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Acute Lymphoblastic Leukaemia in Adults: Clinicopathological Correlations with the French–American–British (FAB) Co-operative Group Classification

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Abstract—*The clinical, haematological and cell surface marker findings in 54 adults with acute lymphoblastic leukaemia have been correlated with the French–American–British (FAB) co-operative group classification of acute leukaemias. A significant relationship ($P=0.03$) was found between Burkitt-like cytology, (FAB) L3 and Central Nervous System (CNS) disease at clinical and haematological remission. The incidence of primary CNS relapse was significantly greater in the FAB, L1 group than L2 ($P=0.03$). The classification did not predict for differences in haematological or cell surface marker findings. There was also no apparent correlation with the rate or duration of complete remission.*

INTRODUCTION

MANY clinicopathological features have been studied in childhood acute lymphoblastic leukaemia (ALL) that will reliably predict patients most at risk of initial treatment failure or early relapse. Light microscopy is still the basic technique for diagnosing leukaemia but despite attempts at relating blast cell cytology to clinical and immunological findings, few studies have shown consistent results. A major problem has been the lack of a generally acceptable classification of blast cell morphology.

In 1976, the French–American–British (FAB), co-operative group proposed criteria for the classification of acute leukaemias [1]. The relationship of this classification to clinical, haematological and cell surface marker findings, in 54 adults with ALL, are presented in this paper.

MATERIALS AND METHODS

Between November 1972 and November 1977, 61 previously untreated adults ($\geq$15 yr of age) were referred to St. Bartholomew's Hospital for treatment of ALL. Morphological and cytogenetic studies indicated that 7 had either a non-Hodgkin's lymphoma or chronic granulocytic leukaemia, in lymphoid blast crisis (CGL-LBC). These cases are excluded.

Remission induction was with vincristine, adriamycin, prednisolone and L-asparaginase [2]. At complete remission (CR), patients received central nervous system (CNS) prophylaxis and then continuous maintenance therapy [2].

May–Grunwald–Giemsa stained blood and marrow films were classified prospectively and retrospectively by the FAB criteria (Table 1). All were Sudan Black (SB) negative. Cases negative for both SB and periodic-acid–Schiff (PAS), were also negative for naphthol AS acetate esterase. Cerebrospinal fluid was examined after cytocentrifugation.

Blast cell surface phenotype was defined by sheep erythrocyte rosettes (E^+) [3], surface membrane immunoglobulin ($SmIg^+$) [3], and reactivity with a rabbit antiserum functionally specific for non-T, non-B, ALL (α-ALL^+, E^-, $SmIg^-$) [4–6] and some cases of CGL–LBC [7].

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Table 1. *FAB criteria for classification of ALL*

Cytological features	L1	L2	L3
Cell size	Predominantly small	Large and heterogeneous	Large and homogeneous
Nuclear chromatin	Homogeneous	Variable	Homogeneous and finely stippled
Nuclear shape	Regular; occasional clefting or indentation	Variable, clefting and indentation	Regular, oval to round
Nucleoli	Absent; small or inconspicuous	One or more often large	Prominent, one or more vesicular
Amount of cytoplasm	Scanty	Variable; often moderately abundant	Moderately abundant
Basophilia of cytoplasm	Slight or moderate	Variable; deep in some	Very deep
Cytoplasmic vacuolation	Variable	Variable	Often prominent

RESULTS

The age and sex distribution of L1 and L2 are shown in Fig. 1. Two males and 2 females with L3 had a mean age of 24 yr. The differences are not significant. The response to therapy and the incidence of CNS disease (CNS^+) are summarised in Table 2, and indicate no significant differences in the rate of CR or relapse.

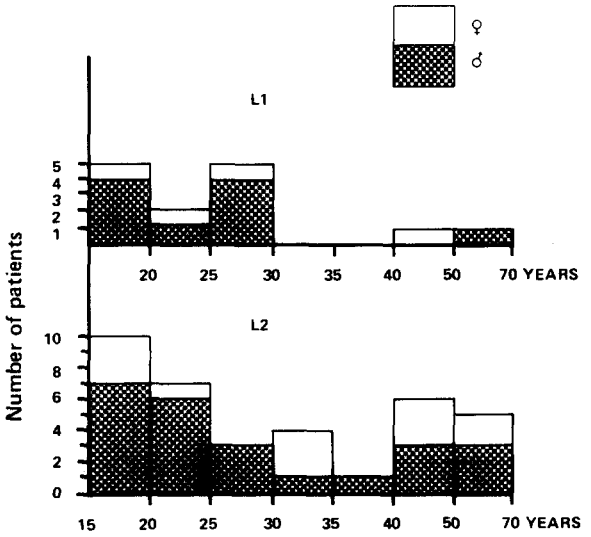

Fig. 1. Age and sex distribution of L1 and L2.

Occult CNS^+ was detected at clinical and haematological remission, or during the first week of CNS prophylaxis in 7 cases. The incidence is highest in L3, and when compared to L1 plus L2 this is significant ($P=0.03$). All these patients subsequently achieved CR. CNS^+ was found in 7 of 22 patients at relapse. In 3 patients with L1, CNS^+ was the primary site of relapse (1° CNS^+). The incidence of 1° CNS^+ at relapse is significantly higher in L1 than L2 ($P=0.03$). CNS^+ at any stage, did not correlate with any of the other clinicopathological features.

Analysis of actuarial remission duration curves of all the groups (Fig. 2) and for L1

Table 2. Clinical features

	L1		L2		L3	
	n	%	*n*	%	*n*	%
Rate of CR	10	71	28	78	2	50
Rate of relapse	5	50	15	54	2	100
CNS^+ at CR	3	30	2	7	2	100
CNS^+ at relapse	3	60	3	20	1	50
1° CNS^+ at relapse	3	60	1	7	1	50

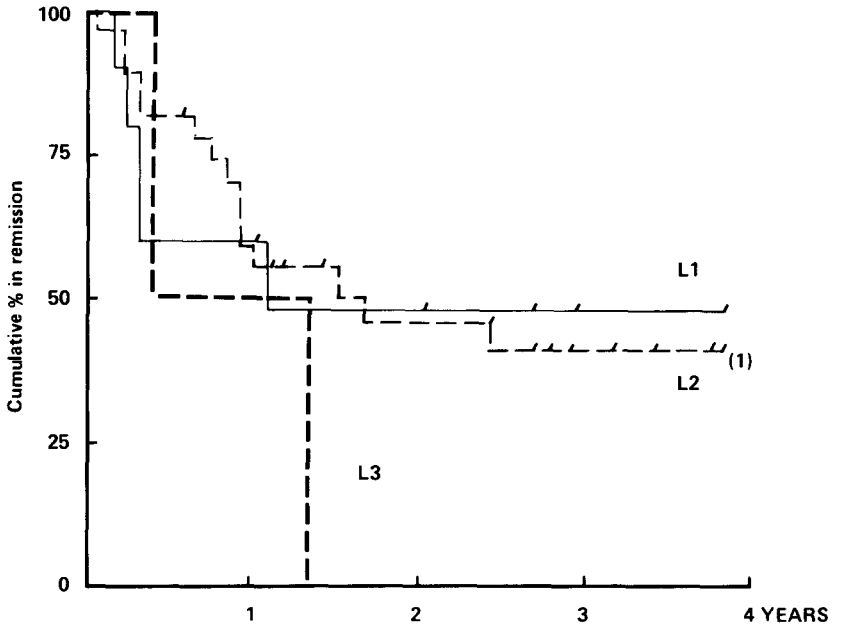

Fig. 2. Actuarial remission duration curves for all cases.

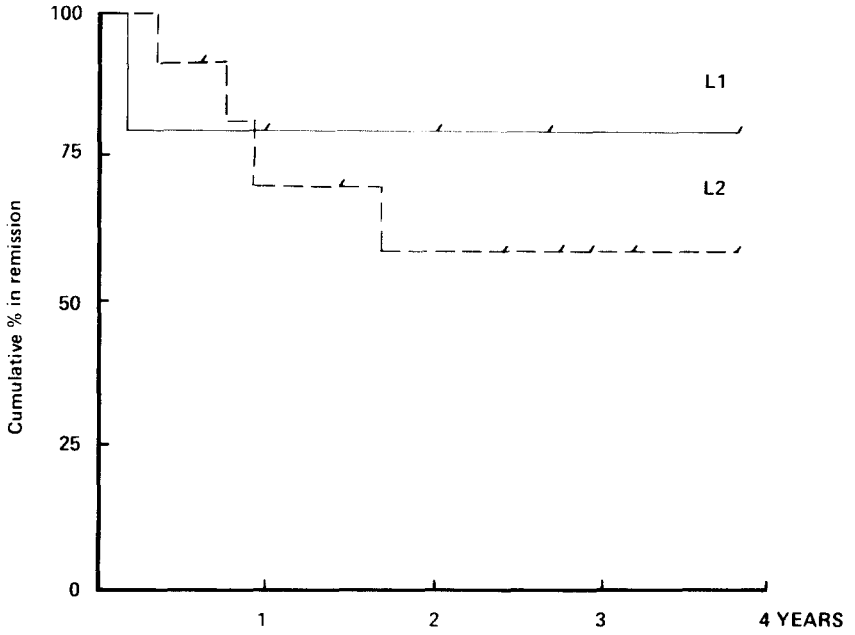

Fig. 3. Actuarial remission duration curves for L1 and L2 with α-ALL⁺, E⁻, SmIg, surface markers.

Table 3. Haematological findings

	L1	L2	L3
Haemoglobin g/dl			
Mean	8.1	9.6	10.9
Range	5.5–12.6	4.4–16.6	7.9–13.6
Blast cells $\times 10^9$/l			
Mean	36.2	40.9	15
Range	0.1–300	0.1–282	0.1–274
Platelets $\times 10^9$/l			
Mean	89	55	85
Range	10–300	10–300	10–274
PAS Positive *n* (%)	9 (64)	22 (61)	—

and L2 with α-ALL⁺, E⁻, SmIg⁻ surface phenotype, (Fig. 3) indicates no significant differences, to July 1978.

Haematological findings at presentation are shown in Table 3 and the results of surface marker studies in Table 4. The PAS reaction is negative by definition in L3 [1, 8]. A single case of L3 was investigated for surface markers and showed α-ALL⁻, E⁻, SmIg⁺. The results indicate that the FAB classification does not predict for significant differences in haematological features or cell surface phenotype.

Table 4 Blast cell surface markers

	L1		L2	
Surface phenotype	*n*	%	*n*	%
α-ALL⁺, E⁻, SmIg⁻	7	58	14	54
α-ALL⁻, E⁺, SmIg⁻	1	8	4	15
α-ALL⁻, E⁻, SmIg⁻	4	33	8	31
Total	12	86	26	72

DISCUSSION

The FAB classification divides common ALL into 2 main groups; L1 which is usually seen in children and L2 which is more frequent in adults. L3 is isomorphous with Burkitt's lymphoma. In the present study, L2 was found in 67% of cases, but there were no significant differences in the mean age (or sex)

of L1 and L2. The classification did not predict haematological findings such as a high blast cell or low platelet count, which are associated with a poor prognosis in children [9, 10].

Adults have a worse prognosis than children, even when treated with similar regimens [11]. Catovsky [12] has suggested that in non-T, non-B, ALL, possession of L2 morphology may be one of the factors involved. We observed no significant differences in the rate or duration of CR, in any of the sub groups, or any significant difference in the duration of remission in L1 and L2 with an α-ALL$^+$, E$^-$, SmIg$^-$ surface phenotype.

A poor prognosis for Burkitt-like leukaemia has been documented previously [2, 13, 14]. In this study, L3 was associated with the lowest rate and duration of CR and the highest incidence of early CNS$^+$ ($P=0.03$).

Brouet *et al.* [15] using a classification similar to FAB, were unable to relate cytology to T, or non-T, non-B, surface phenotype in 100 children and adolescents. Our findings are in agreement with these results. In addition, the FAB classification did not distinguish between α-ALL$^+$ and α-ALL$^-$ in the non-T, non-B (E$^-$, SmIg$^-$) cases.

Belpomme *et al.* [16] classifying ALL on cell size and on assessment of the degree of differentiation, have reported a correlation between 5 morphological sub groups, surface markers and survival in 50 children and adolescents. Thirty-five of the cases, however, were distributed among 4 of their sub groups and had a non-T, non-B, phenotype. With the antiserum of Greaves and co-workers [4–6], the non-T, non-B phenotype (E$^-$, SmIg$^-$) can be divided into α-ALL$^+$ and ALL$^-$. Chessells *et al.* [17] in a study of 94 children, have shown longer remission durations in the α-ALL$^+$ group than in α-ALL$^-$, and Lister *et al.* [18] have shown significant differences in remission duration in 42 adults.

Finally there was a higher incidence of 1° CNS$^+$ at relapse in L1 than in L2 ($P=0.03$). This could not be explained by analysis of other clinical, haematological or immunological data and we are unaware of other studies showing a positive correlation of CNS$^+$ to either L1 or L2.

In conclusion, the proposed FAB classification of acute leukaemias was applied both retrospectively and prospectively to adults with ALL and related to clinicopathological features at presentation. Positive correlations were found between the incidence of early CNS$^+$ and L3 and between 1° CNS$^+$ at relapse and L1. Many more cases must be studied to fully evaluate the FAB classification, and to confirm the present findings.

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