

## DIAGNOSIS OF CENTRAL NERVOUS SYSTEM LEUKAEMIA

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### Summary

Over a 4% year period, 35 patients were diagnosed to have CNS leukaemia after cerebrospinal fluid (CSF) examination following cytocentrifugation. Most of the patients were children who had acute lymphoblastic leukaemia (ALL). It is felt that cytocentrifuge provides a satisfactory cytological preparation and is a more reliable method compared to CSF mononuclear cell count for diagnosis of CNS leukaemia.

Keywords : Central nervous system leukaemia, diagnosis, cytocentrifuge.

### INTRODUCTION

The diagnosis of central nervous system (CNS) leukaemia is important because of its associated morbidity<sup>1,2</sup> and implications for haematological relapse<sup>3,4</sup>. CNS leukaemia occur in about 5–10% of children with acute lymphoblastic leukaemia (ALL) despite prophylactic therapy.<sup>5</sup> Moreover, as more leukaemic patients experience longer bone marrow remissions with modern chemotherapy regimens, CNS leukemia remains a major limiting factor for disease control.<sup>6</sup> There is a need for a fast and reliable method for diagnosis of CNS leukaemia. This report reviews our experience with the use of the cytocentrifuge in the diagnosis of CNS leukaemia at the University Hospital, Kuala Lumpur. The cytocentrifuge method was also compared with the CSF cell count method for diagnosis of CNS leukaemia.

### MATERIALS AND METHODS

*Patients:* Between January 1983 and July 1987, 2280 samples of cerebrospinal fluid (CSF) were examined in the Clinical Diagnostic Laboratory, University Hospital, Kuala Lumpur for of CNS leukaemia. The CSF samples were taken from all paediatric (<14 years old) and adult ALL patients and paediatric acute myeloid leukaemia (AML) patients at diagnosis. Samples from patients during subsequent prophylactic intrathecal treatment and those suspected of CNS leukaemia on follow-up were also examined. The diagnosis of acute leukaemia was based on bone marrow smears and classified using the French, American and British group (FAB) classification.<sup>7</sup>

*Method:* CSF was processed by cytocentri-

fuge (Shandon-Elliot Cytospin SCA – 0030) and the CSF cell count done using a Neubauer chamber within 1 hour of collection.

A) Cytocentrifuge method: 0.5 ml aliquot of CSF was placed in the sample chambers. The chamber, fluid absorption stump and labelled slides were inserted into the cytocentrifuge head. The samples were rotated at 1500 rpm for 10 minutes. Completed slides were dried and stained with Leishman stain for 10 minutes. The diagnosis of CNS leukaemia was based on finding blasts (any number) without clinical evidence of infection and a negative bacteriological culture.<sup>8</sup>

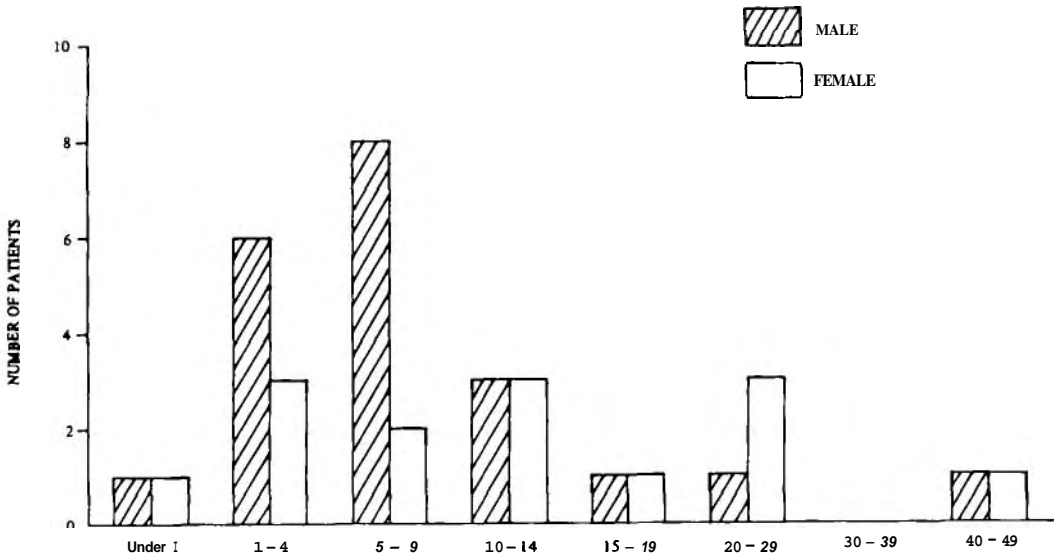
B) CSF cell count: 5 drops of reconstituted CSF was mixed with 5 drops of 0.05% Toluidine stain diluent and then charged into a Neubauer chamber. The number of mononuclear cell/ul was then counted. A CSF cell count > 10 mononuclear cells/ul in the absence of a positive bacteriological culture or gross blood contamination<sup>9</sup> was taken as indicative of CNS leukaemia.

### RESULTS

From 2280 CSF samples examined, 35 cases of CNS leukaemias were detected. The age and sex distribution of these cases are shown in Fig. 1. CNS leukaemia occurred mainly in children as 27 (77%) of patients were ≤ 14 years old. Males outnumbered females by a ratio of 3 to 2.

31 (88.6%) patients with CNS leukaemia had ALL (Table 1). 11 (35%) of ALL patients had L2 subtype. There appeared to be no increase in incidence of CNS leukaemia in L2 subtype as L2 subtype constituted 34%

FIG. 1. AGE AND SEX DISTRIBUTION OF 35 PATIENTS WITH CNS LEUKAEMIA (JANUARY 1983 - JULY 1987)



of the 300 cases of ALL (Department registry) diagnosed in this hospital over the same study period.

Table 2 shows that the cytocentrifuge method detected all cases of CNS leukaemia in this study. Based on the criterion for diagnosis of CNS leukaemia using CSF cell count (> 10 mononuclear cells/ul), 6 patients with positively identifiable blasts by the

TABLE 2  
COMPARISON OF PICK UP OF CNS LEUKAEMIA BY THE CYTOCENTRIFUGE METHOD AND THE CSF COUNT METHOD

	Cytocentrifuge		
	Positive	Negative	Total
CSF Count			
- Positive	29	0	29
Negative	6	2245	2251
	35	2245	2280

TABLE 1  
DISTRIBUTION OF CNS LEUKAEMIA PATIENTS BY FAB CLASSIFICATION

Diagnosis	Number of patients	
ALL	L1	20
	L2	11
AML	M1	1
	M4	1
AUL		2
Total		35

AUL: acute undifferentiated leukaemia.

cytocentrifuge method would have been missed (Table 3). Clearly, diagnosis of CNS leukaemia based on cell count alone is inadequate. The morphology of blasts were satisfactorily preserved in the cytocentrifuge preparation (Fig. 2).

DISCUSSION

Though methods of detecting leukaemic cells in the CSF have improved since the 1960s,

the definition of CNS leukaemia remained inconsistent and controversial.<sup>10</sup> The diagnostic criteria of CNS leukaemia in this study was based on finding morphologically unequivocal blasts in cytocentrifuge samples. However, it is important to exclude specimens contaminated by accidental introduction of peripheral blood blasts or introduction of vertebral bone marrow during a traumatic tap. Any cytocentrifuge preparation showing the presence of red cells should be interpreted with great caution and CSF examination

repeated whenever indicated. False positives can also arise as activated lymphocytes which simulate lymphoblasts can occur in viral infection and also as a reaction to intrathecal drugs.<sup>11</sup> Hence, the cytocentrifuge results should be interpreted in the light of the entire clinical and laboratory picture.<sup>12</sup> The finding of rare blasts by cytocentrifuge with normal CSF findings (i.e. cell count, protein and sugars) should be followed up with a repeat spinal tap in a week's time to clarify the situation. The "traditional" way of diagnosing CNS leukaemia based on a CSF mononuclear cell count of  $>10/\mu\text{l}$  is clearly unsatisfactory. This study showed that leukaemic blasts were identified by the cytocentrifuge method even when CSF cell count was normal. It is thus of advantage to use it as a routine for assessing CSF samples from leukaemic patients.

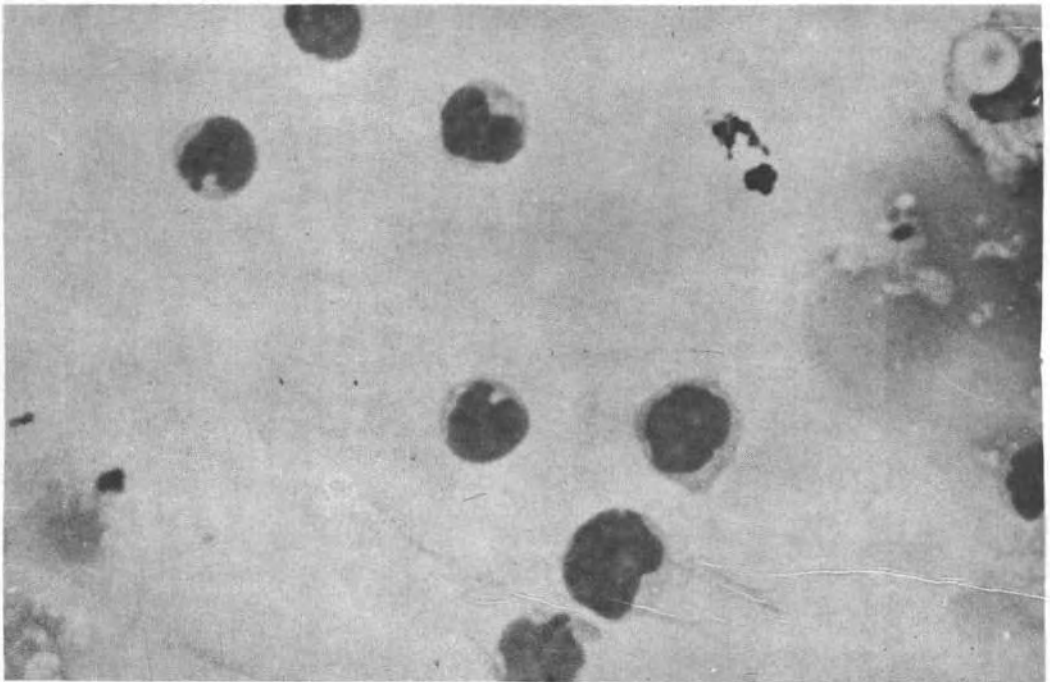
**TABLE 3**  
**CSF CELL COUNT OF**  
**CNS LEUKAEMIA PATIENTS**

Mononuclear cell count/ $\mu\text{l}$	No. of Patients
0-4	4
5-9	2
$> 10$	29

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FIG. 2 Lymphoblasts in cytocentrifuge preparation. Leishman X400.



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