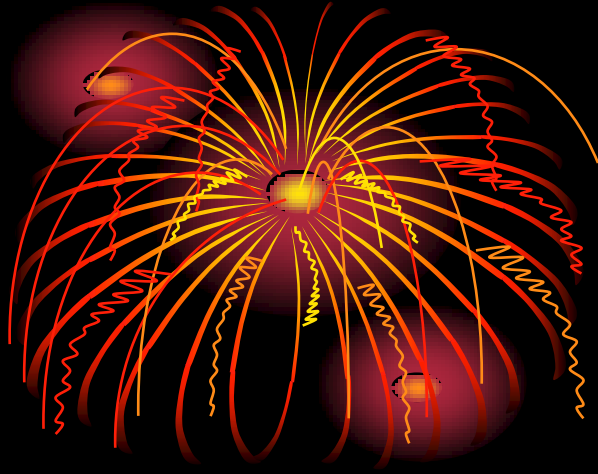
Acute Myeloid Leukemia: The Aga Khan experience

Dr Mzee Ngunga
Aga Khan University Hospital
Nairobi

AML

- Characterized by an increase in the number of myeloid cells in the marrow and an arrest in their maturation
- Granulocytopenia, thrombocytopenia, or anemia
- leukocytosis.

Epedemiology



- United States
  - Annual incidence - 2.4 per 100,000
  - 12.6 per 100,000 > 65 years
- Median age approx. 25 to 30 years
- 5YSR <65 yr less than 40%

- Kosary CL, Ries LAG, Miller BA, Hankey BF, Edwards BK, eds. SEER cancer statistics review, 1973-1992: tables and graphs. Bethesda, Md.: National Cancer Institute, 1995

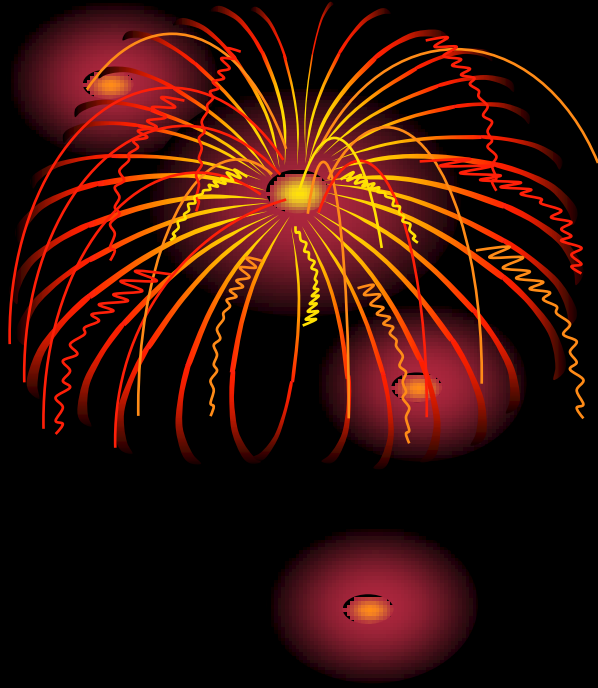
TABLE 1. THE FRENCH–AMERICAN–BRITISH (FAB) CLASSIFICATION OF AML AND ASSOCIATED GENETIC ABNORMALITIES.

FAB SUBTYPE	COMMON NAME (% OF CASES)	RESULTS OF STAINING			ASSOCIATED TRANSLOCATIONS AND REARRANGEMENTS (% OF CASES)	GENES INVOLVED
		MYELOPEROXIDASE	SUDAN BLACK	NONSPECIFIC ESTERASE		
M0	Acute myeloblastic leukemia with minimal differentiation (3%)	–	–	–*	inv(3q26) and t(3;3) (1%)	*EVI1*
M1	Acute myeloblastic leukemia without maturation (15–20%)	+	+	–		
M2	Acute myeloblastic leukemia with maturation (25–30%)	+	+	–	t(8;21) (40%), t(6;9) (1%)	*AML1-ETO*, *DEK-CAN*
M3	Acute promyelocytic leukemia (5–10%)	+	+	–	t(15;17) (98%), t(11;17) (1%), t(5;17) (1%)	*PML-RARα*, *PLZF-RARα*, *NPM RARα*
M4	Acute myelomonocytic leukemia (20%)	+	+	+	11q23 (20%), inv(3q26) and t(3;3) (3%), t(6;9) (1%)	*MLL*, *DEK-CAN*, *EVI1*
M4Eo	Acute myelomonocytic leukemia with abnormal eosinophils (5–10%)	+	+	+	inv(16), t(16;16) (80%)	*CBFβ-MYH11*
M5	Acute monocytic leukemia (2–9%)	–	–	+	11q23 (20%), t(8;16) (2%)	*MLL*, *MOZ-CBP*
M6	Erythroleukemia (3–5%)	+	+	–		
M7	Acute megakaryocytic leukemia (3–12%)	–	–	+†	t(1;22) (5%)	Unknown

*Cells are positive for myeloid antigen (e.g., CD13 and CD33).

†Cells are positive for α-naphthylacetate and platelet glycoprotein IIb/IIIa or factor VIII–related antigen and negative for naphthylbutyrate.

AML

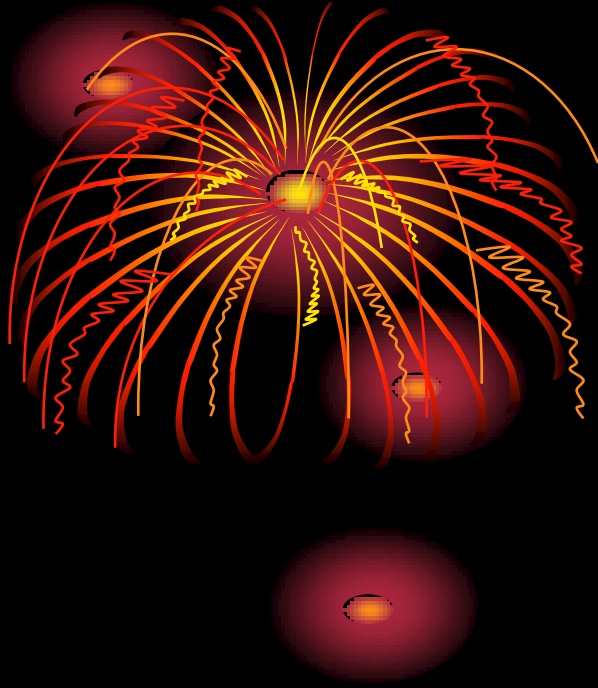


- Primary
- Secondary
  - From CMML
  - Myelodysplastic syndromes
  - Chemotherapy
  - Congenital neutropenia, Blooms syndrome, Fanconis anemia

Bone Marrow Audit: AKUH

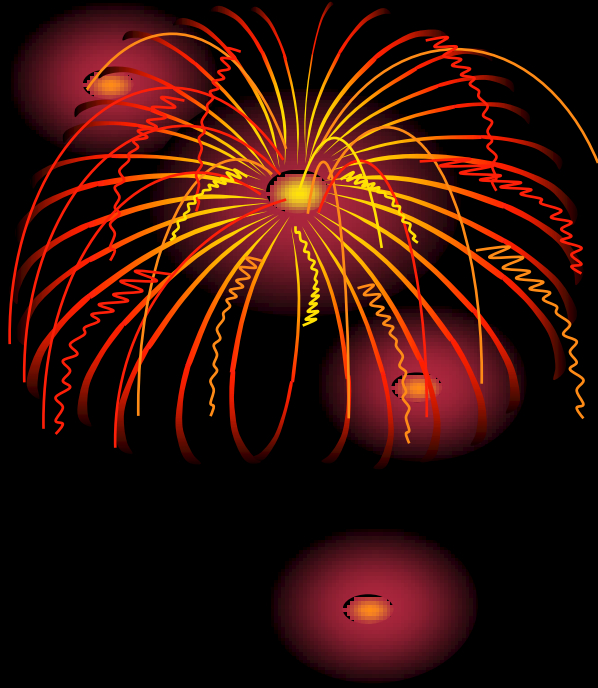
- Feb 2003 to Feb 2006
- To determine the relative frequencies of hematological malignacies
- To establish the AML subtypes in our patients

Patients



- 356 pts
- 18 mo. To 91 yrs
- Male 180 (50.6%)
- Female 176 (49.4%)

Indications



- Anaemia 26.9%
- PUO 17.5%
- Pancytopenia 17.1%
- Possible leukemia 10.9%
- Leukoerythroblastic picture 7.5%
- Staging lyphomas 6.1%
- Monocytopenias 5%
- Undetermined 9%

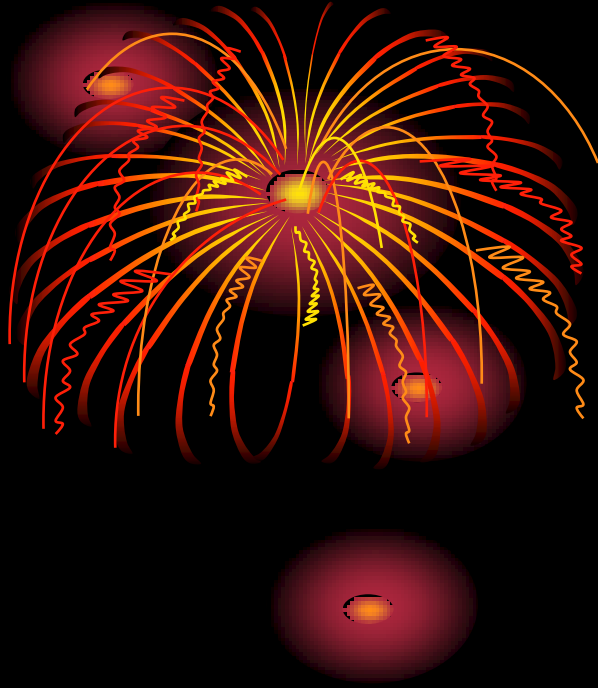
Findings

Disease	Cases	%
Acute myeloid leukemia	29	8.6%
Lymhoproliferative disorder	24	6.7%
Multiple myeloma	20	5.6%
Myeloproliferative disorder/myelodysplastic syndrome	9	2%
Metastatic tumour	9	2%
Acute lymphoblastic	6	1.7%

AML: FAB subtypes

- M0 – 2 (6.7%)
- M1- 7 (23%)
- M2 – 11(36%)
- M3 – 2 (6.7%0
- M4 – 5 (16%)
- M5 – 3 (10%)
- M6 - 1 (3.3%)
- M7 – 0

AML: Patients characteristics

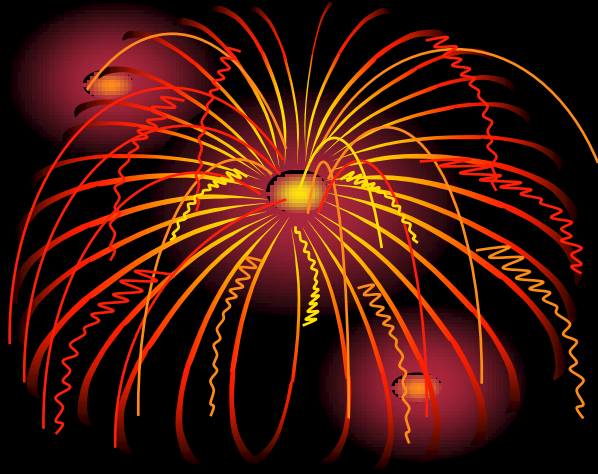


- Male – 18 (60%)
- Female – 12 (40%)
- Avg. age – 45yrs (22 – 85yrs)

Outcomes

- Declined treatment – 10
- Died while undergoing treatment – 8
- On follow up – 1
- Lost to follow up - 10

Outcomes

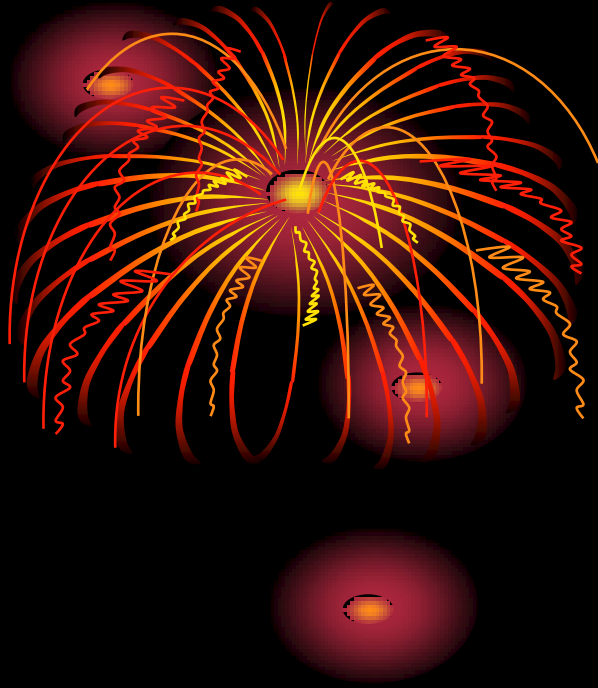


- **Average hospital stay – 30 days**
- **Cost – avg Sh. 1.2m (564,000 – 2.6m)**

Complications

- Severe thrombocytopenia
- Febrile neutropenia
- Cellulitis
- Metrorrhagia
- Blood reaction
- Depression
- Diarrhoea

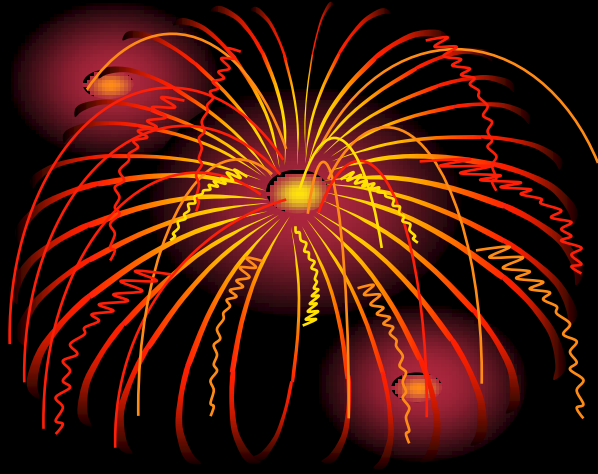
Complications



- Purulent conjunctivitis
- UTI
- Anemia
- Alopecia

Treatment

- Complete remission approx .65%
- Decreases with increasing age and the presence of unfavorable cytogenetic abnormalities.
- With postremission therapy, disease-free survival at five years ranges from 10 to 15% with low-dose maintenance therapy to 25 to 35% with intensive courses of chemotherapy



Chemotherapy

Adriamycin 70mg od *3/7

Cytosine arabinoside Ara-C 300mg od *5/7

Then

- **Ara C 2g IV infusion x2/7**

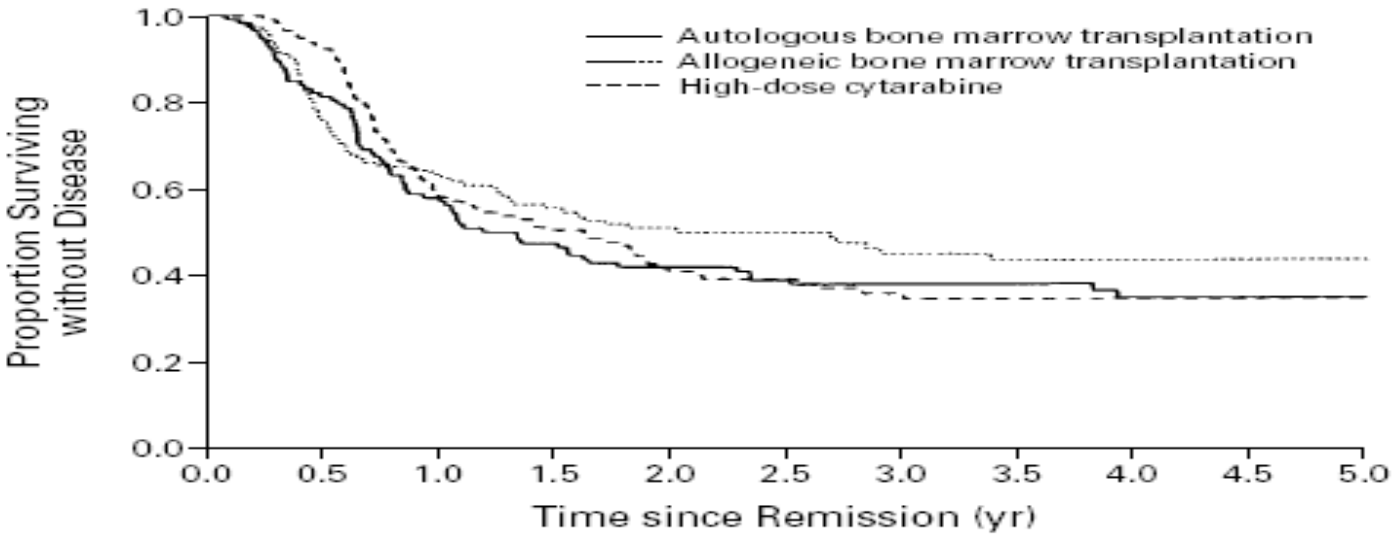
Complete Remission

- Blood neutrophil > 1500
- Plt > 100,000
- No blasts in circulation
- Bone marrow
  - >20% trilineage maturation
  - <5% blasts

Bone marrow transplant

- Allogeneic or autologous bone marrow transplant may not give any additional benefit to high dose cytarabine
- 740 pts, 70% went into remission
- More studies on the pipeline

- Nejm Volume 339:1649-1656
- 1998



Group	No. of Events/No. at Risk				
Autologous transplantation	48/116	18/66	4/45	2/34	0/22
Allogeneic transplantation	41/113	14/71	5/55	1/32	0/22
Cytarabine	48/117	21/69	5/47	1/29	0/18

Figure 1. Probability of Disease-free Survival According to Postremission Therapy.

Table 2. Adverse Prognostic Factors in Patients with AML.

Factors Used to Predict Response to Induction Chemotherapy	Factors Used to Predict Relapse
Unfavorable karyotype	Unfavorable karyotype
Age >60 yr	Age >60 yr
Secondary AML	Delayed response to induction chemotherapy
Poor performance score*	Features of multidrug resistance
Features of multidrug resistance	White-cell count of >20,000/mm^3
White-cell count of >20,000/mm^3	Female sex
Unfavorable immunophenotype	Elevated lactate dehydrogenase level
CD34 positivity†	Autonomous growth of leukemic cells

*The extent of a patient's disabilities are assessed according to a well-defined set of criteria.[50]

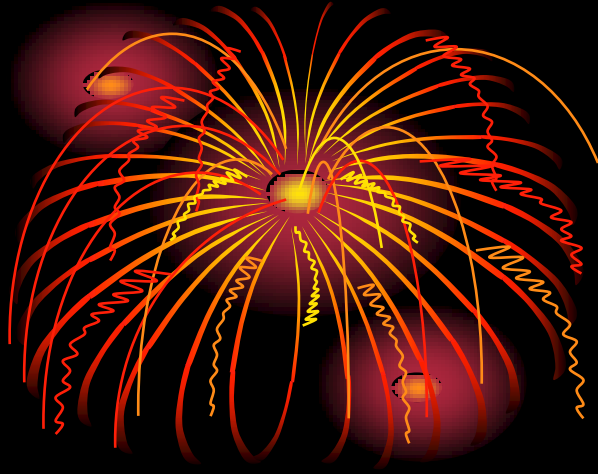
†Unlike the other factors listed, this factor is considered to be minor.

TABLE 4. PATIENTS COMPLETING ASSIGNED THERAPY IN RANDOMIZED TRIALS OF BONE MARROW TRANSPLANTATION FOR ACUTE MYELOID LEUKEMIA.

STUDY	PATIENTS REMAINING IN THE STUDY AFTER COMPLETE REMISSION	PATIENTS ASSIGNED TO THERAPY WHO COMPLETED THE THERAPY		
		CHEMOTHERAPY*	AUTOLOGOUS BONE MARROW TRANSPLANTATION*	ALLOGENEIC BONE MARROW TRANSPLANTATION†
	number/total number (percent)			
Current study	346/518 (67)	106/117 (91)	63/116 (54)	92/113 (81)
Zittoun et al.[15]	422/623 (68)	104/126 (83)	95/128 (74)	144/168 (86)
Burnett et al.[16]	759/1509 (50)	186/191 (97)	126/190 (66)	NA/378
Harousseau et al.[17]	252/367 (69)	71/78 (91)	75/86 (87)	73/88 (83)
Ravindranath et al.[18]	321/552 (58)	113/117 (97)	71/115 (62)	79/89 (89)

*Patients were randomly assigned to therapy.

†Patients were assigned to therapy on the basis of the availability of a suitable donor. NA denotes not available.



Thank You