Influence of Mercurial Diuretics on the Excretion of Sodium, Potassium and Chlorides

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IT has been shown repeatedly that both mercurial diuretics and low sodium diets cause diuresis in patients with congestive heart failure, providing there is an adequate fluid intake. Most patients find a low sodium diet most unpalatable and many would prefer an occasional injection of a mercurial diuretic with less extreme sodium reduction in the diet. This study was undertaken to determine if possible the exact value of mercurial diuretics in augmenting or partially replacing the unpalatable extremely low sodium diets which have recently been used as an effective diuretic measure.

METHOD OF STUDY

This is a report based upon the study of ten patients, nine of whom had congestive heart failure, and one of whom had portal cirrhosis. They were maintained on digitalis and were given no aminophyllin. Ammonium chloride was used in Cases Nos. 1, 3 and 9. All patients were maintained on a daily fluid intake of 3,000 cc. They were given diets containing one gram of sodium chloride daily except for Case No. 6 where the sodium chloride was raised during the course of the study to determine the effect of this increase in sodium intake upon its excretion. Urinary output was measured from 8:00 a.m. to 8:00 a.m. Two cc. (one cc. in Case No. 7) of a mercurial diuretic (mercuhydrin) was administered intravenously every third or fourth day. This was given at the beginning of the 24-hour period so that on the day of injection the mineral excretion was measured for the following 24-hour period.

Determinations of sodium and potassium were made by means of a flame photometer. This apparatus is similar to that described by Barnes et al[1] but the Beckman Spectrophotometer was used as a monochromator and light measuring instrument. Satisfactory concentrations were obtained by diluting the urine 1 to 50 with distilled water. The calibration was made by using standard sodium and potassium solutions containing 5 to 50 parts per million.

Chloride determinations were performed by direct potentiometric titration with silver nitrate using a National Tech. Lab. pH meter with silver and glass electrodes.

These determinations were done by Albert L. Chaney, Ph.D.

REPORT OF CASES

CASE No. 1.—(Figure 1.) The patient received ammonium chloride 4 gm. per day during the entire period of observation. On the first three days he was digitalized and thereafter received only maintenance doses of digitalis. On the day before the first mercuhydrin injection was given, the total sodium excretion was greater than at any subsequent time. This was probably due to the fact that the patient was being digitalized at that time. Thereafter the total sodium excretion was greater in the 24-hour urine specimen after injection of the diuretic than on any of the other 24-hour urine specimens.

The percentage of sodium excretion or grams per liter was also increased in the 24-hour urine specimens following the mercurial diuretic.

CASE No. 2.—The patient was digitalized prior to hospital entry. When he entered the hospital there was evidence of digitalis intoxication with anorexia, nausea, vomiting and multiple ventricular premature contractions. These disappeared after six days, and digitalis therapy was resumed. Following the resumption of digitalis on the sixth day there was again noted an increase of total sodium excretion. Along with this increase of sodium excretion there was a corresponding increase of both the percentage and the total chloride excretion. With each injection there was a decrease of the percentage of potassium excretion, but due to the increased urinary output there was no corresponding decrease in the total potassium excreted.

CASE No. 3.—This patient received on the first day 1.2 mg. of digitoxin with no observed effect on the mineral excretion. The findings were essentially the same as in Case No. 2. On the days of the mercurial injection the percentages of sodium and chloride excretion were increased while the potassium excretion was decreased.

CASE No. 4.—This patient was on maintenance doses of digitalis before and during the study. The sodium and chloride excretion was increased on the days the mercurial was used. This was more marked with the first injection. As the patient depleted his reserves of body sodium by an output of sodium which exceeded the 1 gm. daily sodium chloride intake the total excretion of sodium became progressively lower. In spite of this the percentage of sodium and chloride continued to be higher on the days the diuretic was administered.

The output was not recorded on the last day that mercuhydrin was injected so we were unable to determine the total sodium output for that day.

CASE No. 5.—This patient was on maintenance doses of digitalis during the entire study, as he had been previously digitalized.

There was an increase in both the percentage and total excretion of sodium and chloride on the days of mercuhydrin injection but unlike the previous cases no material change in the potassium excretion was observed.

CASE No. 6.—(Figure 2.) This patient was on digitoxin 0.2 mg. daily during the entire study. Regardless of urinary output there was an increase in the percentage of sodium and chloride excretion on the days of mercuhydrin administration. The values for potassium were inconstant though

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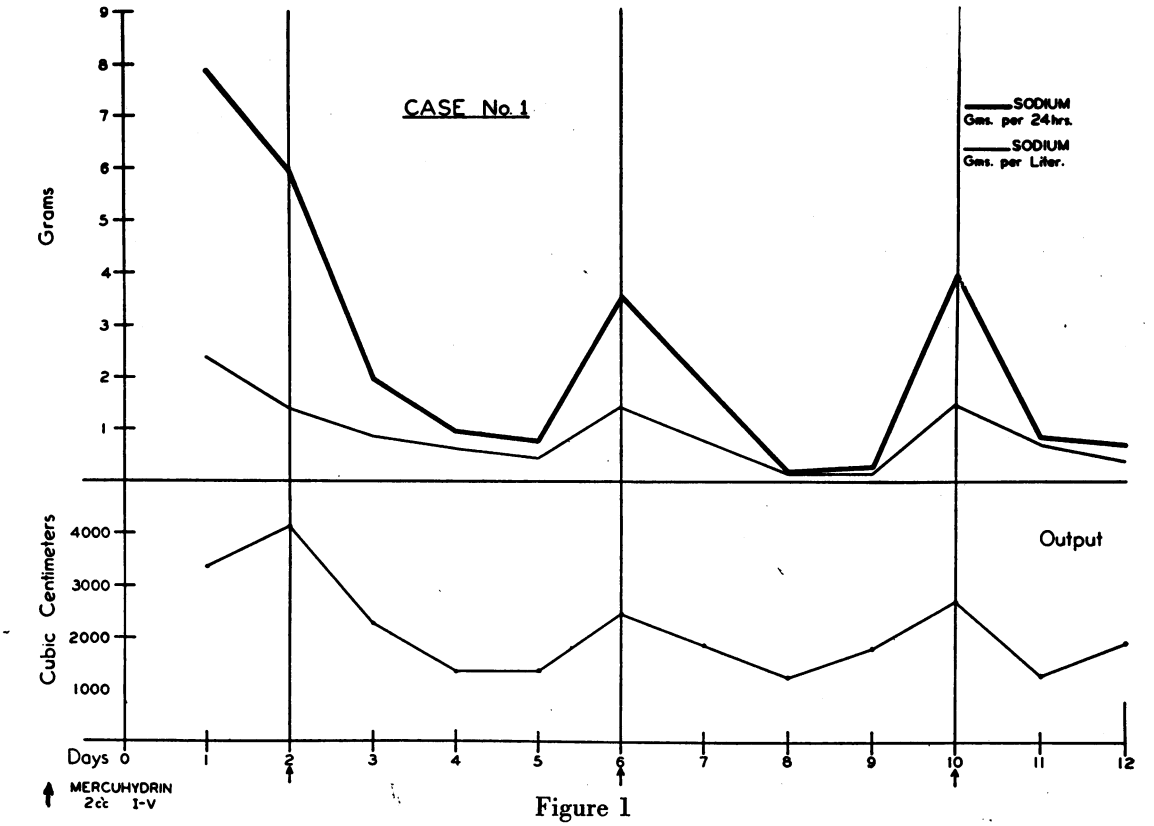

Figure 1

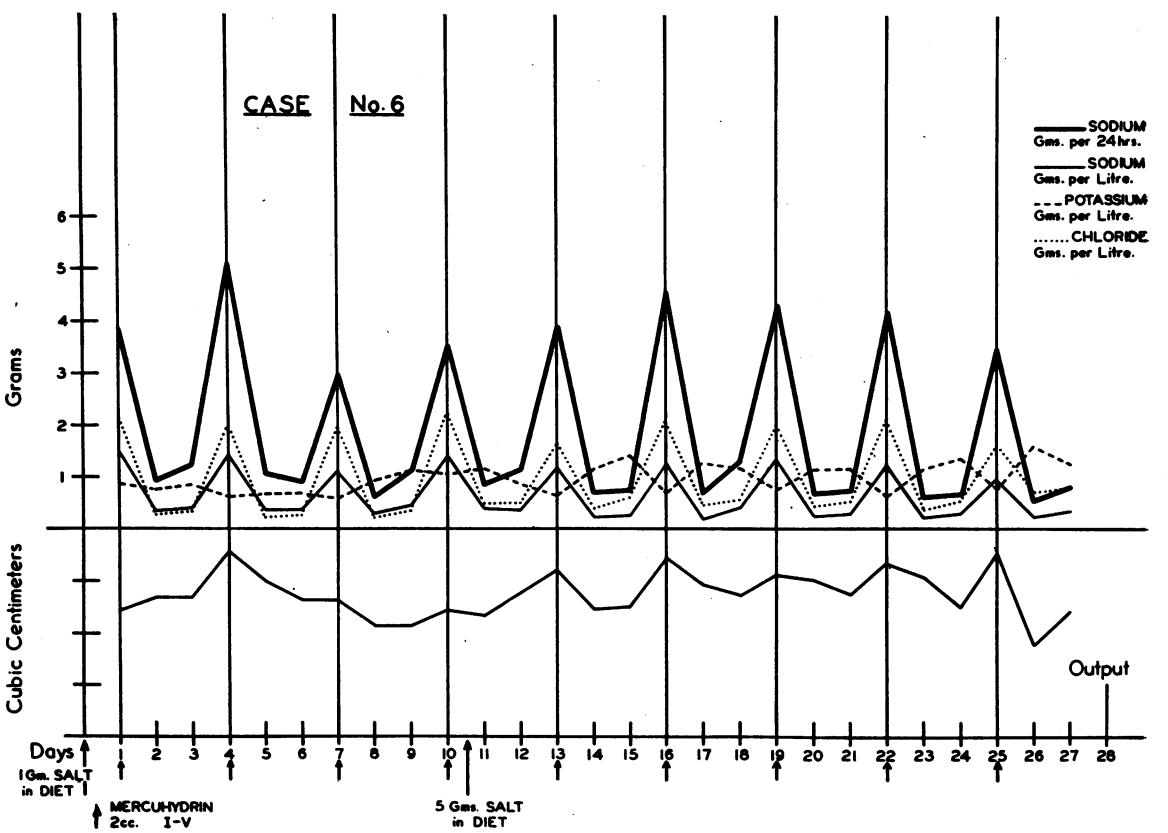

Figure 2

they tended to be lower on the days of the injection. On the eleventh day the sodium chloride intake was increased from 1 gm. to 5 gm. with no significant change in urinary output of sodium. In spite of the increase of sodium chloride intake he had no recurrence of signs or symptoms of congestive failure. This may be due to the fact that the sodium chloride excretion with the diuretics practically equalled this 5 gm. intake.

This patient had three thoracenteses, done on the first, tenth, and eighteenth days of our study. A total of 3,350 cc. of pleural fluid was removed. Only two specimens were analyzed for the sodium content of the pleural fluid. The first contained 2.85 gm. per liter and the second 4.5 gm. per liter. The pleural fluid had a higher sodium content than the average percentage in the urine so that this seems to be an important method of removing sodium from the body.

CASE No. 7.—(Figure 3.) This patient was digitalized with digitoxin during the first two days of our study. As with all the other cases more sodium was excreted on the days of mercurial injection than on the other days. The percentage of sodium was also greater. This case demonstrates the fact that as the sodium in the body is depleted the sodium excretion becomes progressively lower. This case also shows the amount of sodium excreted on six successive days without mercurial diuretics. In this patient only 1 cc. of mercuhydrin was administered every third day. While the urinary output in this patient was not large the total and percentage sodium excretion was almost as great as in the other patients who were given 2 cc. injections of mercuhydrin.

CASE No. 8.—This patient received ammonium chloride 4 gm. daily during the entire study. He was digitalized during the first three days of the study. The high sodium excretion on the second day may in part be due to the digitalis. This case demonstrates again the decrease in sodium excretion as the sodium in the body is depleted by an excretion exceeding the 1 gm. daily sodium chloride intake.

CASE No. 9.—This patient was on maintenance doses of digitoxin. Ammonium chloride 4 gm. daily was given during the entire study. Following the first two mercurial injections the sodium excretion, both the percentage and the total, was greater than at any other time. This was not true of the third injection.

CASE No. 10.—This patient had portal cirrhosis with no evidence of congestive failure. The albumin globulin ratio was 3.6:3.0 gm. The 5 mg. bromsulphalein test showed a retention of 60 per cent after one-half hour and 35 per cent after one hour. The intravenous hippuric acid test showed an excretion of 0.16 gm. of benzoic acid in one hour. The non-protein nitrogen was 45. No digitalis or ammonium chloride was given. The sodium excretion was greater following the mercurial injections than at any other time. The total daily sodium excretion never exceeded 1 gm. even on the days the diuretic was given. The reason for this is not clear. This case is not included in the averages of the cases.

DISCUSSION

The average of the nine cases showed a sodium output of 0.81 gm. per liter on the days without the diuretic (Figure 4) and 1.96 gm. per liter on the days mercuhydrin was injected. The average total 24-hour output of sodium was 1.09 gm. on the days without injection and 4.83 gm. on the days of injection. This shows that the concentration of sodium in the urine was increased nearly two and one-half times

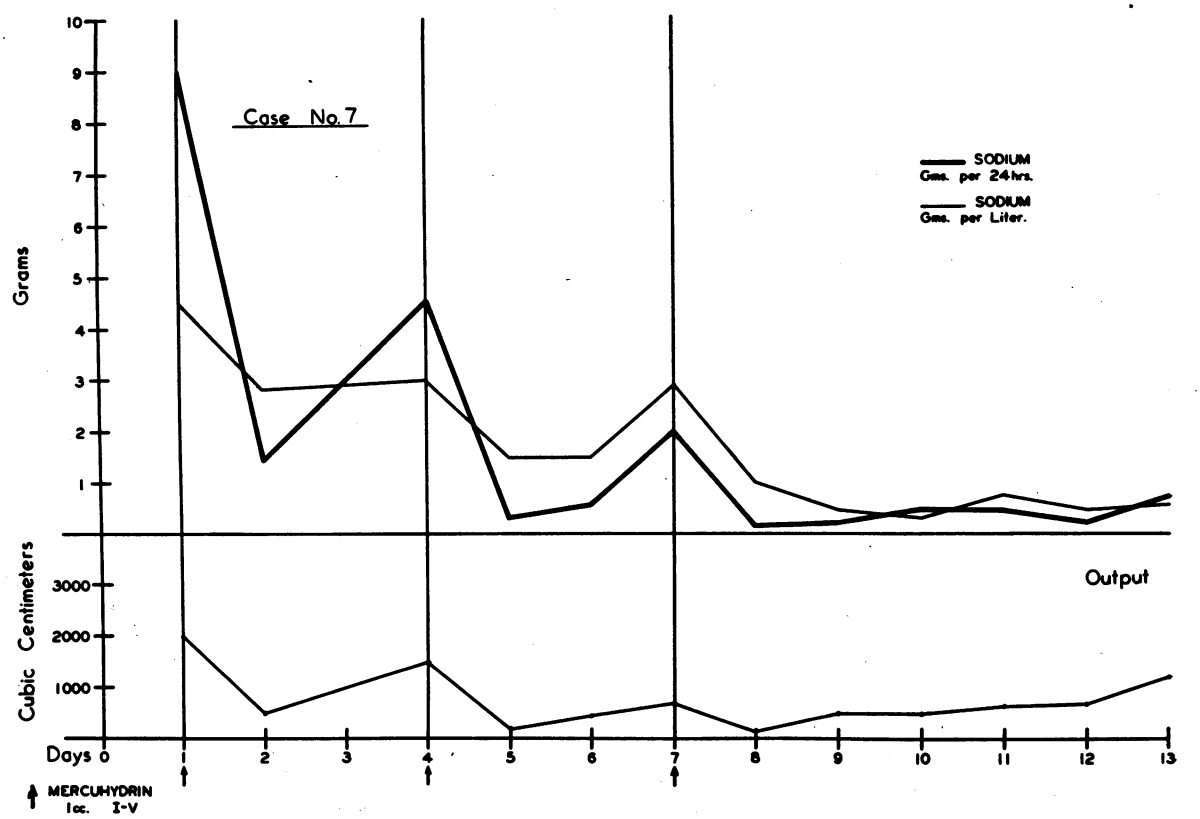

Figure 3

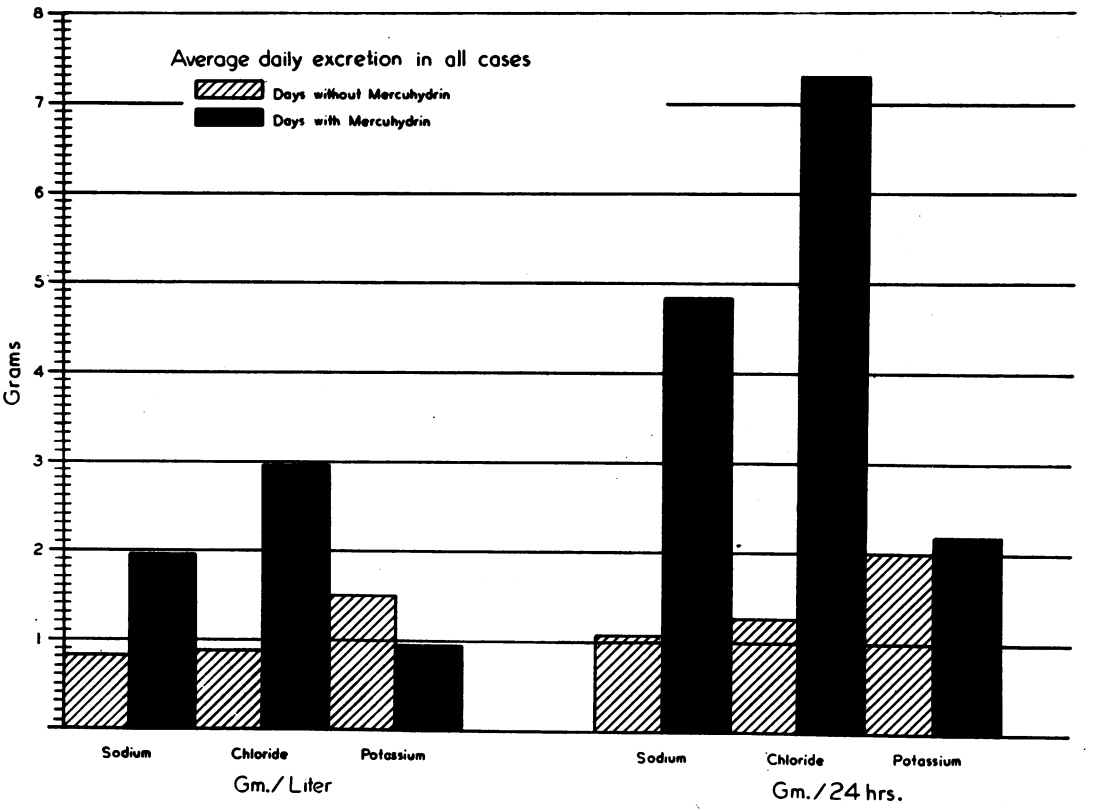

Figure 4

by the injection of the mercurial diuretic, while the average total excretion of sodium in 24 hours was increased more than four times by mercuhydrin injections. Reaser and Burch,[5] in an independent study, recently also found a marked increase both in the total and percentage sodium excretion after injections of a mercurial diuretic in a patient with congestive heart failure. They used a radioactive tracer Na^{22} to determine sodium excretion.

One gram of sodium (as we have measured it in the urine) is the equivalent of 2.54 gm. of sodium chloride which is the form in which dietary sodium is usually measured.

The average 24-hour excretion of 1.09 gm. of sodium on the days without injection is equivalent to 2.77 gm. of sodium chloride.

The average excretion of the 4.83 gm. of sodium for the 24 hours following the injection of mercuhydrin is equivalent to 12.27 gm. of sodium chloride or an increase of 9.5 gm. over the days the diuretic was not given. It would appear therefore from this small series that it may be possible by giving two injections of a mercurial diuretic weekly to increase the sodium chloride intake by 2.7 gm. per day. This would enable the patient to have a much more palatable diet without increasing sodium retention.

There was an actual decrease in the average percentage of potassium excreted in the urine following the injection of the mercurial diuretic. The average potassium in grams per liter decreased from 1.51 to 0.9 following the injections. Due, however, to the diuresis on the days of mercurial injection the total excretion of potassium was slightly greater on those days—2.16 gm. in 24 hours as compared with 2.01 gm. in 24 hours. Melville and Stehle[4] also found that the potassium excretion following the injection of mercurial diuretics is less than the sodium excretion.

The average percentage chloride excretion following an injection of the mercurial diuretic increased more than three and one-half times, from 0.83 to 2.94 gm. per liter. The average total 24-hour excretion of chlorides increased sixfold, from 1.17 to 7.3 gm.

This increased urinary concentration of chlorides was noted by Hatzieganu, Gavrila and Borbil,[3] and Bouyoucos[2] and Stockton.[6]

SUMMARY AND CONCLUSION

1. In a study of nine patients with congestive heart failure who were maintained on a low sodium diet, the injection of 2 cc. of a mercurial diuretic, mercuhydrin, caused the following changes in the urine during the 24 hours after its injection:

(a) The average concentration of sodium in the urine was increased nearly two and a half times. The total sodium excretion was increased more than four times.

(b) The average concentration of potassium in the urine was decreased 40 per cent, although due

to the diuresis there was a slight increase in the total excretion of potassium.

(c) The average chloride concentration in the urine was increased more than three and a half times. The total chloride excretion was increased six times.

2. The average total sodium excretion after the administration of 2 cc. mercuhydrin was 4.81 gm. This is the equivalent of 12.3 gm. of sodium chloride, which is the form in which dietary sodium is usually measured. This is an increased excretion of 9.5 gm. of sodium chloride over the days on which the mercurial diuretic was not given.

3. It appears possible that for brief periods at least, the injection of mercurial diuretics will permit a more palatable, higher sodium chloride diet without any increase in sodium retention.

REFERENCES

1. Barnes, R. B., Richardson, D., Berry, J. W., and Hood, R. L.: Flame photometry, Indust. & Eng. Chem., 17:605, 1945.

2. Bouyoucos, B. G.: Chloride and water content of urine and of blood in course of diuresis with organic mercury salts, Compt. Rend. Soc. de biol., 115:1170-1172, 1934.

3. Hatzieganu, I., Gavrila, I., and Borbil: Effect of mercurial diuretics on hydremia, chloruremia, azotemia and urinary eliminations, Compt. Rend. Soc. de biol., 99:1813 (Dec. 14)., 1928.

4. Melville, K. I., and Stehle, R. L.: Mercury diuresis, J. Pharmacol. and Exper. Ther., 34:209-222 (Oct.), 1928.

5. Reaser, P. B., and Burch, G. E.: Radiosodium tracer studies in congestive heart failure, Proc. Soc. Exper. Biol. Med., 63:543-546 (Dec.), 1946.

6. Stockton, A. B.: Actions of diuretic drugs and changes in metabolites in edematous patients, Arch. Int. Med., 58:891-900 (Nov.), 1936.