The distribution of magnesium following the parenteral administration of magnesium sulfate

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There is reason to believe that sodium, chloride, bromide, sulfate, and thiocyanate ions when injected into the body are distributed through the extracellular fluid alone (2, 5-7, 9, 10). Potassium on the other hand is distributed through a much larger proportion of the body water (11). Thus, of the two cations thus far studied, one, sodium, is excluded from cells, while the other, potassium, appears to enter cells with some freedom. In order to observe the behavior of another naturally occurring cation the distribution of magnesium after injection has been studied and is the subject of the present report.

The general method of study is similar to that previously applied to a study of potassium distribution, and discussed in detail in a previous communication (11). Isotonic magnesium sulfate solution was injected intravenously into dogs, and serum and urine collections made at intervals following injection. By the use of the formula:

\[
\text{Apparent volume} = \frac{\text{amount injected minus amount excreted in urine}}{\text{increase in concentration in serum water}}
\]


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‡ From a thesis submitted by Bernard M. Schwartz to the faculty of the Yale University School of Medicine in candidacy for the degree of Doctor of Medicine, 1939.
independent calculations of the volumes of distribution of magnesium and of sulfate were made. By a comparison of these figures it could be determined whether magnesium behaved as did sulfate, and, assuming a purely extracellular distribution of sulfate, whether or not it remained confined to the extracellular fluid.

In another group of experiments the problem was approached in a somewhat different manner. Following the injection intraperitoneally of magnesium sulfate all urine and feces were collected during the next 24 hours. The concentration of magnesium in the serum at the end of the period was compared with the concentration preceding injection. From these data the retention of any magnesium in the body could be determined, and the amount of magnesium still left in the extracellular fluid could be calculated. If some of the magnesium retained could not be accounted for in the extracellular fluid, then of necessity it must have been deposited elsewhere.

**Materials and Methods**

Adult, unanesthetized female dogs were used. In some a preliminary dose of morphine (10 mg. per kilo) was administered. Urine specimens were obtained by means of a retention catheter. Injections were made into the femoral vein and blood specimens obtained from either the femoral or the jugular vein. Isotonic magnesium sulfate solution (0.154 M) was used in all experiments, the rate of injection approximating 10 cc. per minute. Injections were terminated before the appearance of respiratory arrest. In the stool recovery experiments carmine was given by mouth at the time of injection and all stools saved until they became carmine-free.

Magnesium was determined in serum, urine, and stools by a modification of the method of Hald (4). The calcium was first removed by precipitation as the oxalate at pH 4.2, 0.2 N acetate buffer being used. The magnesium was precipitated as magnesium ammonium phosphate, some hours being allowed for complete precipitation and care being taken to preserve a constant temperature during the process. Finally the magnesium was determined colorimetrically as phosphate by the method of Fiske and Subbarow (3). Sulfate was determined in serum and in urine by the method of Cope (1). Concentrations in terms of
serum water were obtained by dividing determined serum concentrations by 0.92.

Results

In Table I are summarized the results of five experiments with four dogs, in which the volume of distribution was determined

<table>
<thead>
<tr>
<th>Experiment No.</th>
<th>Dog</th>
<th>Dog weight (kg)</th>
<th>MgSO₄ given (m.eq.)</th>
<th>Time after administration (min)</th>
<th>Mg in serum (m.eq. per l.)</th>
<th>Mg in remaining in body (m.eq.)</th>
<th>SO₄ in serum (m.eq. per l.)</th>
<th>SO₄ in remaining in body (m.eq.)</th>
<th>Volume of distribution (liters)</th>
<th>Volume of distribution (per cent body weight)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 A</td>
<td>17.4</td>
<td>55.4</td>
<td>9</td>
<td>14.5</td>
<td>45.0</td>
<td>12.7</td>
<td>49.9</td>
<td>3.1</td>
<td>3.5</td>
<td>18</td>
</tr>
<tr>
<td>2 A</td>
<td>18.9</td>
<td>50.5</td>
<td>12</td>
<td>11.6</td>
<td>40.9</td>
<td>11.2</td>
<td>39.4</td>
<td>3.5</td>
<td>3.5</td>
<td>19</td>
</tr>
<tr>
<td>3 B</td>
<td>18.8</td>
<td>49.6</td>
<td>16</td>
<td>13.9</td>
<td>47.3</td>
<td>13.5</td>
<td>46.3</td>
<td>3.4</td>
<td>3.4</td>
<td>18</td>
</tr>
<tr>
<td>4 C</td>
<td>11.7</td>
<td>36.0</td>
<td>6</td>
<td>13.6</td>
<td>30.5</td>
<td>11.3</td>
<td>28.6</td>
<td>2.2</td>
<td>2.5</td>
<td>19</td>
</tr>
<tr>
<td>5 D</td>
<td>30.3</td>
<td>77.0</td>
<td>8</td>
<td>12.9</td>
<td>68.6</td>
<td>10.9</td>
<td>62.3</td>
<td>5.3</td>
<td>5.7</td>
<td>18</td>
</tr>
</tbody>
</table>

* The increment of sulfate in serum was too small for accurate calculation.

after intravenous injection. The apparent volumes of distribution of magnesium are in general identical with those of sulfate. The only possible exceptions occur in the third period of Experiment 3, in which that of magnesium is somewhat higher, and in the second period of Experiment 4, in which it is somewhat lower. There is a tendency in all experiments for the apparent volume of
distribution of both ions to rise in later periods. No experiments were continued beyond 3 or 4 hours, since by that time the concentration increments of both ions in the serum had fallen too nearly to normal levels for accurate calculations to be made. The actual volumes of distribution corresponded to 18 to 32 per cent.

Table II
Recovery of Magnesium in Urine 24 Hours after Intravenous Injection

<table>
<thead>
<tr>
<th>Experiment No.</th>
<th>MgSO₄ given</th>
<th>Recovered in urine within 24 hrs.</th>
<th>Unaccounted for in urine</th>
<th>Increase in concentration in serum water at end of 24 hrs.</th>
<th>Extracellular fluid volume</th>
<th>Accounted for in extracellular fluid</th>
<th>Unaccounted for in urine or extracellular fluid</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>55.4 m.eq.</td>
<td>27.6 m.eq.</td>
<td>27.8 m.eq. per l.</td>
<td>0.3 m.eq.</td>
<td>5 liters</td>
<td>1.5 m.eq.</td>
<td>5.4 m.eq.</td>
</tr>
<tr>
<td>2</td>
<td>50.5 m.eq.</td>
<td>43.6 m.eq.</td>
<td>6.9 m.eq.</td>
<td>0.1 m.eq.</td>
<td>5 liters</td>
<td>0.5 m.eq.</td>
<td>26.2 m.eq.</td>
</tr>
<tr>
<td>3</td>
<td>49.6 m.eq.</td>
<td>27.6 m.eq.</td>
<td>26.7 m.eq.</td>
<td>2.3 m.eq.</td>
<td>3 liters</td>
<td>6.9 m.eq.</td>
<td>4.1 m.eq.</td>
</tr>
<tr>
<td>4</td>
<td>36.0 m.eq.</td>
<td>26.4 m.eq.</td>
<td>11.0 m.eq.</td>
<td>1.8 m.eq.</td>
<td>7 liters</td>
<td>12.6 m.eq.</td>
<td>12.1 m.eq.</td>
</tr>
<tr>
<td>5</td>
<td>77.0 m.eq.</td>
<td>52.3 m.eq.</td>
<td>24.7 m.eq.</td>
<td>3 m.eq.</td>
<td>4 liters</td>
<td>15.8 m.eq.</td>
<td>75.5 m.eq.</td>
</tr>
</tbody>
</table>

Table III
Recovery of Magnesium in Urine and Feces in 24 Hours after Intraperitoneal Injection

<table>
<thead>
<tr>
<th>Experiment No.</th>
<th>MgSO₄ given</th>
<th>Recovered in urine in 24 hrs.</th>
<th>Recovered in feces in 24 hrs. or more</th>
<th>Increase in concentration in serum water at end of 24 hrs.</th>
<th>Extracellular fluid volume</th>
<th>Accounted for in extracellular fluid</th>
<th>Unaccounted for</th>
<th>SO₄ recovered from urine alone during same period</th>
</tr>
</thead>
<tbody>
<tr>
<td>6</td>
<td>77.0 m.eq.</td>
<td>18.0 m.eq.</td>
<td>10.5 m.eq.</td>
<td>1.8 m.eq. per l.</td>
<td>4 liters</td>
<td>7.2 m.eq.</td>
<td>41.3 m.eq.</td>
<td>54 m.eq.</td>
</tr>
<tr>
<td>7</td>
<td>46.2 m.eq.</td>
<td>23.6 m.eq.</td>
<td>3.3 m.eq.</td>
<td>0.0 m.eq.</td>
<td>4 liters</td>
<td>0.0 m.eq.</td>
<td>19.5 m.eq.</td>
<td>42 m.eq.</td>
</tr>
<tr>
<td>8</td>
<td>46.2 m.eq.</td>
<td>39.7 m.eq.</td>
<td>2.3 m.eq.</td>
<td>0.0 m.eq.</td>
<td>3 liters</td>
<td>0.0 m.eq.</td>
<td>4.2 m.eq.</td>
<td>9 m.eq.</td>
</tr>
<tr>
<td>9</td>
<td>77.0 m.eq.</td>
<td>40.3 m.eq.</td>
<td>19.9 m.eq.</td>
<td>0.4 m.eq.</td>
<td>4 liters</td>
<td>1.6 m.eq.</td>
<td>15.8 m.eq.</td>
<td>21 m.eq.</td>
</tr>
</tbody>
</table>

* Includes stools for 4 days after injection.

of the body weight, a range consistent with the magnitude of the extracellular fluid.

In Table II are summarized the total amounts of magnesium recovered from the urine in the 24 hours after injection in the five experiments of Table I. Initial and final determinations of
the concentrations in the serum are included. Even without allowance for endogenous magnesium excretion during the 24 hour period, failure to recover the injected magnesium in the urine is evident. The magnitude of the changes in serum concentration indicates that this retention can only in part be accounted for by the amount of magnesium still present in the extracellular fluid.

In Table III are presented four complete recovery experiments on four dogs. The magnesium sulfate was given intraperitoneally. In three of the four experiments the same marked retention of magnesium is present. The stool excretion figures are if anything too high, since they include the magnesium already present; in spite of this the amounts are small and in no way account for the failure of recovery in the urine. Therefore, in three of the four experiments magnesium in significant quantities is clearly retained within the body, but not in the extracellular fluid. Simultaneously injected sulfate was completely recovered from the urine within 24 hours.

**DISCUSSION**

The nearly identical volumes of distribution of magnesium and of sulfate in the first 3 or 4 hours after injection indicate that both ions are distributed throughout the same portion of the body water. The magnitude of this portion, corresponding to about one-fourth the body weight, indicates that it is reasonable to identify it with the extracellular fluid volume. Thus magnesium resembles sodium rather than potassium in its initial distribution after injection, since sodium and sulfate distributions are virtually identical. The apparent gradual increase in the volume of distribution of the ions as time elapses is probably due to concentration gradients, first from serum to extracellular fluid and then in the reverse direction. In other words the earlier calculated volumes of distribution are probably lower, the later higher, than the true volume of distribution.

The failure in most experiments to recover all the injected magnesium in stools and urine within 24 hours is probably even more marked than the figures in Tables II and III indicate, since the stool and urine values include endogenous magnesium and so represent maxima for the period. Indeed there is no evidence that any of the injected magnesium is excreted by way of the
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feces, since the figures for 24 hour loss in stools after injection fall within the limits of normal daily fecal excretion. This failure of recovery is a confirmation of the work of Mendel and Benedict (8), who, after injection of magnesium salts, were unable to recover the magnesium completely for days or weeks. Since it cannot be accounted for in the extracellular fluid, the conclusion seems inescapable that sometime between the 4th and the 24th hour after injection some of the magnesium may leave extracellular fluid to be segregated elsewhere. There is no evidence from these experiments as to the mode or the place of this deposition.

SUMMARY

1. The magnesium of magnesium sulfate injected intravenously into dogs distributes itself immediately through approximately the same volume of fluid as does the sulfate ion, corresponding to some 20 or 25 per cent of the body weight.

2. This volume is believed to approximate the extracellular fluid of the body, so that magnesium behaves in respect to its distribution like sodium rather than potassium.

3. Between 4 and 24 hours after injection a variable proportion of the magnesium injected, over and above what can be accounted for in urine and stools, may leave the extracellular fluid and be segregated in unknown form elsewhere in the body.

BIBLIOGRAPHY

THE DISTRIBUTION OF MAGNESIUM FOLLOWING THE PARENTERAL ADMINISTRATION OF MAGNESIUM SULFATE
Paul K. Smith, Alexander W. Winkler and Bernard M. Schwartz