

Serum Sodium Values in Essential Hypertension.* (18850)

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(Introduced by Emmett B. Carmichael.)

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Numerous investigations in recent years have indicated that a relationship exists between the sodium ion and certain hypertensive states(1-4). Beneficial effects of a rice diet in hypertension are thought to be due, at least in part, to a decreased sodium intake(5-7). The effectiveness of sodium restriction in some types of hypertensive cardiovascular disease, while without effect in others, points to a relationship between this cation and the hypertensive syndrome(2,8,9). Selye(2) has shown conclusively that the sodium ion is necessary for the production of experimental hypertension with desoxycorticosterone administration. Likewise, Tobian(4) has shown that this electrolyte is essential to the production of hypertension in certain experimental conditions. Grollman(10) has found an elevated sodium content in various viscera of animals made hypertensive for experimental purposes. Still later, Tobian(11) showed that the sodium content was elevated in the renal artery of hypertensive patients. There have been relatively few reports on the concentration of sodium ion in the serum of hypertensive sub-

jects. Kylin and Elmquist(12) have reported a small series of serum sodium values obtained in hypertensive patients, all of which showed a small but definite elevation from the accepted normal values.

Recently the development of the flame photometer has brought about a simpler procedure for the determination of the sodium concentration in the serum. This method was used to determine serum sodium values in 75 of our hypertensive patients. The purpose of this paper is to present these findings, together with a correlation with those of a normotensive series.

Subjects studied. The outpatient department of the Jefferson-Hillman Hospital offered the source of the patients studied. In this clinic the admissions are made up of Negroes and whites in a ratio of 3 to 1. Sixty-four Negro ($\frac{2}{3}$ were female) and 11 white patients from the Hypertensive Clinic, who had a diastolic blood pressure reading of 100 mm of mercury or above, were examined. None of these patients presented any symptoms or findings of congestive failure. The ages ranged from 35 years to over 70 years of age, but the majority were between 40 and 55 years. In these patients the diagnosis of essential hypertension was arrived at merely on the basis of exclusion of known causes of hypertension, such as pyelonephritis or other primary renal diseases. These patients had been observed over a period of several years before the diagnosis of essential hypertension was substantiated. No cases of so-called hormonal hypertension as described by Schroeder were examined. Therapy had been discontinued at least 30 days before tests were made. For comparison we used a normotensive series of patients that besides being composed of apparently healthy individuals, were known to have normal blood pressures, and were

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1. Selye, H., *J. Clin. Endocrinol.*, 1946, v6, 117.
2. Selye, Hans, Stone, Helen, Timiras, Paola, S., and Schaffenburg, Carols, *Am. Heart J.*, 1949, v37, 1009.
3. Schroeder, H. A., *Am. Heart J.*, 1949, v4, 578.
4. Tobian, Louis, Jr., Personal communication.
5. Kempner, W., *North Carolina, M. J.*, 1945, v1, 72.
6. Flipse, M. E., and Flipse, J. J., *South. M. J.*, 1947, v40, 771.
7. Behrendt, F., and Burgess, A. M., *Rhode Island M. J.*, 1947, v31, 25.
8. Grollman, A., Harrison, T. R., Mason, M. F., Baxter, J., Crampton, J., and Reichsman, F., *J. A. M. A.*, 1945, v129, 533.
9. Grollman, A., *J. Am. Diet A.*, 1946, v22, 864.
10. Grollman, A., *Proceedings of hypertensive conference*, Sept., 1950.
11. Tobian, Louis, Jr., Personal communication.

12. Kylin, Eskil and Elmquist, Hilding, *Acta Med. Scand.*, 1936, v88, 507.

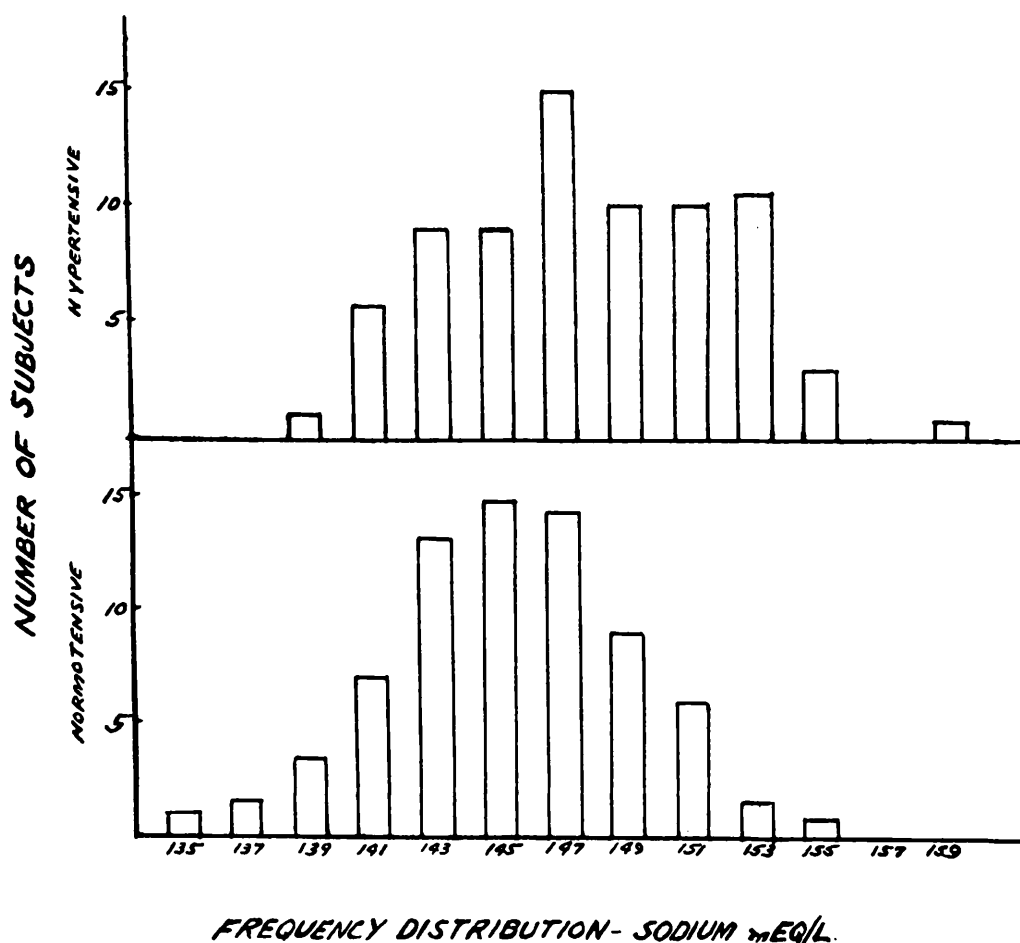


FIG. 1. Frequency distribution curve of serum sodium values in hypertensives as compared to those of normotensive individuals.

otherwise comparable in both sex, race, and age. This normal study was carried out concurrently with the studies on hypertensive patients.

Technic. Blood samples were obtained from nonfasting patients routinely on admission to the clinic and the serum immediately separated. The flame photometric technic used throughout the study was essentially that described by Mosher *et al.*(13). Samples were analyzed in duplicate and the average value of these readings was taken as the correct value. In a series of studies of experimental error it was found that serum sodium

can be determined consistently with less than 1% error. The normotensive frequency distribution curve(14), illustrated in Fig. 1, is based on 400 determinations of serum sodium values in 400 different, apparently normal individuals. The technic described above was used. In order to have a basis for comparison with the 75 hypertensive subjects, the number of subjects in each distribution group of the normotensives was multiplied by 75/400 giving the values plotted in Fig. 1.

Results. The mean value for "normal" serum sodium, as determined by this work, was 144.8 mEq/l. The mean value found in

13. Mosher, R. E., Boyd, A. J., Bird, E. J., Jacobson, S. D., Batchelor, T. M., Iseri, L. T., and Myers, G. B., *Am. J. Clin. Path.*, 1949, v19, 461.

14. Elliott, Howard C., Jr., and Holley, Howard L., *Abstract, Fed. Proc.*, 1951, v10, 1, 180; accepted for publication by the *Am. J. Clin. Path.*

75 hypertensive patients was 147.3 mEq/l, an increase of 2.5 mEq. A statistical analysis based on 400 normotensive determinations and 75 hypertensive determinations using Fisher's "t" test(15) showed the difference between the means to be significant. The value of "t" was 6.16 and that of "P" was less than .01. The standard deviation in the 400 normal determinations was 3.81 mEq/l, and the standard error 0.19 mEq/l. In the 75 hypertensive patients the standard deviation was 4.07 mEq/l, and the standard error was 0.45 mEq/l. In the frequency distribution curves shown in Fig. 1 it is obvious that there is a tendency toward an increase in the sodium values present in the serum of hypertensive individuals. Forty-three per cent of "normal" values fall to the right of the normal mean on the curve, while 66% of the hypertensive values fall in these same limits.

Twenty-four of the patients were recalled for further examination two months after the initial values were obtained. This was thought necessary in order to determine the constancy of the values previously found. Ninety-two per cent of the values checked were within plus or minus 0.5%. We believe that these deviations were within the range of technical error.

15. Fisher, Ronald, A., *Statistical methods for research workers*, 8th edition, Edinburgh, Oliver, 1941.

Discussion. The results obtained would seem to indicate that there is a tendency toward an elevation in the serum sodium concentration of hypertensive patients. Surprisingly enough, statistically this elevation was found to be very significant. These data indicate a wide overlap between the serum sodium values found in normotensive and hypertensive patients, with a definite trend for a large group of the hypertensives to have a value in the upper normal range. One might be tempted to conclude that this finding supports the concept of adrenal participation in the production of the hypertensive syndrome, and that this might offer a basis for sodium restriction therapy in this disease. However, until the significance of these findings is more clearly understood, it may perhaps be better to avoid any conclusion concerning these findings as to their therapeutic or etiologic concepts.

Summary and conclusions. A series of serum sodium determinations made on uncomplicated hypertensive patients has been presented. The range and average serum sodium values in these patients were found to be slightly above those found in a concomitant series of 400 normotensive subjects. We have intentionally avoided any conclusions at this time as to the significance of these findings.

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Apoerythein Studies. IV. Nonidentity of Salivary, Gastric Juice, and Gastric Mucosal Apoerythein Activities. (18851)

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Previous papers in this series have reported the normal variations which occur in salivary apoerythein (intrinsic factor) levels(1) and demonstrated the unique manner in which heating affects salivary apoerythein activity

(2,3). The heating of saliva at 70°C for 15 seconds results in a complete loss of apoerythein activity, but heating below 65°C or at 75°C-100°C results in no diminution of activ-

1. Beerstecher, E., Jr., and Altgelt, S., *J. Biol. Chem.*, 1951, v189, 31.

2. Beerstecher, E., Jr., *Fed. Proc.*, 1951, v10, 161.

3. Beerstecher, E. Jr., and Edmonds, E. J., *Science*, in press.