# Serum Magnesium Concentration in Acute Viral Disease in Man

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## INTRODUCTION

The role of magnesium (Mg) in infection (bacterial, viral, or parasitic) has been reviewed by Péchery et al. (1971). In experimentally induced Mg deficiency in male Sprague-Dawley rats, Alcock and Shils (1974) reported decreased serum levels of immunoglobulin G (IgG) and McCoy and Kenney (1975) noted depression of serum antibody titers, along with increased values for ribonucleic acid (RNA) and deoxyribonucleic acid (DNA) in the spleen, which was enlarged in male Wistar rats. Since these studies provided evidence of the significance of Mg in the immune response, we investigated the serum magnesium (S-Mg) concentration during acute viral disease in man.

## MATERIAL AND METHODS

Twenty seven ambulant male patients 20-37 years of age (mean: 25.4, S.E.M.: 0.8 ) who visited the Skin Outpatient Department of the Karolinska Hospital were studied. Viral disease diagnosis (Table 1) was based on the presence of a significant rise of titer on complement fixation test. The patients were adequately nourished, showed no clinical evidence of dehydration, and received neither diuretics nor infusions. There was no known chronic concomitant disease present.

Table 1. Viral Disease Diagnosis

| Diagnoses | No. of patients |
|---|---|
| Herpes simplex | 20 |
| Varicella zoster | 4 |
| Rubella | 2 |
| Influenza A | 1 |
| Total | 27 |

Blood was sampled from patients when they were first seen, the 1st to 15th day of the illness in 22 cases (in 7 cases the date of onset could not be ascertained), and again during convalescence, 6 to 31 days later.

Blood from 11 apparently healthy nonalcoholic men, aged 18-43, serving as controls, was sampled in the postprandial state in the morning, between 8-12 a.m. The sampling was repeated under identical conditions after an interval of 10-14 days in order to compare the intraindividual variation with the intraindividual variation in the patient group.

Serum Mg concentration was estimated by the atomic absorption flame spectrophotometry method, using a Perkin Elmer spectrometer No. 403 (variation coefficient 1.18% at the 95% level).

Complement fixation for antibodies against the respective virus was carried out using the method described by Germanis and Jeansson (1973).

The Wilcoxon nonparametric sign test was used to compare the values of S-Mg concentration obtained on the first sampling, with those obtained on the second, in the patient group. The Wilcoxon rank sum test was used for analysis of the difference between the intraindividual variation of the patient group in comparison with the intraindividual variation in the controls. The means of the controls of the first and of the second sampling were compared with each other using the Student's *t*-test for dependent means. The means of the two groups on the two respective sampling occasions were compared with each other using the Student's *t*-test for independent means.

## RESULTS

There was no significant difference upon comparison of the means of the first with those of the second sampling in the healthy controls. The means of the first sampling in the patients compared with the first sampling in the controls, as well as the means of the second sampling of the patients compared with the second sampling of the controls, did not differ significantly (Table 2). However, on comparison between the

Table 2. Serum Magnesium Concentrations in Healthy Controls and Patients with Viral Disease

| | | $\bar{x}$ | S.D. | S.E.M. | n | Range in mmol/liter |
|---|---|---|---|---|---|---|
| Healthy controls | I | 0.797 | 0.037 | 0.011 | 11 | 0.73 - 0.87 |
| | II | 0.792 | 0.031 | 0.009 | | 0.74 - 0.85 |
| All patients; all diagnoses | I | 0.851 | 0.086 | 0.016 | 27 | 0.75 - 1.05 |
| | II | 0.815 | 0.172 | 0.034 | | 0.66 - 1.16 |

I denotes first sampling; II denotes second sampling.

first and the second sampling of the S-Mg concentration of the patient group, we found 12 cases of increase and 13 cases of decrease of the S-Mg concentration and unchanged values in 2 patients (Table 3). The Wilcoxon sign test showed no significant difference.

There was no systematic difference between the first and the second sampling in the patients with herpes simplex, nor in the remaining group of patients with other viral disease. However, on closer scrutiny we found that the reason for it was, that in the former group, 9

cases showed a rise and 9 cases a fall in S-Mg concentration and 3 cases a rise and 4 patients a fall in the latter group (Table 4).

Table 3. Serum Magnesium Concentration in Viral Disease

| | | $\bar{x}$ | S.D. | S.E.M. | n | Range in mmole/liter |
|---|---|---|---|---|---|---|
| All patients with a rise of serum Mg conc. [a] | I | 0.821 | 0.105 | 0.035 | 12 | 0.69 - 1.05 |
| | II | 0.908 | 0.154 | 0.044 | | 0.77 - 1.16 |
| All patients with a fall of serum Mg conc. [a] | I | 0.883 | 0.055 | 0.015 | 13 | 0.81 - 0.95 |
| | II | 0.816 | 0.058 | 0.016 | | 0.79 - 0.90 |
| Patients with no change in serum Mg conc. [b] | | | | | 2 | 0.76 - 0.76<br>0.88 - 0.88 |

[a] I denotes values on first sampling; II denotes values on second sampling.
[b] These two patients had the diagnosis of herpes simplex.

Table 4. Serum Magnesium Concentration in Viral Disease

| | | $\bar{x}$ | S.D. | S.E.M. | n | Range in mmol/liter |
|---|---|---|---|---|---|---|
| Herpes simplex patients with a rise of serum Mg conc. [a] | I | 0.823 | 0.098 | 0.032 | 9 | 0.76 - 1.05 |
| | II | 0.896 | 0.154 | 0.187 | | 0.77 - 1.16 |
| Herpes simplex patients with a fall of serum Mg conc. [a] | I | 0.876 | 0.062 | 0.022 | 9 | 0.78 - 0.92 |
| | II | 0.807 | 0.064 | 0.021 | | 0.66 - 0.89 |
| Patients with other viral disease and a rise of serum Mg conc. [a] | I | 0.816 | 0.148 | 0.086 | 3 | 0.69 - 0.98 |
| | II | 0.943 | 0.183 | 0.105 | | 0.80 - 1.15 |
| Patients with other viral disease and a fall of serum Mg conc. [a] | I | 0.900 | 0.040 | 0.020 | 4 | 0.86 - 0.94 |
| | II | 0.832 | 0.045 | 0.022 | | 0.81 - 0.90 |

[a] I denotes first sampling; II denotes second sampling.

In order to establish whether the absolute variation between the first and the second sampling in the patients (i.e., either a rise or a fall of S-Mg concentration) differed from those in the healthy controls, we used Wilcoxon rank sum test. This showed a significant difference ($p < 0.01$) between the intraindividual variation of the patients and the healthy controls (Fig. 1). The intraindividual variation range of the healthy controls was 0-0.02 mmol/liter and that of the patients was 0-0.27 mmol/liter.

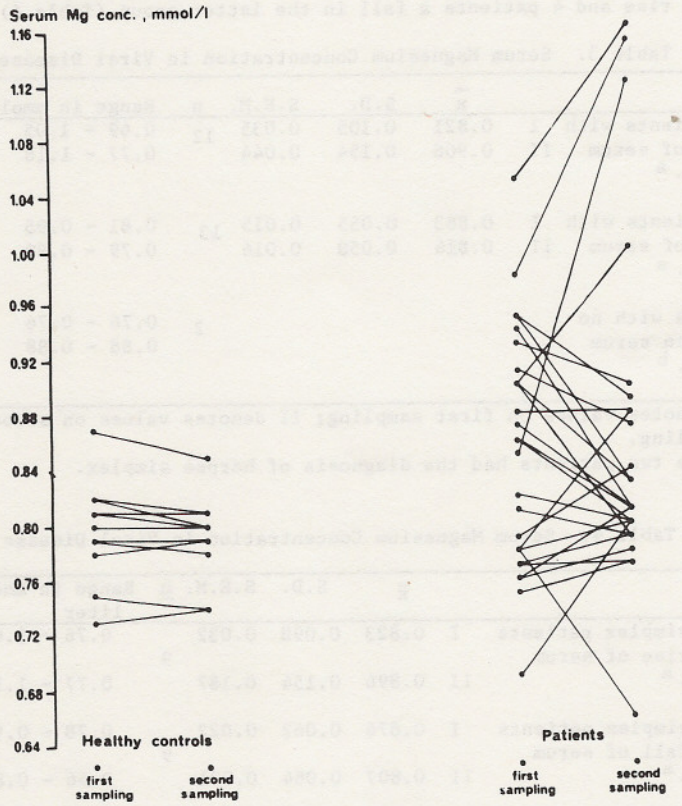


Figure 1. Intraindividual variations of serum Mg concentration in healthy conrols and in patients with viral disease. The time interval between the first and second sampling in the healthy controls is 10-14 days and in the patients 6-31 days.

## DISCUSSION

The S-Mg concentration of healthy subjects is remarkably constant (Wacker and Parisi, 1968a-c). This is confirmed by our findings of the very slight intraindividual variation of S-Mg concentration in the healthy nonaddicts used as controls.

In the patients with acute viral disease, we found a wide range of S-Mg concentration on both sampling occasions and a very marked intra-individual variation, highly significantly different from that of the controls.

Only 2 patients had values below the normal range, one on each sampling occasion. Serum Mg concentration above the normal range was seen

in 14 patients (9 on the first and 5 on the second sampling) of these, 4 (1 on the first and 3 on second sampling), had values exceeding 1.00 mmol/liter. Acute tubular necrosis of the kidney, as well as a number of other pathological conditions, are known to cause hypermagnesemia (Wacker and Parisi, 1968a-c). Our patients showed no evidence of concomitant disease.

Efflux of intracellular Mg during an acute viral attack, with a resultant rise in the serum, and consequent fall during convalescence is ruled out as an explanation because of the lack of a consistent trend of rise, or of fall, on either sampling. No explanation can therefore be offered at present for the striking finding. None the less, it is essential that repeated random studies of populations with acute viral disease be carried out, using serial sampling and the statistical analysis described, to establish whether the marked variation is characteristic of all acute viral disease in man.

## SUMMARY

Marked interindividual and intraindividual variation of S-Mg concentration on two consecutive samplings, collected at an interval of 6-31 days, was seen in 27 male patients, 20-37 years of age (mean: 25.4; S.E.M.: 0.8 ) with acute viral disease, diagnosed on the basis of presence of a significant rise of titer on complement fixation test (herpes simplex, varicella zoster, rubella, or, influenza A. The intraindividual variation of the patients was 0-0.27 mmol/liter whereas that of 11 apparently healthy nonaddict controls, matched for age, sex, and the time interval between the samplings, was 0-0.02 mmol/liter. The difference was statistically significant ($p < 0.01$; Wilcoxon rank sum test). Repeated random studies of viral disease populations, using serial sampling and the statistical analysis described, are essential to establish whether the observed marked variation in S-Mg concentration is a characteristic of all acute viral disease in man.

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