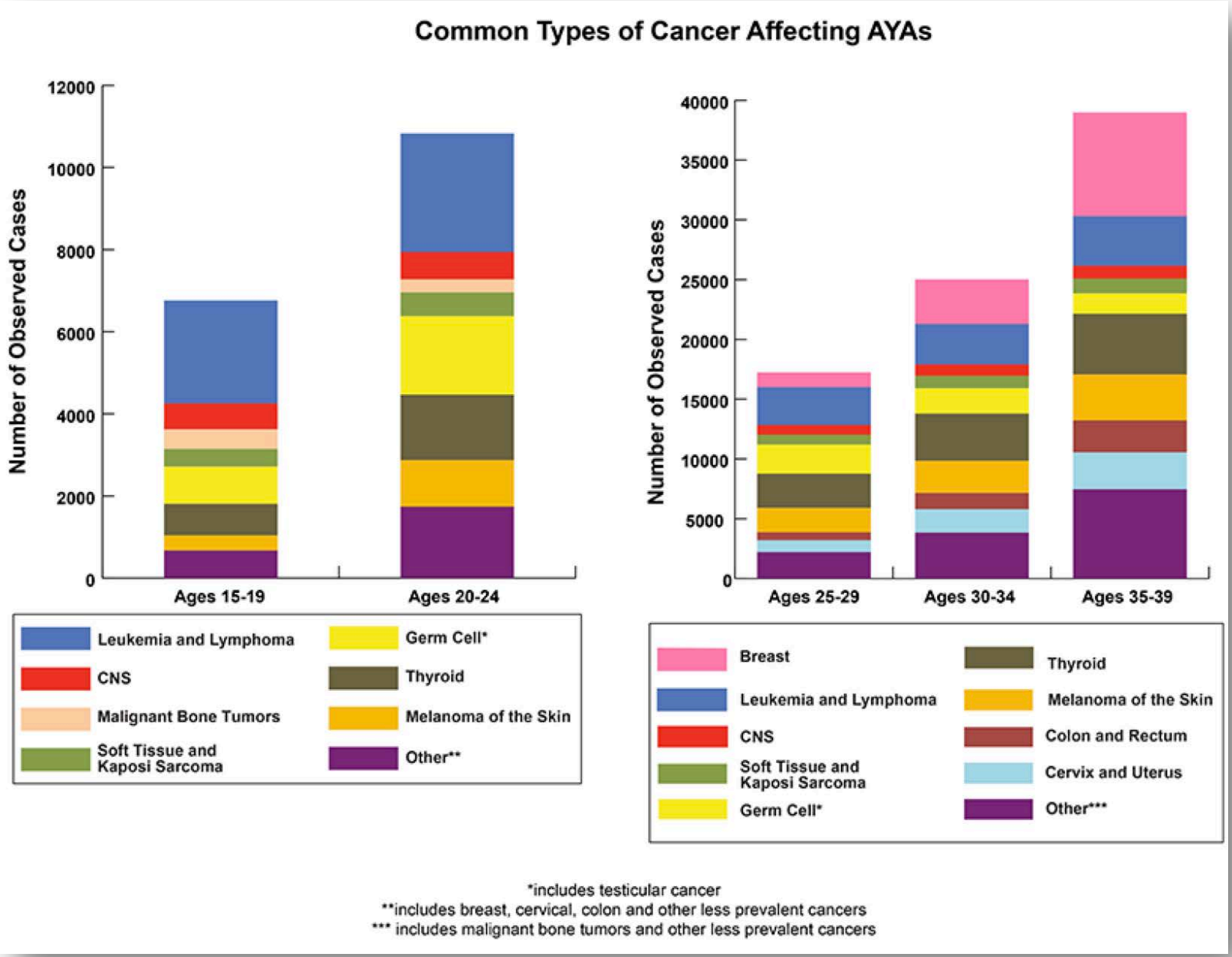
Treatment of Acute Leukemia In Adolescents and Young Adults



Source: http://www.cancer.gov/types/aya

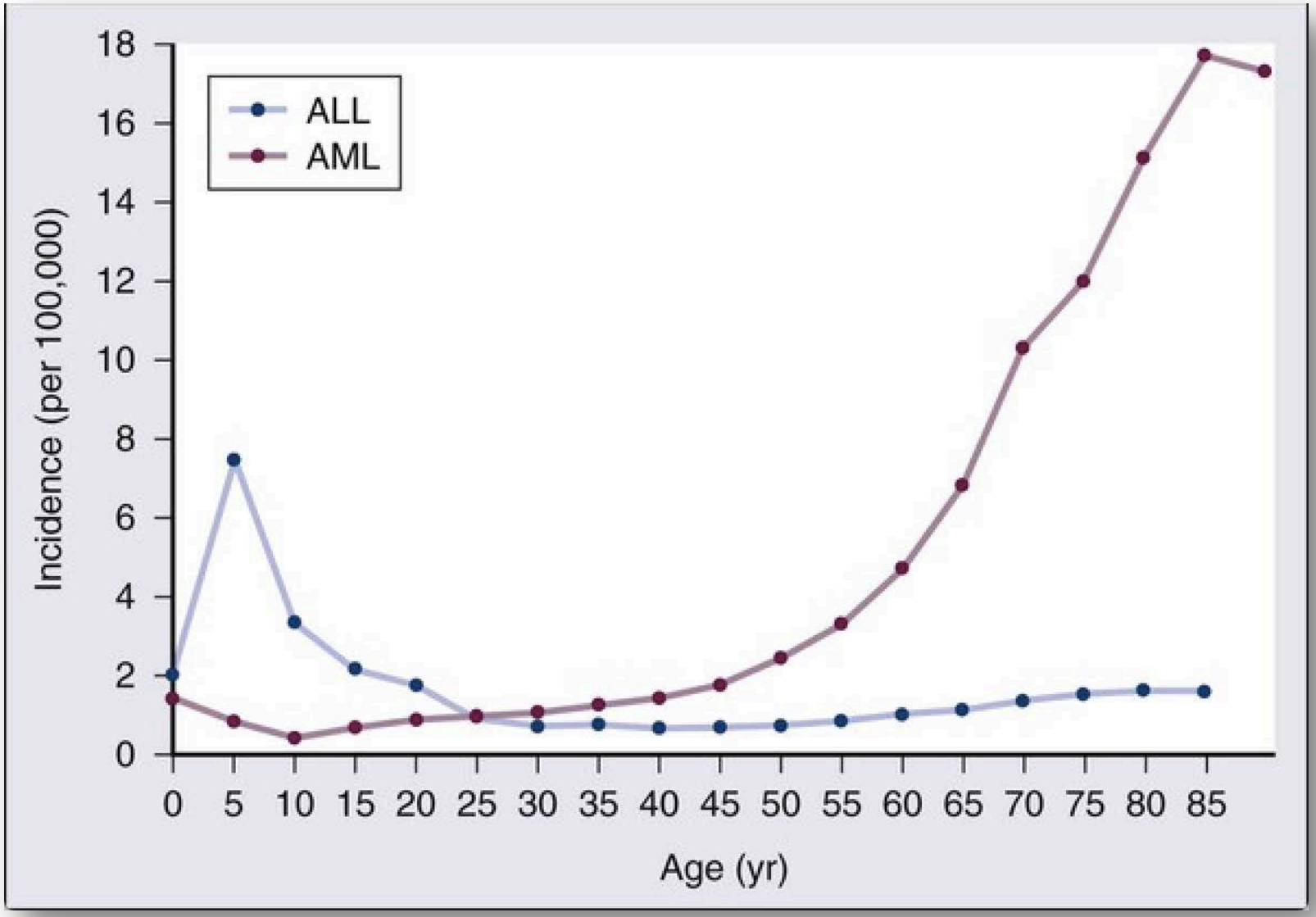
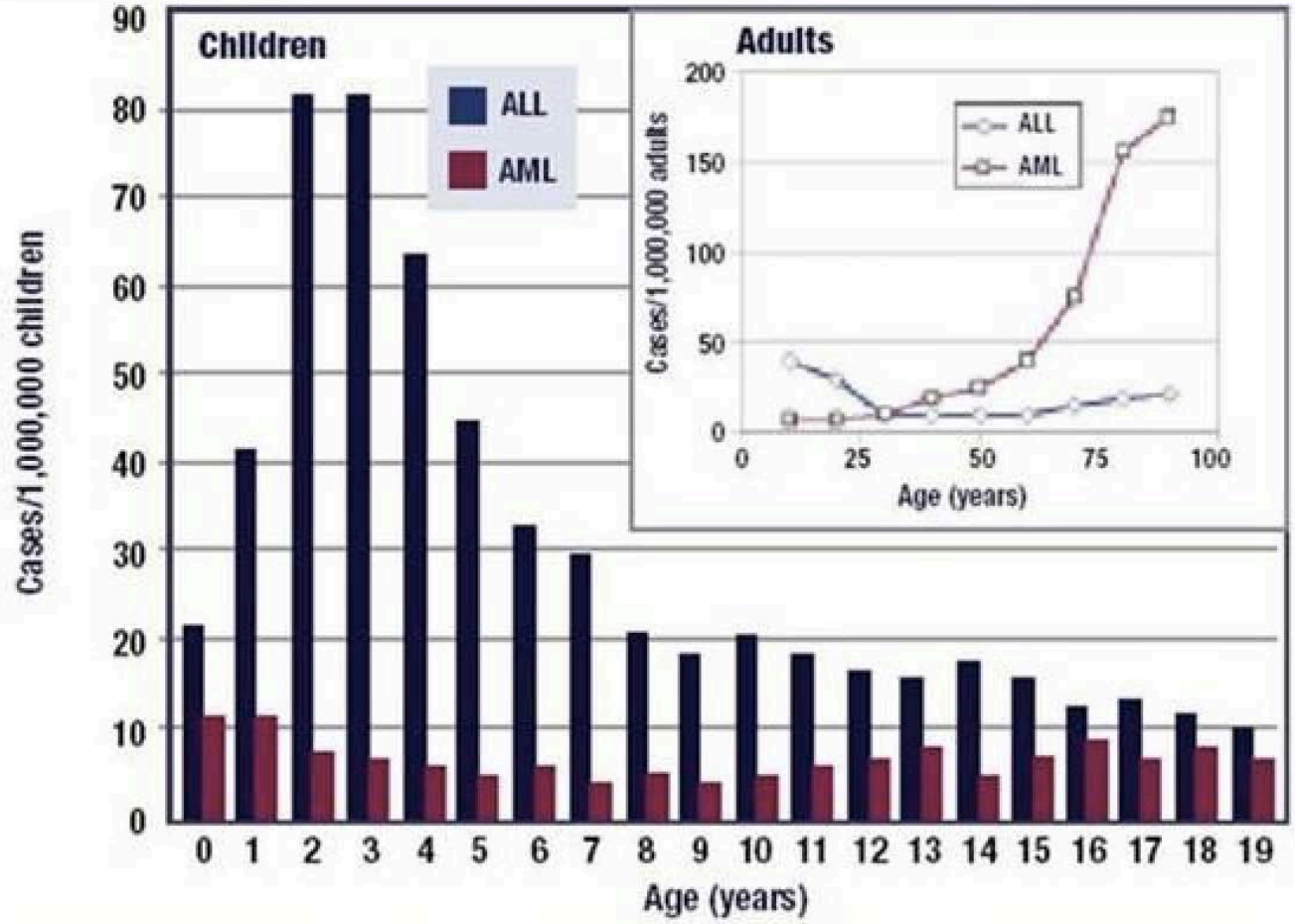

ALL
AML
Incidence (per 100,000)
0
2
4
6
8
10
12
14
16
18
0 5 10 15 20 25 30 35 40 45 50 55 60 65 70 75 80 85
Age (yr)

FIGURE 3

Age-specific incidence of ALL and AML, children and adults



Case 1

BP

- 22 Yo Female, Ugandan
  - High school student
- ºh/o Alcohol, ºtobacco use
- HIV Negative
- Nulliparous

2 June 2016

Referral Diagnosis

POORLY DIFFERENTIATED ACUTE LEUKEMIA

(BMA/Bx)

Case 2

MI

- 21 Yo Male Ugandan (African)
- DJ,
- Single, with no children
- +ve Hx of alcohol intake
- HIV-Ve

August 2016

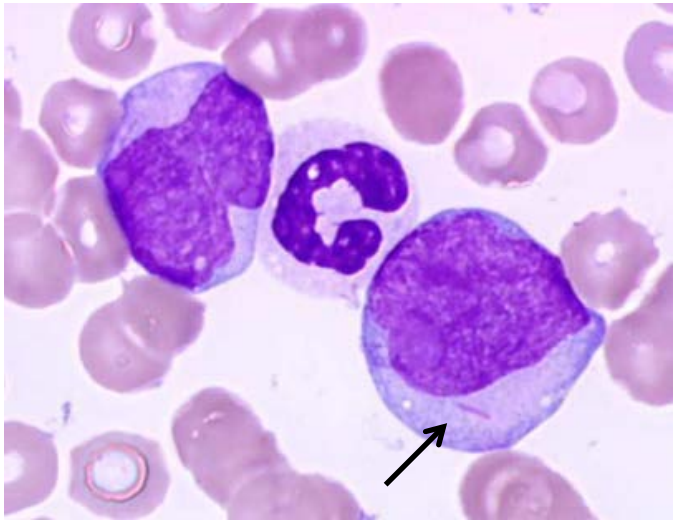
Referral Diagnosis

– **ACUTE LYMPHOBLASTIC LEAUKEMIA**

Distinguishing between AML and ALL by morphology*

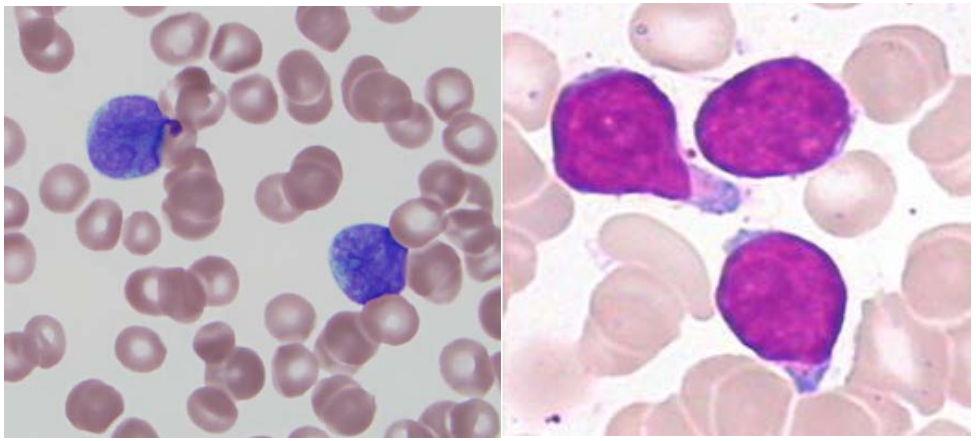
Myeloid

- Larger blasts with more voluminous cytoplasm
- Auer rods (most specific)



Lymphoid

- Smaller blasts with very little cytoplasm
- “Hand mirror” sign with pinched cytoplasm



*Except for Auer rods, these features are helpful, but not entirely specific

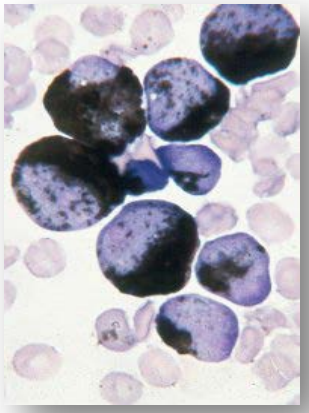
Distinguishing between AML and ALL using cytochemical stains (1)

Cytochemical Reaction	Cellular Element Stained	Positive Staining	Negative Staining
Myeloperoxidase (MPO)	Myeloid granules	**Myeloblasts** **Promyelocytes (strong)** Monoblasts (weak +/-)	Lymphoblasts Early myeloblasts
Sudan Black B (SBB)	Phospholipid	**Myeloblasts** Lymphoblasts (+/-)	Erythroblasts Megakaryoblasts
Non-specific esterase (NSE)	Cellular enzyme	**Monoblasts and promonocytes** Megakaryoblasts (+/-)	Most myeloblasts and lymphoblasts
Periodic-Acid Schiff (PAS)	Glycogen	**Erythroblasts** Lymphoblasts (granular)	Most myeloblasts/monoblasts

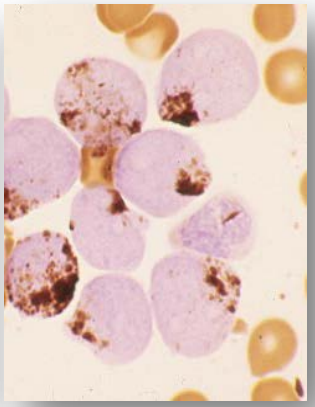
Distinguishing between AML and ALL using cytochemical stains (2)

	MPO	SBB	SPE	NSE	PAS
Myeloblasts	++	++	++	+	Diffuse-Weak
Lymphoblasts	-	- / weak +	-	-/+	Block-Granular
Monoblasts	+/-	++	-	++	Diffuse-Weak

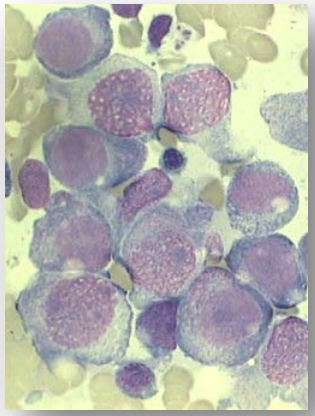
a. Myeloblast: M0: neg for all; M1 through M6: +MPO; M7: neg for MPO
b. Lymphoblast: +PAS and acid phosphatase, +/- sudan black, neg for others
c. Monoblast: strong +NSE, Lysozyme; neg to weak for MPO



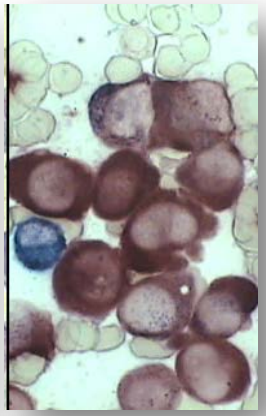
SBB



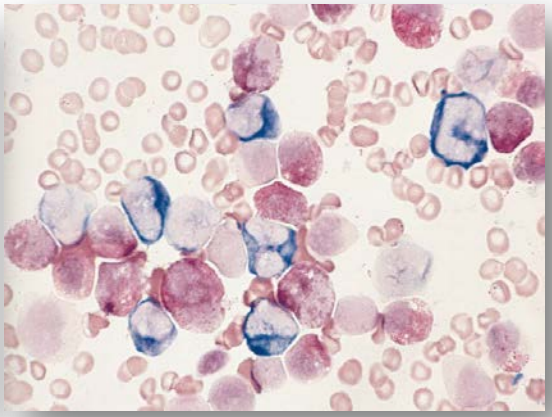
MPO



Wright-Giemsa



Brown: α-naphthyl acetate esterase (NSE)



Blue: chloroacetate esterase (SPE)

Adolescents and Young Adults with ALL

- Acute Lymphoblastic Leukemia (ALL) survival rate is close to 90% in young children.
- In older adolescents and young adults (AYA), event-free survival is only 30-45%.
- Improved outcome, with disease-free survival rates of 60-70%, are achieved when AYA patients are treated with “pediatric-inspired” approaches.
- National Cancer Institute has defined the AYA population as those between 15 and 39 years of age.

Treatment Regimens - ALL

- Adult Regimens:
  - Intensive use of myelosuppressive agents:
    - Daunorubicin
    - Cytarabine
    - Cyclophosphaminde
    - Allogeneic stem cell transplantation (SCT)
- Pediatric Regimens:
  - Berlin-Frankfurt-Munster (BFM) backbone:
    - Glucocorticoids
    - Vincristine
    - Asparaginase
    - Early and frequent CNS prophylaxis and prolonged maintenance therapy

Standard supportive care and monitoring

- Allopurinol is recommended for the first 10 days of induction therapy to prevent hyperuricemia.
- Antimicrobial prophylaxis: antiviral and *Pneumocystis jiroveci* prophylaxis should be used throughout treatment.
- Fungal prophylaxis should include mold coverage throughout induction therapy.
  - Broader spectrum azole antifungals cannot be used with vincristine.
- Asparaginase-related toxicities
  - Asparaginase-related hypersensitivity reactions can occur in 20% of children and adults.

Adolescent and Young Adults with AML

- Acute Myeloid Leukemia (AML) represents 33% of adolescent and 50% of young adult leukemia.
- Diagnosis should be based on cytogenetic and molecular factors to avoid overtreatment.
- Poorer prognosis of AYAs with ALL can be overcome with intensive pediatric protocols; whether a similar approach would benefit AYAs with AML has not yet been established.
- Intensifying therapy, or “one-size-fits-all” therapy, does not improve survival rates.

Treatment Regimens - AML

- "3+7" continues to be the backbone of induction therapy.
  - (daunorubicin 60–90 mg/m^2/day idarubicin 10–12 mg/m^2/day or mitoxantrone 10–12 mg/m^2/day) and seven days of cytarabine (100–200 mg/m^2/day)

- AYA patients usually receive one or two cycles of induction therapy.

- Additional CNS therapy is routine in most pediatric protocols.

- Bone marrow assessment on the 7th or 10th day after completion of induction treatment.

AML in AYA is often curable with chemotherapy alone

Retrospective analysis of 432 AYA (16-29) with AML at MDACC, 1965-2009:

- Median age 23
- 17% had core binding factor (CBF; t(8;21) or inv(16) AML)
- 12% had acute promyelocytic leukemia (APL; t(15;17))
- CR rates:
  - 93% for CBF AML
  - 78% for APL
  - 77% with diploid karyotype
  - 68% for other AML
- AML outcome in AYA superior to that in older adults

Factors contributing to improved AML outcome in AYA

- Disease biology is different in AYA
  - Lower incidence of abnormal/complex cytogenetics
  - Reduced incidence of secondary/therapy-related AML than is seen in older patients
- Better tolerance of AML chemotherapy
  - Better suited for more dose-intense regimens
- Less comorbid conditions at baseline
- Taking less concomitant medications
  - Fewer drug-drug interactions and toxicities
- Lower incidence of abnormal/complex cytogenetics

References

- http://www.cancer.gov/types/aya
- http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4470138/
- Pemmaraju *et al*., Clinical characteristics and outcomes of AYA with AML. Clin Lymph Myel Leuk, in press (2016).
- Curran, E., & Stock, W. (2015). How I treat acute lymphoblastic leukemia in older adolescents and young adults. Blood, 125(24), 3702-3710. Accessed June 14, 2016. http://dx.doi.org/10.1182/blood-2014-11-551481