

# Leukemia

General:

Definition: A cancer involving the blood forming cells Acute leukemia is the most common malignancy in children. It is due to a clonal proliferation of hematopoietic cells (usually white blood cells). In leukemia, abnormal immature white cells increase greatly and invade other tissues and organs. These white cells are not able to function at their normal task of fighting disease which makes the leukemic child vulnerable to infection or hemorrhage.

## Types of Childhood Leukemia

- 1 Acute Lymphoblastic Leukemia (ALL) 75%
- 2 Acute Myeloid Leukemia (AML) 20%
- 3 Mixed Lineage Leukemia 2%
- 4 Chronic Leukemia 3%

## Signs and Symptoms

- Fever and recurrent infection - Due to low white count
- Easy bruising and bleeding -Due to low platelets
- Lethargy and pallor -Due to low hemoglobin
- Bone pain -Due to marrow infiltration
- Lymphadenopathy and hepatosplenomegaly

## Diagnostic Evaluation – done at BCCH

- CBC and differential
- Chemistry panel: BUN, creatinine, uric acid, electrolytes, calcium, phosphate, liver function tests, LDH
- Coagulation profile: PT, PTT, Fibrinogen. There may be a bleeding tendency, particularly in AML
- Blood type and cross match if there is anemia or thrombocytopenia
- Chest x-ray: mediastinal mass is often found in T-cell ALL
- Bone marrow
  - ~ Aspirate and Biopsy - essential for diagnosis
  - ~ Cytogenetic evaluation - Essential for classification
  - ~ Immunophenotyping of leukemia
- Spinal tap. Send fluid for cell count and chemistry.

## Acute Care and Supportive Care

Contact BCCH immediately as Intravenous fluids, blood transfusions and antibiotics are frequently required even before the diagnosis is established.

# Leukemia

## Acute Lymphoblastic Leukemia

### Classification of ALL

Before determining treatment, the type of ALL is sub-classified according to morphology, immunophenotype, or risk factors.

- a. Immunologic Classification Pre-B cell, Progenitor B-cell, early pre-B ALL, transitional pre-B ALL, B-cell ALL (Burkitts) NB these patients are treated in a similar fashion to B-Cell lymphomas, T-cell ALL
- b. Classification according to risk factors:

	<b>Good Risk</b>	<b>High Risk</b>
Age at Diagnosis	>1 yr <10 yrs	<1 yr >10 yrs
White Cell Count at Diagnosis	<50 x 10 <sup>9</sup> /L	>50 x 10 <sup>9</sup> /L
DNA Index	>1.16	<1.16
Cytogenetics	Hyperdiploidy	Hypodiploidy (<45 chromosomes) t(9;22) (q34;q11)t(4;11 (q21;q23) Balanced t(1;19) (q23;p13)
CNS Disease	Absent	Present
Lymphoma Syndrome	Absent	Present

### Etiology

Unknown

### Treatment of ALL

Treatment is usually stratified according to the known risk factors +/- the immunologic, cytogenetic and morphologic classification. Children age < 1yr (infant ALL) have a generally poorer outcome and are currently treated with intensive multiagent chemotherapy.

#### 1 Chemotherapy

- ~ Chemotherapy is the mainstay of treatment. There are many different protocols but they follow a similar pattern with different phases of treatment with varying intensity: Induction (4 weeks); Consolidation (4 weeks); Interim maintenance I (8 weeks); Delayed Intensification I (8 weeks); Interim maintenance II (8 weeks); Maintenance (2 years girls, 3 years boys)
- ~ Commonly used drugs: vincristine, steroids, l'asparaginase, +/- anthracyclines, cyclophosphamide, cytarabine, 6-mercaptopurine, dexamethasone, intrathecal methotrexate
- ~ 95% of children obtain bone marrow remission (no evidence of leukemia) after the induction phase.
- ~ Some patients may receive a second delayed intensification
- ~ The maintenance phase is less intensive and children are able to attend school and rarely require hospitalization

#### 2 Radiotherapy

This is used if patients have leukemic infiltration of the central nervous system or testes. "Somnolence syndrome", i.e. extreme tiredness and lethargy lasting approximately 1 week may occur 4-8 weeks after cranial radiation.

### 3 Blood and Bone Marrow Transplant

Only used for patients who have relapsed or ultra high risk patients in first remission.

#### Prognosis

65%-90% 5 year event free survival depending on the presence or absence of risk factors at diagnosis.

## **Leukemia**

### **Acute Myeloid Leukemia**

FAB Morphologic Classification: This classification is the most commonly used.

- M1 - Myeloblastic without maturation
- M2 - Myeloblastic with differentiation
- M3 - Acute Promyelocytic - APL (usually has translocation t (15:17))
- M4 - Myelocytic and Monocytic with differentiation
- M5 - Monocytic with poorly differentiated +/- well differentiated monocytoid cells
- M6 - Erythroleukemia
- M7 - Megakaryoblastic leukemia (more common in Down's syndrome)

### Etiology

Unknown although associated with radiation, etoposide and intensive chemotherapy

### Treatment of AML

#### 1 Chemotherapy

- ~ All children with AML (with the possible exception of APL) require intensive chemotherapy and significant bone marrow hypoplasia to achieve remission
- ~ Induction: Intensive. Lasts 4-8 weeks
- ~ Useful drugs: anthracyclines (doxorubicin, daunorubicin, idarubicin), cytarabine, etoposide
- ~ 80-85% remission
- ~ Consolidation - Often omitted if patient goes on to bone marrow transplant. Lasts 4-6 months Useful drugs: high dose cytarabine/l'asparaginase, etoposide, anthracyclines (doxorubicin, daunorubicin)
- ~ Maintenance - None. Does not improve disease free survival
- ~ Bone Marrow Transplant (BMT)
  - Allogeneic BMT - Recommended in first remission if matched sibling available
  - Autologous BMT - Advantage over chemotherapy not established

#### 2 Radiotherapy

Radiotherapy is rarely indicated except as a preparative regimen for BMT

### Prognosis

With chemotherapy alone 5 year disease free survival approximately 40%

With allogeneic bone marrow transplant 5 year disease free survival approximately 50%

Downs syndrome patients with M7 AML - have a better prognosis than non-Down's syndrome patients.

## **Leukemia**

### **Acute Promyelocytic Leukemia (APL)**

#### Treatment:

All Trans Retinoic Acid (ATRA, tretinoin, Vesanoïd) can induce remission in many patients with APL. It is not yet known whether it is more effective long term than chemotherapy induced remission.

Bleeding is a complication of APL and its treatment.