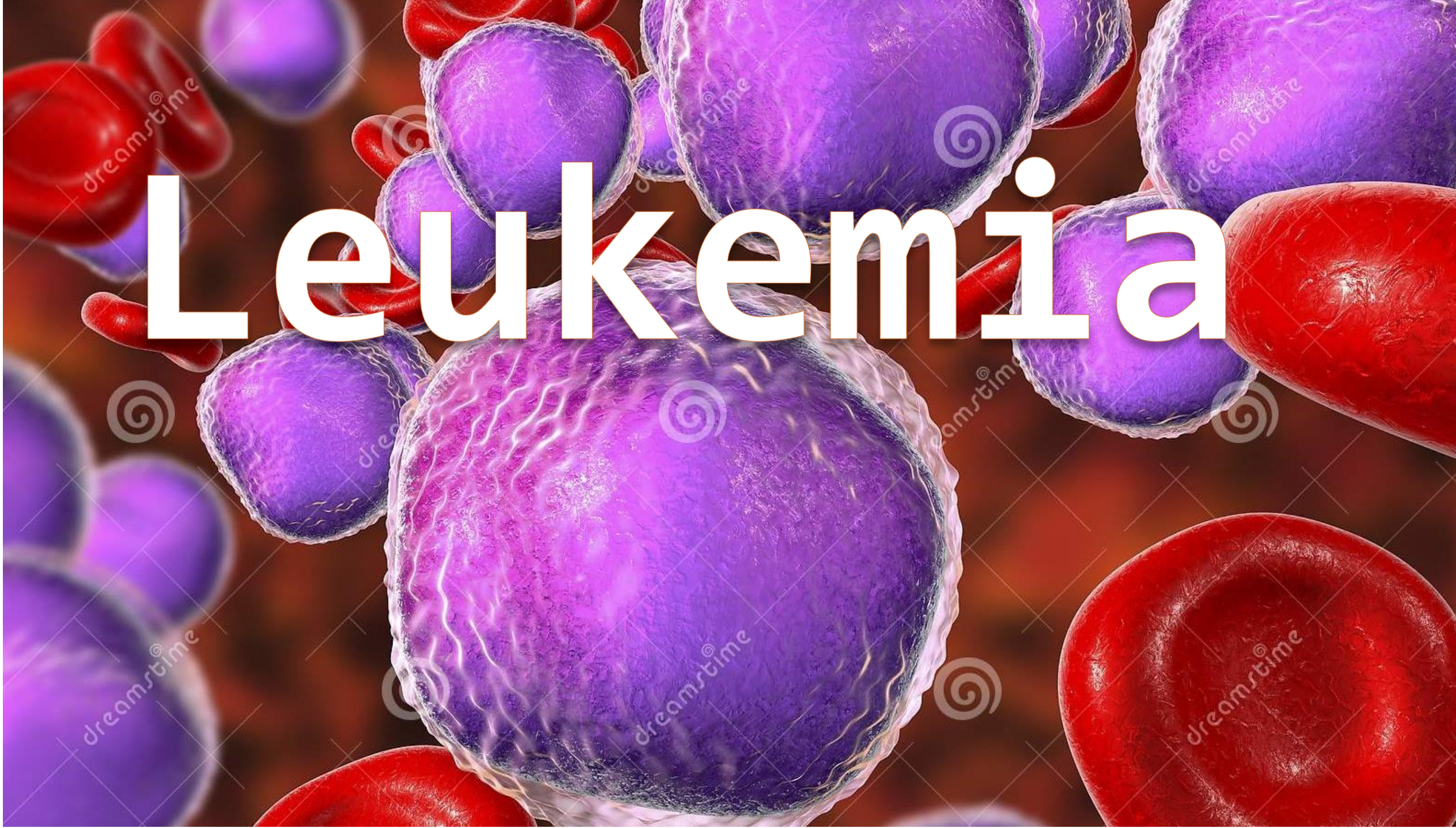
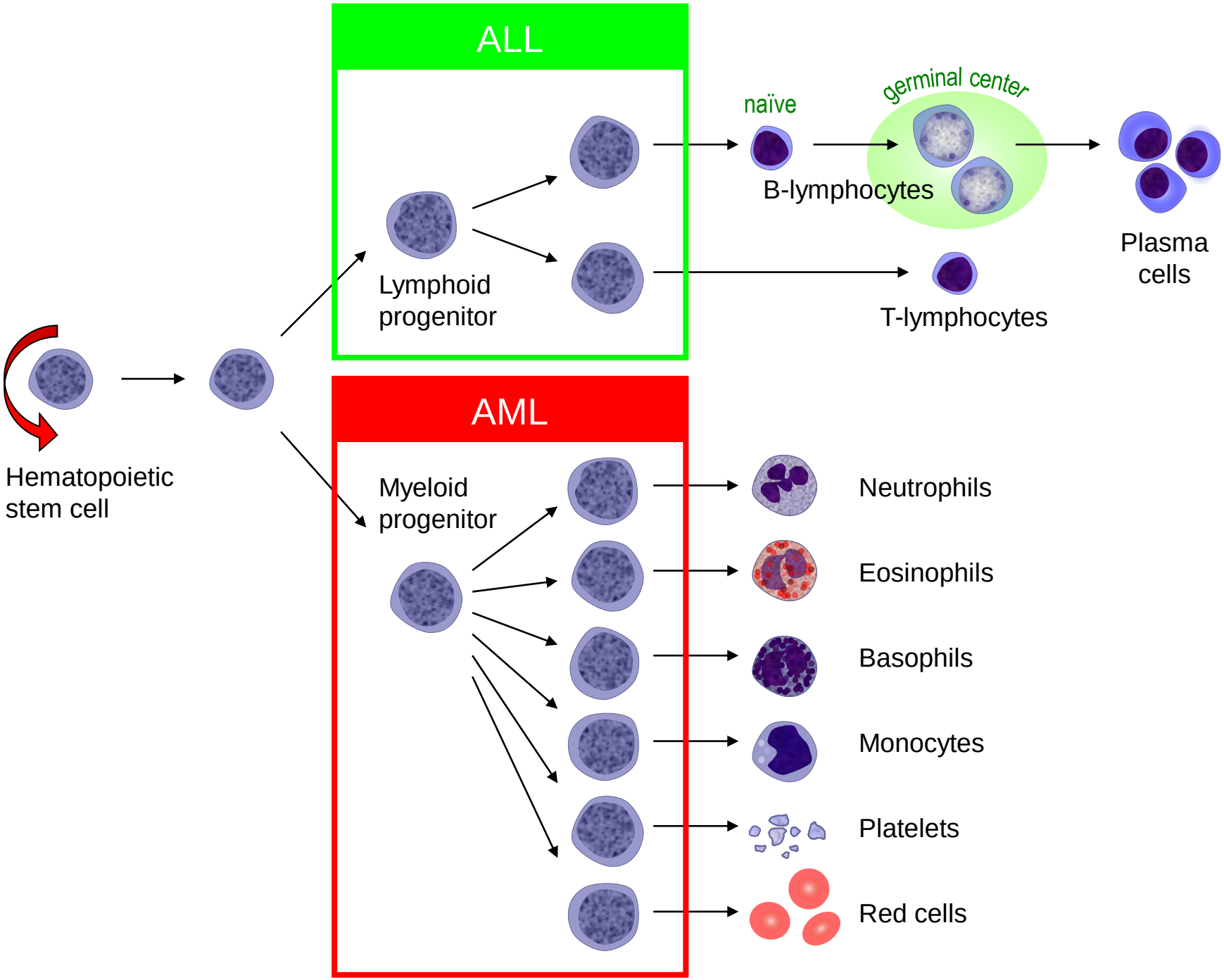

Leukemia

7th Lecture Objectives (LEUKEMIA)

1. To understand the definition of leukemia and recognize its different types
2. To be able to approaches to patient with leukemia (investigations and treatment)
3. To be able to recognize the complications of leukemia and treating it
4. To be able to recognize leukemia treatment (chemotherapy and radiotherapy) complications and side effects

Leukemia

Acute leukemias represent a clonal expansion and arrest at a specific stage of myeloid or lymphoid hematopoiesis.


ALL
naïve
germinal center
B-lymphocytes
Plasma cells
Lymphoid progenitor
T-lymphocytes
Hematopoietic stem cell
AML
Myeloid progenitor
Neutrophils
Eosinophils
Basophils
Monocytes
Platelets
Red cells

Epidemiology

The leukemia are the most common malignant neoplasm in childhood, accounting for about **41%** of all malignancies that occur in children <15 yr of age.

Most common age: 2-5 years
Male > Female.

Acute Leukemia constitute **97%** of all childhood leukemias and consist of the following types:

- **Acute lymphoblastic leukemia (ALL) 80%:** of which 85% are B-cell acute lymphoblastic leukemia (B-ALL)
and 15% are T-cell acute lymphoblastic leukemia (T-ALL)
- **Acute myeloblastic leukemia (AML), 15%**
- **Acute leukemias of ambiguous lineage 2%**

Chronic myeloid leukemias constitute **3%** of all childhood leukemias and consist of

- Philadelphia chromosome-positive (Ph1) myeloid leukemia
- Juvenile myelomonocytic leukemia

Causes of acute leukaemia

- Idiopathic (most)
- Hematologic disorders (e.g., Fanconi anemia, Kostmann syndrome, Diamond-Blackfan anemia)
- Chemicals, drugs
- Ionizing radiation

Clinical features

Duration: few weeks – few months
Symptoms: Anorexia, fatigue, irritability, intermittent low-grade fever , bone pain, joint pain, pallor, bruising, or epistaxis .
Signs: pallor, purpuric and petechial skin lesions, or mucous membrane hemorrhage, lymphadenopathy, Splenomegaly, hepatomegaly.

Rarely, patients show signs of increased intracranial pressure, meningeal irritation signs, papilledema, retinal hemorrhages, and cranial nerve palsies .

Non-malignant conditions mimicking leukemia

- ITP (Immune Thrombocytopenic Purpura)
- Aplastic anemia
- Streptococcal/viral pharyngitis
- Trauma, rheumatologic diseases, collagen vascular diseases, osteomyelitis
- CMV, EBV infection

Laboratory investigations

CBP(complete Blood Picture)

-Hb : mostly low <10 g/dL (s.t. Normal)

-Total WBCs: low, normal, or high (normal 4-11 X 10^9/L). May be very high (hyperleukocytosis) > 100 X10^9/L; causing increasing viscosity of blood, bleeding diathesis, ARDS, CVA.

Leukopenia→ infection.

-Platelets: usually thrombocytopenia (plt<50 X10^9/L cause mucocutaneous bleeding).

-Blood film: normochromic normocytic anemia. Blasts in peripheral blood (%).

-ESR: increased (not specific).

Bone marrow examination:-

necessary for diagnosis, useful for determining type of leukaemia

ALL is defined by the presence of >25% blasts in bone marrow

AML is defined by the presence of >20% blasts

Done in diagnosis, during therapy and during follow-up in certain spots; and when suspect BM relapse.

Classification of subtypes of leukemia depends on

Morphology: FAB classification

ALL : L1, L2, L3

AML : M0, M1, M2, M3, M3v, M4, M4 Eo, M5, M6, M7

Immunophenotype: flowcytometry;e.g

ALL: Pre-B, B-cell , T-cell

Cytogenetic:

ALL : t(12,21)

AML : t(15,17)in M3

CML : t(9,22) – Philadelphian chromosome

Biochemical investigations

-S.uric acid : (NV: 120-420 mmol/L).
DNA (destructed by chemotherapy)→purine nucleotide→hypoxanthine→xanthine→urate→ nephropathy
-LFT: SGOT, SGPT, S.Alk Ph, TSB (direct & indirect)
-RFT: S. creatinine, BUN
-S. electrolyte: Na, Cl, K
-S. minerals: Ca, Ph, Mg
-Others: bl. Sugar, S. albumin

Imaging studies

- Chest X-ray (AP & lateral): anterior mediastinal mass, pulmonary infiltrates, ARDS, pneumonia.
- X-ray of long bones and vertebrae: osteoporosis, pathologic fracture .
- Abdominal U/S: size and texture of liver, spleen, abdominal LN groups, kidneys, GB, UB, ascites,…
- CT scan of brain (ICH), of lungs (pneumonia, pul. hemorrhage), of abdomen (liver & spleen)
- MRI : rarely requested

Treatment

Supportive measures

-For anemia --- packed RBCs (10 mL/Kg)

-For infections--- broad-spectrum antibiotics(often 3rd generation cephalosporin+ aminoglycoside) , antifungal, antiviral; systemic & local

-For bleeding--- platelets concentrate,antifibrinolytic

-Hydration --- twice maintenance i.e., 3000mL/m2/d (dilutional effect, increase GFR, corrects electrolyte imbalance, enhance excretion of toxic metabolites e.g. uric acid)

-Nutrition

Specific measures(CHEMOTHERAPY)

ALL

Induction of remission: vincristine, prednisone, daunorubicin, L-asparginase

CNS prophylaxis: intrathecal(methotrexate ,cytosar, steroid), cranial radiation

Consolidation of remission: cytosar, cyclophosphamide, methotrexate, etoposide

Maintenance of remission: 6-MP, oral MTX

Total duration of Rx: for boys 3 years
for girls 2.5 years

Bone Marrow Transplantation

Allogeneic : from matched related or unrelated donor

S.E.: life-threatening infections, GVHD, secondary malignancies,….
Indication: very HR ALL, relapse, many cases of AML

Prognosis

Acute lymphoblastic leukemia

Criteria	Good prognosis	Bad prognosis
Age (yr)*	1-10	<1 , >10
Gender	Female	Male
Race	White	Black, Hispanics
Mediastinal mass	No	Yes
Extramedullary involvement	No	Yes
WBCs count X 10^9/L*	<50	>50

Prognosis in AML

Good prognosis:

Down's syndrome

AML-M3 (APL) with t(15,17)

AML-M4Eo with inv(16)

Bad prognosis:

Secondary AML

Monosomy 7

Complications

Of disease:-

- BM infiltration(anemia, thrombocytopenia, neutropenia)
- Medullary &/or extramedullary relapse (CNS, testis)
- Hyperuricemia, hyperleukocytosis
- SVC syndrome & tracheal obstruction (mediastinal mass)
- Delayed growth.
- Psychologic problems (chronic disease)

Of chemotherapy:-

- ❖myelosuppression (most drugs except VCR & steroid),
- ❖nephrotoxicity (MTX, cyclophosphamide)
- ❖hepatotoxicity (MTX, 6-MP)
- ❖cardiotoxicity (adriamycine)
- ❖ alopecia, infertility, mucositis (MTX, cytosar)
- ❖secondary malignancies (etoposide)

Of supportive measures

transfusion-related infections (HBV, HCV, HIV, CMV), allergic reactions, fluid overload, S.E. of antibiotics

References

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- *Nelson* TEXTBOOK *of* PEDIATRICS EDITION 21 (2020)

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