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Bromide partition test in the evaluation of the blood-cerebrospinal barrier in children with congenital hypothyroidism and central nervous system disease

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Serum and cerebrospinal fluid bromide partition was studied in 11 children with congenital hypothyroidism, in 12 children with tuberculous meningitis, and in 10 children with various neurological disorders. The ratio serum bromide per cerebrospinal fluid bromide (bromide index) was below the critical value of 1.65 in 5 of 11 children with hypothyroidism as compared with 10 of the 12 children with tuberculous meningitis. No clear correlation was found between the test and the clinical and laboratory signs of hypothyroidism. The test is a valuable index of blood-cerebrospinal fluid barrier involvement in hypothyroidism.

The estimation of differences in the bromide concentration of blood serum and cerebrospinal fluid (CSF) is considered one of the methods for evaluating the integrity of the blood-CSF barrier. In bacterial meningitis, unlike in viral meningitis, an increased leakage of bromide into the CSF was shown [4, 5, 9]. The concentration of bromide in these cases was sometimes higher in the CSF than in the blood serum, so that the method is suitable for differentiating serous meningitis and particularly for the diagnosis of tuberculous meningitis [2], and also for evaluting the course of the disease. The barrier may be disturbed in other diseases too, for example in hypothyroidism with myxoedema [1, 6].

The aim of the present study was to test the bromide partition in cases of congenital hypothyroidism, in a group of children with tuberculous meningitis, and in a group of various central nervous system diseases.

Material and Methods

The material comprised three groups of children. *Group 1.* Eleven children with clinically obvious hypothyroidism. Their data are seen in Table I; a diagnostic lumbar puncture was indicated in all of them. *Group 2.* Twelve children with tuberculous meningitis. The diagnosis was established on the grounds of the symptoms, the course of the disease, the changes in CSF, and by its bacteriological examination. *Group 3.* Ten children with neurological disorders in consequence of inflammatory processes such as bacterial menin-

TABLE I

Main clinical features and results of some specific tests in children with congenital hypothyroidism

Case No.	Initials	Age, years	Sex	Mental retardation	Physical and motor handicap	Typical face, appearance, and body proportions	Typical skin and hair anomalies	Bone age retardation	PBI, µg per 100 ml	Radioiodine uptake per cent	Scintigraphic activity
1.	M. E.	3/12	F	+	+	+++	+	?		0	
2.	Z. A.	16/12	M	+	+	−	+	++			
3.	M. S.	3	F	+++	++	+	+	++	4.2	5	
	after a month			+++	++	+	+	++			
4.	A. T.	12	F	−	−	−	++	−			
5.	P. G.	1	F	+++	+++	+++	++	+++	0.5	3	−
	after 4 years			+++	+++	+++	++	++			
6.	K. G.	6/12	F	+	+	+	+	+	0.5		
7.	S. M.	2	M	+++	++	++	+	++	2.0		+
8.	C. W.	4	M	++	++	++	++	++			
9.	K. E.	5/12	F	++	+++	+++	+++	+			−
10.	S. E.	2/52	F	?	?	+	+	?	0.5		−
11.	K. K.	2/12	F	+	++	++	++	?			−

gitis (2 cases) and viral meningitis (1 case), perinatal cerebral injury and other disturbances.

For three days, sodium bromide solution was given orally in a dose of 0.5—1.5 g daily. On the fourth day venous blood and CSF were obtained, the latter by lumbar puncture. Estimation of bromide in serum and CSF was done by the method of HUNTER and GOLDSPINK [3], first in a macromodification [8], subsequently as a micromethod [7]. The bromide index was calculated as the serum bromide/CSF bromide ratio. Values for the index lower than 1.65 were considered abnormal [2, 5, 9].

RESULTS

In six children with hypothyroidism, the bromide index was normal, while the value was reduced in five cases. A correlation could not be detected between the bromide index and the duration or severity of the disease or the thyroid function tests. In two cases the low bromide index displayed an increasing tendency in the course of substitution therapy (Table II).

In the group of tuberculous meningitis a decrease of the bromide index below the normal level was evident in 10 of 12 children at the beginning of treatment. After 5—6 weeks the values were as a rule higher than the initial ones. In one case the test was repeated after 5 months and the index was normal. In two cases a normal value was obtained in spite of a typical tuberculous meningitis; the ne-

TABLE II
Bromide partition between blood serum and CSF in children with hypothyroidism

Case, No.	Initials	Bromide concentration, mg/100 ml		Bromide index (serum bromide/ CSF bromide ratio)
		in serum	in CSF	
1.	M. E.	9.2	3.6	2.5
2.	Z. A.	25.4	4.5	5.6
3.	M. S.	6.9	11.3	0.6
	after a month	8.9	7.7	1.15
4.	A. T.	24.3	13.0	1.9
5.	P. G.	7.8	4.9	1.6
	after four years	26.1	12.6	2.1
6.	K. G.	0.7	0.7	1.0
7.	S. M.	1.4	0.7	2.0
8.	C. W.	11.2	4.6	2.4
9.	K. E.	15.0	2.0	7.5
10.	S. E.	18.1	31.0	0.6
11.	K. K.	9.7	12.8	0.8

TABLE III
Bromide partition test in children with tuberculous meningitis

Case, No.	Initials	Age years	Bromide concentrations mg/100 ml		Bromide index (serum bromide/ CSF bromide ratio)
			in serum	in CSF	
1.	S. L.	10	10.5	19.2	0.5
	after 5 months		12.2	5.0	2.4
2.*	B. K.	11	9.6	2.7	3.5
3.	H. T.	7	10.0	13.4	0.7
	after 6 weeks		7.6	7.0	1.1
4.	C. E.	8	7.6	6.2	1.2
	after 5 weeks		6.6	4.5	1.5
5.	H. Z.	10	11.6	16.0	0.7
	after 6 weeks		8.8	9.8	0.9
6.*	P. B.	7	13.4	7.6	1.8
	after 6 weeks		15.3	3.3	4.6
7.	M. T.	6	10.6	6.8	1.55
8.	G. T.	10	3.5	3.4	1.0
9.	Z. E.	8	4.3	4.9	0.9
10.	H. U.	7	16.2	22.2	0.7
11.	K. J.	15	6.9	5.5	1.25
12.	J. I.	7	5.0	4.2	1.2

The test was done in an early stage of the disease. The course was mild and only minimal changes were found in the CSF.

TABLE IV

Bromide partition test in children with various CNS diseases

No. of case	Initials	Age, years	Diagnosis	Bromide concentration mg/100 ml		Bromide index
				in serum	in CSF	
1.	B. J.	9	Lymphocytic meningitis	12.8	4.6	2.8
2.	K. J.	4	Purulent meningitis	6.4	6.0	1.1
3.	R. Z.	6/12	Purulent meningitis, pyocephalus	4.6	3.2	1.4
4.	A. K.	6	Recovered from purulent meningitis	8.2	4.4	1.9
5.	S. R.	2/12	Recovered from purulent meningitis	4.4	1.8	2.4
6.	K. J.	1	Recovered from purulent meningitis	12.5	5.6	2.2
7.	Z. K.	3/12	Subdural haematoma	13.6	11.0	1.2
8.	R. D.	10/12	Brain injury	26.4	13.2	2.0
9.	M. D.	5/12	Congenital heart defect, encephalopathy	24.0	14.6	1.6
10.	P. R.	5/12	Coeliac syndrome with encephalopathy	27.6	14.8	1.8

gativity of the test was ascribed to the mild course of the disease in these patients (Table III).

In the group of other CNS lesions, a low bromide index was found in three cases. In two of these, bacterial purulent meningitis was diagnosed (Table IV).

DISCUSSION

Tuberculous meningitis may be considered a model of the permeability of the blood–CSF barrier [5, 6, 10]. The usefulness of the bromide test for evaluating the integrity of that barrier was shown in previous papers and it was stated that the test is particularly helpful for diagnostic purposes and for evaluation of the success of treatment [2].

In meningitis caused by other infections, the permeability to bromide of the blood–CSF barrier was also increased, although not so constantly as in tuberculous meningitis [4, 5]. This was revealed by the present observations, too. In serous meningitis of viral aetiology the bromide index was normal and it was also normal in CNS diseases with or without disorders in CSF circulation.

Reports are scarce concerning the behaviour of the blood — CSF barrier in children with hypothyroidism. Our results seemed to confirm the

lack of any correlation between the clinical and biochemical alterations. It is, however, worthy of note that in five such cases we have found a low bromide index, and that its value was increasing under the effect of substitution treatment.

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