

## THE EFFECTIVE USE OF SMALL NON-DEHYDRATING DOSES OF EPSOM SALT IN EPILEPSY: A STUDY OF ONE HUNDRED AND NINE CASES\*

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ELEVATION of blood magnesium to excess produces coma.<sup>1</sup> Elevation of blood magnesium in moderation produces drowsiness. This sedative effect is applied therapeutically in the control of uræmic<sup>2</sup> and eclamptic<sup>3</sup> convulsions by intravenous magnesium sulphate.

The converse of this, depression of blood magnesium, produces parathyroid tetany. The latter has been developed experimentally in rats<sup>4</sup> on diets deficient in magnesium and may occur clinically with low blood magnesium.<sup>5</sup> Nevertheless, there is no change in magnesæmia after removal of the parathyroid glands in animals.<sup>6</sup> Convulsions with hypomagnesæmia have been described in other conditions, such as chorea and pneumonia.<sup>5</sup>

Hirschfelder<sup>5</sup> recently reported 10 patients with low blood magnesium, who suffered from convulsions or muscular twitchings. Four of these patients had kidney lesions. After single 20 to 25 gm. doses of Epsom salt were administered by mouth to these four, the magnesium in the plasma rose almost to double the normal concentration within four to six hours, and the twitchings or seizures subsided. Hirschfelder concluded that convulsions are relieved by oral magnesium sulphate in patients with renal insufficiency.

### METHOD

In view of these findings the blood magnesium in a series of patients subject to epileptiform seizures was studied at St. Elizabeth's Hospital. A normal value for magnesium in blood was first established. Colorimetric estimation on Folin-Wu blood filtrate with titan yellow as the specific reagent, a modification of the Hirschfelder and Serles technique,<sup>7</sup> was used. In a group of 15 controls findings ranged from 2.9 to 4.0 mgm. of magnesium per 100 c.cm. of whole blood. The controls were individuals most of whom had never taken a dose of Epsom salt or milk of magnesia, the remainder not having had either cathartic for six months prior to the estimations. They

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consisted of nine cases of dementia præcox, two of general paresis not subject to convulsions, one patient formerly epileptic, but free from fits for ten years, two technicians and the writer. An average normal value of 3.61 mgm. of magnesium per 100 c.cm. of whole blood was calculated.

One hundred and nine male patients subject to generalized convulsive seizures with loss of consciousness were selected. Prior to similar blood magnesium determinations in these, they were prohibited from having Epsom salt or milk of magnesia for a period of two months to forestall unnaturally high concentrations of magnesium in the blood. In spite of this, estimations in 100 of these patients ranged from 2.67 to 4.8 mgm., with an average value of 3.47 mgm. They were studied for a preliminary six-month period, when the usual methods employed in the treatment of epilepsy were used: phenobarbital, sodium bromide, belladonna, ketogenic diet, fluid limitation, general hygiene, psychotherapy and in some cases an occasional dose of Epsom salt. Following this, the above medication was discontinued, and for a succeeding six-month period, daily, small, measured, oral feedings of magnesium sulphate were administered at 6 a.m. to a group of those patients, who presented low concentrations of magnesium in the blood, using another lot as control epileptics. Doses were so small that diarrhoea did not follow; and fluids were not limited, so that dehydration played no part.

It was thought that the frequency of seizures might be reduced by this procedure for the following reasons:—

1. Rats on magnesium-free diets develop convulsions.
2. Reduction of the plasma magnesium is accompanied by hyper-irritability of the neuromuscular system, occasionally muscular twitchings or convulsions.
3. Intravenous magnesium sulphate controls seizures.

The cases for the administration of magnesium sulphate were selected on the following basis: (1) Comparatively low blood magnesium; (2) frequent seizures; (3) good kidney function, estimated by frequent urine examinations, a blood non-protein nitrogen and concentration and dilution tests when indicated, Hirschfelder<sup>5</sup> having demonstrated the importance of avoiding hypermagnæmia and resultant coma in kidney disease.

These numbered 74. Their doses of magnesium sulphate were measured in 0.6, 1.0, 2.5, 5.0, 8.5, 11, and 17 gm. quantities, each patient receiving the largest dose that he could take without developing watery stools. The salt was always given in a full 8-ounce glass of water, additional fluid being permitted in unlimited quantity. Each patient was carefully questioned and watched for diarrhoea.

The cases used as control epileptics were selected as such, because: (1) they had normal or high blood magnesium; (2) fewer seizures; (3) poor kidney function or severe illness; (4) they were uncooperative due to psychosis. These numbered 35. They received  $\frac{1}{2}$  to 2 ounces of mineral oil every morning.

## RESULTS

Under Epsom salt treatment 33 patients (30·3 per cent.) were benefited, improvement being estimated from the decrease in frequency of seizures. For example, convulsions were reduced from 29 to 0, 8 to 0, 3 to 0, 11 to 1, 4 to 1, 3 to 1, 19 to 7, 8 to 3, 17 to 7, etc. One patient who took milk of magnesia was included in this group. Two (1·8 per cent.) died before studies could be completed, six (5·5 per cent.) neither improved nor became worse, and 33 (30·3 per cent.) developed more convulsions. Under mineral oil therapy eight patients (7·3 per cent.) improved, 13 (11·9 per cent.) showed no change and 14 (12·8 per cent.) developed more seizures.

At first glance it would appear that the improvement in 33 and the decline in 33 others under an Epsom salt regime indicated that each group benefited or became worse respectively, purely by chance, and that magnesium sulphate was without effect. Careful study demonstrates that this is not the case. Whereas those patients who improved took magnesium sulphate regularly for the most part, the unimproved by contrast frequently took their medication irregularly. One patient had no convulsions in the six months of salt therapy until the last, when medication was refused. In another case there was a steady decrease in the number of seizures, until the last month, when salts were taken irregularly. Four patients showed terminal increases in seizures with little or no medication in the last months. One man made slight improvement under irregular medication. Of the group who showed the same number or more convulsions with Epsom salt, 15 were extremely uncooperative, rarely taking their medication, and one on milk of magnesia had had the same medicine plus luminal for the first six months. In this salt-poor group there were many who continued to improve, until they began taking the magnesium sulphate irregularly, when occasionally a status epilepticus developed. In these, luminal in heavy dosage had to be administered to terminate a series of convulsions. Even here in these unresponsive cases it was striking that whenever *daily* Epsom salt was taken, that patient did well as long as he maintained this regularity. If, therefore, this large, uncooperative group were added, as it should be, to the controls, those who fared poorly with salts would be decreased by approximately half.

On this basis it may be said that 33 out of 57 cooperative patients benefited, and 15 out of 15 uncooperative patients did poorly under a salt regime. More exactly then, under Epsom salt treatment 33 patients (30·3 per cent.) were benefited, two (1·8 per cent.) died of causes unrelated to treatment, five (4·6 per cent.) neither improved nor became worse and 19 (17·4 per cent.) developed more convulsions. To the mineral oil control group as given may be added a number of uncooperative salt control cases: 14 (12·9 per cent.) who became worse and one (0·9 per cent.) who remained unimproved. Of the eight who improved under mineral oil treatment, two refused medication, leaving only six patients in this group. The actual

decrease in frequency of seizures in these six was practically negligible except in one case in which the fits were reduced from 14 to 5.

As has been stated, salt dosage varied from 0.6 to 17.0 gm. Cases improved on quantities of magnesium sulphate ranging between these values. There was no correlation between degree of improvement and quantity of Epsom salt administered.

In all but three cases the blood magnesium increased under Epsom salt medication. The average blood magnesium after six months of the salt by mouth was 4.43 mgm. per 100 c.cm. of whole blood, the lowest value being 3.5 mgm. and the highest 6.6 mgm. The average increase in blood magnesium over its previous concentration was 0.99, low : 0.10, high : 3.48. There was never sufficient hypermagnesæmia to produce drowsiness or coma, no patients in the salt improved group being nephritic.

Correlation of age and average per cent. improvement (based on the decrease in frequency of seizures) in each diagnostic group indicates that patients with *psychosis with cerebral arteriosclerosis* improved 76.6 per cent. ; *dementia præcox*, 72 per cent. ; *general paresis*, 60 per cent. ; *epilepsy without psychosis*, 59 per cent. ; *epilepsy with mental deficiency*, 49 per cent. ; and *psychosis with epilepsy*, 33.8 per cent. The only unusual age group, necessarily advanced, lay in the *psychoses with cerebral arteriosclerosis*. No particular colour group, Indian, Negro or Caucasian, benefited more than another.

#### COMMENT

Nerve tissue normally contains a high percentage of magnesium.<sup>8</sup> It was this fact combined with Hirschfelder's<sup>5</sup> discovery of low blood magnesium in a few epileptics that led to the idea of an elemental deficiency in some forms of paroxysmal convulsive disorder. This conception fails to maintain itself in the light of finding hypermagnesæmia prior to Epsom salt administration in 17 out of 33 patients, who were definitely improved under salt regimen. A low blood magnesium is not therefore by any means a constant in epilepsy. Hirschfelder's idea<sup>5</sup> that there might be a variability of blood magnesium in epileptics, and that periods of hypomagnesæmia might precede or accompany the attacks, is borne out to a certain extent in the finding of 2.89, 3.15 and 3.59 mgm. of magnesium per 100 c.cm. of blood during seizures in three patients. Not one of these responded well to magnesium therapy, however, although two made 9 and 5 per cent. improvement respectively.

It is notable that those patients, who showed more marked increases in blood magnesium after medication, did not develop lesser numbers of seizures. Hirschfelder's<sup>5</sup> patients, however, whose twitchings or convulsions were relieved by Epsom salt, all suffered from renal insufficiency. None of the patients in the present series, who responded to treatment, had pathological kidneys.

The improvement in some, without dehydration, somewhat impugns the idea<sup>9</sup> that Epsom salt is effective in epilepsy through its water-eliminating

power. Besides, recent work<sup>10</sup> indicates that decrease in brain hydration is not of therapeutic aid in epilepsy. The temptation is too great not to record the dubious double entendre : the idea just does not hold water.

Rather, the impression is made that in some cases magnesium sulphate alters physicochemical cell relationships in the brain in a way as yet unknown. Magnesium may have sedative powers by interfering with brain-cell metabolism. Neural charges may be neutralized by the salt in the microscopic batteries that are nerve-cells. Perhaps electrical conductivity or cell charge is reduced—or cell resistance increased—to lessen the frequency of convulsions. But speculation is admission of ignorance. Let it rather be said : magnesium sulphate lessens the frequency of convulsions, not by filling a need where there is deficiency or by dehydrating a brain where there is plethora, but how—we do not know. Further study is required on a group of cooperative, non-psychotic epileptics.

#### SUMMARY AND CONCLUSIONS

1. The normal range of magnesium is 2·9 to 4·0 mgm. per 100 c.cm. of whole blood with an average value of 3·61 mgm.

2. In 100 epileptics the blood magnesium ranged from 2·67 to 4·80 mgm., with an average value of 3·47 mgm.

3. Thirty-three (58 per cent.) out of 57 cooperative epileptics were helped by small, daily, non-dehydrating doses of Epsom salt.

4. In a control group of 35 patients taking mineral oil and 15 uncooperative patients taking Epsom salt irregularly, only six patients (12 per cent.) showed slight improvement.

5. There was no correlation between degree of improvement and quantity of Epsom salt administered, blood magnesium level, colour or age, except in the *psychoses with cerebral arteriosclerosis*, in which ages, necessarily advanced, ranged from 60 to 73.

6. In 33 improved cases, six diagnostic groups showed the following percentage improvement :—

Psychosis with cerebral arteriosclerosis . . . . .	76·6 per cent.
Dementia præcox . . . . .	72·0 " "
General paresis . . . . .	60·0 " "
Epilepsy without psychosis . . . . .	59·0 " "
Epilepsy with mental deficiency . . . . .	49·0 " "
Psychosis with epilepsy . . . . .	33·8 " "

7. Kidney disease was not present in the patients who responded to treatment ; and hypermagnesiæmia was never sufficient to produce drowsiness or coma.

8. Three patients showed lower than average blood magnesium during convulsions, but reacted poorly to magnesium therapy.

9. Magnesium in small daily dosage is effective in some epileptics neither by filling an elemental deficiency nor by dehydration.

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