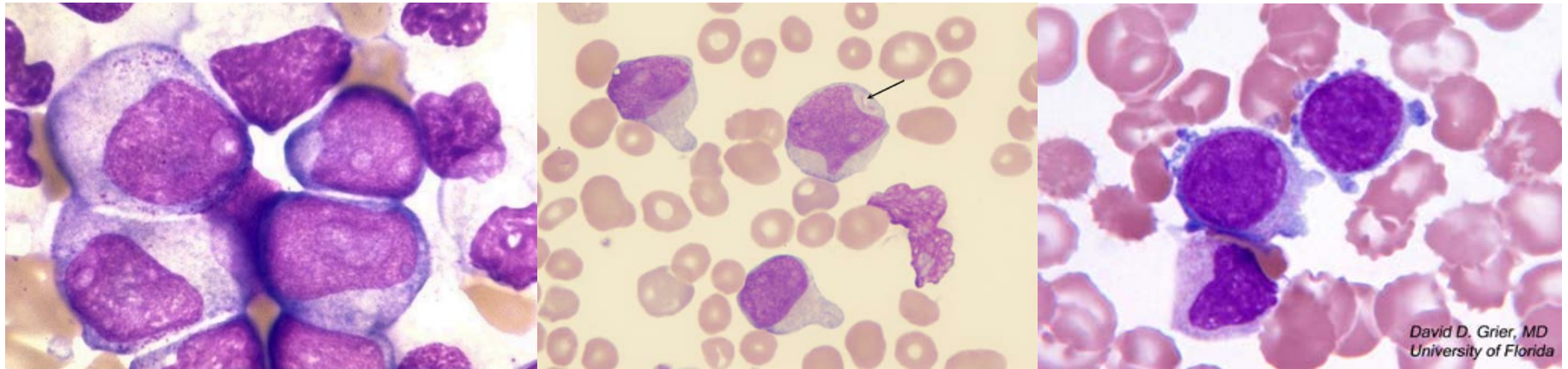


Easy Trick to Spot Leukemia for Pediatricians



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Department of Pediatrics
Phramongkutklao Hospital***

Most Common Pediatric Cancers

Age 0-14

▪ Leukemia	32%
▪ CNS	20
▪ Lymphoma	11
▪ Neuroblastoma	8
▪ Rhabdo/STS	7
▪ Kidney	6
▪ Bone	6
▪ Germ cell	4
▪ Retinoblastoma	3
▪ Liver	1

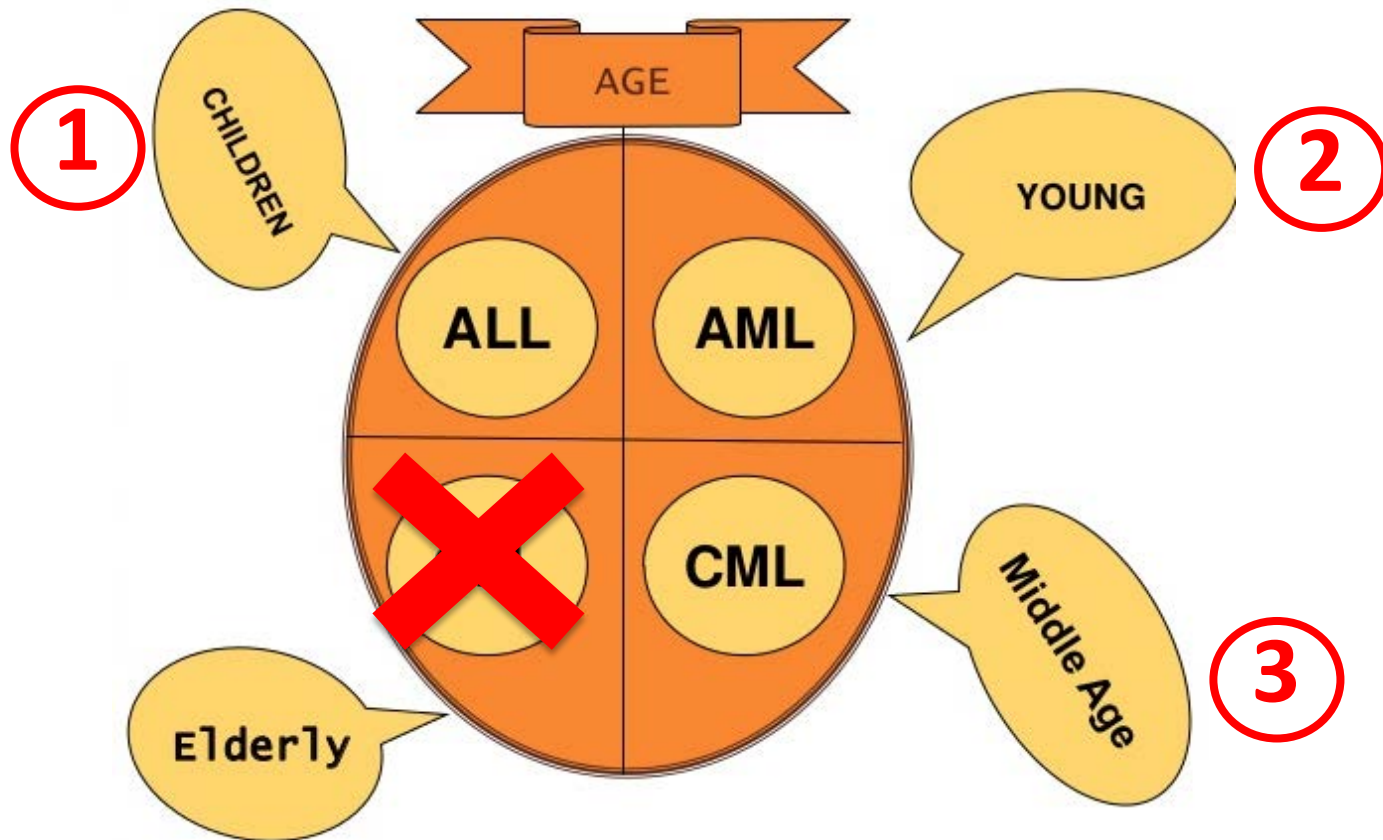
Age 15-19

▪ Lymphoma	25%
▪ Germ cell	14
▪ Leukemia	12
▪ CNS	10
▪ STS	8
▪ Bone	8
▪ Thyroid cancer	7
▪ Melanoma	7

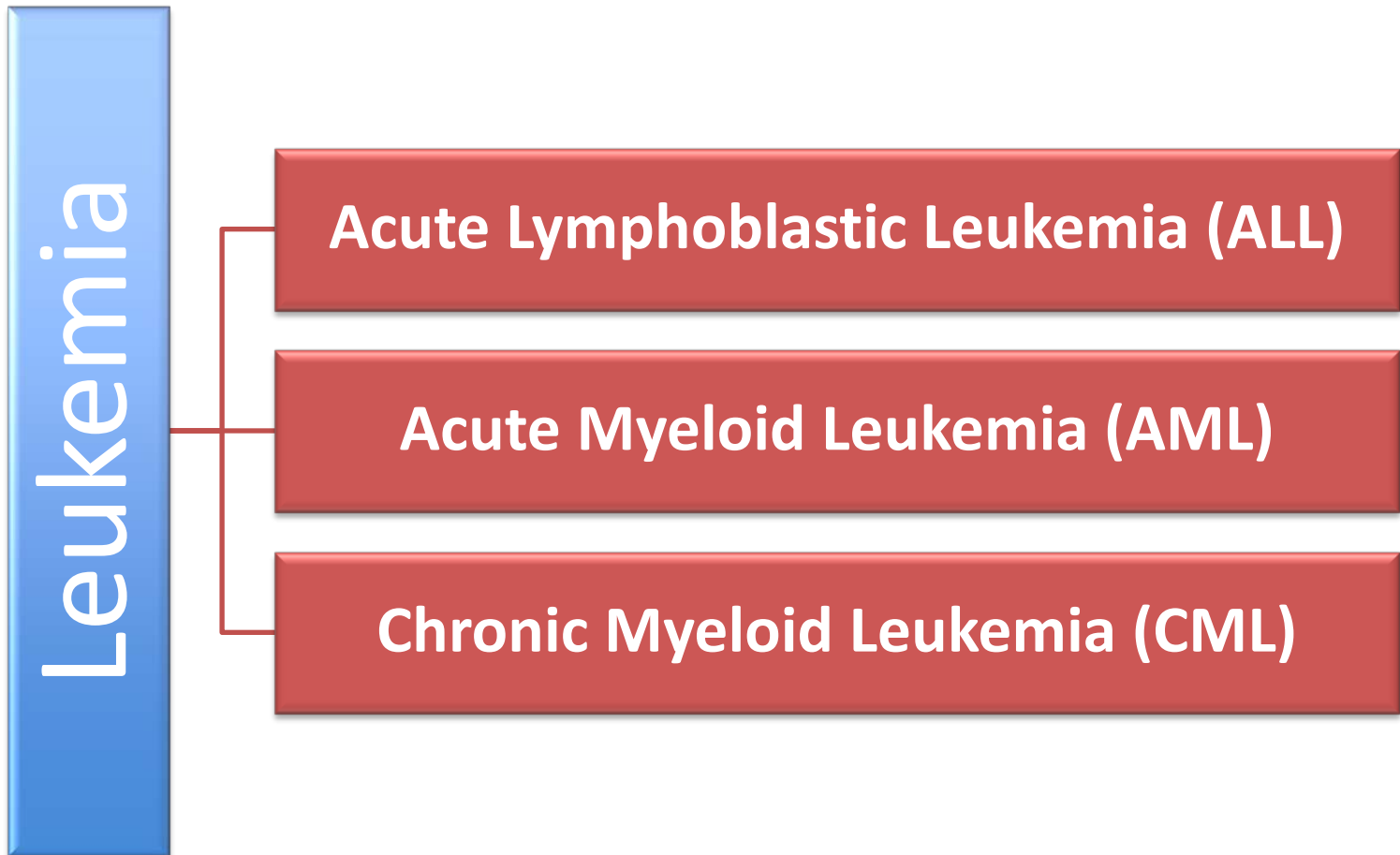
Leukemia

Leukemia = Leuk + emia
(white) (blood)

Leukemia Types



Pediatric leukemia



Survival Rate in Childhood Acute Leukemia

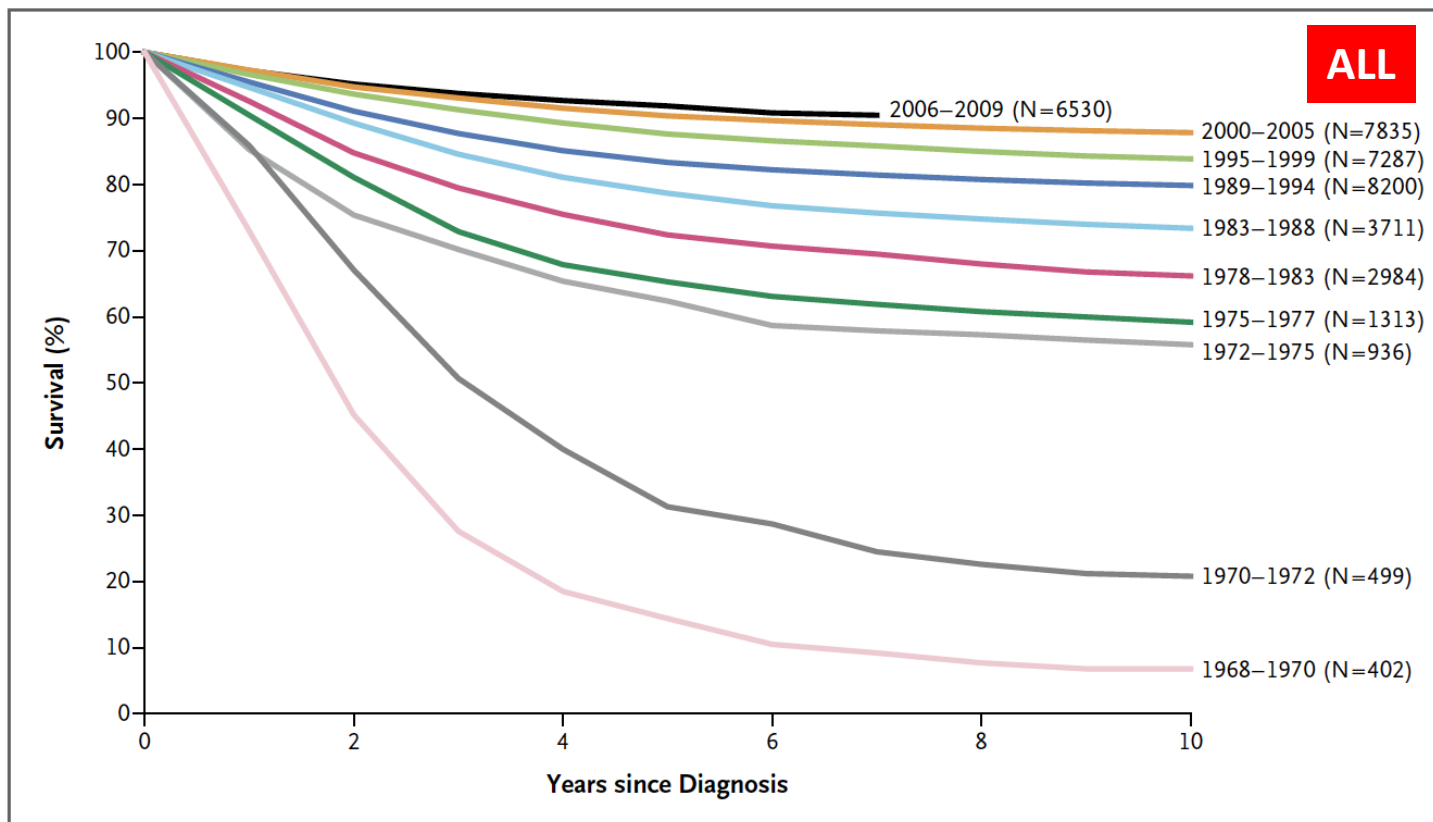
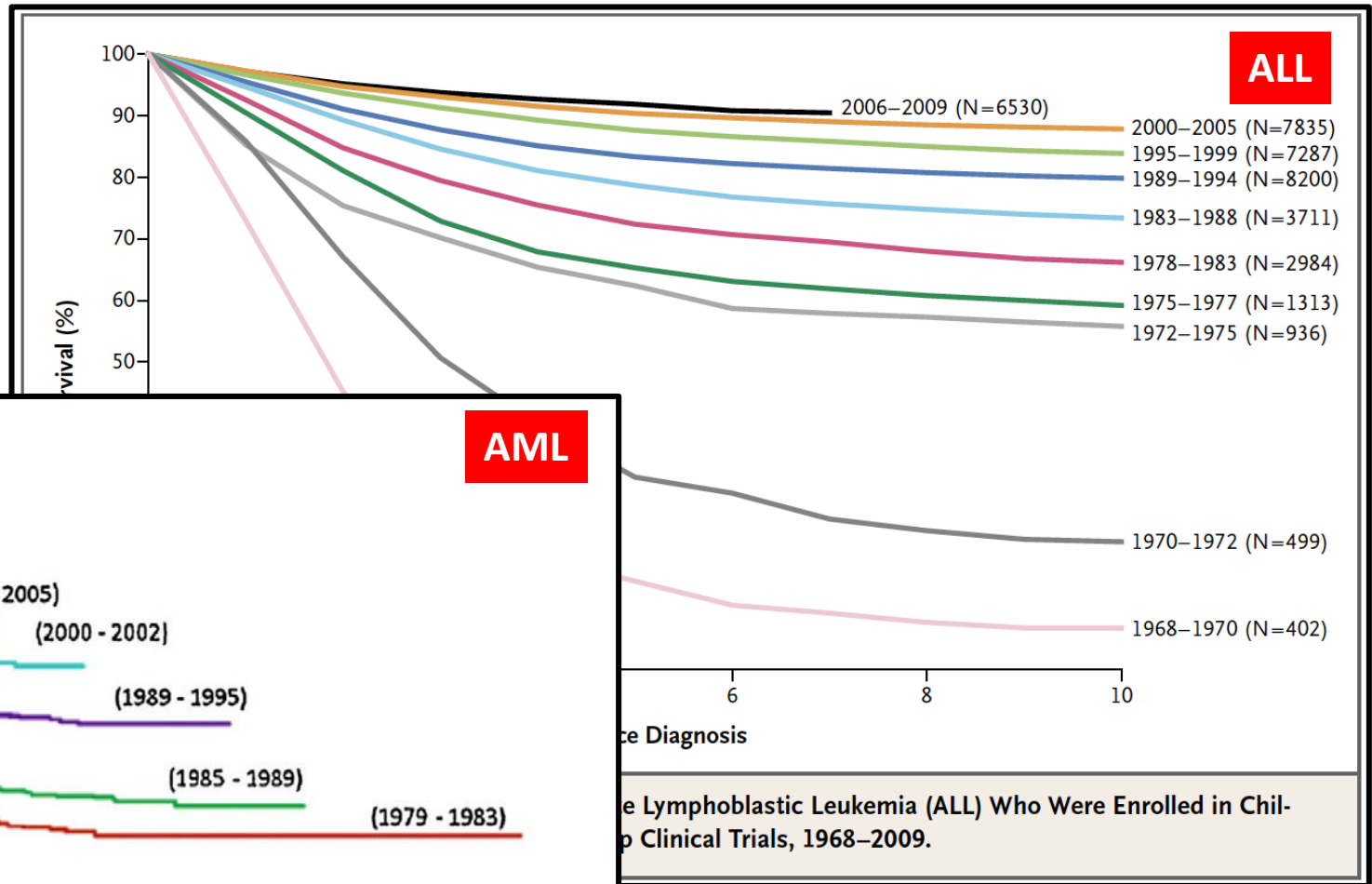


Figure 1. Overall Survival among Children with Acute Lymphoblastic Leukemia (ALL) Who Were Enrolled in Children's Cancer Group and Children's Oncology Group Clinical Trials, 1968–2009.

Hunger et al, NEJM 2015
Rubnitz et al, Lancet Oncology 2010

Survival Rate in Childhood Acute Leukemia

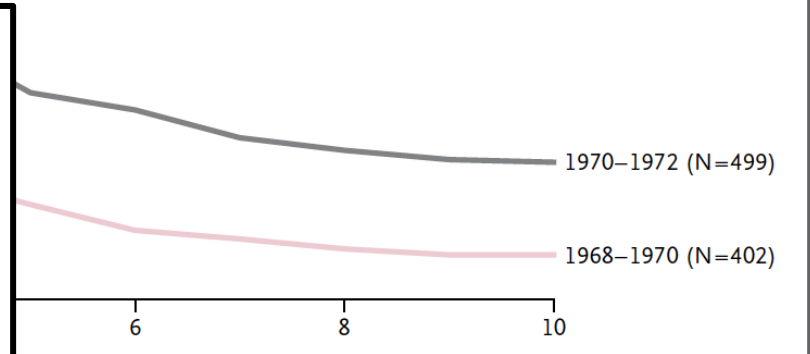
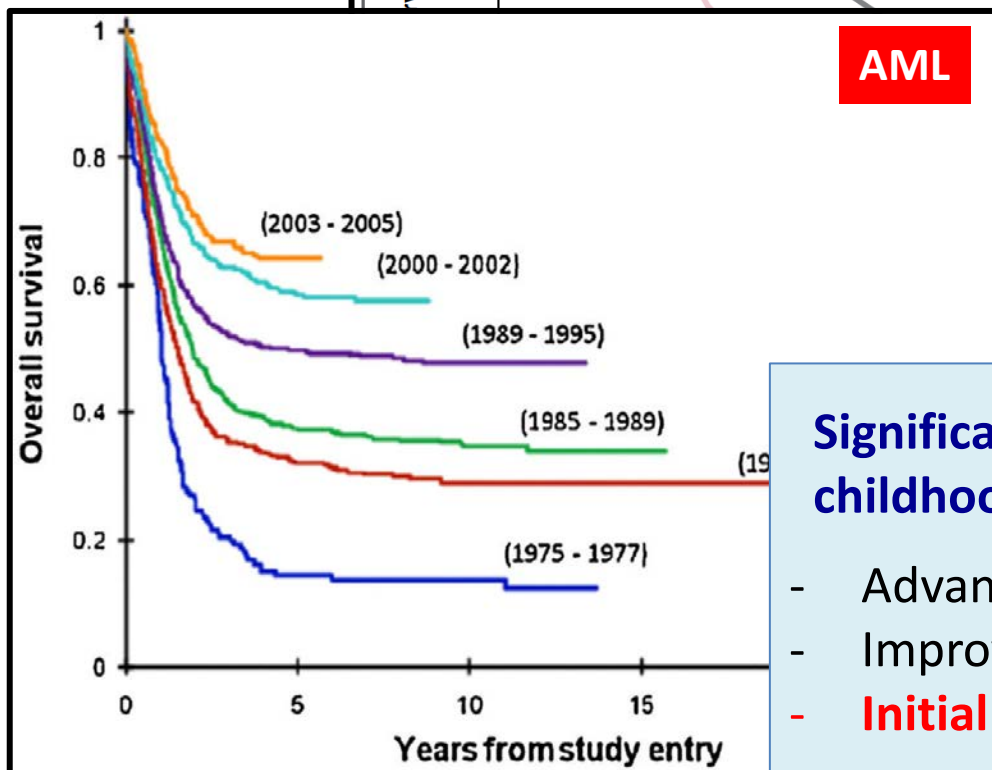
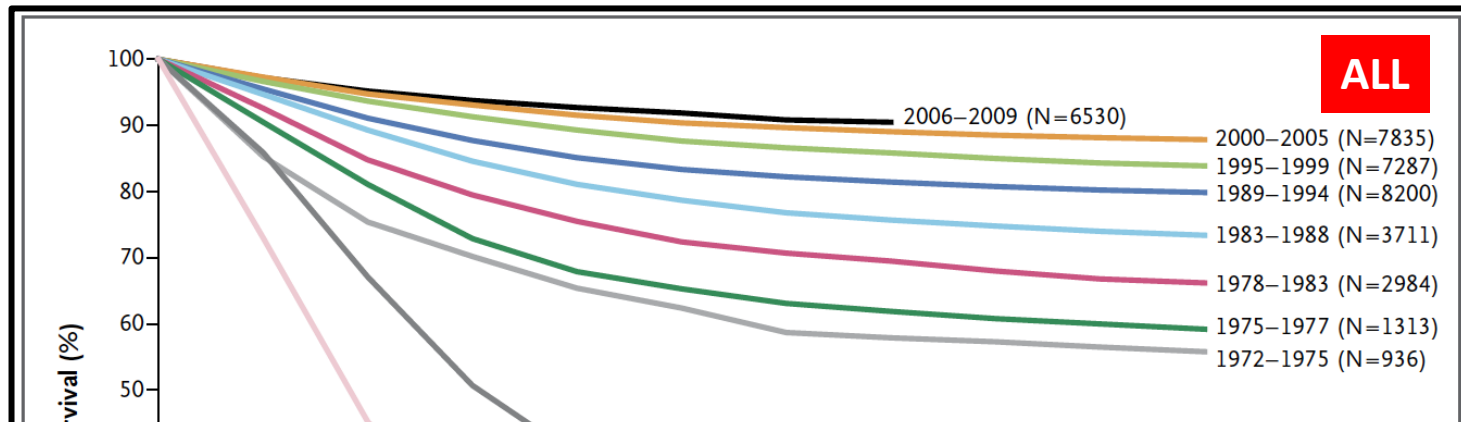


Age at Diagnosis

Overall Survival in Childhood Acute Lymphoblastic Leukemia (ALL) Who Were Enrolled in Childhood Clinical Trials, 1968-2009.

Hunger et al, NEJM 2015
Rubnitz et al, Lancet Oncology 2010

Survival Rate in Childhood Acute Leukemia



Significant improvement of the current childhood leukemia survival rate due to

- Advanced treatment strategies
- Improved supportive care
- **Initial recognition & management**

Outlines

Easy Trick

- ✓ Spot leukemia
- ✓ Basic laboratory tests
- ✓ Initial management

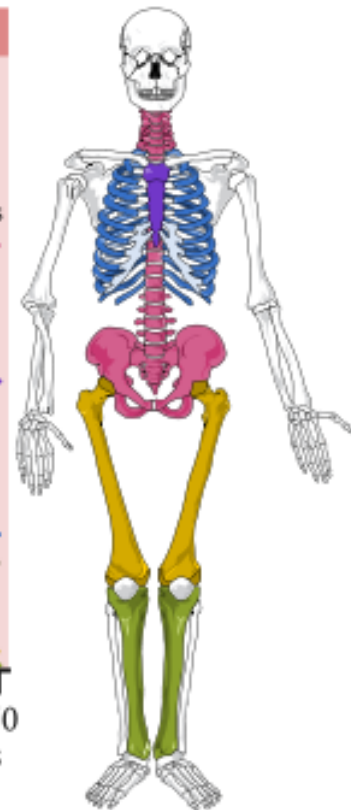
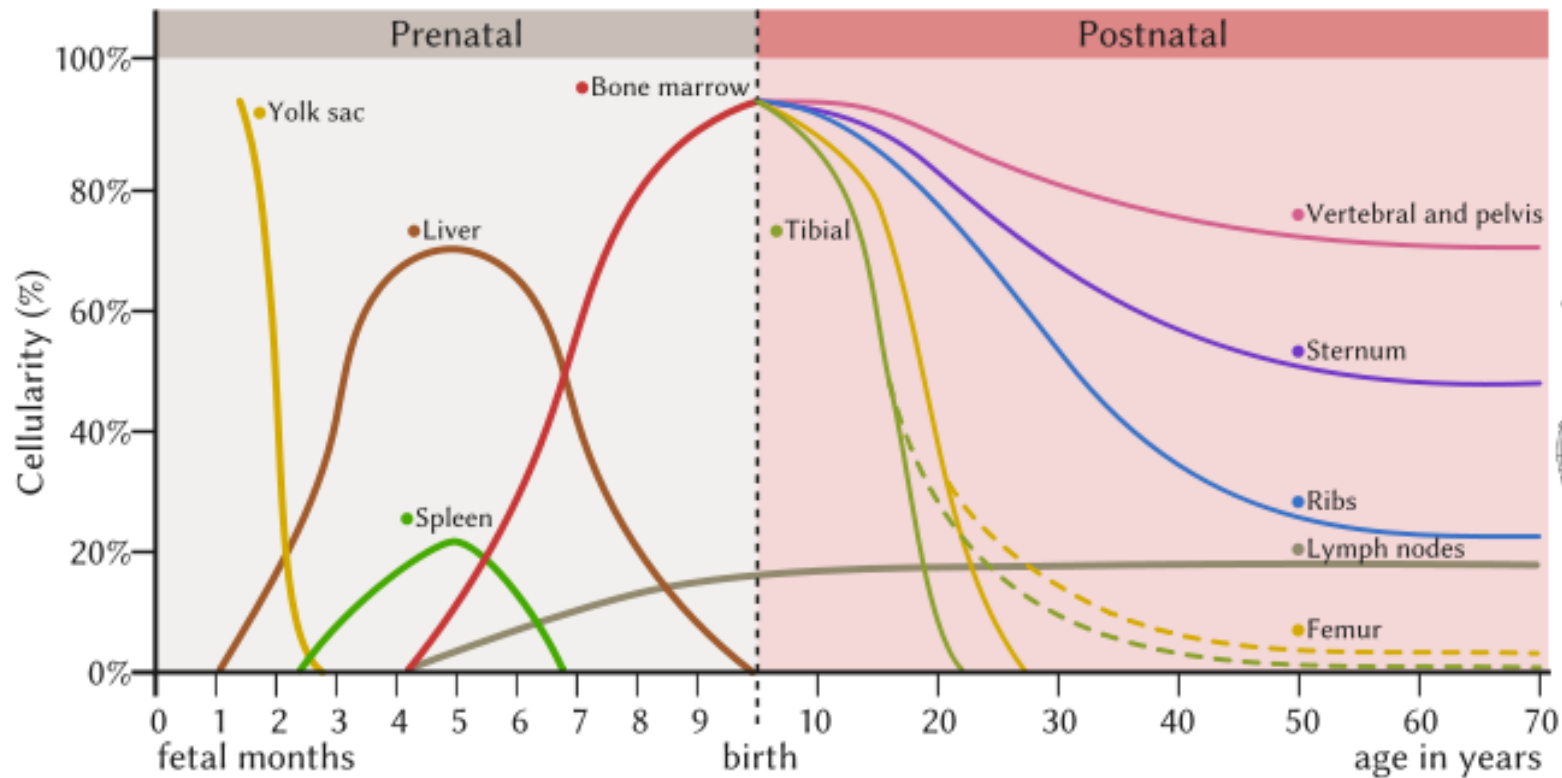
Case

- 3 yo boy presents to OPD
 - 2 weeks history of ~~fever~~, lethargy, ~~spontaneous bruising and epistaxis~~

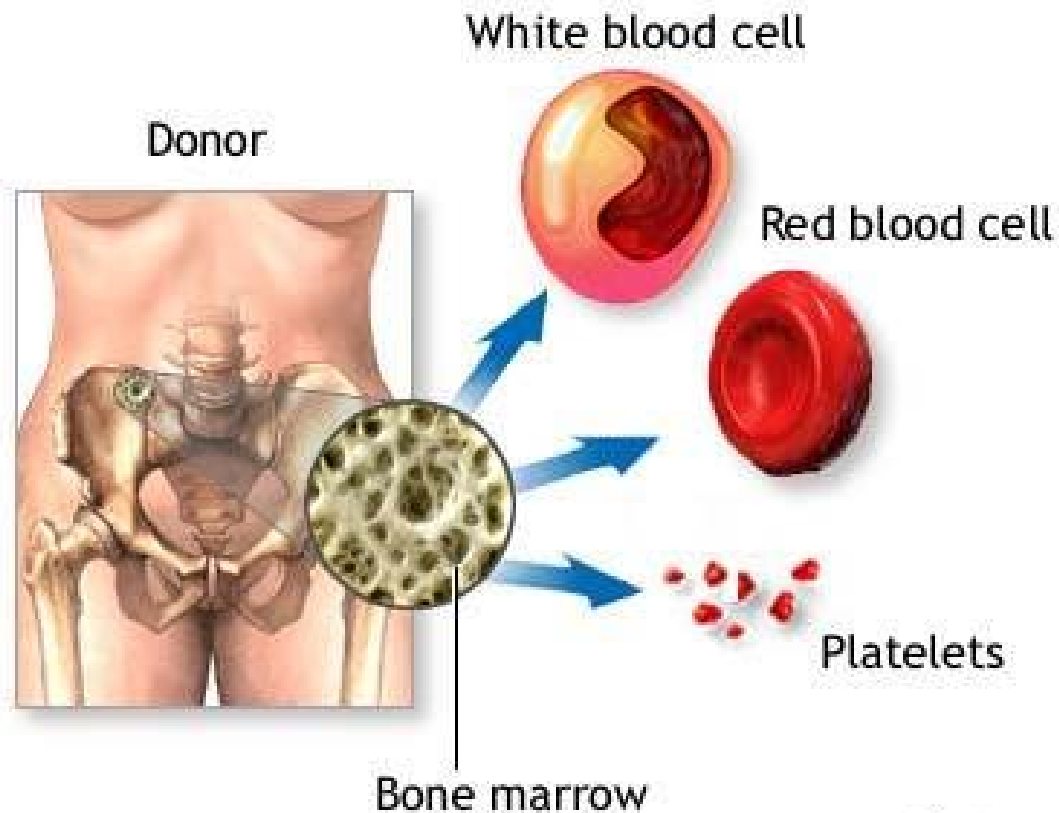


Development of Hematopoiesis

HEMATOPOIESIS

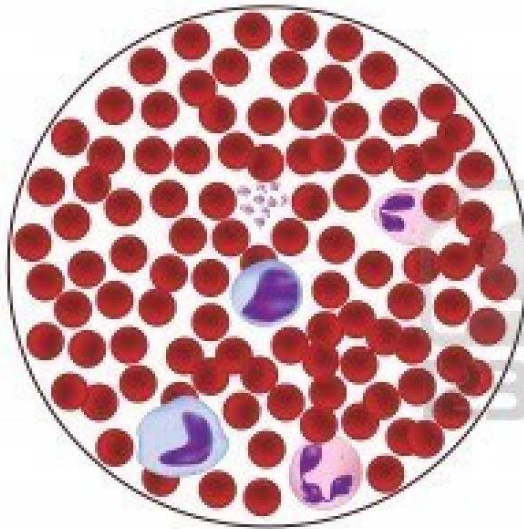


Bone Marrow Function

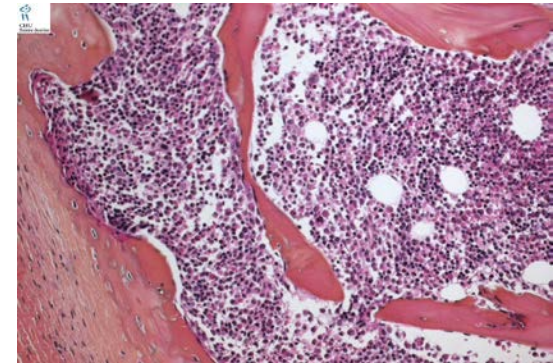
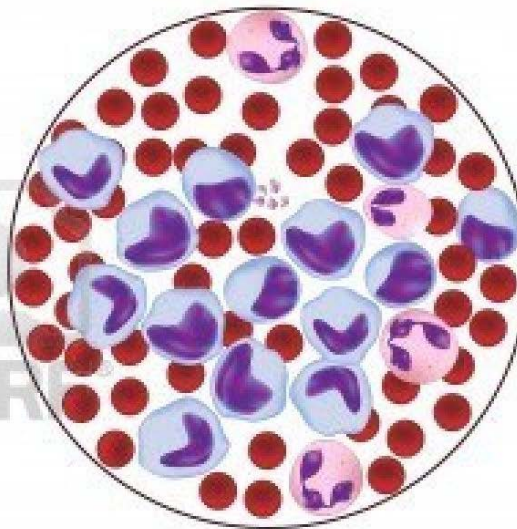


Acute Leukemia

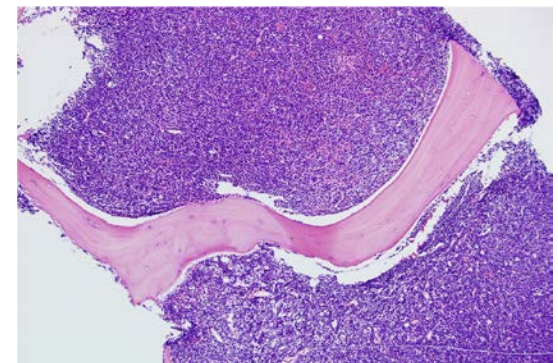
Normal Bone marrow



Leukemia



Normocellular marrow



Hypercellular marrow

Clinical Presentations

Fatigue

Weakness

Anorexia

RBC

Fever

Prolonged infection

WBC

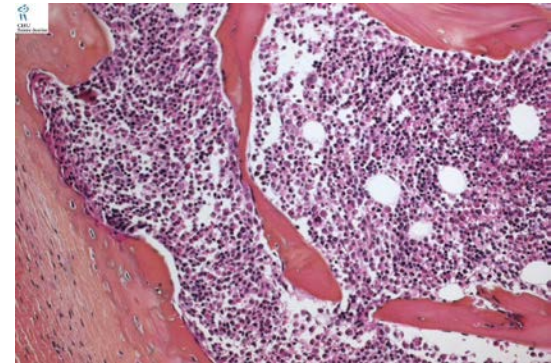
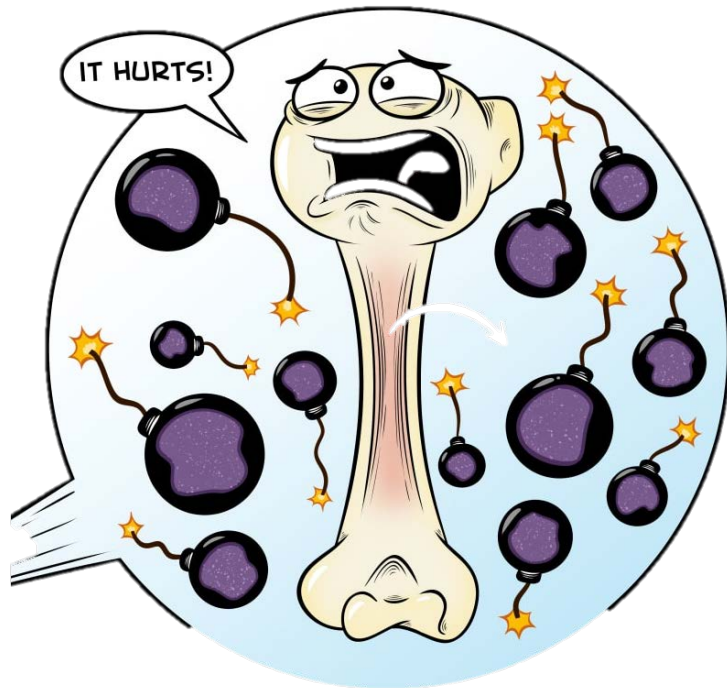
Easy bruising

Bleeding

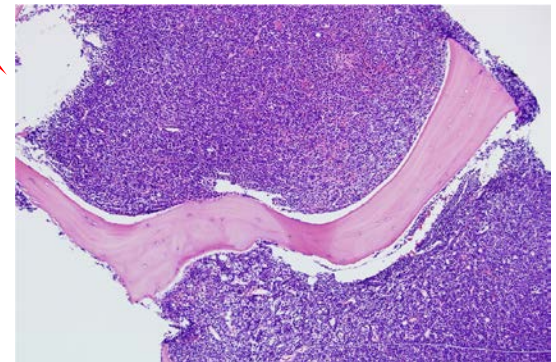
Platelets

Acute Leukemia

Bone Pain

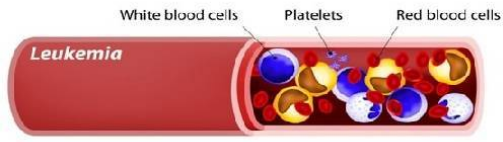
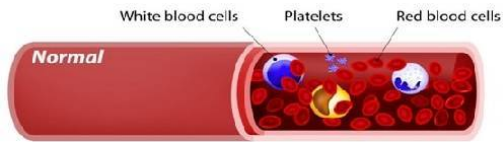
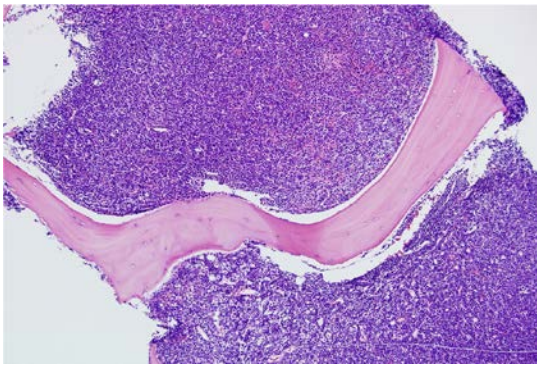


Normocellular marrow

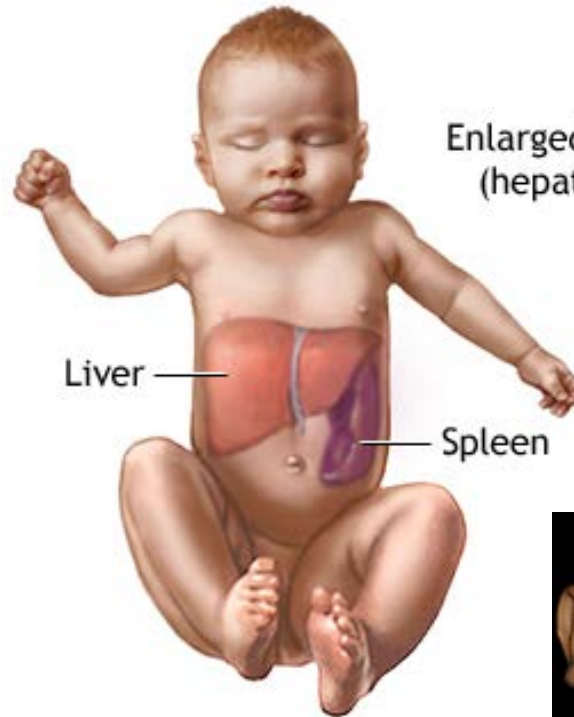
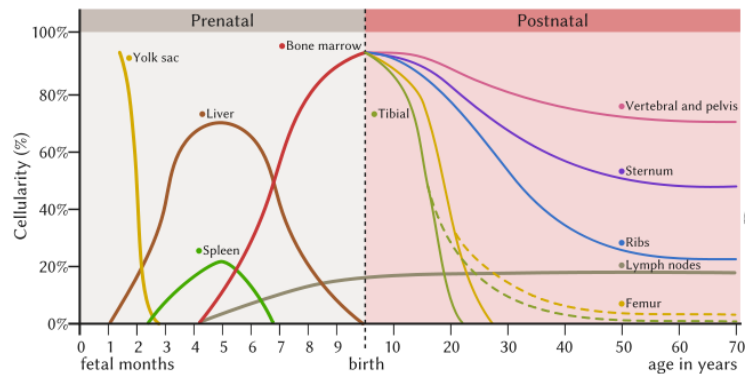


Hypercellular marrow

Clinical Presentation



HEMATOPOIESIS •



Clinical Presentations

Fatigue

Weakness

Anorexia

RBC

Fever

Prolonged infection

WBC

Easy bruising

Bleeding

Platelets

Lymphadenopathy

Hepatosplenomegaly

RE system

Specific Signs & Symptoms

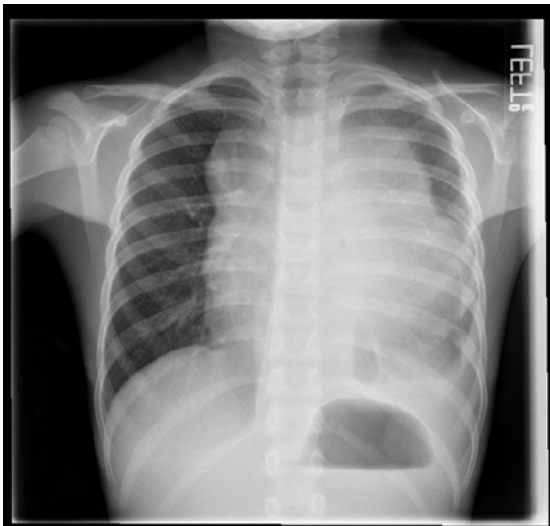


Leukemia cutis (AML-M5 > ALL)



CNS leukemia (<5% at diagnosis)

- CNS1 : no lymphoblasts
- CNS2 : <5 cells/cm³ with blasts on cytopsin
- CNS3 : ≥5 cells/cm³ with blasts or CN palsy



Anterior mediastinal mass with
Superior vena cava syndrome



Specific Signs & Symptoms



Clinical Characteristics of 724 Children with ALL (CCSG)

Clinical characteristics	Percent (%)
Age (years) distribution	
<1	6
1 – 3	18
3 – 10	54
>10	22
General symptoms	
Fever	61
Bleeding	48
Bone pain	23
Lymphadenopathy	
None	50
Moderate	43
Extended	7
Splenomegaly	
None	37
Moderate	49
Extended	14
Hepatosplenomegaly	
None	32
Moderate	55
Extended	13
Mediastinal enlargement	7

Other Risk Factors

- Radiation exposure
- Chemical exposure eg. Benzene (AML)
- Drugs eg. chemotherapy in (AML)
- Genetics

Genetic Disorders with Increased Risk of Developing Leukemia

Trisomy 21 (Down syndrome)

Fanconi anemia

Shwachman-Diamond syndrome

Diamond-Blackfan anemia

Kostmann disease

Li-Fraumeni syndrome (germ line p53 mutation)

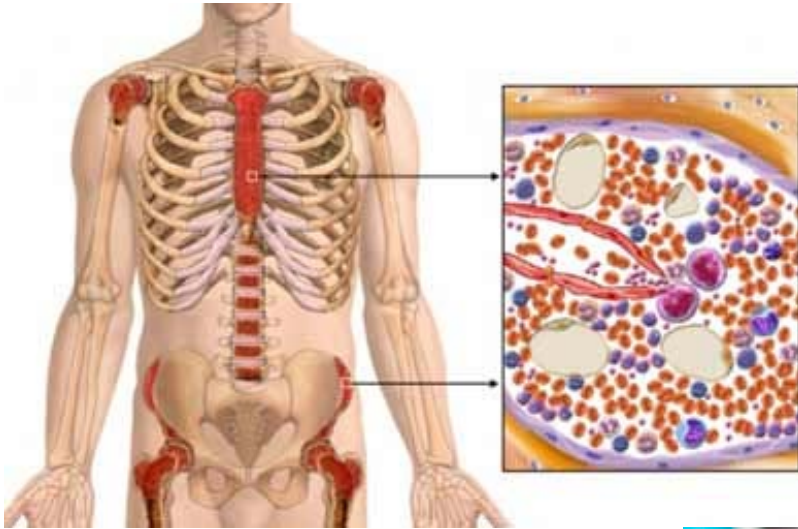
Neurofibromatosis

Case

- 3 yo boy presents to OPD
 - 2 weeks history of fever, lethargy, spontaneous bruising and epistaxis
- **Looking for ...**
 - Infectious etiology
 - Bone pain
 - Well being : appetite , weight loss
 - Risk factors : environmental , genetics , underlying
 - Respiratory and cardiovascular status
 - Pallor , lymphadenopathy , hepatosplenomegaly
 - CNS and testicular involvement // extramedullary lesions





Basic Laboratory Tests



Complete Blood Count



CBC in Acute Leukemia

CBC	Percentage (%)
WBC ($\times 10^9/L$)	
< 10	53
10 – 49	30
> 50	17
Hemoglobin (g/dL)	
< 7.0	43
7.0 – 11.0	45
> 11.0	12 
Platelets ($\times 10^9/L$)	
< 20	28
20 – 99	47
> 100	25 

Pizzo PA, Poplack DG. *Principles and Practice of Pediatric Oncology*. 5th ed. Philadelphia: Lippincott-Williams and Wilkins, 2006

Pancytopenia in Hospitalized Children

- N=64 (5 year period), median age = 8 years
- Median blood counts = ANC 1080, Hb 9.3, platelets 82K
- **64% infectious etiology** (bacterial sepsis, non-EBV virus, etc.)
- 28% hematologic etiology
 - Aplastic anemia – 11%
 - ITP – 5%
- 8% miscellaneous (drug-induced, SLE)

Case – Complete Blood Count

- 3 yo boy presents to OPD **Cut-point Hb = $11 + (0.1 \times \text{Age})$**
 - 2 weeks history of fever, lethargy, spontaneous bruising and epistaxis

	WBC (cells/mm ³)	Hb (g/dL)	Platelets (cells/mm ³)
1	250,000	7	30,000

Case – Complete Blood Count

- 3 yo boy presents to OPD
 - 2 weeks history of fever, lethargy, spontaneous bruising and epistaxis

	WBC (cells/mm ³)	Hb (g/dL)	Platelets (cells/mm ³)
1	250,000	7	30,000
2	2,500	7	30,000

Case – Complete Blood Count

- 3 yo boy presents to OPD
 - 2 weeks history of fever, lethargy, spontaneous bruising and epistaxis

	WBC (cells/mm ³)	Hb (g/dL)	Platelets (cells/mm ³)
1	250,000	7	30,000
2	2,500	7	30,000
3	4,500	11	4,000

Case – Complete Blood Count

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	WBC (cells/mm ³)	Hb (g/dL)	Platelets (cells/mm ³)
1	250,000	7	30,000
2	2,500	7	30,000
3	4,500	11	4,000
4	7,000	10	80,000



Case – Complete Blood Count

- 3 yo boy presents to OPD
 - 2 weeks history of fever, lethargy, spontaneous bruising and epistaxis

	WBC (cells/mm ³)	Hb (g/dL)	Platelets (cells/mm ³)
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4	7,000	10	80,000
5	7,000	13	80,000



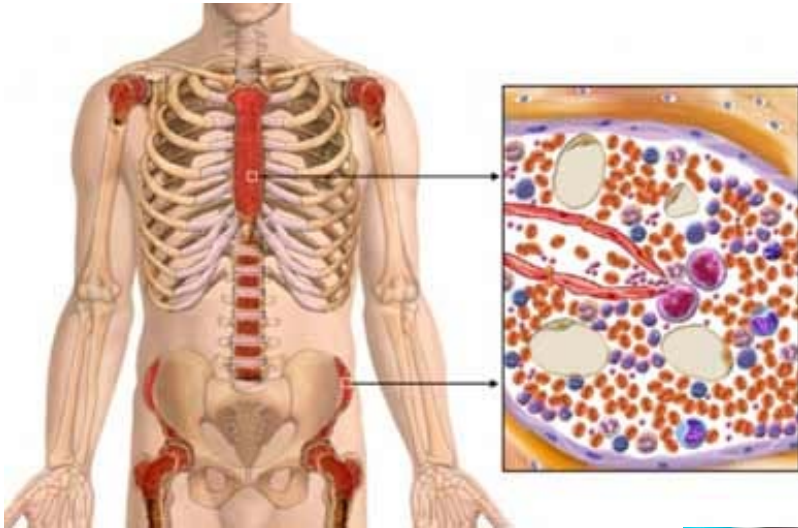
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4	7,000	10	80,000
5	7,000	13	80,000
6	7,000	13	120,000



Basic Investigation



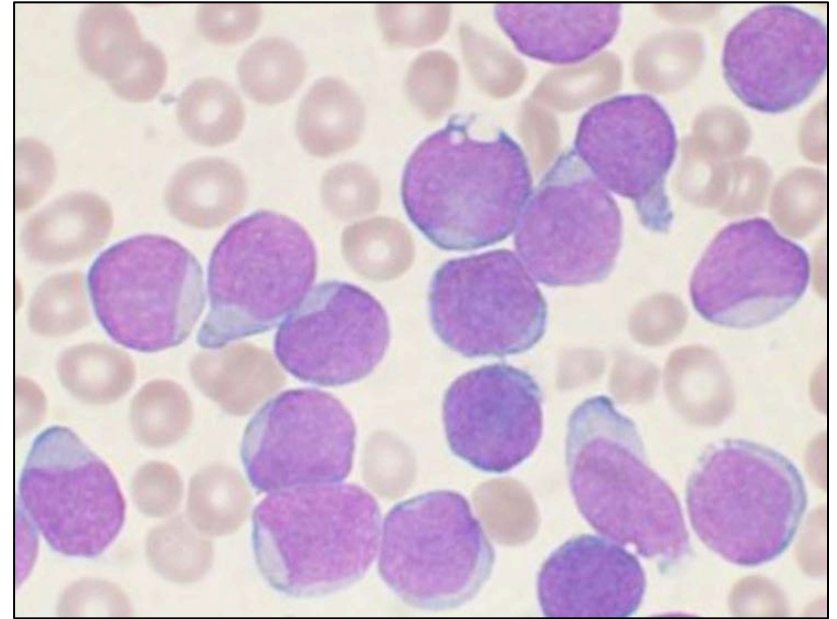
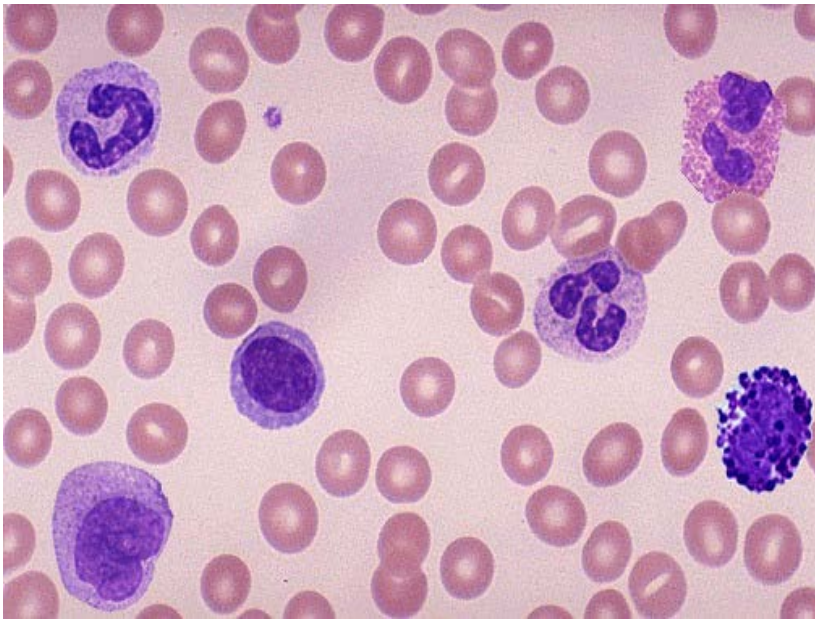
Complete Blood Count

+

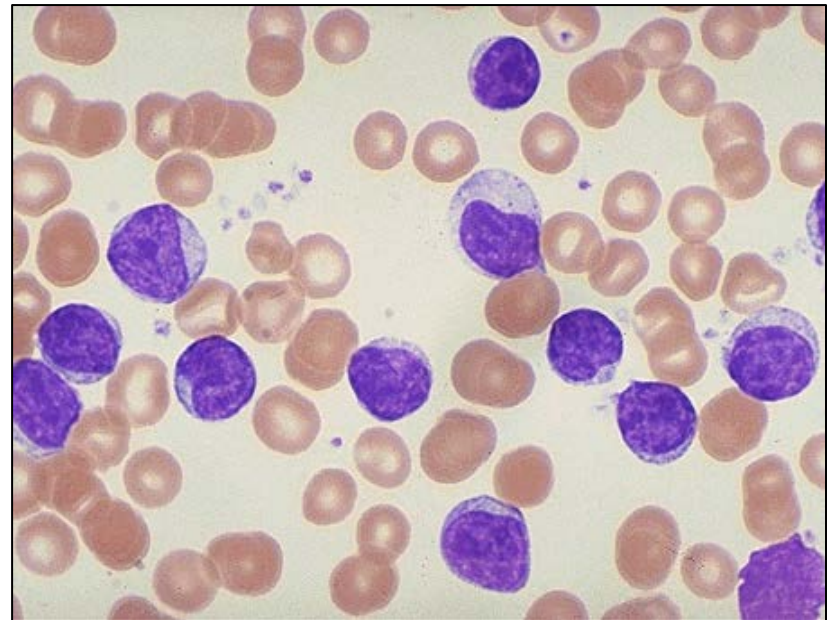
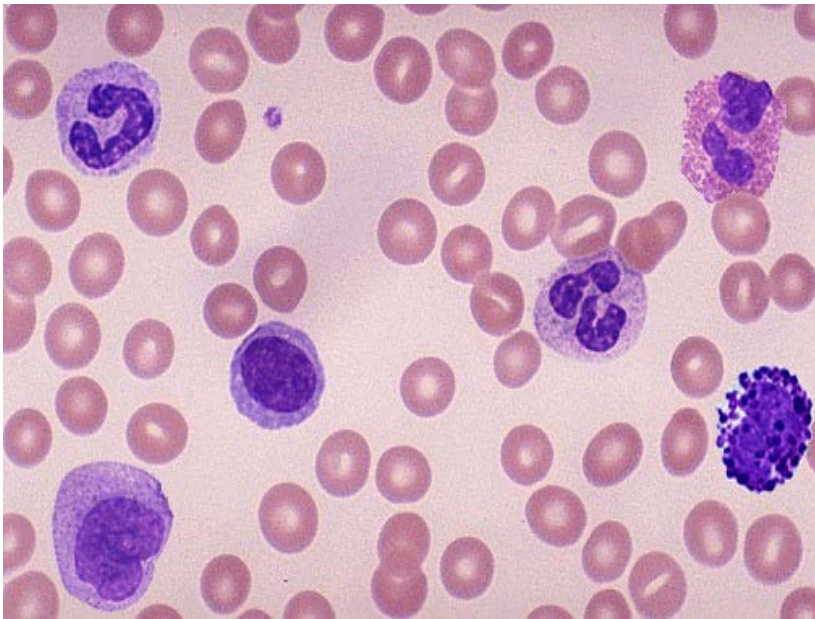
Peripheral Blood Smear



Peripheral Blood Smear

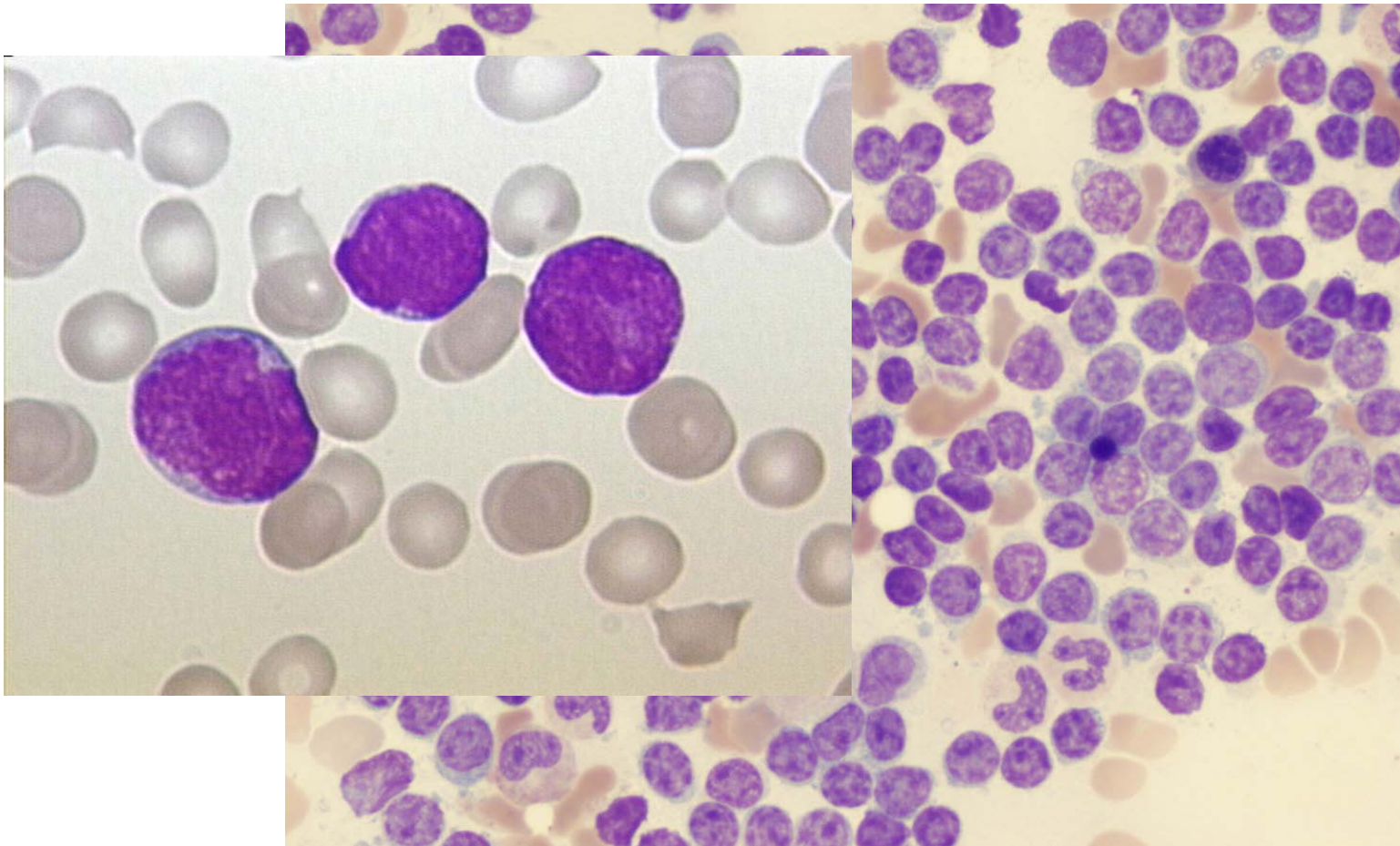


Peripheral Blood Smear



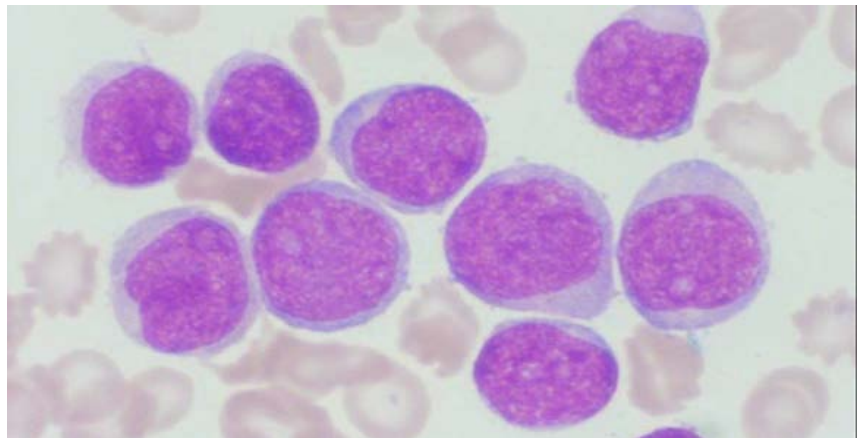
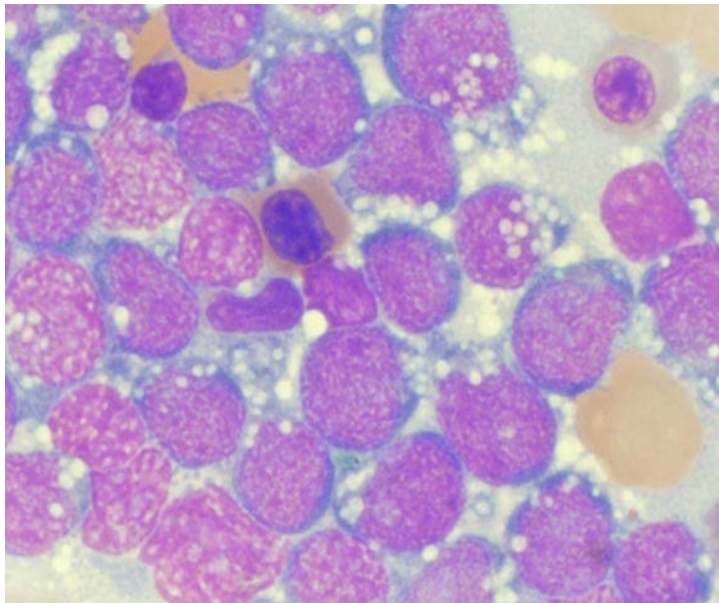
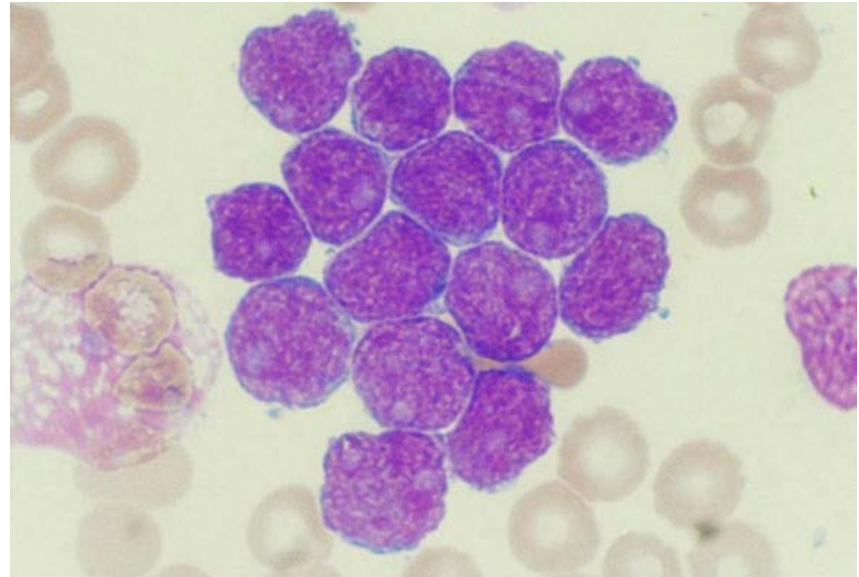
Homogenous distribution of abnormal mononuclear cells

ALL – Blood smear

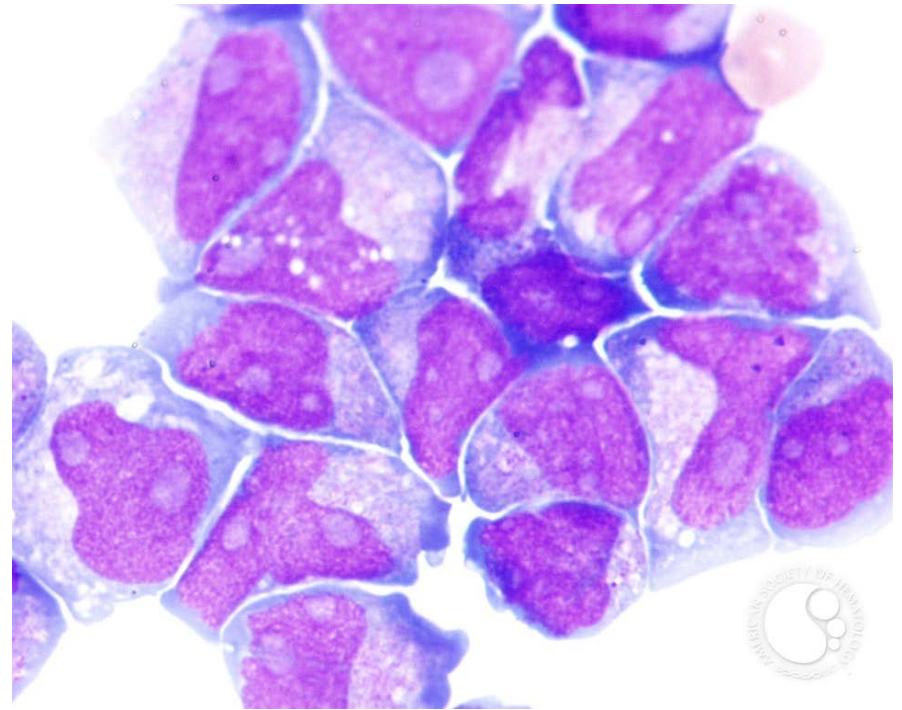


ALL – FAB Classification

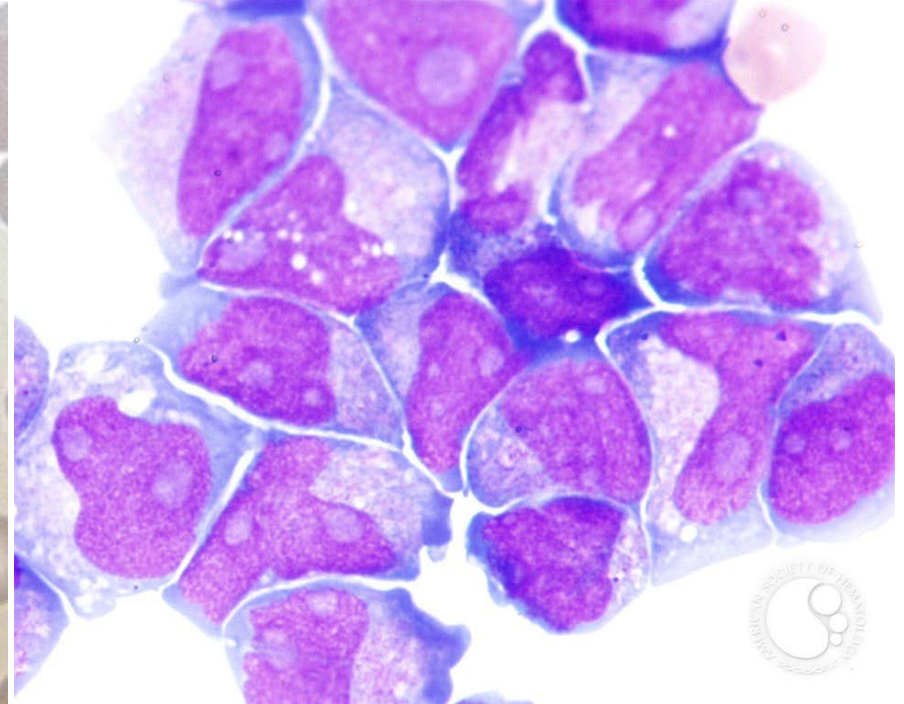
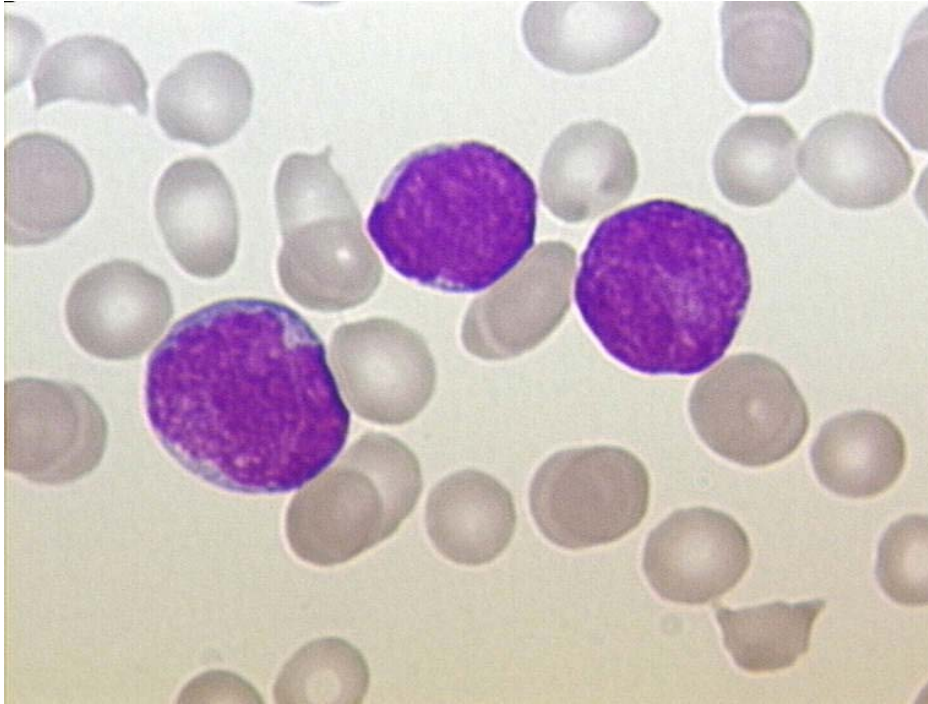
L-1	85%
L-2	14%
L-3	1%



AML – Blood Smear

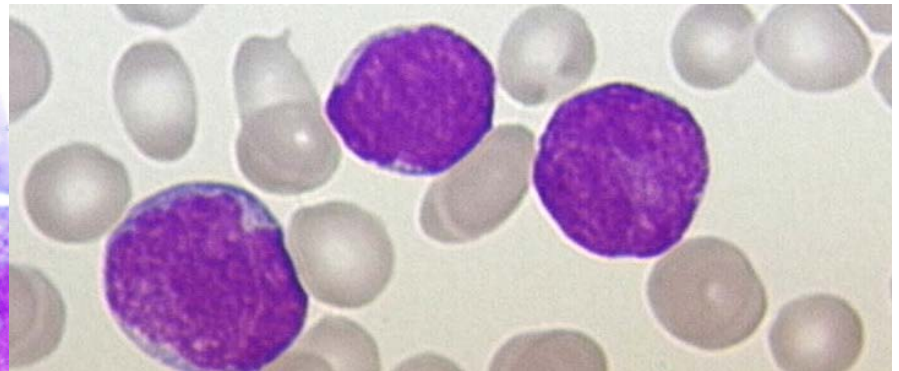
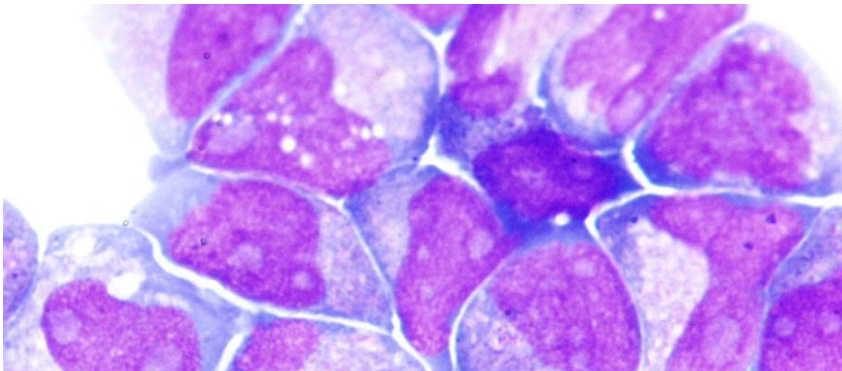


AML – Blood Smear



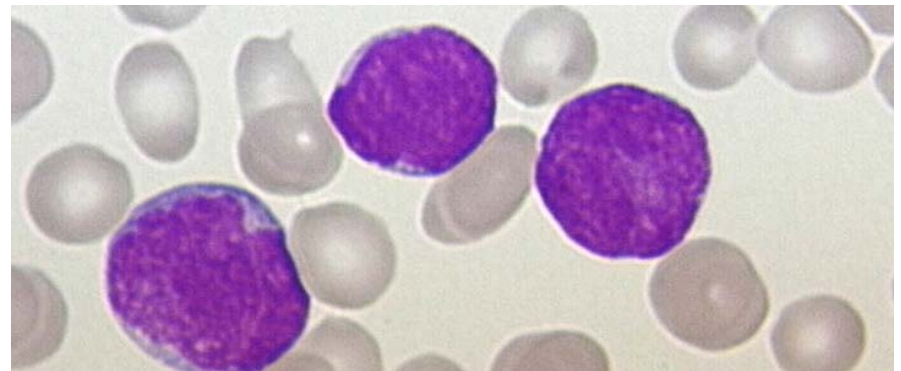
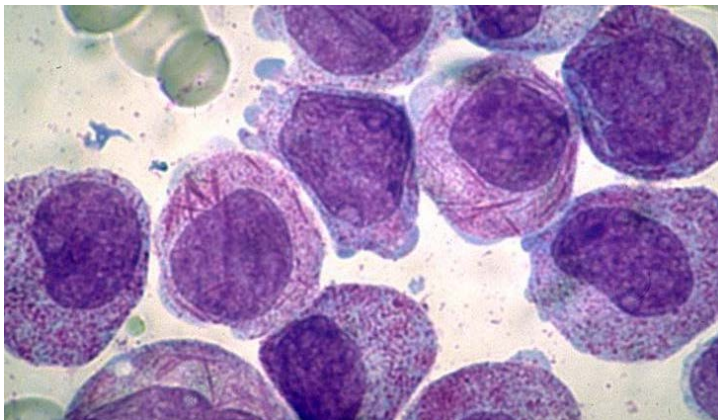
Cytologic Features of Blasts in AML vs. ALL

Feature	AML	ALL
Blast size	Large, often uniform	Variable, small to medium size
Nuclear chromatin	Usually finely dispersed	Coarse to fine
Nucleoli	1-4, often prominent	Absent or 1-2
Cytoplasm	Moderately abundant, granules often present	Usually scant, coarse granules sometimes present (7%)
Auer rods	Present in 60-70% of cases	Not present



Cytologic Features of Blasts in AML vs. ALL

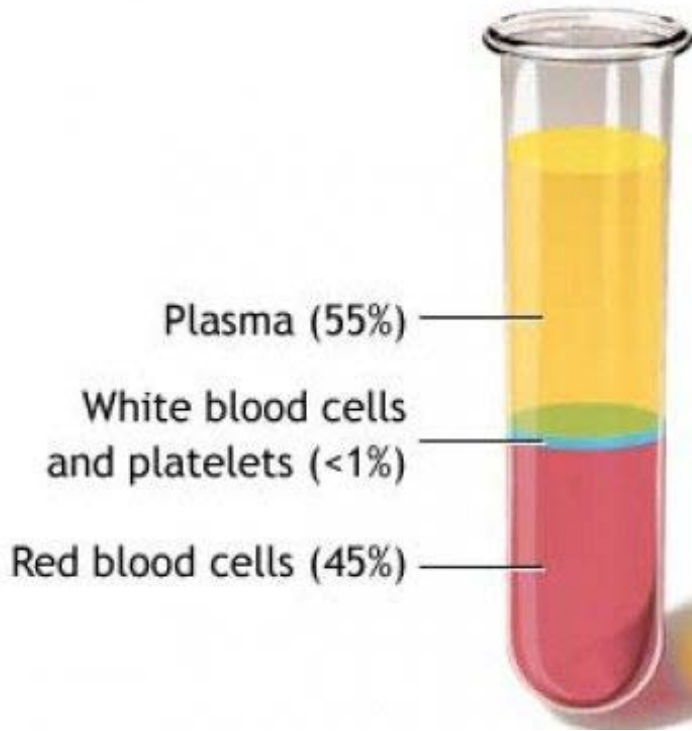
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Cytoplasm	Moderately abundant, granules often present	Usually scant, coarse granules sometimes present (7%)
Auer rods	Present in 60-70% of cases	Not present



Other Useful Investigations

- LDH
- Tumor lysis syndrome labs
 - Potassium
 - Phosphorus
 - Uric acid
 - Calcium
- Hemoculture and/or urine culture
- Types and Crossmatch for blood and platelets
- Chest X-ray


Tumor Lysis Syndrome



Extracellular electrolytes  (+++)

Intracellular electrolytes  (+)

 TLS

Intracellular electrolytes  (+)
(*elevated K, Phosphorus, Uric acid*)
(*but low calcium*)

Case

- 3 yo boy presents to OPD
 - 2 weeks history of fever, lethargy, spontaneous bruising and epistaxis

	WBC (cells/mm ³)	Hb (g/dL)	Platelets (cells/mm ³)
1	10,000	7	30,000

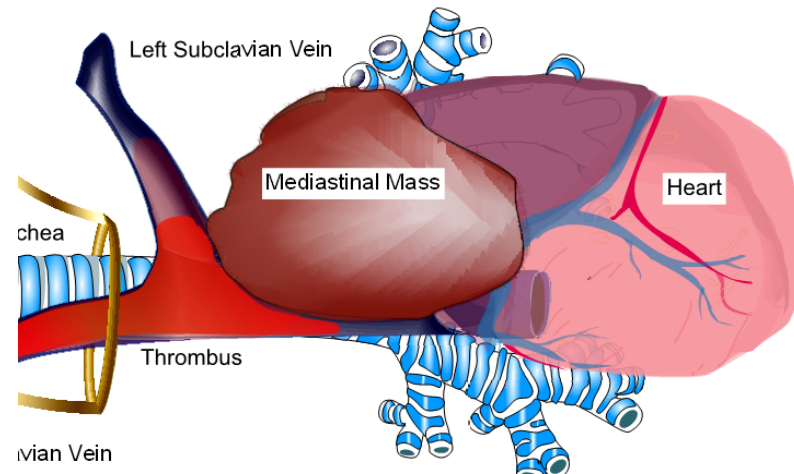
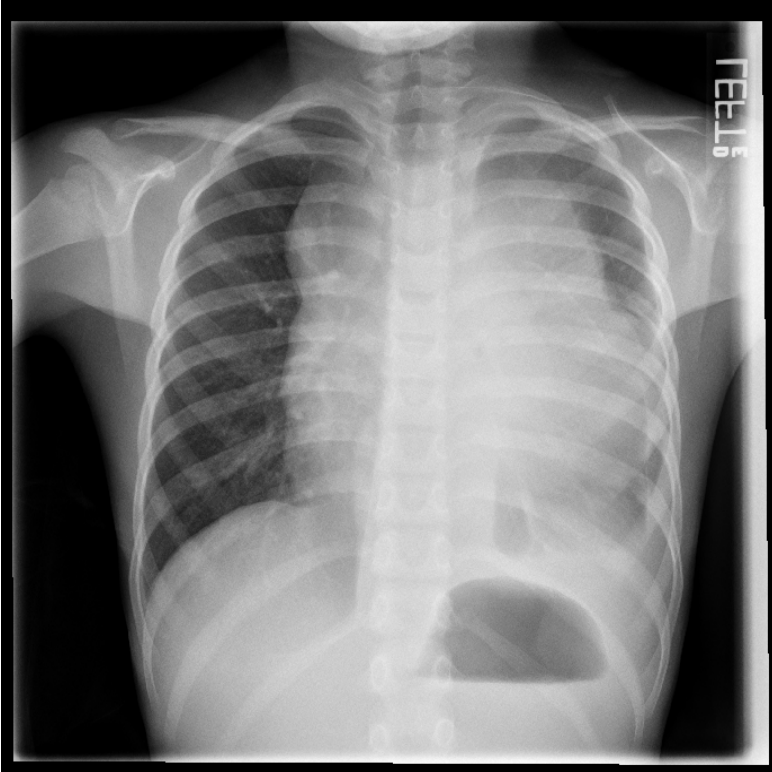
BUN 5.5 mg/dL Cr 1.2 mg/dL

E'lytes: Na 142 K 5.5 Cl 101 CO2 19 (mEq/L)

Uric acid 14.9 Ca 8.8 PO4 7.1

LDH 986 U/L (135-225)

Chest X-ray



Sedation might be fatal

Initial Management

Leukocytosis and Hyperleukocytosis

Initial Management	
IV hydration	2,500 – 3,000/m ² /day
Diuretic	Avoid unless having appropriate hydration
Transfusion	Avoid blood transfusion – hyperviscosity Platelet and FFP can be given – keep plt high !!!
Fever	Appropriate empiric antibiotics
Pain control	Avoid NSAIDs
Sedation	Always check CXR first
Hyperuricemia	Aggressive hydration and allopurinol
Hyperphosphatemia	Phosphate binder

Initial Management

Pancytopenia

Initial Management	
IV hydration	2,500 – 3,000/m ² /day
Transfusion	Can be given if clinically indicated
Fever	Appropriate empiric antibiotics
Pain control	Avoid NSAIDs
Sedation	Always check CXR first
Hyperuricemia	Aggressive hydration and allopurinol
Hyperphosphatemia	Phosphate binder

Back too the **CASE**

- 13 yo boy presents to OPD

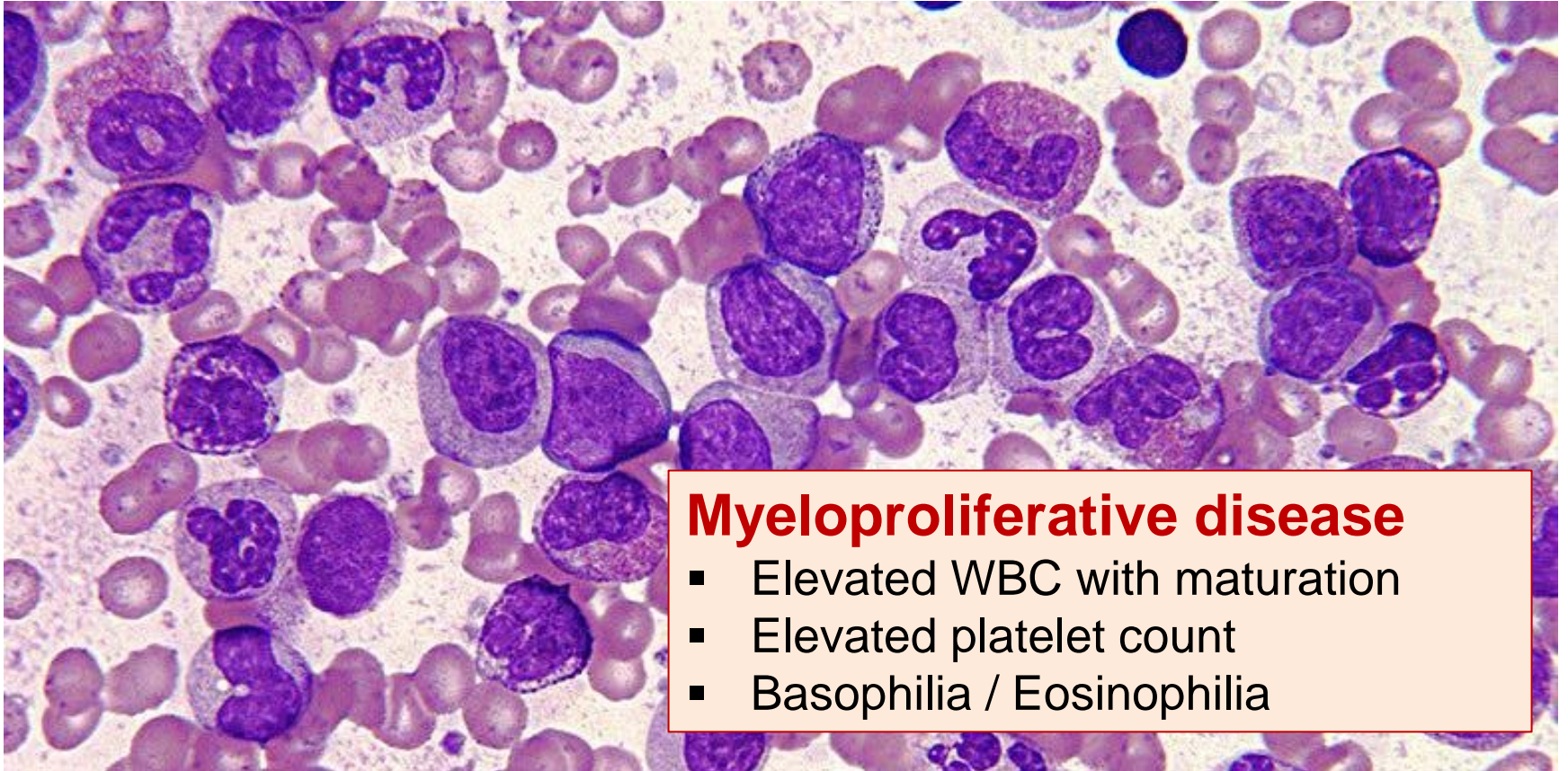
	WBC (cells/mm ³)	Hb (g/dL)	Platelets (cells/mm ³)
1	250,000	7	30,000
2	2,500	7	30,000
3	4,500	11	4,000
4	7,000	10	80,000
5	7,000	13	80,000
6	7,000	13	120,000

Case – Complete Blood Count

- 13 yo boy presents to OPD

	WBC (cells/mm ³)	Hb (g/dL)	Platelets (cells/mm ³)
1	250,000	7	30,000
2	2,500	7	30,000
3	4,500	11	4,000
4	7,000	10	80,000
5	7,000	13	80,000
6	7,000	13	120,000
7	250,000	11	750,000

Peripheral Blood Smear



Myeloproliferative disease

- Elevated WBC with maturation
- Elevated platelet count
- Basophilia / Eosinophilia

Chronic Myeloid Leukemia

CML - Clinical Features

- At diagnosis – **70% symptomatic**
 - Easy fatigability
 - Loss of sense of well-being
 - Decreased tolerance to exertion
 - Anorexia
 - Abdominal discomfort
 - Weight loss
 - Excessive sweating
- On physical examination
 - **Pallor**
 - **Splenomegaly**
 - Sternal tenderness



Case 2

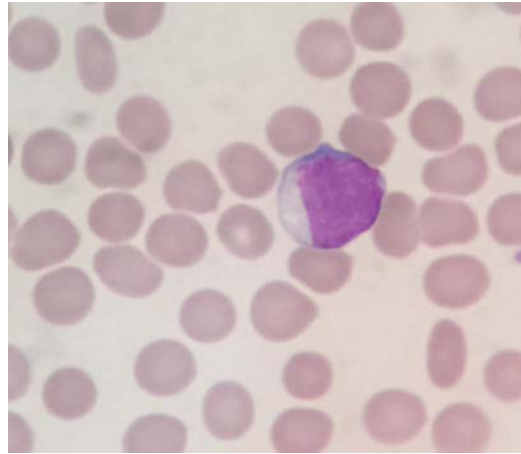
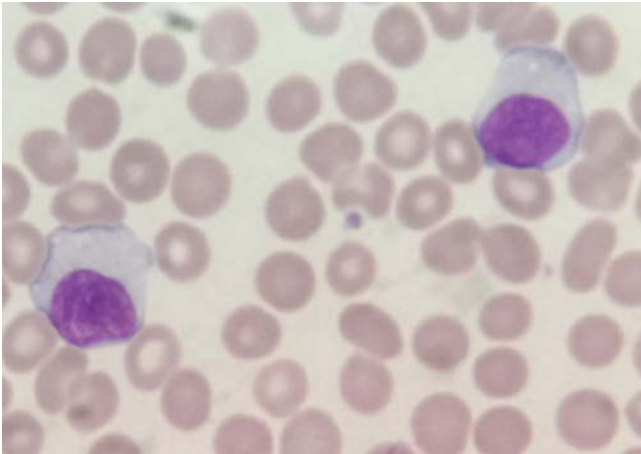
- 5 years old boy presented with fever with producing cough
- PE : tonsil 3+ with exudate, injected pharynx, both cervical LN enlargement and supraclavicular enlargement, liver 2 FB BRCM, spleen 1 FB BRCM



Patient and parents' permission obtained

Lab investigation – CBC

- CBC : **WBC 18,700/mm³** (N 46%, L 35%, M 4%, **Blasts 15%**)
Hb 10 g/dL Hct 29.7%, **Platelet 540,000/mm³**
- **LDH 540 (H)**



- **Blasts => Downey cells in PBS**



Hoagland's sign

Patient and parents' permission obtained

Summary

- Patients with leukemia usually present with fever, anemia and abnormal bleeding

But ... Not Always

- Careful history taking and physical examination are important to guide further investigation in order to identify definite diagnosis
- If still not sure ... **serial follow up** is the BEST approach

Thank You

