CEREBROSPINAL FLUID LACTATE LEVEL IN CHILDHOOD PURULENT MENINGITIS

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INTRODUCTION

Purulent meningitis is a life-threatening disease which requires prompt diagnosis and management to reduce morbidity and mortality. The diagnosis of purulent meningitis would be definite only if cerebrospinal fluid studies and cultures are used to verify the diagnosis. In clinical practice, physicians may not always be able to differentiate bacterial meningoencephalitis from non-bacterial infection. Antimicrobial agents may have to be prescribed and continued during the course of illness and without bacteriologic confirmation of the diagnosis. The determination of cerebrospinal fluid lactate has been recommended to differentiate bacterial meningitis from other causes of meningitis (Bland *et al.*, 1974; Controni *et al.*, 1977; Brook *et al.*, 1978). However, some controversy remains (Berg *et al.*, 1982). This study was carried out to re-evaluate the diagnostic usefulness of this determination.

MATERIALS AND METHODS

The patients studied were selected from the Department of Pediatrics, Siriraj Hospital, Mahidol University, Bangkok, Thailand. A total of 54 pediatric patients were grouped according to disease. Purulent meningitis was diagnosed by bacterial growth or bacteria found by Gram stain from the cerebrospinal fluid. The combination of negative culture and Gram stain of the cerebrospinal fluid but with a clinical pattern suggestive of bacterial meningitis was grouped as clinical purulent meningitis. Viral or toxic encephalopathy was diagnosed to be non-purulent meningitis. Controls were obtained from normal cytochemical studies of the cerebrospinal fluid. The cerebrospinal fluid protein was measured according to turbidimetric method of Kingsbury (Varley, 1969). The cerebrospinal fluid lactate was determined by enzymatic method of Marbach and Weil (1967).

Table 1

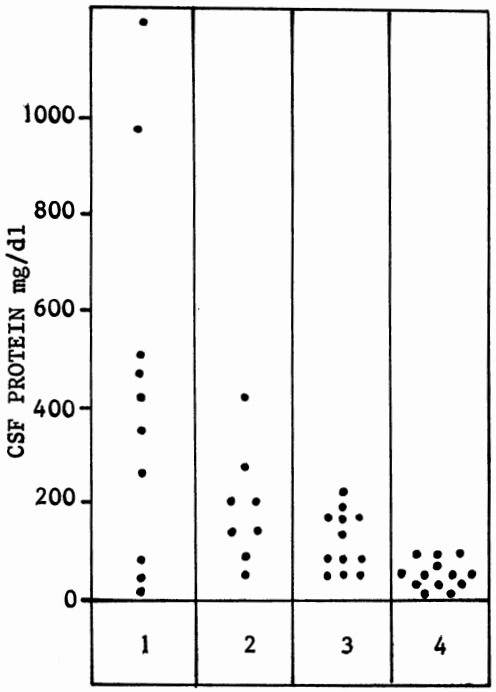
Details of patients and laboratory findings in cerebrospinal fluid.

Diagnosis	No. patients	Sex		Mean age (months)	Mean cell count(c.mm)	Polymorph (%)	Protein (mg/dl)	Lactate (mg/dl)
		male	female					
Purulent meningitis	13	11	2	25	3456	85	504.6	80.4
Clinical purulent meningitis	9	4	5	9	3830	78	188.1	72.7
Nonpurulent meningitis	18	10	8	46	1001	27	78.6	17.0
Controls	14	4	10	29	1	0	27.3	11.8

RESULTS

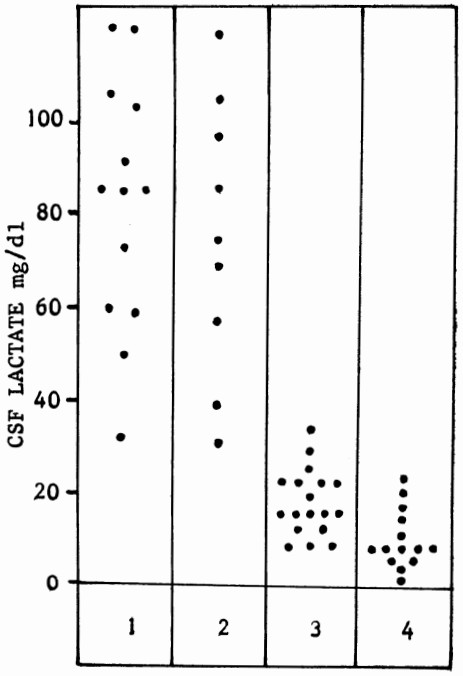
The sex and age of patients and the cytochemical studies of the initial diagnostic sample of the cerebrospinal fluid and lactate measurement in proven purulent meningitis, clinical purulent meningitis, non-purulent meningitis and controls are summarized in Table 1.

The distribution of the cerebrospinal fluid protein and lactate for all groups including the statistically significant differences are demonstrated in Figs. 1 and 2.



1 = Purulent meningitis;
2 = Clinical purulent meningitis;
3 = Non-purulent meningitis;
4 = controls.
1 vs 2, $p > 0.2$; 1 vs 3, $p < 0.05$;
1 vs 4, $p < 0.02$; 2 vs 3, $p < 0.01$;
2 vs 4, $p < 0.001$; 3 vs 4, $p < 0.001$

Fig. 1—Protein in cerebrospinal fluid in patients and controls.



1 = Purulent meningitis;
2 = Clinical purulent meningitis;
3 = Non-purulent meningitis;
4 = Controls.
1 vs 2, $p > 0.5$; 1 vs 3, $p < 0.001$;
1 vs 4, $p < 0.001$; 2 vs 3, $p < 0.001$;
2 vs 4, $p < 0.001$; 3 vs 4, $p < 0.01$

Fig. 2—Cerebrospinal fluid lactate in patients and controls.

The mean lactic acid of the 4 cases of *Hemophilus influenzae* meningitis was found to be 58.2 mg/dl which was lower than the mean of 8 cases of pneumococcal meningitis (89.2 mg/dl). The level of cerebrospinal fluid lactate in the two dead cases of pneumococcal meningitis were not different from those of the survivors. Follow up study of the cerebrospinal fluid lactate was performed in 6 cases of proven purulent meningitis, 5 cases of clinical purulent meningitis and 8 cases of non-purulent meningitis. These values are shown in the Figs. 3 and 4.

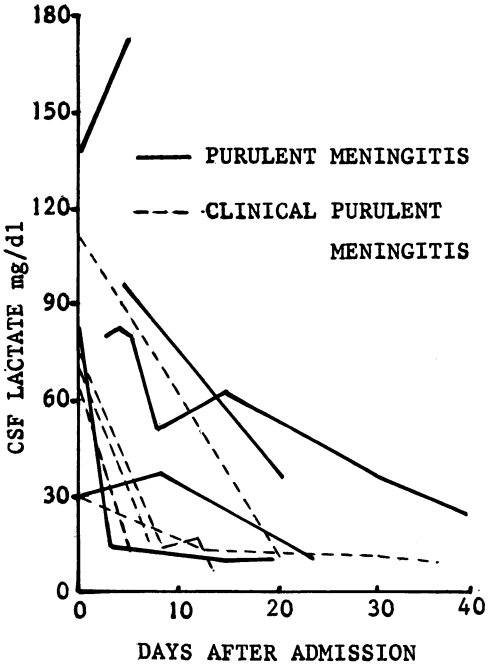


Fig. 3—The cerebrospinal fluid lactate level in each patient with purulent meningitis and clinical purulent meningitis after antimicrobial agents was repeated and showed a decline in lactate level.

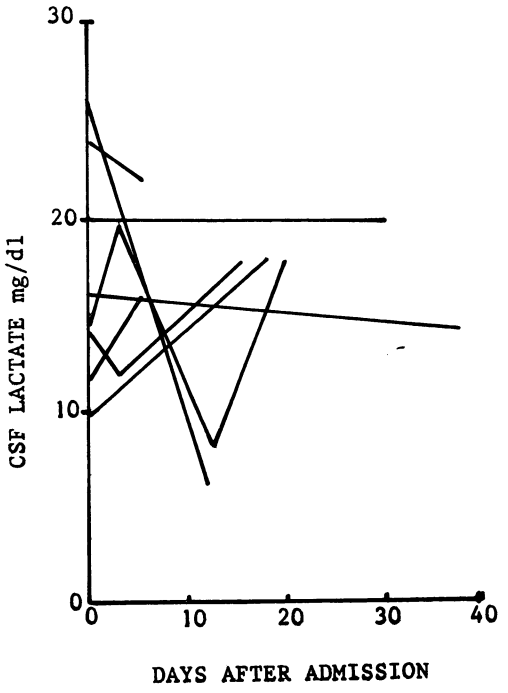


Fig. 4—The cerebrospinal fluid lactate level of non-purulent meningitis remained the same during hospitalization.

DISCUSSIONS

The definitive diagnosis of bacterial meningitis requires positive culture. Occasionally there is only small number of infective organisms in the cerebrospinal fluid and culture may take some time. Counter immunoelectrophoresis with the specific high titer antisera of *Hemophilus*, *Pneumococcus* and *Meningococcus* can be performed when the antimicrobial agents have been given prior to obtaining cerebrospinal fluid. This is less time consuming but is expensive and can provide false positives (Controni *et al.*, 1977). Limulus lysate testing for gram negative endotoxin also requires a large quantity of bacteria (Ross *et al.*, 1975).

Over 50 years ago Nishimura (1924) reported a raised cerebrospinal fluid lactate in bacterial meningitis. A value over 35 mg/dl differentiates bacterial from non-bacterial infection (Bland *et al.*, 1974; Controni *et al.*, 1977; Brook *et al.*, 1978). The mechanisms responsible for this finding are still uncertain. There may be an increase in glucose metabolism via anaerobic glycolysis of cellular elements (Osnato and Killian, 1926; De-Sanctis *et al.*, 1938; Baltch and Osborne, 1957), a decrease in cerebral blood flow due to an increase intracranial pressure (Kopetsky and Fishberg, 1933), or slow clearance of lactate from the cerebrospinal fluid (Alexander *et al.*, 1962; Prokop, 1968). Many studies have shown that lactic acid formation occurs in other bacterial infected spaces such as synovial, peritoneal and pleural cavities (Check, 1979; Chavalittamrong and Angsusingha, 1980). There was no correlation

between blood lactate and lactic acid in these sites or the subarachnoid space. The determination of lactic acid in these sites has been recommended as a diagnostic aid (Check, 1979; Chavalittamrong and Angsusingha, 1980).

This study demonstrated that the mean value of cerebrospinal fluid cell count and polymorphonuclear count were higher in proven purulent and clinical purulent meningitis than in non-purulent meningitis and controls, and cerebrospinal fluid protein was also significantly higher. The cerebrospinal fluid lactate was significantly higher in purulent and clinical purulent meningitis than in non-purulent and controls. This difference was great enough to be of diagnostic usefulness. Although the cerebrospinal fluid lactate in one case of *Streptococcus pneumoniae* was 33.1 mg/dl on the first lumbar puncture, the seven day follow up cerebrospinal fluid lactate remained 42 mg/dl despite appropriate treatment. Lactate determination should be performed simultaneously with culture in every case of clinical purulent meningitis, for when the culture results are negative the lactate level may be helpful.

Cytochemical studies showed an overlap between clinical and non-purulent meningitis. Cerebrospinal fluid lactate (over 35 mg/dl) is a more sensitive discriminant as it was found only in clinical purulent meningitis. Furthermore by the modification of enzymatic determination of lactic acid using the Monotest Lactate Kit (Boehringer-Mannheim. Mannheim, West Germany) and following the technique of Noll, the entire assay required 15 minutes to complete (Noll, 1974).

This study demonstrated correlations between decreasing cerebrospinal fluid lactate and pattern of clinical improvement. The two cases in which cerebrospinal fluid lactate fell slowly developed hydrocephalus later. Follow up cerebrospinal fluid lactate determination may have some predictive value for the development of hydrocephalus.

In conclusion, cerebrospinal fluid lactate is one of the parameters to be considered in suspected cases of bacterial meningitis. With its rapid and sensitive results, physicians are able to decide whether or not to continue antimicrobial agents in suspected cases. A cerebrospinal fluid lactate of over 35 mg/dl may be considered as an absolute indication for the treatment of bacterial meningitis. This should be interpreted along with careful clinical examinations and the standard laboratory tests. Furthermore follow up cerebrospinal fluid studies are important to confirm the diagnostic monitoring improvement of the patients.

SUMMARY

Cerebrospinal fluid lactate was determined in 54 pediatric patients by means of enzymatic method of Marbach and Weil. The mean value of cerebrospinal sfluid lactate in 13 purulent meningitis patients was 80.4 mg/dl, in 9 clinical purulent meningitis patients was 72.7 mg/dl, in 18 non-purulent meningitis patients and 14 controls were 17.0 and 11.8 mg/dl respectively. The present study demonstrated that a cerebrospinal fluid lactate level of 35 mg/dl may be used as a cut off point to differentiate bacterial from non-bacterial infection of the central nervous system. It should served as a supplementary aid to clinical examinations and conventional methods to diagnose bacterial meningitis.

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