Some observations on magnesium in cerebrospinal fluid

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SYNOPSIS Investigation of 67 patients with neurological disorders (excluding meningitis) showed a mean level of Mg in cerebrospinal fluid of 1.93 ± 0.03 mEq./l. These figures are significantly lower than earlier figures published in the literature. Patients with polyradiculo-neuritis do not show the fall in cerebrospinal fluid Mg levels reported in cases of infective meningitis. The level of Mg in cerebrospinal fluid is maintained in the presence of low levels of plasma Mg.

As pointed out elsewhere (MacIntyre, 1963; Alcock, MacIntyre, and Radde, 1965), our knowledge of the physiology of Mg has remained scanty because based until recently on laborious and rather imprecise methods of estimation. A rapid and accurate flame spectrophotometric method is now available (Alcock, MacIntyre, and Radde, 1960; MacIntyre, 1961), and we have therefore re-examined some basic data relating to Mg in human cerebrospinal fluid and sought to extend them.

PREVIOUS OBSERVATIONS

Cohen (1927) first pointed out that Mg concentrations in human cerebrospinal fluid were on average 20 to 30% higher than in serum. This finding is even more remarkable when it is remembered that only some 70% of serum Mg is freely diffusible. Cohen's original observations were later confirmed by McCance and Watchorn (1931, 1934) and by Hunter and Smith (1960).

Examining the serum and cerebrospinal fluid of 18 hospital in-patients suffering from a variety of neurological disorders, other than meningitis, Cohen (1927) found the mean serum Mg level to be 2.11 mEq./l.¹ and the mean concentration in lumbar cerebrospinal fluid 2.70 mEq./l. McCance and Watchorn (1931), using the same technique, investigated 68 hospital in-patients (37 of them with parenchymatous neurosyphilis) and found mean values of 2.23 mEq./l. and 2.74 mEq./l. respectively. Hunter and Smith (1960), however, using a different microchemical method (Hunter, 1959) give figures nearly 20% lower. They found the mean concentra-

tion of serum Mg in 38 patients 'with mild non-inflammatory neurological conditions' to be 1.61 ± 0.11 mEq./l. and of cerebrospinal fluid 2.23 ± 0.089 mEq./l. It is clear that the normal range of Mg concentration in human cerebrospinal fluid has not yet been established beyond dispute. We have sought to obtain more data to this end.

Cohen (1927) also stressed the constancy of the cerebrospinal fluid level of Mg. He showed that it did not rise in response to an intramuscular injection of $MgSO_4$ which significantly, although transiently, raised the serum Mg level. McCance and Watchorn (1931) confirmed that the cerebrospinal fluid Mg did not rise when plasma levels were raised. The level in cerebrospinal fluid remained remarkably constant under these circumstances; in fact as the plasma Mg rose the cerebrospinal fluid values, expressed as a percentage of plasma levels, fell from 134 to 89%. Although these authors did not report any cases with low plasma Mg levels they concluded that 'the constancy of cerebrospinal fluid Mg can be regarded as an established fact'. Evidence will be presented that this is true, even in cases of tetany with very low plasma Mg levels.

Cohen (1927) finally mentioned that in three patients with meningitis the level of Mg in lumbar cerebrospinal fluid was low, the values approximating those in plasma. Eisler (1928), on the other hand, stated that 'in infective meningitis the cerebrospinal fluid Mg was so constantly raised as to be of diagnostic value'. McCance and Watchorn (1931, 1934) questioned Eisler's 'normal' readings and later confirmed Cohen's observations in relation to meningitis. Hunter and Smith (1960) also confirmed Cohen's data, showing that in tuberculous meningitis a definite gradient occurred between the concentrations of Mg in ventricular, cisternal, and lumbar

¹ Values given in early papers (expressed in mg. per 100 ml.) have been converted into mEq./l. for comparison with more recent data.

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fluids. These facts seem so well established that we have not sought to confirm them. We have demonstrated, however, that in polyradiculo-neuropathy (Guillain-Barré syndrome), a disorder still sometimes suspected of being of infective origin, this breakdown of the 'cerebrospinal fluid plasma barrier' does not occur.

METHODS

We have performed simultaneous estimations of Ca and Mg in both plasma and cerebrospinal fluid in 67 patients suffering from a variety of neurological disorders. Samples were obtained during diagnostic lumbar punctures or during myelography or air encephalography. At the same time blood was collected into heparin, the plasma being promptly separated. Concentrations of Mg and Ca were determined by flame spectrophotometry (MacIntyre, 1961).

RESULTS AND DISCUSSION

The results are recorded in Table I. Three points seem worthy of comment.

1 In 50 patients suffering from psychoneurosis, cerebrovascular disease, cerebral tumours, idiopathic epilepsy, degenerative neurological disorders, and degenerative disorders of the spine with neurological complications, the mean cerebrospinal fluid Mg was $1.88 \text{ mEq.} \pm 0.03 \text{ mEq./l.}$ There were no significant differences between the clinical subgroups. We confirm Cohen's (1927) original observation that in such cases the concentration of Mg is higher in cerebrospinal fluid than in plasma, although our readings for both are substantially lower than those of early investigators. It has been shown that in the dog radioactive ^{28}Mg ions move rapidly and in both directions between plasma and cerebrospinal fluid (Oppelt, MacIntyre, and Rall, 1963). If the same applies to man the 'cerebrospinal fluid/plasma barrier' to Mg must be a functional, not a structural one.

2 Fifteen patients with polyradiculo-neuropathy (Guillain-Barré syndrome) were found to have a normal cerebrospinal fluid Mg (mean $2.09 \text{ mEq./l.} \pm 0.10$). Their spinal fluids did not differ significantly in this respect from those obtained in the various types of non-infective neurological disorder. Unlike what happens in infective meningitis, the gradient between cerebrospinal fluid and plasma Mg is maintained in polyradiculo-neuropathy.

3 The concentration of Mg in cerebrospinal fluid may be maintained in the presence of a low plasma Mg. This has not been previously reported. Particularly interesting in this respect were our observations on two cases of infantile tetany.

ILLUSTRATIVE CASES

H.R. (H.H. 264653) A full-term female infant, born at home by normal delivery, was admitted eight days after birth. Forty-eight hours previously she had refused feeds and vomited. Later she had had three major seizures. Her general condition was good. The Moro response was excessively brisk and a positive Trousseau sign was noted. Serum Ca was 3.5 mEq./l. , serum Mg 0.7 mEq./l. ; cerebrospinal fluid Ca 2.1 mEq./l. , cerebrospinal fluid Mg 1.8 mEq./l. She improved on parathormone and vitamin D and did not relapse when these were discontinued.

K.B. (H.H. 265381) A female infant, the second of twins, was born in hospital by assisted breech delivery. On the eighth day twitching was noticed in the right arm, right leg, and right side of the face. She had several further attacks in the next 48 hours. She was very irritable and the Trousseau sign was positive. Serum Ca was 3.8 mEq./l. , serum Mg 1.2 mEq./l. , later falling to 0.9 mEq./l. ; cerebrospinal fluid Ca 3.0 mEq./l. , cerebrospinal fluid Mg 2.2 mEq./l. She responded promptly to parathormone and did not relapse when this was discontinued.

These two cases provide further evidence that cerebrospinal fluid is not a plasma ultrafiltrate but is produced by mechanisms involving active transport.

TABLE I
SUMMARY OF RESULTS

Diagnosis	Number of Cases	Blood (mEq./l.)		Cerebrospinal Fluid (mEq./l.)	
		Ca	Mg	Ca	Mg
Psychoneurosis	7	5.13 ± 0.08	1.69 ± 0.06	1.91 ± 0.03	1.79 ± 0.03
Cerebral arteriosclerosis	5	5.16 ± 0.07	1.66 ± 0.07	1.98 ± 0.02	1.90 ± 0.05
Cerebral tumours (primary)	7	5.17 ± 0.03	1.54 ± 0.04	1.87 ± 0.03	1.99 ± 0.07
Idiopathic epilepsy	6	5.12 ± 0.05	1.74 ± 0.06	1.97 ± 0.06	1.77 ± 0.13
Disseminated sclerosis	5	5.05 ± 0.05	1.68 ± 0.10	1.98 ± 0.04	1.90 ± 0.05
Motor neurone disease	5	5.06 ± 0.04	1.60 ± 0.08	1.96 ± 0.07	1.94 ± 0.07
Syringomyelia	2	5.25	1.65	2.1	1.85
Trigeminal neuralgia	3	4.93	1.47	1.87	1.80
Spondylosis	10	5.12 ± 0.06	1.71 ± 0.03	2.03 ± 0.06	1.94 ± 0.06
Polyradiculo-neuritis (Guillain-Barré syndrome)	15	5.16 ± 0.05	1.67 ± 0.05	1.99 ± 0.03	2.09 ± 0.10
Infantile tetany	Case H.R.	3.5	0.7	2.1	1.8
	Case K.B.	3.8	1.2 (later 0.9)	3.0	2.2

They illustrate a further point, namely, that even when seizures occur in magnesium-depleted patients, a low level of magnesium in the cerebrospinal fluid plays no part in their pathogenesis.

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