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CSF magnesium levels in diseases with brain symptoms in Ghanaian children*)

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Zusammenfassung

Bei 1 300 Kindern aus Ghana wurden die Mg-Konzentrationen mittels AAS (Hitachi) ermittelt in Plasma (P-Mg), Erythrozyten (E-Mg) und Liquor cerebrospinalis (L-Mg); weiter wurden die Blutgaswerte mit der Astrup-Methode gemessen.

Als Normalwerte wurden ermittelt: P-Mg: $1,79 \pm 0,14$ mEq/l; E-Mg: $4,22 \pm 0,40$ mEq/l; L-Mg: $1,97 \pm 0,41$ mEq/l; P-pH: $7,358 \pm 0,028$; L-pH: $7,320 \pm 0,053$. — Bei Meningitiden und anderen, mit Krämpfen einhergehenden Erkrankungen lagen P-Mg und E-Mg im Normbereich, dagegen waren L-Mg und das Verhältnis L-Mg zu P-Mg in der akuten Phase erhöht; eine Normalisierung erfolgte im Zuge der Genesung. P-pH war bei beiden Kollektiven gegenüber der Norm erniedrigt und normalisierte sich ebenfalls während der Genesung. Es wird angenommen, daß ein Übertritt von intracellulärem Mg in den Liquor für die erhöhten L-Mg-Gehalte verantwortlich ist.

Summary

Mg concentrations were studied in plasma (P-Mg), red cells (E-Mg), and cerebro-spinal fluid (C.S.F.-Mg), using Shimadzu Atomic Absorption Spectrophotometer, and blood gas analyses were performed using the Astrup method, on 1 300 Ghanaian children.

The normal values were established thus: P-Mg, 1.79 ± 0.14 mEq/L. E-Mg 4.22 ± 0.40 mEq/L. C.S.F.-Mg 1.97 ± 0.41 mEq/L. P-pH 7.358 ± 0.028 . C.S.F.-pH 7.320 ± 0.053 . In the meningitides and other convulsive diseases the P-Mg and E-Mg were within normal limits, but the C.S.F.-Mg and the ratio of C.S.F.-Mg to P-Mg showed values higher than normal in the acute phase, these values returning to normal in the

Abbreviations used:

P-Mg:	plasma magnesium concentration
E-Mg:	erythrocyte magnesium concentration
CSF-Mg:	cerebrospinal fluid magnesium concentration
CNS:	central nervous system
B-pH:	venous blood pH

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convalescent phase. P-pH was found to be lower in the convulsive group as compared with the normal value and with the meningitides group as compared to the normal values, and returned to normal during convalescence. We suggest that movement of Mg from inside brain cells into the C.S.F. accounts for the higher C.S.F.-Mg values obtained.

Résumé

Les concentrations du Mg ont été étudiées dans le plasma (P-Mg), les érythrocytes (E-Mg), et le LCR (LCR-Mg), en utilisant un spectrophotomètre d'absorption atomique Shimadzu, et les analyses des gaz sanguins ont été effectuées en utilisant le procédé d'Astrup, chez 1 300 enfants Ghanéens.

Les valeurs normales ont été établies ainsi: P-Mg: $1,79 \pm 0,14$ meq/l, E-Mg: $4,22 \pm 0,40$ meq/l, LCR-Mg: $1,97 \pm 0,41$ meq/l, P-pH $7,358 \pm 0,028$, LCR-pH: $7,320 \pm 0,053$. Dans la méningite et dans d'autres affections convulsives, les P-Mg et E-Mg ont été à l'intérieur des limites normales, mais le CSF-Mg et le rapport de LCR-Mg à P-Mg a présenté des valeurs plus élevées que la normale dans la phase aiguë, ces valeurs retournant à la normale dans la phase de convalescence. Nous suggérons que le déplacement du Mg de l'intérieur des cellules cérébrales dans le LCR rend compte des valeurs plus élevées obtenues de LCR-Mg.

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Introduction

Magnesium, existing much in an intracellular phase next to potassium, has direct effects on muscle contraction and nervous stimulation system and then takes part in energy production as a co-activator to many enzymes. The study of magnesium metabolism has lagged behind of other electrolytes because of technical difficulties with the method of determination. Since the recent development of the Atomic Absorption Spectrophotometer, many investigators have reported on various aspects of the subject. In pediatrics, the cause of hyper and/or hypomagnesemia were reported to be depend on neonatal speciality [1—4], gastrointestinal, renal, endocrine disorders, diuretic, radiation, dialytic therapy, excess Mg intake, dehydration and so on [5, 6]. Looking through these literatures we were unable to find the subject of metabolism in diseases with brain symptoms dealt with. We therefore set out to look into this, and our findings from the basis of this report.

Materials and method

From June 1976 to December 1977 magnesium concentration and acid-base balance were measured in the plasma, erythrocyte and CSF in 326 Ghanaian children, who were seen at the clinics or ward of Dept. of Child Health, University of Ghana Medical School, aged ranging between

0 and 15 years old. Specimens collected from 222 cases on the convalescent period were analysed to establish standard values in Ghanaian children.

3 ml of venous blood specimen, collected from cubital or femoral vein using a heparinized disposable syringe, was separated into Wintrobe tube and a disposal test tube and then these tubes were sealed tightly by Parafilm. After a hundred times dilution with 1 % SrCl₂ solution, whole blood and plasma Mg concentration were determined with the Shimadzu Atomic Absorption Spectrophotometer model AA-660-S. The erythrocyte Mg concentration was calculated by the indirect method as follows;

$$E-Mg = \frac{\text{whole blood Mg} - P-Mg(1 - Ht.)}{Ht.}$$

Acid-base balance in blood and CSF was measured by Radiometer Blood-Gas Analyzer model BMS-MK2.

Results

(A) Studies in normal Ghanaian children

These were taken from children whose investigation included examination of blood and CSF though they did not necessarily have diseases referable to these organs.

1. P-Mg

The 222 children in this category were grouped as follows in the Table 1. The overall normal value was found to be 1.79 ± 0.14 mEq/L. Group (b) had higher values, and group (d) lower values than the overall normal. Group (a) was further subdivided according to the differences in month after birth. The steady rise in P-Mg concentration from birth to age one is noted.

2. E-Mg

The E-Mg, calculated by the indirect method, is shown in the Table 1, with the normal value found to be 4.22 ± 0.40 mEq/L.

3. CSF-Mg

The Table 1 also shows our established CSF-Mg value for normal Ghanaian children. There is no significant difference between the groups.

4. Ratio of CSF-Mg to P-Mg

This ratio we established to be 1.070 ± 0.231 (Table 1).

5. Venous blood pH

The value for the overall normal of 7.358 ± 0.028 is shown in the Table 2.

6. CSF-pH

The CSF and blood samples were collected and analysed at the same time. The value of 7.320 ± 0.053 has been established as the normal for Ghanaian children (Table 2).

7. Ratio of CSF-pH to venous blood-pH

This value has been found to be $0.995 \pm 0,008$ (Table 2).

(B) Studies in diseases showing brain symptoms

Categories of diseases studied in this connection are shown in the Table 3. All the 104 patients were acutely ill on admission.

(a) Various meningitides.

1. CSF-Mg (Fig. 1)

On admission most of these patients had CSF-Mg levels well above normal. In each individual as well as in the group as a whole the CSF-Mg

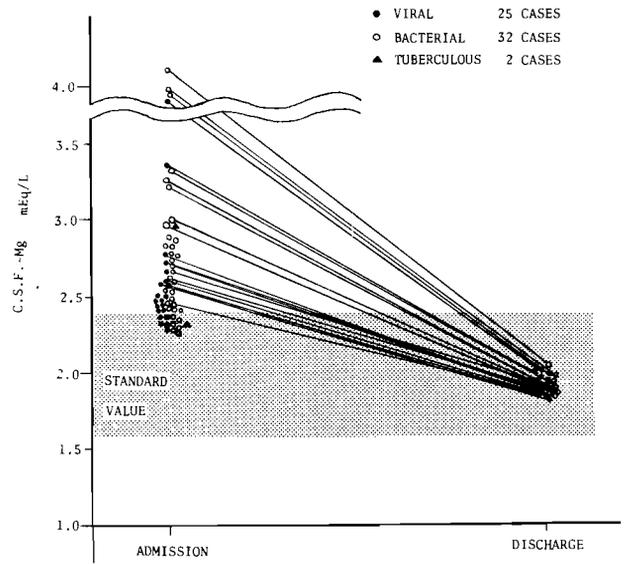


Fig. 1: C.S.F.-Mg levels in various meningitides

Tab. 1: Standard values in normal Ghanaian children

Ages (years)	P-Mg (mEq/L)	E-Mg (mEq/L)	No. of cases	CSF-Mg (mEq/L)	Ratio of CSF-Mg to P-Mg	No. of cases
(a) 0—1	1.78 ± 0.19	4.26 ± 0.39	78	1.99 ± 0.06	1.08 ± 0.243	18
1) 0—1/12	1.60 ± 0.17	4.35 ± 0.36	20			
2) 1/12—2/12	1.71 ± 0.16	4.25 ± 0.24	4			
3) 2/12—3/12	1.79 ± 0.16	4.31 ± 0.42	6			
4) 3/12—11/12	1.82 ± 0.19	4.22 ± 0.27	48			
(b) 1—3	1.84 ± 0.17	4.24 ± 0.41	57	1.97 ± 0.08	1.07 ± 0.196	20
(c) 3—5	1.79 ± 0.15	4.33 ± 0.45	32	1.96 ± 0.07	1.09 ± 0.185	21
(d) 5—10	1.70 ± 0.12	4.05 ± 0.45	28	1.98 ± 0.05	1.14 ± 0.158	16
(e) over 10	1.79 ± 0.11	3.91 ± 0.32	28	1.97 ± 0.05	1.10 ± 0.175	15
Overall value	1.79 ± 0.14	4.22 ± 0.40	222	1.97 ± 0.41	1.70 ± 0.231	90

Tab. 2: Standard values in normal Ghanaian children

Ages (year)	Venous blood-pH	CSF-pH	Ratio of CSF-pH to blood-pH	No. of cases
(a) 0—1	7.353 ± 0.030	7.314 ± 0.048	0.994 ± 0.010	59
(b) 1—3	7.351 ± 0.030	7.325 ± 0.052	0.992 ± 0.007	43
(c) 3—5	7.357 ± 0.030	7.318 ± 0.056	0.997 ± 0.008	28
(d) 5—10	7.358 ± 0.024	7.320 ± 0.049	0.993 ± 0.008	26
(e) over 10	7.357 ± 0.032	7.196 ± 0.048	0.995 ± 0.007	24
Overall value	7.358 ± 0.028	7.320 ± 0.053	0.995 ± 0.008	191

Tab. 3: Mg and pH values in diseases with brain symptoms

On admission

Diseases	No. of cases	P-Mg (mEq/L)	CSF-Mg (mEq/L)	Ratio of CSF-Mg to P-Mg	Blood-pH	CSF-pH	Ratio of CSF-pH to blood-pH
Normal children	222	1.79 ± 0.14	1.97 ± 0.41	1.070 ± 0.231	7.358 ± 0.028	7.320 ± 0.053	0.995 ± 0.008
All meningitides	59	1.77 ± 0.35	2.63 ± 0.48	1.530 ± 0.284	7.346 ± 0.032	7.263 ± 0.911	0.987 ± 0.010
Bacterial meningitis	32	1.60 ± 0.31	2.73 ± 0.68	1.714 ± 0.248	7.361 ± 0.035	7.253 ± 0.105	0.987 ± 0.010
Virus meningitis	25	1.86 ± 0.23	2.51 ± 0.40	1.304 ± 0.056	7.325 ± 0.023	7.277 ± 0.071	0.988 ± 0.010
T.B. meningitis	2	1.54 ± 0.38	2.48 ± 0.46	1.610 ± 0.089	7.338 ± 0.016	7.211 ± 0.003	0.984 ± 0.006
Febrile convulsion	7	1.74 ± 0.18	2.65 ± 0.20	1.436 ± 0.116	7.310 ± 0.069	7.320 ± 0.064	0.998 ± 0.006
Epilepsy	6	1.78 ± 0.33	2.50 ± 0.38	1.426 ± 0.244	7.330 ± 0.028	7.333 ± 0.032	1.000 ± 0.002
Cerebral malaria	32	1.75 ± 0.21	2.56 ± 0.21	1.430 ± 0.231	7.336 ± 0.036	7.322 ± 0.054	1.000 ± 0.020

On discharge

All meningitides	27	1.69 ± 0.20	1.91 ± 0.10	1.125 ± 0.021	7.344 ± 0.021	7.317 ± 0.037	0.993 ± 0.007
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reverted to normal with treatment. Patients with bacterial meningitis had higher CSF values on admission when they were compared with other groups, with the t-test at 5% significance. The presenting symptoms improved in parallel with CSF-Mg levels (Fig. 2).

2. Relation between CSF-Mg and CSF-K

CSF-Mg showed a positive correlation with CSF-K and the coefficient was -0.589 .

3. Ratio of CSF-Mg to P-Mg

It will be noted that the values are distinctly higher in the group with bacterial meningitis as compared with the viral meningitis group.

4. CSF-pH

Most patients had lower CSF-pH than normal on admission, with correlation to normal before discharge. In most cases the improvement in CSF-pH matched the clinical impression of recovery from symptoms as shown in the Fig. 3.

5. Relation between CSF-pH and Mg

The coefficient of correlation was -0.694 . CSF-pH also negatively correlated with CSF-K and the coefficient was -0.672 .

b) Various convulsive diseases.

There were seven cases of febrile convulsion and six of epilepsy, all with acute symptoms, for

whom full results are available. They are included, in spite of the small numbers, because of the close proximity of the convulsion to the time of studying the samples.

1. CSF-Mg

Complete results are available in only a few patients. On the whole the high admission values tended to fall to within the normal range with treatment as shown in the Fig. 4.

2. Ratio of CSF-Mg to P-Mg

The ratio of CSF-Mg to P-Mg had again the high admission values tending to return to normal in the convalescent period.

Discussion

Apart from the P-Mg and the E-Mg, we found no significant difference in the values between the groups and also between the sexes. Our P-Mg value of 1.79 ± 0.14 mEq/L is comparable with the values of 1.60 to 2.10 mEq/L published for other national groups [2, 3, 5—7]. Our finding of a gradual rise in P-Mg levels with age up to age one is also in accord with other authors' results. Normal E-Mg values have been quoted as 3.5 to 5.0 mEq/L [7, 8]. Our figures of 4.22 ± 0.40 mEq/L are not different. Our CSF and venous pH values are also similar to other published figures. The reported normal CSF-Mg values

MENINGOCOCCAL MENINGITIS (O.H., 5 Y. 8 M., ♀)

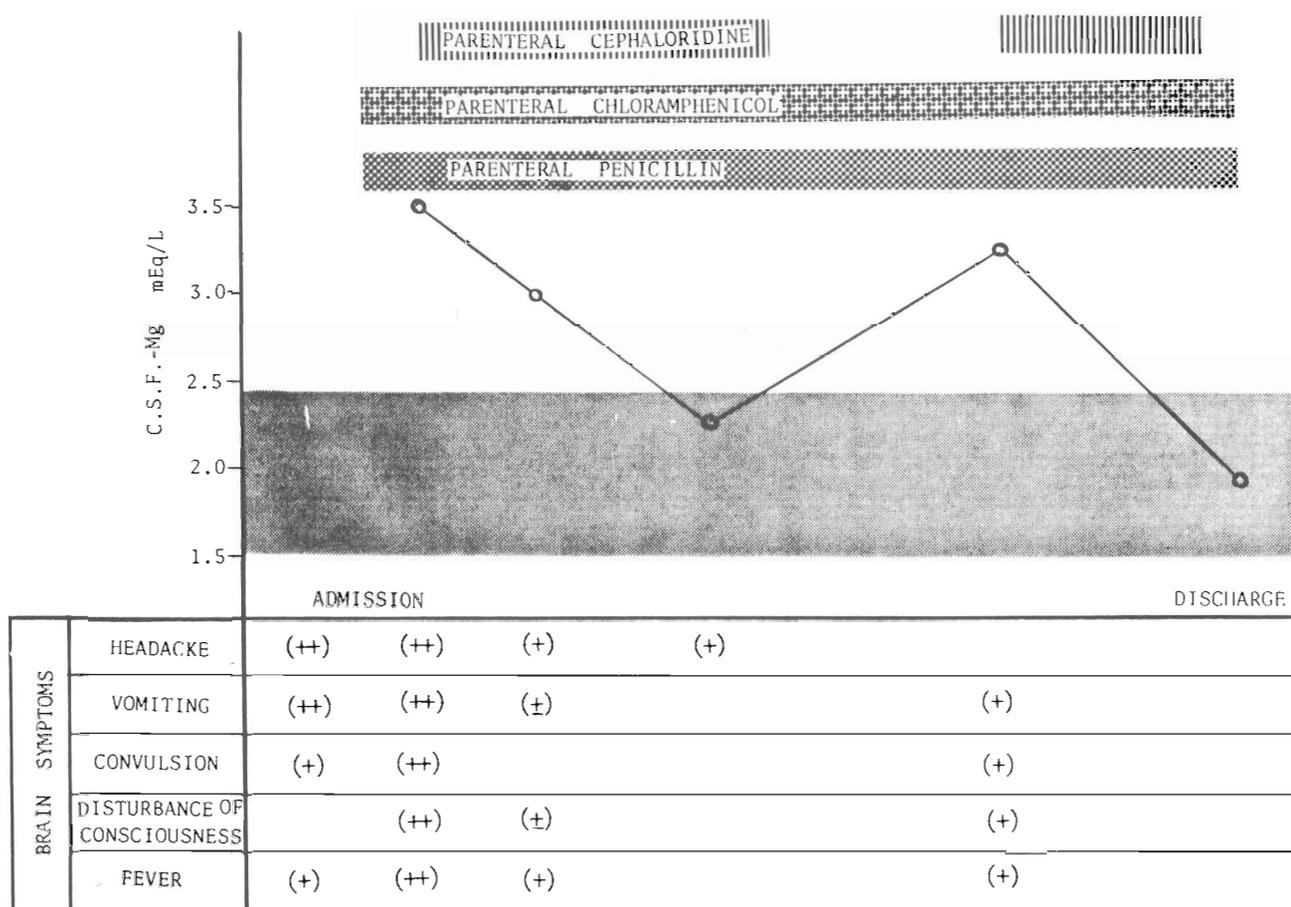


Fig. 2: Correlation between C.S.F.-Mg and brain symptoms

measured by the Atomic Absorption Spectrophotometer, ranging from 2.02 to 2.30 mEq/L are significantly higher than our value of 1.97 ± 0.41 mEq/L. Since Cohen [9] reported that CSF-Mg was 20—30% higher than P-Mg, there have been several reports, some performed by the atomic absorption method, confirming his statement. However we were unable to find any specific reports where the P-Mg and CSF-Mg were collected and analysed at the same time. This is what we have done, with a ratio of 1.071 ± 0.231 . Furthermore we have not found any reports of the ratio of CSF-pH to venous blood-pH, with both samples taken and analysed at the same time. We have established that for normal Ghanaian children this ratio is 0.995 ± 0.008 .

Several authors have shown a rise in CSF-GOT [10], LDH [11], CPK [12] and Cholinesterase enzymes in various CNS diseases. Our patients with meningitides and other convulsive

diseases demonstrated a variation in the CSF-Mg and pH levels in parallel with symptoms, a positive correlation in the CSF-K to Mg values, and a negative correlation between the CSF-pH and CSF-Mg. Our samples were taken and examined concurrently and in particular the admission specimens were obtained fairly close to the actual convulsive episodes. In the past derangement in the plasma to CSF electrolyte composition has been thought to be due to abnormality of the blood-brain barrier. If that were so our results and those of the previous authors would be difficult to explain. We propose the following alternative mechanism. Mg, like potassium, is an intracellular cation, and therefore requires intact cell membrane metabolism to maintain it in the intracellular compartment. Damage to the cell membrane's functional system will predispose to escape of intracellular cation K and Mg, as well as enzymes-GOT, LDH and CPK, etc. without neces-

MENINGOCOCCAL MENINGITIS (O.H., 5 Y. 8 M., ♀)

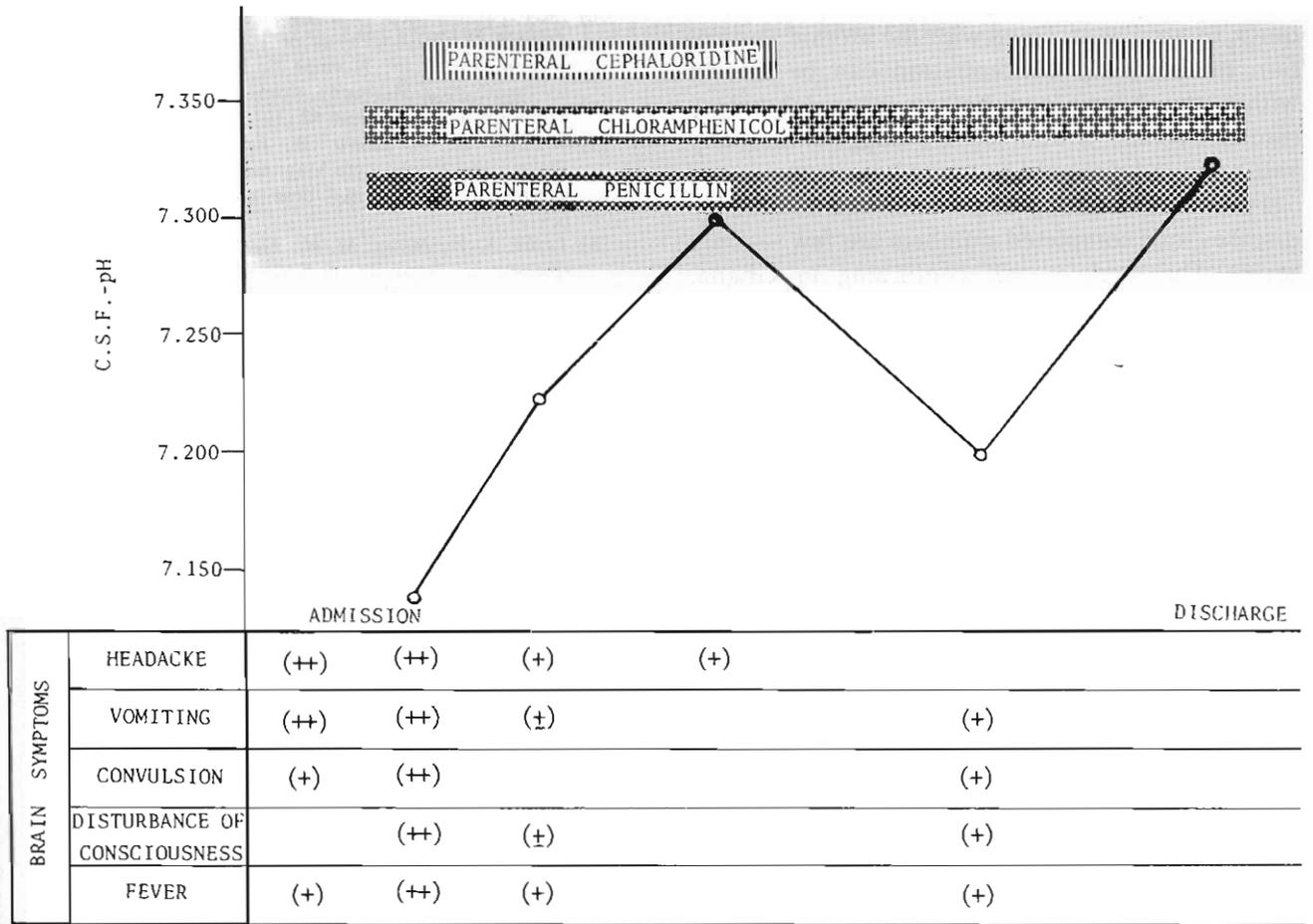


Fig. 3: Correlation between C.S.F.-pH and brain symptoms

sarily causing cell death. Factors likely to cause this type of damage are infective toxins as in meningitis, or hypoxia as in prolonged convulsions. The more severe the damage the more deranged the biochemical findings, as in our patients with bacterial meningitis, in whom there was a positive correlation between the CSF-K and Mg. It will be remembered that these patients also had very high CSF-Mg levels on admission. However we were not able to show a clearly negative correlation between the CSF-pH and Mg in our patients who presented with convulsion without meningitis. We think that this is explained by the episodic nature of convulsions, allowing brain cells to start recovering very soon after the ictal episodes.

We recommended adoption of the ratio of CSF-Mg to P-Mg as a useful indicator of the derangement in cellular metabolism. In our figures the normal was found to be 1.070 ± 0.231 . The patients with meningitis had an overall figure of

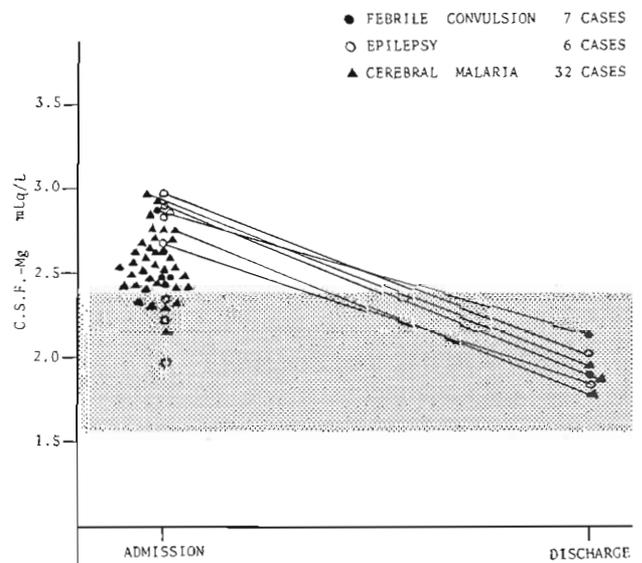


Fig. 4: C.S.F.-Mg levels in various convulsive diseases

1.530 \pm 0.284. The lowest group, with viral meningitis, had a value of 1.304 \pm 0.056. The ratio is quick to arrive at, since with the atomic absorption method, Mg concentration can be known within the hour, long before other laboratory results become available. We suggest that any value above 1.4 should be treated as urgent.

Finally in the group of patients with convulsive diseases, our completed numbers are few — only seven. The work is still continuing in Ghana. However our conclusion is, so far, in accord with the previous findings of Tanuma [13] in Japanese children.

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