Effects of Posture on Renal Excretion of Sodium and Chloride in Orthostatic Hypotension

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Large decreases in the rates of sodium excretion, chloride excretion, and glomerular filtration were observed in patients with orthostatic hypotension when they assumed the upright posture following a period of recumbency. When they returned to the recumbent position, sodium excretion typically was not restored immediately in spite of immediate restoration of filtered sodium load. The decreased sodium excretion found to occur in patients with orthostatic hypotension when they are in the upright posture is considered to be due in part to the decreased filtered sodium load and in part to changes in tubular reabsorption that are independent of filtered sodium load.

When the normal human subject changes from the recumbent to the erect position, arterial blood pressure is maintained, and there is either no change or only a moderate decrease in renal sodium excretion. When the patient with orthostatic hypotension changes from the recumbent to the upright posture a marked fall in arterial blood pressure occurs; therefore, it might be anticipated that the decreased arterial blood pressure in the upright posture would be reflected by a decreased intraglomerular pressure, decreased glomerular filtration rate, and decreased sodium excretion.

The effect of posture upon the renal excretion of sodium in human subjects with orthostatic hypotension has not been reported previously. Studies of renal function in orthostatic hypotension have demonstrated a decreased rate of urine flow when such patients change from the recumbent to the upright position, while at the same time, phenolsulphonphthalein excretion and uric acid clearance remain unchanged. Corcoran and associates have demonstrated decreased inulin and Diodrast clearances in patients with orthostatic hypotension who were tipped by means of a tilt-table to the 60 degree head-up passive erect posture.

In the present study it has been demonstrated that in orthostatic hypotension large changes in the renal excretion of sodium result from changes in body posture. Filtered sodium loads have been measured, and the changes in sodium excretion have been interpreted in terms of alterations in the glomerular filtration and tubular reabsorption of sodium.

Methods

1. Clinical Methods. Studies of renal function were performed upon three patients with orthostatic hypotension and upon one hypertensive patient under the influence of Dibenamine. Changes in renal function were obtained simply by requesting the patient either to assume a position of recumbency or to sit, stand quietly, or walk. In general, a period of erect posture was interposed between two periods of recumbent posture. Arterial blood pressures, pulse rates, fluid intake, and urine output were recorded. Diets were unrestricted except in experiment 6, in which case the patient was fasting, and in experiment 7, in which instance the patient was on a diet containing about 1.5 Gm. of sodium chloride per day. To assure an adequate urine output for urine volume measurements the patients drank varying quantities of water at the beginning of each study and throughout the course of the study. No intravenous infusions were employed. Urine samples were obtained without employment of catheterization. Blood samples were withdrawn from an antecubital vein either at the midpoint of the urine collection period or at the beginning and end of the urine collection period.

The endogenous creatinine clearance was employed as a measure of glomerular filtration rate. Although endogenous creatinine clearance is not always equal to inulin clearance, evidence is accumulating that this function is a reliable measure of changes in glomerular filtration rate. In some
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experiments urinary creatinine excretion was measured instead of endogenous creatinine clearance.

2. Analytic Methods. Sodium and potassium ions were determined by means of a Barclay Flame
samples were determined by an aeration method described by West and Todd. creatinine was determined in urine and plasma samples by a modification of the method of Hare.

| TABLE 1.—Summary of Fluid Intake and Urine Output for All Experiments |
|-------------------------------|-------------------|-------------------|-------------------|
| Time                         | Position          | Water Drunk (ml.) | Urine Output (ml.) | Urine Specific Gravity |
| Experiment 1                 |                   |                   |                   |                       |
| 10:30 p.m. to 7:30 a.m.      | Recumbent         | Unrestricted      | 715               | 1.015                 |
| 7:30 a.m. to 3:30 p.m.       | Upright           | Unrestricted      | 163               | 1.025                 |
| Experiment 2                 |                   |                   |                   |                       |
| 10:00 p.m. to 6:00 a.m.      | Recumbent         | Unrestricted      | 1510              | 1.008                 |
| 6:00 a.m. to 2:00 p.m.       | Recumbent         | Unrestricted      | 44                | 1.028                 |
| 2:00 p.m. to 10:00 p.m.      | Upright           | Unrestricted      | 302               | 1.031                 |
| Experiment 3                 |                   |                   |                   |                       |
| 7:15 p.m. to 10:05 p.m.      | Standing          | 800               | 175               | 1.010                 |
| 10:05 p.m. to 11:05 p.m.     | Recumbent         | 385               | 1.001             |
| 11:05 p.m. to 3:05 a.m.      | Recumbent         | 1200              | 1.003             |
| 3:05 a.m. to 7:05 a.m.       | Recumbent         | 285               | 1.013             |
| 7:05 a.m. to 8:05 a.m.       | Standing          | 500               | 22                |
| 8:05 a.m. to 11:05 a.m.      | Standing          | 45                | 1.025             |
| 11:05 a.m. to 3:17 p.m.      | Standing          | 800               | 85                | 1.027                 |
| 3:17 p.m. to 7:00 p.m.       | Standing          |                   |                   |                       |
| Experiment 4                 |                   |                   |                   |                       |
| 7:45 p.m. to 6:30 a.m.       | Recumbent         | Unrestricted      | 1010              | 1.015                 |
| 7:45 a.m. to 4:00 p.m.       | Upright           | Unrestricted      | 310               | 1.035                 |
| Experiment 5                 |                   |                   |                   |                       |
| 8:15 a.m. to 12:53 p.m.      | Recumbent         | 500               | 1860              | 1.008                 |
| 12:53 p.m. to 5:14 p.m.      | Standing and walking | 1000             | 94                | 1.021                 |
| 5:14 p.m. to 6:17 p.m.       | Recumbent         | 250               | 192               | 1.007                 |
| 6:17 p.m. to 8:00 p.m.       | Recumbent         | 940               |                   | 1.003                 |
| Experiment 6                 |                   |                   |                   |                       |
| 2:55 p.m. to 5:50 p.m.       | Recumbent         | 1040              | 76                | 1.035                 |
| 5:50 p.m. to 8:55 p.m.       | Sitting           | 800               | 167               | 1.015                 |
| 8:55 p.m. to 9:50 p.m.       | Head-down 27 min.; recumbent | 500          | 277               | 1.005                 |
| 9:50 p.m. to 1:00 p.m.       | Recumbent         | 450               | 363               | 1.003                 |
| 8:35 a.m. to 11:29 a.m.      | Recumbent         | 400               | 402               | 1.002                 |
| 11:29 a.m. to 2:30 p.m.      | Recumbent         | 350               | 160               | 1.004                 |
| 2:30 p.m. to 5:30 p.m.       | Recumbent         | 350               | 440               | 1.001                 |

Photometer with lithium ion employed as the internal standard. The average deviation of the sodium determinations was about 5 per cent.

Chlorides were determined by the method of Vollard.

Ammonia nitrogen and urea nitrogen in urine This method allows for determination of "true creatinine" and not "total creatinine chromogen."

RESULTS

Data concerning fluid intake, urine output, and urine specific gravity are listed in table 1
In figures 1 to 7 the postural variations in urinary sodium excretion are shown graphically with the simultaneous variations in either endogenous creatinine clearance* or in urinary creatinine excretion. In those cases in which serum sodium was measured, the filtered sodium load, which is equal to the product of the endogenous creatinine clearance and the serum sodium,† is also shown. Protocols of

* Endogenous creatinine clearances are uncorrected for body surface area.
† Correction for the Donnan equilibrium and for plasma water content is not applied.

the individual experiments are presented as the legends of figures 1 to 7. In figure 8 the simultaneous excretion rates of potassium, ammonia nitrogen, and urea nitrogen are graphed with the postural changes in the creatinine and sodium excretion rates. The rate of urinary chloride excretion was determined in all cases and found to approximate closely the rate of sodium excretion. An example of this correlation is presented in figure 9.

![Fig. 1. Effects of posture upon sodium excretion and creatinine excretion in patient, R. N., experiment 1. Patient R. N. was diagnosed as having orthostatic hypotension. From 10:30 p.m., June 8, 1950 to 7:30 a.m., June 9, 1950 the patient was recumbent, asleep most of the time. From 7:30 a.m. to 3:30 p.m., June 9, 1950, the patient was in either the sitting or standing posture.](image1)

![Fig. 2. Effects of posture upon sodium excretion and creatinine excretion in patient, S. B., experiment 2. Patient S. B. had idiopathic orthostatic hypotension. He remained recumbent from 10:00 p.m., Dec. 4, 1950 until 6:00 a.m., Dec. 5, 1950. For the next 16 hours the patient was in either the sitting or standing position, occasionally walking.](image2)

The renal excretion of sodium was found to decrease greatly in the patients with orthostatic hypotension when they assumed the upright posture after a period during which they were recumbent. The rate of sodium excretion of the patient in the upright posture was found to be one-third to one-hundredth of the rate in the recumbent posture. A large percentage decrease in sodium excretion while the patient was in the upright posture occurred even in experiment 7, in which the patient was on a "salt-free" diet and excreting only minute quantities of sodium during the control period.

The decreased sodium excretion rate in-
duced by the upright posture was observed to be accompanied by decreases in glomerular filtration rate and filtered sodium load. Relatively small percentage decreases in glomerular filtration rate or filtered sodium load were accompanied by relatively large decreases in sodium excretion rate. In three experiments, 3, 5, and 6, filtered sodium load and urinary sodium excretion were found to change simultaneously in opposite directions.

In experiment 5 restoration of the glomerular filtration rate and filtered sodium load to the levels obtained while the patient was in the recumbent position occurred without restoration of urinary sodium excretion. In experiment 3, the initial rise in filtered sodium load is accompanied by a delayed increase in sodium excretion. The trend is also seen in experiment 2, in which urinary creatinine excretion returned to the value obtained during the period of recumbency, while urinary sodium excretion remained depressed. On the other hand, in experiment 7, urinary sodium excretion returned to the value obtained while the patient was recumbent in spite of the failure of the filtered sodium load to return to the level observed during recumbency.

**Fig. 3.** Effects of posture upon endogenous creatinine clearance, filtered sodium load, and sodium excretion in patient, S. B., experiment 3. The patient, S. B., the same as in experiment 2, was hospitalized from Jan. 23, 1951 to Jan. 24, 1951. Average blood pressure during this experiment when the patient was in the recumbent position was 130/80; pulse, 64; average blood pressure while the patient was standing was 95/80; pulse, 90.

**Fig. 4.** Effects of posture upon sodium excretion and creatinine excretion in patient, S. B., experiment 4. This study of patient, S. B., was made about one year after experiments 2 and 3. Blood pressure was 110/70 in the recumbent position and 60/40 in the standing position. The patient was not hospitalized but was instructed carefully in the collection of urine samples at home. Diet and fluid intake were unrestricted. The patient remained recumbent from 7:45 p.m., Dec. 15, 1951 to 6:30 a.m., Dec. 16, 1951. He then arose and remained in the upright position, either sitting or standing, from 6:30 a.m. until 4:00 p.m., Dec. 16, 1951.

In experiment 3, figure 3, during hour 12, a decrease in sodium excretion is seen to accompany a decrease in the endogenous creatinine clearance. During hour 13 a further decrease in sodium excretion occurs in the face of an unchanged glomerular filtration rate and filtered sodium load. While it is possible that the urine sample of hour 12 may have been contaminated with sodium from the urine of hours 8 to 12, inspection of figure 8, concerning the same experiment, reveals no corresponding
trend in the excretion of ammonia nitrogen or potassium.

**Discussion**

In patients with orthostatic hypotension the renal excretion of sodium decreases markedly when the subject assumes the standing posture. The decreased sodium excretion in the patient in the upright posture is accompanied by large decreases in glomerular filtration rate and filtered sodium load. This is in contrast to the situation in the normal individual who is up and about in whom, at most, relatively minor decreases in sodium excretion and glomerular filtration rate occur.

In recent years the relative importance of the glomerular filtration and the tubular reabsorption of sodium upon sodium excretion by the kidney has been the subject of many investigations in both man and in experimental animals. Some workers have demonstrated that changes in renal sodium excretion are...
frequently associated with, and possibly are caused by, somewhat parallel changes in glomerular filtration rate.\textsuperscript{27, 28} Others have reported changes in sodium excretion occurring independently of changes in glomerular filtration rate.\textsuperscript{29-33}

That alterations in amount of sodium filtered play a role in the decreased sodium excretion which occurs in subjects with orthostatic hypotension when they assume the erect posture is indicated by the results of experiment 3 shown in figures 3 and 8. Ammonia nitrogen and potassium, substances excreted by tubular secretion, are little affected by the decrease in glomerular filtration rate occurring during the second period of standing. Creatinine, a substance which is considered to be excreted only by glomerular filtration, under the conditions of the experiment, is decreased

\textbf{Fig. 7.} Effects of posture upon endogenous creatinine clearance, filtered sodium load, and sodium excretion in patient, S. D., experiment 7. S. D. was hospitalized with the diagnoses of pernicious anemia and orthostatic hypotension. In the outpatient department, prior to her hospital admission, her blood pressure in the recumbent position was 110/70 and in the standing position, 60/40. The patient had been on a "salt-free" diet (1.5 Gm. NaCl per day) for at least 10 days prior to the renal function studies and was maintained on the same diet for the duration of the studies. She drank 200 ml. of water at the beginning of the experiment and then 100 ml. of water hourly until its conclusion. During the upright period the patient sat in a wheelchair most of the time. Two periods of ambulation, each of 20 minutes duration, were included in the upright period. Blood pressure while the patient was recumbent averaged 100/70; pulse, 56. Systolic blood pressure, taken while the patient was in the sitting position, was 90 mm. Hg and diastolic pressure could not be determined by the indirect method. Pulse was 72. Hemoglobin, 13.3 Gm.; red cell count, 4.7 million per cubic millimeter.

\textbf{Fig. 8.} Effects of posture upon urinary excretion of ammonia nitrogen, potassium, creatinine, urea nitrogen, and sodium, experiment 3. The data depicted here were recorded simultaneously with those shown in figure 3. For further explanations see text.
proportionately to the decrease in glomerular filtration rate. In the case of urea, a substance not reabsorbed by an active process, the decrease in urea excretion results from the decreased glomerular filtration rate. Since the percentage decrease in urea excretion is greater than the percentage decrease in creatinine excretion, the decreased glomerular filtration of urea must secondarily result in more complete tubular reabsorption of urea by simple physical processes. Sodium resembles urea insofar as it is also a freely-diffusible substance. By analogy, the decreased filtered sodium load occurring when the subject is in the upright posture may also allow for more complete tubular reabsorption of sodium by simple physical processes. The greater percentage decrease in the excretion of sodium as compared with the percentage decrease in the excretion of urea is evidence that in addition to simple physical processes, an active tubular transport mechanism may be operating to effect reabsorption of sodium.

To prove the occurrence of changes in the active tubular reabsorption of sodium it is necessary to demonstrate different rates of sodium excretion at the same filtered load\textsuperscript{14, 15} or to show that sodium excretion and filtered sodium load are changing simultaneously in opposite directions. Many of the investigators claiming to have demonstrated altered tubular reabsorption of sodium have not measured filtered sodium loads. They determined glomerular filtration rates and assumed that the plasma sodium level remained unchanged. In the present work serum sodium levels have been determined and the filtered sodium loads calculated. Evidence has been obtained that sodium excretion may vary independently of filtered sodium load. In experiment 3, figure 3, during the recumbent period, sodium excretion is seen to increase while filtered sodium load is decreasing. During the early part of the second period of standing, a marked decrease in sodium excretion occurs in the face of an unchanged filtered sodium load. During the last period of standing, sodium load tends to be restored towards control values without an accompanying increase in sodium excretion. In experiment 6, during hour 6, sodium excretion increased in spite of a decreasing filtered sodium load. In experiment 7, figure 7, filtered sodium load remains below the level observed during the last recumbent period, while sodium excretion returns to above the control level.

The results indicate that changes in sodium excretion which are due to altered filtered sodium load occur rapidly, whereas the adjustments in tubular reabsorption occurring in-

![Fig. 9. Comparison of the changes in urinary sodium excretion and chloride excretion resulting from changes of posture in experiments 3, 5, and 7. The sodium excretion is indicated by the solid horizontal lines, while the chloride excretion is indicated by the broken horizontal lines. When the two were equal, a single solid horizontal line is employed.](image-url)

dependently of changes in filtered sodium load occur more slowly. During the recumbent period in experiment 3, figure 3, an immediate rise in filtered sodium load is accompanied by a gradual increase in sodium excretion. In the same experiment a sudden decrease in filtered sodium load is accompanied by a simultaneous decrease in sodium excretion; however, a further decrease in sodium excretion occurs with the passage of time, in spite of no further change in filtered sodium load. In experiment 5, figure 5, an immediate restoration of filtered
sodium load to the previous value for the recumbent posture is seen to be accompanied by a more gradual rise in sodium excretion rate. From these studies it appears that a sudden large decrease in glomerular filtration rate and filtered sodium load may cause a sudden severe decrease in sodium excretion. Later adjustments in tubular reabsorption, occurring independently of glomerular filtration rate and filtered sodium load, may tend to alter sodium excretion further, depending upon variables not yet clearly identified.

**SUMMARY**

The changes in renal sodium excretion resulting from changes of posture in patients with orthostatic hypotension have been measured and the results interpreted in terms of alterations in the glomerular filtration and the tubular reabsorption of sodium. The endogenous creatinine clearance was employed as a measure of the glomerular filtration rate, and filtered sodium loads were calculated as the products of the glomerular filtration rates and the serum sodium concentrations.

Large decreases in the rate of urinary sodium excretion and in glomerular filtration rate occurred when subjects with orthostatic hypotension changed from the recumbent to the upright posture. Typically, when they returned to the recumbent posture sodium excretion was not restored immediately in spite of the immediate increases in filtered sodium loads. Other examples of sodium excretion varying independently of filtered sodium load were observed; thus proof was obtained of altered tubular reabsorption of sodium. Changes in chloride excretion resulting from postural changes in patients with orthostatic hypotension were parallel and approximately equal to the changes in sodium excretion.

It is concluded that the decreased sodium excretion found to occur in patients with orthostatic hypotension when they were in the upright position is partly due to the decreased load of sodium filtered and partly due to changes in tubular reabsorption that are independent of filtered sodium load.

**SUMARIO ESPAÑOL**

Gran diminución en la velocidad de excreción del sodio y cloruro, y la filtración glomerular fueron observados en pacientes con hipotensión ortostática al asumir la posición vertical luego de un período de recinación. Cuando volvieron a la posición reclinada, la excreción de sodio típicamente no fue restaurada inmediatamente a pesar de inmediata restauración de la carga de sodio filtrado. La diminución de excreción de sodio encontrada en pacientes con hipotensión ortostática cuando en la posición vertical es considerada como causada en parte a la diminución de carga de sodio filtrado y en parte a cambios en la reabsorción tubular que son independientes a la carga de sodio filtrado.

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