—3.0 years
- Treatment protocol according to risk stratification (low risk, intermediate vs high risk)
- Several phases: Remission induction, consolidation and intensification, maintenance phase
- Several chemotherapeutic agents are used in ALL treatment
  - Corticosteroids, vincristine, methotrexate (IT and IV), daunomycin
  - Mercaptopurine and oral methotreaxate oral

AML

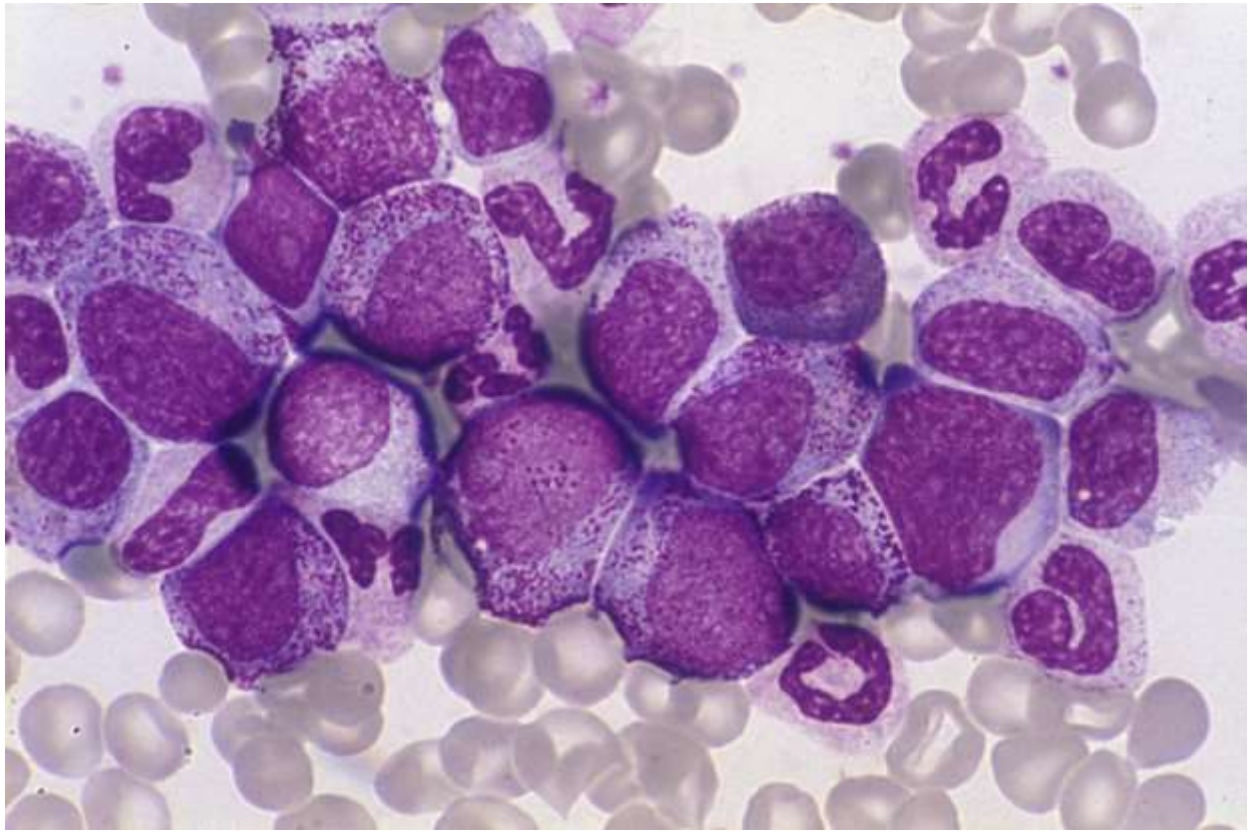


Acute Myelogenous Leukemia

FAB subtype	Name
M0	Undifferentiated acute myeloblastic leukemia
M1	Acute myeloblastic leukemia with minimal maturation
M2	Acute myeloblastic leukemia with maturation
M3	Acute promyelocytic leukemia (APL)
M4	Acute myelomonocytic leukemia
$M4_{eos}$	Acute myelomonocytic leukemia with eosinophilia
M5	Acute monocytic leukemia
M6	Acute erythroid leukemia
M7	Acute megakaryoblastic leukemia

- Signs and symptoms are same as in ALL
- High WBC count at presentation
- M3 may present with DIC
- M4 and M5 may present with gingival infiltration
- M7 is most specific leukemia in Down syndrome
- Carries worse prognosis than ALL
- Treatment : Aggressive chemotherapy, Bone marrow transplant (for unfavorable prognosis)

CML



- Initial chronic phase in which malignant clone produces high WBC. Mild anemia and thrombocytosis
- Splenomegaly
- chronic phase lasts 3-4 years and ends by “Blast crisis” which mimic ALL
- 95% of CML cases have positive Philadelphia chromosome “t(9;22)” resulting in a BCR-ABL fusion protein
- Treatment:
  - hydroxyurea
  - Imatinib: specifically inhibts BCR-ABL production
  - BMT

Lymphoma

- Most common cancer in adolescents
- Two major types:
  - Hodgkin disease
  - Non-Hodgkin lymphoma (NHL)
- Unknown etiology, EBV plays causal role in both conditions
- Hodgkin disease peaks in the adolescent/young adult. NHL increases with age.
- NHL in childhood are diffuse, highly malignant
- NHL has three histologic subtypes
- NHL has association with immunodeficiency

Table 156-1 Subtypes of Non-Hodgkin Lymphoma in Children

HISTOLOGIC CATEGORY	IMMUNOPHENOTYPE	USUAL PRIMARY SITE	MOST COMMON TRANSLOCATION(S)
Small noncleaved (Burkitt lymphoma)	Mature B-cell (surface immunoglobulin present)	Abdomen (sporadic form) Head and neck (endemic form)	t(8;14)(q24;q32) t(2;8)(p11;q24) t(8;22)(q24;q11)
Lymphoblastic	T-cell (rarely pre-B-cell)	Neck and/or anterior mediastinum	Many
Large cell	T-cell, B-cell, or indeterminate	Lymph nodes, skin, soft tissue, bone	t(2;5)(p23;q35)

Clinical manifestation

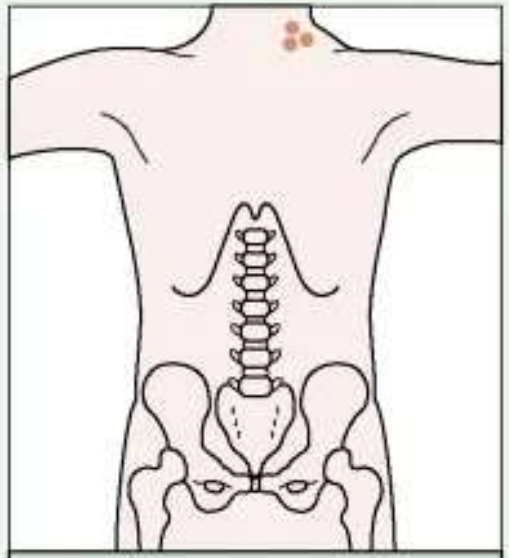
- painless, firm lymphadenopathy usually the supraclavicular and cervical nodes
- Mediastinal lymphadenopathy producing cough or shortness of breath
- **B symptoms**:
  - Fever >38° C for 3 consecutive days
  - drenching night sweats
  - unintentional weight loss of 10% or more within 6 months

- Burkitt lymphoma may present with abdominal mass or jaw mass

Diagnosis

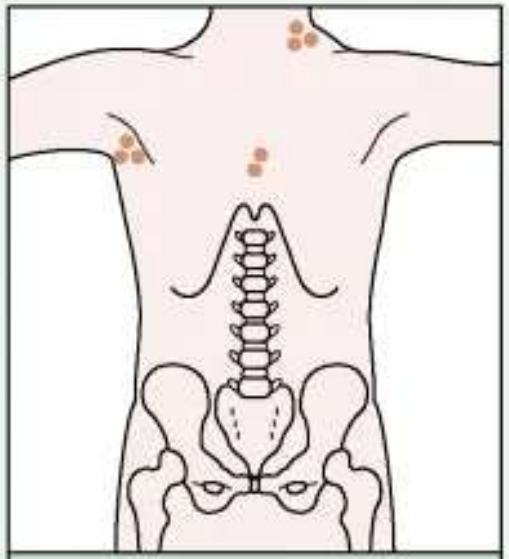
- **Diagnosis** is established by tissue biopsy
- Pathologic hallmark of Hodgkin disease is the identification of **Reed-Sternberg cells.**
- Chest x-ray assesses for a mediastinal mass
- CT scan for staging
- PET scan
- Bone marrow aspiration
- CBC and blood chemistry

Ann Arbor Staging System for Hodgkin Disease and Non-Hodgkin Lymphomas



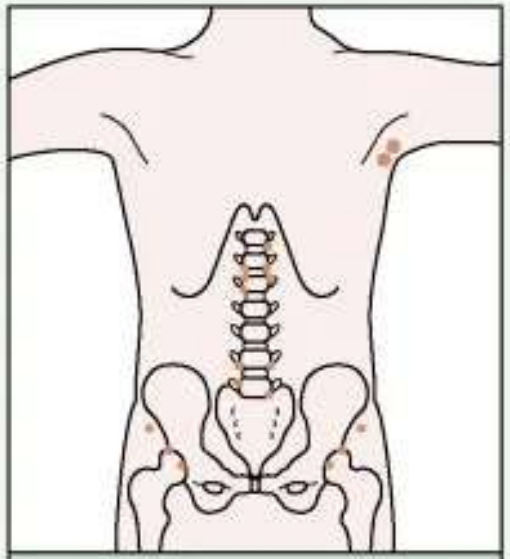
Stage I

- Involvement of single lymph node region
- Or involvement of single extralymphatic site (stage I_E)



Stage II

- Involvement of ≥2 lymph node regions on same side of diaphragm
- May include localized extralymphatic involvement on same side of diaphragm (stage II_E)



Stage III

- Involvement of lymph node regions on both sides of diaphragm
- May include involvement of spleen (stage III_S) or localized extranodal disease (stage III_E) or both (III_{E+S})

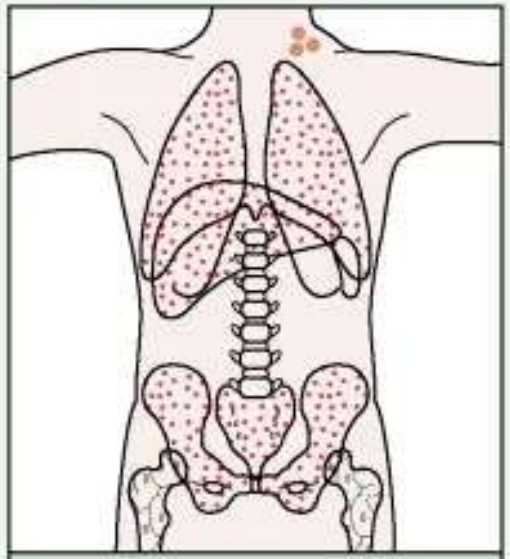
For Hodgkin disease:

III_1

- Disease limited to upper abdomen—spleen, splenic hilar, celiac, or porta hepatis nodes

III_2

- Disease limited to lower abdomen—periaortic, pelvic, or inguinal nodes

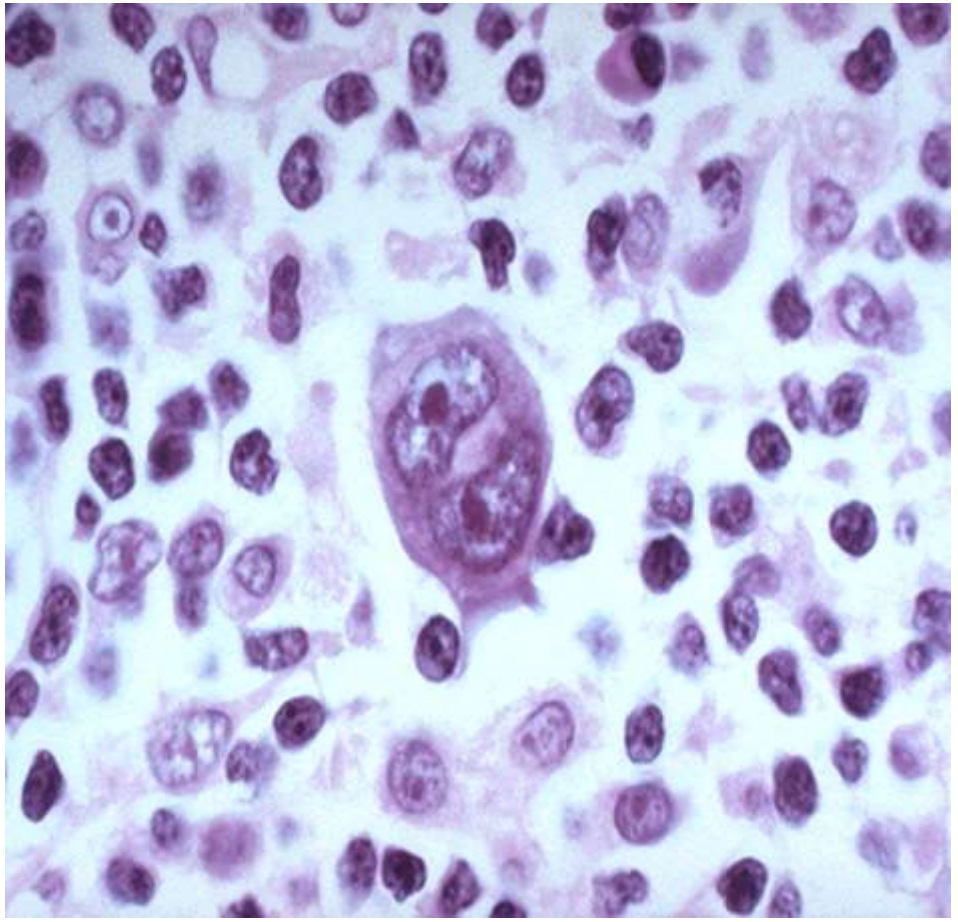


Stage IV

- Disseminated (multifocal) extralymphatic disease involving one or more organs (e.g., liver, bone marrow, lung, skin), +/– associated lymph node involvement
- Or isolated extralymphatic disease with distant (non-regional) lymph node involvement

Reed-Sternberg (RS) cell

- resembling an "owl's eye" appearance



Mediastinal mass

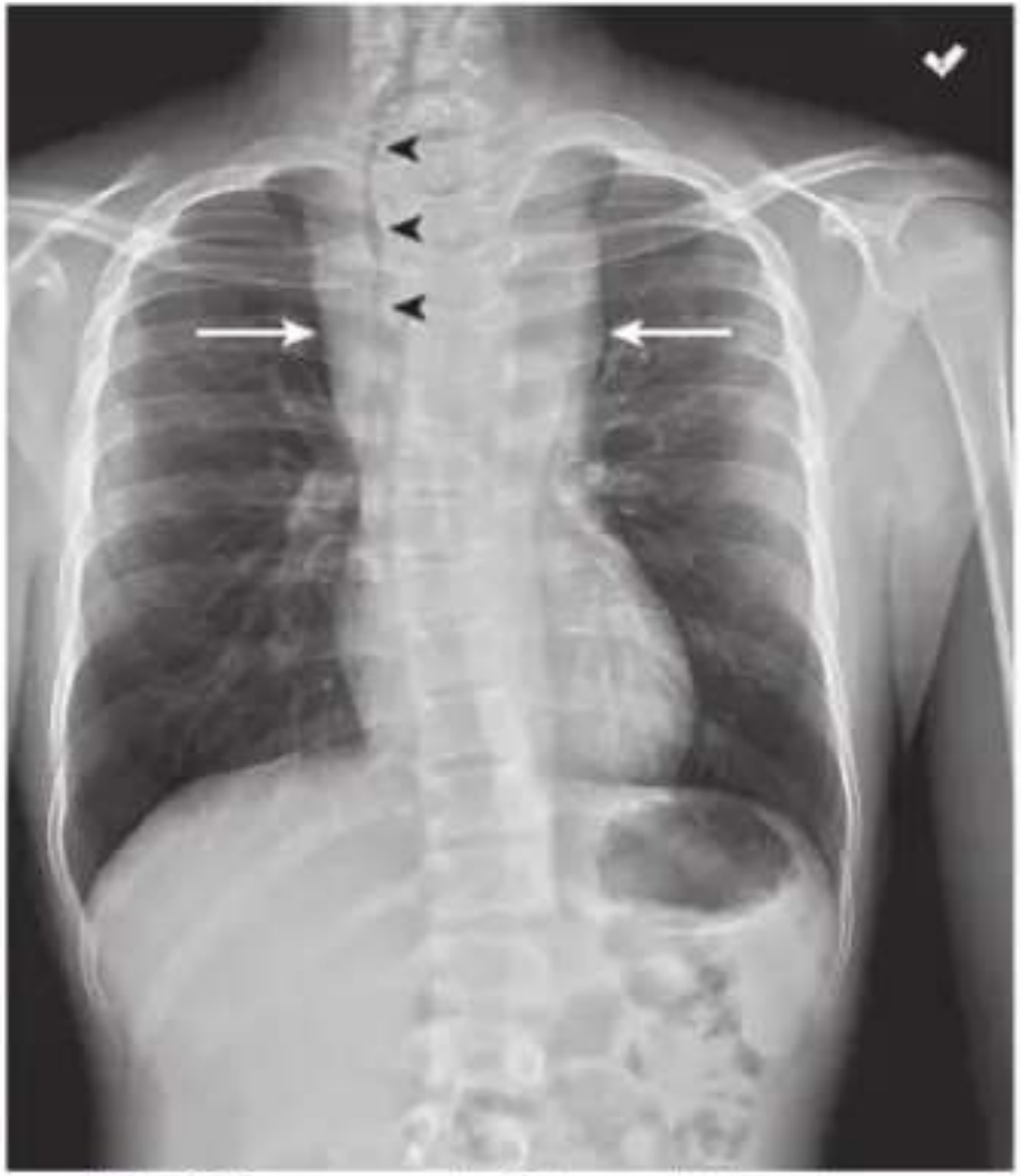
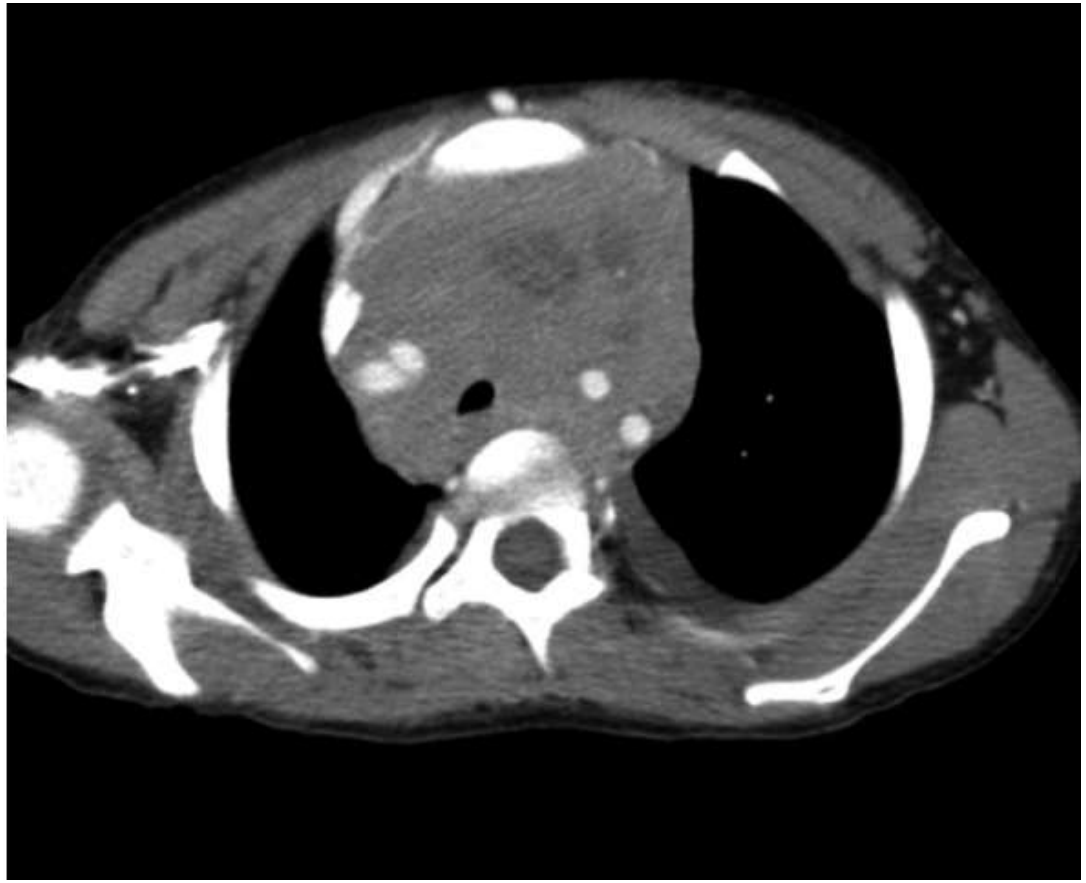


Figure 156-1 Chest x-ray of a 15-year-old boy demonstrating a large superior anterior mediastinal mass *(large arrows)* compressing the trachea and deviating it rightward *(arrowheads)*. Biopsy revealed non-Hodgkin lymphoma.



differential diagnosis

- leukemia, rhabdomyosarcoma, nasopharyngeal carcinoma, germ cell tumors, and thymomas.
- Nonmalignant diagnoses include infectious mononucleosis (EBV infection), branchial cleft and thyroglossal duct cysts, cat scratch disease (Bartonella henselae),
- bacterial or viral lymphadenitis
- mycobacterial infection, toxoplasmosis
- Patients with acute abdominal pain from Burkitt lymphoma may be misdiagnosed as having appendicitis

Treatment

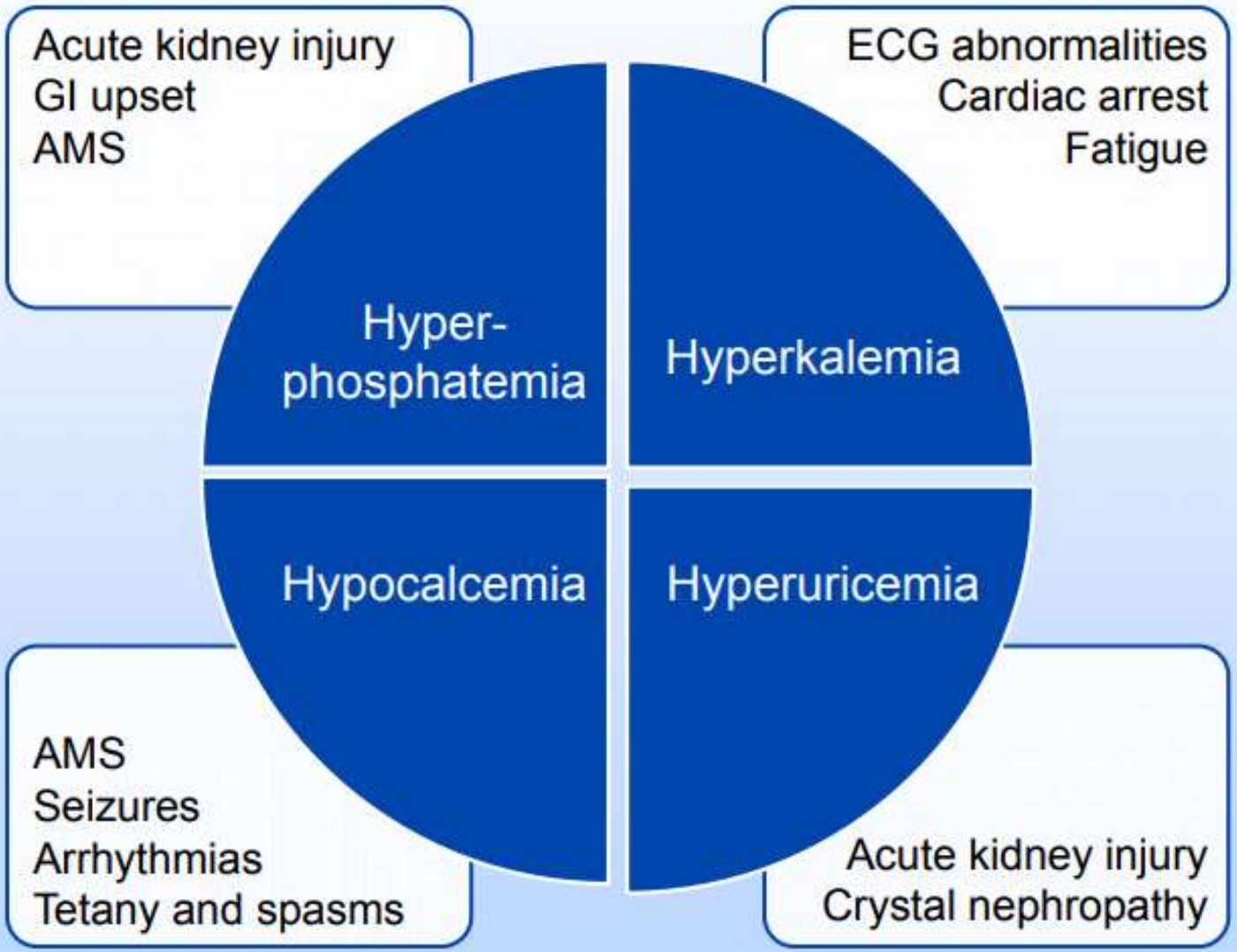
- For Hodgkin disease: a combination of chemotherapy with or without low-dose radiation therapy.
- Chemotherapy usually consists of some combination of cyclophosphamide, vincristine, procarbazine, doxorubicin, bleomycin, vinblastine, prednisone, and etoposide.
- More aggressive chemotherapy is used to treat NHL: cyclophosphamide, moderate- to high-dose methotrexate, cytarabine, doxorubicin, ifosfamide, and etoposide.
- The prognosis is generally excellent. There is an approximately 90% 5-year overall survival rate,

Oncologic emergency

Tumor lysis syndrome (TLS)

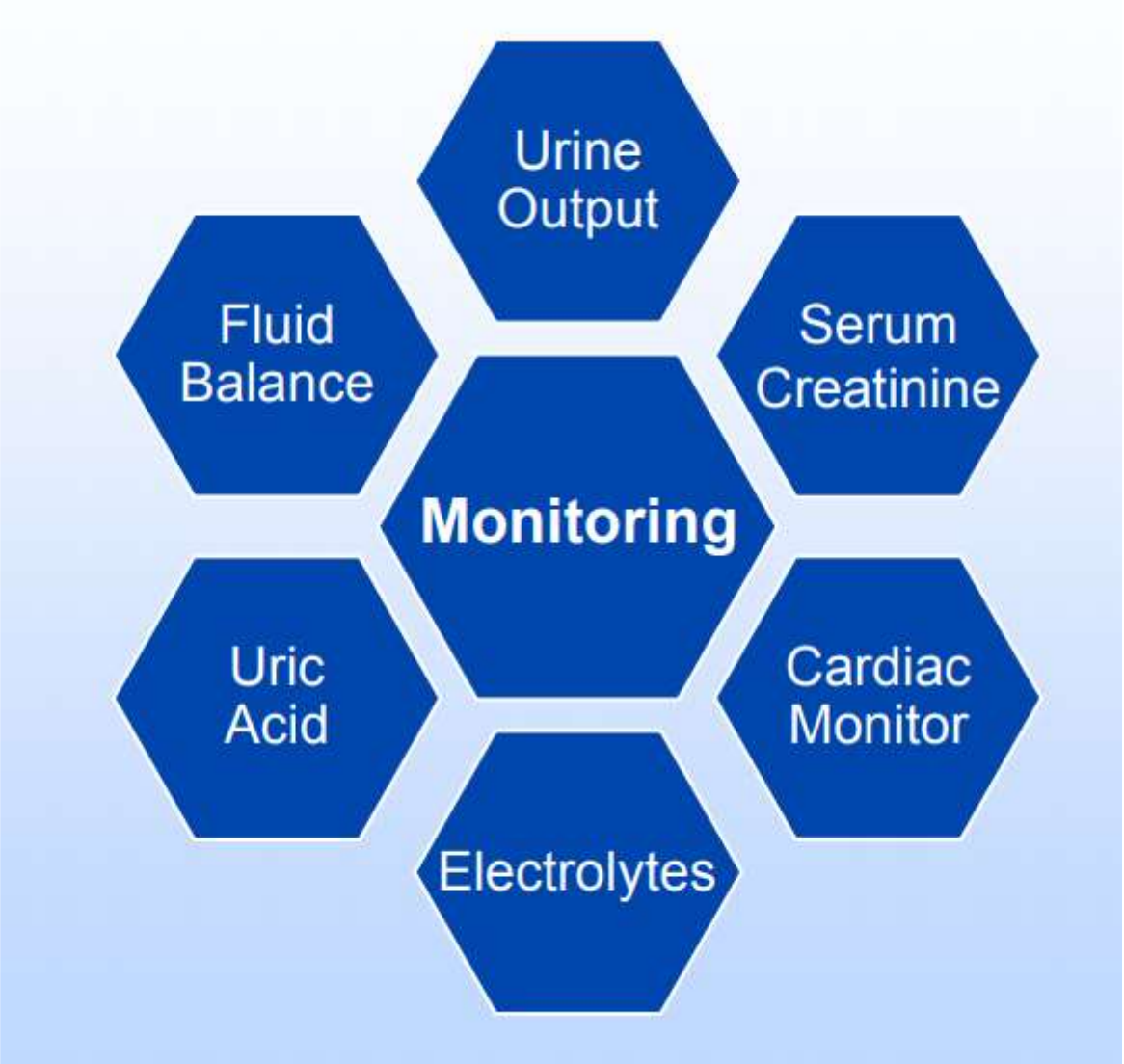
- Sudden massive lysis of tumor cells leading to release their contents into the bloodstream occur spontaneously or after initiation of chemotherapy
- metabolic disorders: hyperkalemia, hyperphosphatemia, hypocalcemia, and hyperuricemia leading to end-organ damage.
- Can lead to acute kidney injury (AKI), fatal arrhythmias, and even death.
- 30% of patients need hemodyalisis
- Morality rate 15%

Clinical Presentation



TLS treatment

- Aggressive hydration plus diuretics
- Medications:
  - Allopurinol: blocks uric acid production
  - OR Rasburicase: in sever cases, high cost
- Dialysis
- Monitoring



- **Thank you**