As the 100 cases of typhoid fever with polyuria reported represent, in some measure, a selected group, the small and diminishing mortality rate is, of course, at the most, suggestive. It is felt, however, that certain conclusions as to the results and usefulness of this mode of treatment, which seems to supply an additional means of combating the toxæmia of the disease, may be submitted with some confidence with the hope that this method of copious water-drinking with its resulting diuresis, may be found by other observers to diminish in some further degree the severity and mortality of typhoid fever in hospital practice.

Our experience and conclusions may be summarized as follows:

1. Large quantities of water internally, a gallon or more in twenty-four hours, may easily be taken by typhoid fever patients, if administered in small quantities at frequent and definite intervals.

2. A copious elimination of watery urine at once follows, the degree of polyuria, day by day, closely corresponding to the quantity of fluid ingested.

3. Patients are more comfortable by this mode of treatment and toxic, nervous symptoms are lessened.

4. The mortality, as well as the severity, of typhoid fever, seems to be still further diminished by this method of hydrotherapy employed as an accessory to the cool-bath treatment of the disease.

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CHLORIDE AND WATER EXCRETION IN TYPHOID FEVER, WITH COPIOUS DIURESIS.

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And

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I. INTRODUCTORY.

The clinical tests of Drs. Cushing and Clarke, described in the preceding paper, offered an opportunity of investigating several interesting features of urine secretion in typhoid fever, as influenced by unusually large diuresis, the consequence of a very free administration of water. This opportunity we were glad to utilize as far as time would permit. To avoid complications, we confined ourselves to the study of the excretion of water and chlorine, neglecting all the other urinary constituents. The practical agreement of the results in all the cases examined shows that the material was sufficient to justify general conclusions.
We wish to take this opportunity to thank Dr. Cushing for the use of this clinical material, and the medical staff of Lakeside Hospital for their ready co-operation.

The details of the results are presented in the appendix, in the form of charts, and we shall confine ourselves to the discussion of the results. We shall touch but lightly on the bibliography of the subject, since this was discussed in the previous papers by Sollmann.¹

While writing this paper, a monograph by Garratt² has come to hand which contains an excellent synopsis of the literature as well as valuable original contributions.

Concerning the cases included in this investigation, we may premise that they were all male subjects with typhoid fever of moderate degree, without fatality. All presented a trifling albuminuria. The study of each case was begun soon after admission to the hospital, and continued for a variable period, but never far into convalescence. The patients were confined to bed during the entire period of observation. For the greater part of the time they were on a milk and albumen diet;³ during convalescence they received the diet noted in the appendix. All patients were given four ounces of distilled water every fifteen minutes. This as well as the food was omitted during sleep, and modified according to circumstances. This showed considerable irregularity.

All the patients excreted a very large quantity of urine of very pale color and of low specific gravity, containing an extremely low percentage of chloride.

II. THE DIURESIS.

THE DEGREE OF DIURESIS. The quantity of urine excreted by these patients was very great. Excluding the period during which the administration of food was temporarily suspended on account

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² Medico-Chirurgical Transactions, 1904, vol. lxxxvii.
³ The usual directions were that each patient should receive, every four hours, four ounces of milk with two ounces of lime-water, and every four hours alternating with the milk the white of one egg dissolved in six ounces of water, with a teaspoonful of sugar and a few drops of lemon-juice. A record of the feeding was directed to be kept. This showed considerable irregularity.

The analysis of these fluids yielded per litre:

<table>
<thead>
<tr>
<th>Sample</th>
<th>Chlorides</th>
<th>Nitrogen</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>1.090</td>
<td>3.64</td>
</tr>
<tr>
<td>II</td>
<td>1.180</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Sample</th>
<th>Albumen-Water</th>
<th>Chlorides</th>
<th>Nitrogen</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>0.445</td>
<td>0.14</td>
<td>1.708</td>
</tr>
<tr>
<td>II</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>III</td>
<td>1.000</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
of hemorrhage, the daily excretion of urine was generally above three litres, averaging over five litres, and exceeding nine litres on several isolated days.

The excretion of this enormous quantity of fluid is conclusive proof that the kidneys are not appreciably injured (at least under the conditions of these experiments) by typhoid fever or by prolonged diuresis. The conclusion is supported by the study of the urinary constituents, since the percentage of chlorides and the total molecular concentration depart very materially from those of the plasma. We will show later that the chlorides fall to extremely low figures, on some days below 0.1 gram per litre. The molecular concentration was only determined twice in the case of Kretzian. On July 16th the depression of freezing point was 0.215° C.; on July 19th, 0.205° C. This was probably the lowest point reached. It is pretty near to the recorded minimum (0.12° C.).1

The lowering of this factor below that of the blood (0.56° C.) under the influence of water has been proposed as a test of renal efficiency. The present kidneys evidently bear the test very well.

The kidneys are also maintained very efficient in the excretion of material. The two cases of typhoid fever studied by Hatcher and Sollmann 2 are valuable for comparison, as the patients were kept under nearly identical conditions, except that only the usual quantities of fluid were administered, the urine measuring 650 c.c. to 1600 c.c. These cases showed a greater depression of freezing point (Δ) than the present series during the period of milk diet: Case N, mean Δ equals 1.163; extremes, 0.859 to 1.446; Case B, mean Δ equals 0.994; extremes, 0.991 to 0.997). On the other hand, the daily excretion of total molecules (Δ × c.c.) was much greater with the water treatment. With Kretzian, Δ × c.c. = 1935.0 on July 16th; 1758.9 on July 19th; whereas, in the cases of Hatcher and Sollmann, Δ × c.c. never exceeded 1428.5, the mean being about 900. We shall show later that the total excretion of chloride is also greater with diuresis than without.

Corresponding to the low molecular concentration, the specific gravity in the present series was also very low. Readings of the urinometer varied between −1.0 and +2.8. No correction was made for temperature (summer heat), so that the real specific gravity is somewhat higher. In the case of Colson, the readings lay between 2 and 5 during polyuria, and between 9.8 and 12.5 when the quantity of urine was small (after hemorrhage).

Dependence of the Diuresis on the Income of Fluid.—The charts show that, with few exceptions, the curves for the income and output of fluid are strictly parallel, day by day. This is interesting as showing that the kidneys are capable of meeting efficiently even

the not inconsiderable task imposed on them by the elimination of nine litres per day of urine of very low molecular concentration. For if the kidneys were at all unequal to the task, an accumulation of fluid would occur in the body, and the fluid would be excreted when the administration of water was discontinued, so that the urine excretion would exceed the fluid income whenever the latter was reduced. This does not occur at all, since the curves for ingestion of fluid and excretion of urine are so nearly parallel. Colson shows strikingly how the urine may fall in one day from 7000 c.c. to 3000 c.c., and Hickock from 5500 c.c. to 1300 c.c. by the reduction of the fluid. It is true that intestinal hemorrhage was present in both cases. If this had any effect it would favor retention of fluid; but the near approach of the output to income shows that this retention cannot be great.

The conclusion that no progressive retention of fluid occurs may also be seen by comparing the income and output of water during longer periods, as seen from the following table:

<table>
<thead>
<tr>
<th>Date of observation</th>
<th>Days of observation</th>
<th>C.c. of fluid administered</th>
<th>C.c. of urine collected</th>
<th>Total deficiency in excreted fluid</th>
<th>Deficiency in excreted fluid, average per day</th>
</tr>
</thead>
<tbody>
<tr>
<td>July 11-19</td>
<td>9</td>
<td>48,720</td>
<td>33,540</td>
<td>15,180</td>
<td>1657</td>
</tr>
<tr>
<td>July 21-30</td>
<td>10</td>
<td>16,820</td>
<td>12,000</td>
<td>4,820</td>
<td>492</td>
</tr>
<tr>
<td>Aug. 15-17</td>
<td>3</td>
<td>18,840</td>
<td>16,900</td>
<td>4,940</td>
<td>1060</td>
</tr>
<tr>
<td>Aug. 19-22</td>
<td>3</td>
<td>5,560</td>
<td>3,060</td>
<td>2,500</td>
<td>830</td>
</tr>
<tr>
<td>Aug. 19-Sept. 12</td>
<td>15</td>
<td>95,040</td>
<td>76,320</td>
<td>18,720</td>
<td>1154</td>
</tr>
<tr>
<td>July 12-30</td>
<td>19</td>
<td>157,020</td>
<td>155,300</td>
<td>1,720</td>
<td>90</td>
</tr>
<tr>
<td>Aug. 15-17</td>
<td>8</td>
<td>17,560</td>
<td>17,610</td>
<td>-50</td>
<td>-17</td>
</tr>
<tr>
<td>Aug. 15-Sept. 2</td>
<td>19</td>
<td>120,780</td>
<td>94,470</td>
<td>&lt;26,310</td>
<td>&lt;1820</td>
</tr>
<tr>
<td>Aug. 7-Sept. 2</td>
<td>6</td>
<td>48,540</td>
<td>15,940</td>
<td>32,600</td>
<td>4650</td>
</tr>
</tbody>
</table>

Excluding Cases 2, 4, 8, and 9, the average daily difference in the entire series equals 763 c.c., being but little larger than the average difference of Cases 2 and 4, with small urine secretion. In Case 6 the income and output practically balance; in Case 7, even more appears to be excreted than is administered. Cases 1 and 2 seem to show, indeed, that a greater amount of fluid is retained when the administration is large than when it is small, but the difference can probably be explained by differences in perspiration, due to the hemorrhages which occurred during the period of the lesser water administration.

We would also point out that the close agreement between the income and output of fluid shows that the elimination of the latter occurs to by far the greatest extent by the urine; only a relatively very small amount remains to be excreted by the bowels.

Accepting the conclusion that no appreciable progressive retention of fluid occurs after the administration of the water is well under way, it might still be supposed that a retention would occur during
the first days of administration, an equilibrium being established, somewhat as occurs in the administration of salt or bromides to normal individuals. Our charts do not answer the question directly, but the prompt and complete response of the urine curves to any change in the administration of the fluid, argues strongly against the initial retention. The chart also shows that the urine responds promptly and efficiently to the income of fluid, even after severe hemorrhage and withdrawal of fluid—i.e., when the need of organism for water might be supposed to be the greatest.

The Effect of Perspiration on the Diuresis. This is seen very prettily in the case of Kordick. Free perspiration was noticed on the last two days of observation, and the chart shows a corresponding increase in the difference between the fluid and urine. Barber is perhaps a still more striking illustration. This patient had frequent chills, with sweating, between August 28th and September 2d. Accordingly the difference between fluid and urine averages 4950 c.c.—very much more than even the maximum average (1687 c.c.) observed in any of the other cases. Allowing 800 c.c. as the average apparent retention, Barber must have eliminated by the perspiration over 4000 c.c. per day more fluid than the other patients. This is very much more than the usual total loss by perspiration, as calculated by Garratt,\textsuperscript{1} namely, 1200 c.c. for high fever, 1500 c.c. for high fever with remittance, 2068 c.c. in crisis, and 1096 c.c. in epicrisis.

This would indicate that the perspiration may be much more free with copious administration of water than it is ordinarily. This must be an important antipyretic measure. We would also emphasize that the quantity of urine was still very high (2500 c.c. to 4500 c.c.), notwithstanding the copious perspiration.

The Effect of Temperature on the Diuresis. Since the administration of fluid was not kept perfectly constant, it would be difficult to determine the effect of the degree of fever, unless this effect were fairly large. The latter was certainly not the case, and it is our belief that the temperature has no great effect on the elimination of urine, except indirectly by influencing perspiration.

The Effect of Cathartics on the Diuresis. These, by abstracting water through the bowels, should increase the difference between the income of fluid and the quantity of urine. This is shown by Kretzian, July 6th and 7th (see chart).

Effect of Diuretics on the Diuresis. The charts show that the following diuretics certainly did not increase the quantity of urine: agurin, 6 grams per day; sodium acetate, 9 grams per day; potassium nitrate, 9 grams per day; urotropin, 2 grams per day. Indeed, the diuresis was generally less than in the control periods, the patients not being able to take as much water. This

\textsuperscript{1} Loc. cit.
inefficiency of the diuretics during the existence of polyuria is an interesting phenomenon.

**CALCIUM CHLORIDE.** J. B. Macallum has recently found that the injection of calcium chloride greatly diminishes the urine excretion in rabbits. Two of these patients, Hickock and Colson, received considerable amounts of this salt by mouth. It is somewhat difficult to judge the effects, as the administration coincided with the period of the water withdrawal; but comparing the hemorrhage period of Hickock, who received 4 grams of calcium chloride per day (August 17th to 22d) with the second hemorrhage of Colson, who did not receive calcium chloride (July 19th to 28th), no essential difference can be detected. It is, therefore, probable that the calcium does not influence the diuresis under these conditions.

**III. THE CHLORIDE EXCRETION.**

The excretion of chlorides was low in these cases, both as concerns the quantity per day and per litre. Since a greatly lessened excretion of chloride is the rule in typhoid fever, it is necessary to compare the present series of polyuric patients with others in which the quantity of urine is no more than ordinary. The study published by Hatcher and Sollmann is especially valuable in this respect, as the conditions other than water administration were practically identical in both series. We shall, however, avail ourselves also of other accessible data.

**The Effect of the Polyuria on the Chlorides.** This may be judged by comparing the averages of the two series of typhoid cases:

<table>
<thead>
<tr>
<th>Quantity of urine.</th>
<th>Chlorides per litre (NaCl)</th>
<th>Chlorides per day (NaCl)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A. Polyuria (present series)</td>
<td>4500 c.c.</td>
<td>0.25 gm.</td>
</tr>
<tr>
<td>B. Ordinary quantity of urine (Hatcher and Sollmann)</td>
<td>885</td>
<td>0.63</td>
</tr>
<tr>
<td>C. Various fevers above 100° (Garratt)</td>
<td>958</td>
<td>0.90</td>
</tr>
</tbody>
</table>

The comparison of A and B shows that the polyuria, of about five times the normal, increased the elimination of chloride to about three times the normal, while it diminished their quantity per litre to about one-third.

This large polyuria, therefore, affects the chloride excretion in the same direction as it would in the normal kidney.

Lesser variations in the urine secretion also cause an inverse change.

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2 American Journal of Physiology.
3 The chlorides are always calculated as sodium chloride.
4 Hickock and Colson are excluded, since they received calcium chloride, which might vitiate the conclusions.
in the concentration of the chlorides, but the daily elimination is scarcely affected. This may be seen from the following table:

<table>
<thead>
<tr>
<th></th>
<th>Mean quantity of urine (c.c.)</th>
<th>Mean chlorides per litre (gm.)</th>
<th>Mean chlorides per day (gm.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kretzian</td>
<td>8000</td>
<td>0.17</td>
<td>1.5</td>
</tr>
<tr>
<td>Kordick</td>
<td>5500</td>
<td>0.22</td>
<td>1.7</td>
</tr>
<tr>
<td>Kiswan</td>
<td>4200</td>
<td>0.27</td>
<td>1.5</td>
</tr>
<tr>
<td>Barber</td>
<td>4000</td>
<td>0.35</td>
<td>1.7</td>
</tr>
</tbody>
</table>

The study of the extremes also shows that the quantity per litre is more variable than the quantity per day.

<table>
<thead>
<tr>
<th></th>
<th>Minima.</th>
<th>Maxima.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Extremes of sodium chloride per litre</td>
<td>0.09-0.20</td>
<td>0.27-0.60</td>
</tr>
<tr>
<td>Extremes of sodium chloride per day</td>
<td>0.60-0.80</td>
<td>2.8-3.2</td>
</tr>
</tbody>
</table>

The constancy in the limits of the daily chloride excretion is certainly very striking. It has been observed by other investigators.¹

All these considerations, based on averages, justify the conclusion that the degree of diuresis causes a parallel but small change in the total excretion of chlorides, and an inverse and considerable change in the percentage of this ion.

It is difficult to verify these conclusions by the study of the individual curves. Indeed, at first glance it would seem that the percentage and daily elimination both varied in the same direction as the diuresis in the majority of cases. (For instance, Kordick, August 25th to September 2d; Kretzian, July 6th to 17th; Colson, July 19th to 28th; Kiswan, August 19th to 24th; Hickock, August 18th to 21st.) This, however, is a mere coincidence. A closer inspection of the curves shows that the percentage of the chlorides is really following the income of chlorides (which we shall study later), and that the latter is parallel to the income of fluid, and hence to the degree of diuresis. Indeed, the curve of the percentage of chlorides agrees better with the curve of the income of fluid than with that of the excretion of urine.

When there is a difference in diuresis independent of the admission of fluids—for instance, by perspiration, as in the case of Barber, and with Kordick on September 2d—the chloride obeys the general rule—i.e., the daily quantity varies with, the percentage inversely to, the diuresis.

**The Effect of Perspiration on the Chlorides.** Sweat contains about 0.3 per cent. of chloride, even in fever. It might be supposed, therefore, that the daily quantity of chloride and its percentage in the urine should both be lessened by profuse perspiration. The observations on Barber and Kordick do not bear this out. Evidently the excretion by the urine predominates so greatly over that by the sweat that the influence of the latter is totally obscured.

**The Effect of the Febrile Condition on the Chlorides.** A careful comparison of the fever and chloride charts fails to reveal

any correspondence. The chlorides usually drop to about 2 grams per day within three days of the inauguration of the milk diet, and tend to continue about this low point as long as the milk diet is continued, independently of the curve of the fever. They increase again when the patients are placed on convalescent diet, and often show very conspicuous oscillation at this time. The increase could, in most cases, be referred to greater chloride in income (broth, etc.). This agrees with the general experience of most other investigators, in all febrile diseases except pneumonia. The only apparent effect of hemorrhage is seen in the simultaneous drop of the temperature and chlorides after hemorrhage (Colson and Barber). However, this is evidently due to the simultaneous stoppage of all food.

The Effect of the Chloride Income on the Chloride Elimination. Excluding the administration of calcium chloride (which will be considered separately), almost every change in the chloride income causes a corresponding change in the chloride elimination. There is apparently little tendency to retention. Even after severe hemorrhage and complete starvation, the chloride excretion responds promptly and completely to our increase of chloride income. It would be difficult to imagine a condition in which the need of the organism for chloride could be greater.

It is well known that the chloride excretion does not usually respond as promptly as this to changes in the chloride income, and that fever patients especially show a tendency to retention. We may perhaps suppose that the polyuria tends to reduce the chloride of the body to the extreme minimum, causing a ready elimination of any excess. It would seem to us that this is in fair agreement with Forster's theory, although it could scarcely be cited as a proof of the latter.

We wished to determine also the effect of large additions of chlorides to the diet. The patient with whom we tried this (Colson) became nauseated, however, by the addition of 1 per cent. of sodium chloride to the water and milk, and absolutely refused to take the salt. In the face of this resistance we did not insist. The prompt and considerable rise in the chlorides in the convalescent period shows sufficiently that the elimination responds to large quantities of chlorides, but it does not permit any conclusions as to the completeness of the elimination.

The Question of Chloride Retention in Fever. We have seen that the degree of hyperpyrexia does not modify the chloride excretion in the present series of cases, and that this is the general result in all fevers, with or without polyuria. This does not, of course, imply that the disease process which underlies the hyperpyrexia has no effect on chloride excretion, independent of the hyperpyrexia. In the previous papers of Sollmann the conclusion

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2 Loc. cit.
was drawn that "the disappearance of chloride from fever urines is due practically entirely to a deficiency of chloride income." This was based mainly on the observation that chloride excretion is influenced in the same direction as in health, arguing that the same mechanism is involved. While we see no reason to modify the latter conclusion, we believe that the phenomena are modified quantitatively in fever, in the direction of a much greater tendency to chloride retention. This may be seen from the following table of averages:

<table>
<thead>
<tr>
<th></th>
<th>Quantity of urine</th>
<th>Sodium chloride per litre</th>
<th>Sodium chloride per day</th>
</tr>
</thead>
<tbody>
<tr>
<td>A. Typhoid fever with polyuria</td>
<td>4500 c.c.</td>
<td>0.25 gm.</td>
<td>1.5 gm.</td>
</tr>
<tr>
<td>B. Typhoid fever with ordinary quantity of urine</td>
<td>885</td>
<td>0.68</td>
<td>0.58</td>
</tr>
<tr>
<td>Hatcher and Sollmann, Moos (quoted by Garratt)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>C. Fevers above 100° (Garratt, loc. cit.)</td>
<td>958</td>
<td>0.90</td>
<td>0.88</td>
</tr>
<tr>
<td>D. Normal individuals on milk diet (Garratt, last day of No. 1, and second and third day of No. 2)</td>
<td>965</td>
<td>2.75</td>
<td>2.7</td>
</tr>
<tr>
<td>Haskins' (fourth and fifth day)</td>
<td>1125</td>
<td>2.10</td>
<td>2.36</td>
</tr>
</tbody>
</table>

In fever, with milk diet (B and C) the daily excretion of chlorides by the urine averages between 0.53 to 0.88 gram, and even with the large polyuria of the present series it averages only 1.6 grams, whereas in normal individuals on a similar diet it averages between 2.35 and 2.7 grams.

In this table the chloride income has not been considered, so that an absolute retention of chloride over the amount administered is not proven.

Haskins' gives data from which the absolute retention of chlorides may be calculated.

From the first to the fifth day, inclusive, the chloride income was 14,508 grams; the excretion by the urine, 20,638 grams, a loss of 6.130 grams, or an average loss of 1.23 grams per day. Selecting the fourth and fifth days, when the conditions had reached a practical constant, the income was 7.25 grams, the output 4.71 grams, an average apparent retention of 1.27 grams per day. The loss by the feces and sweat must be subtracted from this. Röhmann determined the daily loss of chloride by the feces as 0.162 gram; there are no available data as to the loss by the sweat, but we see that even

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2 The higher figure of Moos may be excluded because it evidently does not refer to a milk diet.
3 Loc. cit.
4 In the tables given in Haskins' paper, the sodium chloride of milk is assumed to be 2.7 grams per litre, according to Bunge's figures. This seems to show a considerable chloride retention. There can be little doubt, however, that Bunge's figure is too high for the milk used by Haskins. Röhmann determined the chloride content of milk as 1.56 grams sodium chloride per litre; Schubert gives 1.6 grams; Södner as 1.62 grams; Vanmeister as 1.74 grams; a sample analyzed by us gave 1.76 grams. We shall use 1.6 grams in the calculations.
in health a chloride retention of about 1 gram per day may occur with a chloride income of 3.63 grams per day. This agrees entirely with the figures of Javal, quoted by Garratt (page 37). While there can be little doubt, from the above table, that the retention in fever is greater than this by at least 1.5 grams per day, it is evident that the mere fact of retention is by no means characteristic of fever, and that the difference is merely quantitative and not qualitative.

On account of imperfect records and the variable chloride content of the albumin solution, we do not consider the data of the chloride income in the present series sufficiently exact to determine whether any chloride retention occurred. (In the case of Barber, assuming the albumin solution to contain 0.1 per cent. of sodium chloride, the chloride income was at least 7.282 grams for five days, the output, 5.125 grams, showing an average retention of at least 0.425 gram per day. In another case, however (Kiswan), the income in fourteen days was calculated as 20.603 grams, the output as 29.627 grams.) We are probably not far from right in assuming the average chloride income on a milk diet to be 2.4 grams of sodium chloride. On this assumption an ordinary typhoid patient retains 1.8 grams per day, the polyuria typhoid patient about 0.7 gram, and a normal individual about 1 gram. The conclusion seems justified that the polyuria is able to counteract the excessive chloride retention in fever.

The Effect of Calcium Chloride on the Chloride Excretion. We have shown that the chloride of the urine in this series of cases varies promptly with the chloride of the food. When the chloride is administered in the form of calcium chloride, the phenomena are altogether different. The charts show that in the case of Colson there was a latent period of six days, during which the administration of the calcium chloride did not increase the urinary chloride. A very considerable rise then occurred, especially in the percentage of chloride. It outlasted the stoppage of the calcium chloride by three days. In the case of Hickock there was no rise in the three days during which the urine was observed.

The total amount of chloride (calculated as sodium chloride) administered as calcium chloride to Colson between June 30th and July 9th equals about 31.05 grams. To this must be added at least 10 grams for the food. During this time and in the four days following there were excreted at most 12.88 grams—i.e., scarcely if any more than was given in the food. The calcium chloride has practically disappeared. Hickock shows a similar phenomenon.

It might be supposed that there was in these cases a real retention of chlorides, due to the hemorrhage. The prompt response of chloride excretion of added chloride in the diet inclines us against

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1 This is calculated on the assumption that the crystalline calcium chloride (containing six molecules of water) was given. We made no analysis of the sample, since small differences would not alter the conclusions.
this explanation. It seems more probable that the calcium hinders and delays the absorption of the chloride ion. Further observation would, of course, be required before accepting the latter explanation.

The Effect of Other Salts on the Excretion of Chlorides. The charts show that the following salts did not cause any change beyond the normal accidental variations in the quantity of urine or in the chlorides per litre or per day: agurin, 6 grams per day (one trial of two days); sodium acetate, 9 grams per day (four trials of three days, one trial of two days); sodium nitrate, 9 grams per day (five trials of three days, one trial of four days). This negative result, as concerns the chlorides, does not seem to be due to absence of diuretic effect, for Garratt obtained a similar negative result on the chlorides, in various fevers, with caffeine, digitalis, potassium citrate, sodium bicarbonate, citrate, and salicylate. In normal individuals on a milk diet (Haskins) diuretin and sodium acetate also did not modify the chloride excretion, although the acetate had a considerable diuretic effect.

We intended to make further experiments with iodides, but could not find the time; an experiment was, however, made by accident in the case of Barber. On September 1st the urine contained 0.345 gram of chloride per litre, and 0.95 gram per day, and it averaged about this for the preceding four days. On September 2d the urine after incineration titrated 1.945 grams per litre, and contained iodine. On extracting the latter it was found to correspond to 1.714 grams of sodium iodide, leaving 1.250 grams of sodium chloride per litre or 2.419 grams of chloride per day. It is seen that the accidental administration of the iodide increased the percentage of chloride 3.7 times, the daily excretion 2.6 times—a very conspicuous difference.

In a previous research Sollmann¹ had observed that in dogs, when the urine had been rendered chloride poor by the injection of sodium sulphate, the percentage of chloride was increased by the intravenous injection of sodium iodide and sulphocyanide, but was not increased by diuresis, caffeine, or irritant diuretics, nor by the intravenous injection of the acetate, ferrocyanide, or phosphate of sodium, nor by the injection of urea, alcohol, or glucose. Several investigators had shown, on the other hand, that in rabbits these diuretic measures increase the percentage of chloride (except the administration of water by mouth). This seems to show an important difference in the chloride retaining mechanism in these two classes of animals, and it seems interesting to determine to which class the human kidney belongs. This was the primary object of the present research. The negative effect of the acetate, agurin, and urotropin seems to indicate that the chloride excretion in man resembles that in the dog. This was also the conclusion of

Haskins. It must be remembered, however, that the doses of the salts are much smaller than those which were used on the dogs, and we cannot be certain that correspondingly large doses would not have increased the percentage of chlorides. The positive result with the iodide shows, however, that even moderate doses of this salt, which is effective on dogs, are also effective in man. On the other hand, sodium nitrate, which is very effective in dogs, produced no certain effect in man. This may, however, be due to the rapid destruction of the nitrate ion in the body.

We may conclude, further, that a moderate nephritis does not break down the chloride retaining mechanism, since all the cases had albuminuria. This is also the conclusion of other investigators.

SUMMARY AND CONCLUSIONS.

The free administration of water to typhoid patients causes a large polyuria, exceeding three litres per day and averaging over five litres. On isolated days nine litres are not rarely excreted. The percentage of chlorides and the total molecular concentration are much below normal, while the daily excretion of total dissolved molecules exceeds that of ordinary typhoid cases. The eliminating capacity of the kidneys is, therefore, not injured in typhoid fever, nor by a prolonged polyuria. No accumulation of fluid appears to occur in the body, the excretion being very nearly parallel to the income. The quantity of urine is influenced by the perspiration and to a lesser extent by catharsis. It appears probable that the perspiration is freer under the influence of the large administration of fluid. The temperature has no direct effect on the diuresis. Diuretics do not increase the polyuria, nor does the administration of calcium chloride appear to diminish diuresis.

The effect of the polyuria on the chloride excretion, as compared with ordinary typhoid cases, consists in a diminution of the percentage and an increase of the amount excreted per day. Minor variations in diuresis effect the percentage, but not the daily output. Perspiration acts indirectly, by influencing the diuresis. The course of the fever, the degree of hyperpyrexia, and the convalescence appear to have no direct effect.

The chloride excretion varies strictly with the chloride income. The effect of calcium chloride is, however, delayed and comparatively small. Agurin, sodium acetate and nitrate, and urotropin had no effect on the chloride excretion, but it was increased by iodide. Moderate nephritis was without effect.

The excretion of water and chlorides in typhoid fever appears to obey the same laws as in health. There is, however, a greater tendency to chloride retention in the fever. The difference appears to be only quantitative and not qualitative. It is greatly diminished by polyuria.
The prolonged restriction of the chloride income appears to produce no deleterious effects, and the patients do not develop any "salt hunger."

APPENDIX.

Explanatory Notes. The urines were collected from 7 a.m. to 7 a.m., the last collection being made very close to 7 o'clock. The urines were analyzed soon after their receipt at the laboratory. The chlorides were determined in a 20 c.c. sample of the urine, directly by titration against silver nitrate (1 c.c. = 1 mg. NaCl), using potassium chromate as indicator. This preliminary determination served to show the progress of the case, and to check the second determination. This was made after incinerating 20 c.c. of the urine with sodium nitrate and carbonate. The latter determination was used in calculating the daily excretion. The direct determination gave results but slightly higher than the incinerated samples during the polyuria, when the urine was almost colorless. In the scanty, highly colored urines which were voided after the hemor-rhages the end reaction was indistinct and the values were considerably too high.

The recording of the fluid taken and the collection of the urines had to be left to the nurses and orderlies. As this conflicted somewhat with numerous other duties, occasional errors were only natural. When these were discovered the results were discarded, which accounts for some of the breaks in our charts. There can be little doubt that other errors escaped detection, which may account for temporary, unexplained variations. These we have retained in the charts, but we have tried to eliminate them in drawing our conclusions. A fairly good check of the accuracy of the collection and recording is furnished by comparing the curves for the income of fluid and the quantity of urine, and the income and output of chlorides. From these we may conclude that the accuracy was sufficient.

The figures for the chloride income cannot be considered absolute, and have only a comparative value. In their calculation the first analysis of the albumen solution (0.445 gram per litre) and of the milk (1.09 grams) was employed.

SUPPLEMENTARY NOTES.

(Mention of medicines like strychnine or morphine and the tub-baths are omitted.)

Colson. Admitted to the hospital and placed on milk and albumen diet and water on June 26, 1904, on the eighteenth day of the disease. The urine shows a faint trace of proteid throughout.

Diet. Milk and albumen-water to July 2d; July 2d to 5th, all nourishment stopped and water reduced; July 5th to 15th, milk and
albumen-water; July 15th, soft egg and toast; July 16th to 20th, custard and junket (July 18th, 3 ounces of ice-cream); July 20th to 22d, all nourishment stopped and water reduced; July 22d, albumen-water; July 23d, milk and albumen-water; July 24th, albumen-water; July 25th, milk and albumin water; July 26th, milk, albumen, custard, and 13 ounces of broth; July 27th, custard, junket, and 27 ounces of broth. (Port wine from July 24th on.)

**Medicines** (per day). July 1st to 6th, 8 grams calcium chloride; July 6th to 9th, 6 grams; July 12th to 16th, 2 grams urotropin; July 17th to 19th, 6 grams of agurin.

**Intestinal Hemorrhages.** July 2d, 5 a.m., 3 ounces; 9 a.m., 6 ounces; 3 p.m., 16 ounces; July 20th, 3 p.m., four hemorrhages, aggregating 52 ounces; July 24th, 1 a.m., 12 ounces; 3 p.m., 4 ounces.

**Kordick.** Admitted to the hospital and placed on milk and albumen diet and water on August 17th, on the fourth day of the disease. Faintest trace of albumin throughout. Perspires freely, especially on August 31st and September 1st.

**Diet.** Milk and albumen-water.
Medicines (per day). August 22d to 25th and August 28th to 31st, 9 grams of sodium acetate.

Kretzian. Admitted to the hospital and placed on milk and albumen diet and water on June 28th, on the fourth day of the disease. Slight albuminuria throughout.

**Diet.** To July 28th milk and albumen-water (July 17th, bag of candy found in bed; not known whether any was eaten; no visitors allowed after this); July 18th, 3 ounces of ice-cream; July 22d, 4 ounces of ice-cream; July 28th, custard and junket; July 29th, toast and egg.

Medicines (per day). July 4th to 6th, 9 grams of sodium acetate; July 6th to 10th, 17th to 20th, and 24th to 27th, 9 grams of sodium nitrate; July 6th, 0.2 gram of calomel; July 7th, 15 grams of magnesium sulphate.

Kiswan. Admitted to hospital and placed on milk and albumen diet and water on August 6th, on the eleventh day of the disease.
An active nephritis exists on admission, which tapers off. Some urine is lost through incontinence.

**Diet.** Milk and albumen-water throughout.

**Medicines** (per day). August 18th to September 2d, 0.67 gram of urotropin; July 18th to 19th, 6 grams of sodium nitrate; July 19th to 21st, 23d to 26th, and 28th to 31st, 9 grams of sodium nitrate.

**Hickock.** Admitted to hospital and placed on milk and albumen diet and water on August 8th, the eleventh day of the disease. A very faint trace of albumin throughout.

**Diet.** Milk and albumen-water, except from August 18th to 20th, when all nourishment is withdrawn and the water reduced.
Medicines (per day). August 17th on, 4 grams of calcium chloride; August 18th, 6 grams of sodium acetate; August 19th to 21st, 9 grams of sodium acetate.

Intestinal Hemorrhages. August 17th, 9 to 12 A.M., 6 ounces; August 18th, 5 to 9 A.M., 3 ounces; 3 to 6 P.M., 4 ounces; August 20th, 6 to 9 P.M., 10 ounces.

Barber. Admitted to hospital and placed on milk and albumen diet and water on August 19th, the sixth day of the disease. The urine contained a faint trace of albumin throughout:

Diet. Milk and albumen-water.

Medicines (per day). August 27th to 30th, 9 grams of sodium acetate; August 30th, 0.67 gram of quinine hydrochloride; August 31st to September 2d, 1 gram. Iodide was found in the urine on September 2d.
Chills, accompanied by profuse perspiration, were present from August 7th.

Doyle. Admitted to hospital and placed on milk and albumen diet and water on August 11th, the fourteenth day of the disease.