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Received July 3, 1953. P.S.E.B.M., 1953, v84.

## Electrocardiograms and Serum Electrolyte Levels in Hamsters with Adrenal Insufficiency and Hypercorticalism.* (20617)

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In previous reports, Wyman, Fulton, and Shulman have described the circulatory changes in the transillumined cheek pouch of the hamster, (*Mesocricetus auratus*) after adrenalectomy and during treatment of the normal animal with cortisone(1). Vasoconstriction occurred consistently during cortisone administration. Furthermore, occasional vasomotion, frequent vasoconstriction, bradycardia, and slow blood flow occurred prior to death from adrenalectomy. Zweifach and Chambers, however, described a loss of vascular tone and absence of vasomotion in the mesoappendix of the adrenalectomized rat(2). In view of the evidence that hyperpotassemia may stimulate smooth muscle(3,4), a possible explanation for the discrepancy might be significant differences in serum potassium levels in the 2 species after adrenalectomy. Snyder and Wyman(5) reported a rise in the serum potassium of over 100% in the adrenalectomized hamster as compared with reported elevations of less than 50% in the adrenalectomized rat. In order to test the possible relationship between vasoconstriction, cardiac changes, and serum electrolyte levels, sodium and potassium determinations were made and electrocardiograms taken for each day following adrenalectomy and every other day during cortisone administration.

*Materials and methods.* Twenty-four male hamsters, 80 to 100 g in weight, were adrenalectomized using a dorsolateral approach in a single operation. Purina Laboratory Chow and tap water were given *ad libitum* and the hamsters received the usual postoperative care. The 24 hamsters were divided into 3 groups of 8 animals each, and on every third day an electrocardiogram was taken and blood was drawn by heart puncture for electrolyte determinations on each group so as to provide data for each postoperative day for their period of survival. Three groups of 8 intact hamsters were similarly used for cortisone studies except the electrocardiograms and heart punctures were made every other day throughout the entire period. Each animal was given a daily injection of 5 mg cortisone acetate (Cortone, Merck)‡. *Electrocardiograms* were obtained by means of hypodermic

* This investigation was supported in part by a research grant from the National Heart Institute of the National Institutes of Health, Public Health Service.

† Messrs. Benotti of the Boston Medical Laboratory made the electrolyte determinations. The work has benefitted immeasurably by numerous conferences with Dr. Maurice H. Shulman. We are indebted to Dr. David Littman for advice in interpreting the electrocardiograms, to Mr. Frederick W. Maynard for technical photographic advice, and to Miss Lois L. Smith and Miss Roma Kagan for valuable assistance.

‡ Kindly supplied by Dr. Elmer Alpert, Merck and Co.

TABLE I. Adrenalectomized Hamsters; ECG, Serum Na and K.

| Days after adrenalectomy | No. used and surviving | mEq/liter | | Millivolts | |
|---|---|---|---|---|---|
| | | Na | K | T wave | P wave |
| −3* | 24 | 145 (137–153)† | 5.97 (5 – 8 ) | .33 (.31–.36) | .20 (.18–.22) |
| 1 | 24 | 137.6 (135–141) | 7.1 (6.7– 8 ) | .20 (.16–.24) | .12 (.11–.13) |
| 2 | 22 | 137.2 (134–141) | 10.1 (6.5–12.5 ) | .25 (.19–.31) | .15 (.12–.18) |
| 3 | 16 | 121.5 ( 95–140) | 9.0 (7.7–11.2 ) | .16 (.00–.20) | .09 (.05–.10) |
| 4 | 11 | — | 9.2 (7.7–11.8 ) | .19 (.16–.21) | .09 (.07–.11) |
| 5 | 7 | 132.7 (123–139) | 10.1 (7.3–15+) | .23 (.19–.27) | .10 (.07–.13) |
| 6 | 0 | | | | |

* Three day preadrenalectomy values for 24 hamsters in the group. After adrenalectomy, ECGs and heart punctures were made on 8 hamsters every third day.

† In this and in Table II the figure is the avg; figures in parentheses are the range.

electrodes, a preamplifier (Grass Instrument Co.), and a cathode ray oscilloscope, and were recorded on linograph paper in a kymograph camera (Grass Instrument Co.). Unipolar precordial leads VC-5 and VL were employed. Anesthesia was 10 mg per 100 g body weight sodium pentobarbital (Nembutal, Abbott). Serum for the sodium and potassium determinations was obtained from centrifuged blood taken directly from the heart with hypodermic syringes. The blood serum samples were prepared as follows: 0.1 ml of the serum was pipetted into a 25 ml volumetric flask containing lithium chloride solution, 5000 p.p.m. (0.75 ml for K, 4 ml for Na), and diluted to 25 ml with distilled water. Electrolytic determinations were made on a flame photometer (Barclay) and are reported in mEq/liter. A *control group* of 5 hamsters was used to determine the effect on the electrocardiogram of 5 successive heart punctures at 3-day intervals. Serum sodium and potassium were also determined for this group.

*Results.* After 5 successive heart punctures, the electrocardiogram showed no significant alterations in the control series. The average electrolyte levels on each successive heart puncture were found to be about 145 mEq/liter for sodium and 7 mEq/liter for potassium. These values did not vary significantly on each successive heart puncture and are similar to those reported by Snyder and Wyman(5). The slight differences in absolute values may be attributed to the manner in which the blood was obtained.

Adrenalectomized hamsters gradually lost weight and lived for an average of 5 days. The changes in the electrocardiogram and the serum electrolytes are shown in Table I and Fig. 1 and 2 A, B, C. The most significant electrocardiographic changes were a lowering of the P and T waves accompanied by bradycardia and, in some cases, a prolonged QT interval. The serum electrolyte levels exhibited a rise in potassium and a fall in sodium. It was noted that as the serum potassium rose, the T wave became shallower. In some cases where the potassium level exceeded 15 mEq/liter, a complete reversal of the T wave was observed (Fig. 1).

Cortisone-treated animals also lost weight but lived an average of 16 days. During the entire study the electrocardiogram showed no significant changes related to the electrolyte levels (Table II; Fig. 2D, E, F). This was true even in the stages of treatment where there was marked vasoconstriction in the hamster cheek pouch (10 to 12 days). The two high values for the T and P wave voltages on the twelfth and sixteenth days were correlated chronologically with the appearance and persistence of the vasoconstriction. The values were normal, however, on the intervening fourteenth day. Serum electrolyte levels remained essentially normal, although the potassium values were on the low side of the normal range during the treatment.

*Discussion.* The electrocardiographic changes reported in this paper are comparable with those reported for severe adrenal insufficiency in dogs(6). It is well established that the sodium and potassium concentrations across a cell membrane are of great importance in the maintenance of cellular activity. Moreover, potassium is implicated in the maintenance of the resting potential and an eleva-

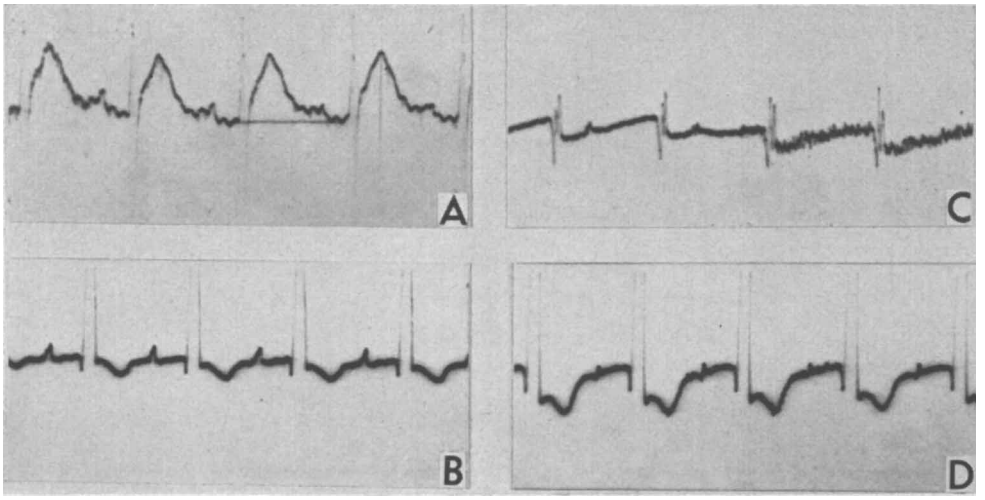


FIG. 1. ECG changes showing reversal of the T wave after adrenalectomy using lead VC-5 (A and B) and VL (C and D). A and C—before adrenalectomy (Na 140 mEq/l; K 6.6 mEq/l). B and D—three days after adrenalectomy (Na 95 mEq/l; K 15+ mEq/l).

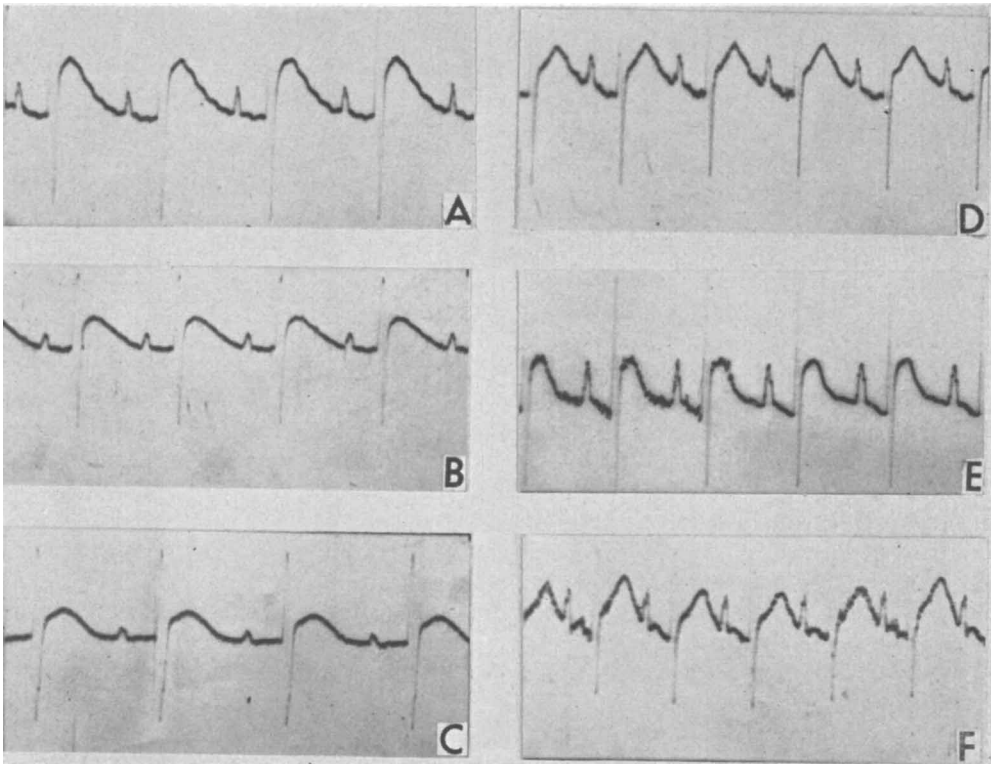


FIG. 2. ECG records (Lead VC-5) showing the effect of adrenalectomy (A, B, C) and cortisone-treatment (D, E, F) on normal hamsters. A. Before adrenalectomy (Na 155 mEq/l; K 5 mEq/l; heart rate 375/min.; T wave .33 mv; P wave .17 mv; QT 98 msec.). B. Two days after adrenalectomy (Na 141 mEq/l; K 10.5 mEq/l; heart rate 384/min.; T wave .24 mv; P wave .14 mv; QT 100 msec.). C. Five days after adrenalectomy (Na 123 mEq/l; K 12 mEq/l; heart rate 330/min.; T wave .2 mv; P wave .08 mv; QT 105 msec.). D. Before cortisone treatment. E and F. After 8 and 16 days of cortisone treatment; no significant changes.

TABLE II. Cortisone-Treated Hamsters; ECG, Serum Na and K.

| Days of treatment | No. used and surviving | mEq/liter | | Millivolts | |
|---|---|---|---|---|---|
| | | Na | K | T wave | P wave |
| −3* | 24 | 142 (130–150) | 6 (4.2 –7.9) | .33 (.31–.35) | .12 (.11–.13) |
| 3 | 23 | 150.2 (147–153) | 5 (4.9 –5.3) | .28 (.27–.30) | .16 (.12–.20) |
| 4 | 22 | 149 (141–151) | 6.3 (4.7 –8.8) | | |
| 6 | 20 | 145.6 (137–152) | 4.85 (4.25–5.5) | .28 (.20–.36) | .12 (.05–.21) |
| 8 | 19 | 138.7 (122–152) | 5.8 (4.1 –8.8) | .31 (.22–.40) | .21 (.14–.28) |
| 10 | 15 | 146.2 (142–150) | 5.8 (5 –8.8) | .32 (.27–.37) | .18 (.17–.19) |
| 12 | 14 | 146.7 (145–150) | 4.27 (3.8 –4.6) | .50 (.45–.52) | .22 (.16–.28) |
| 14 | 8 | 134.5 (127–142) | 5 ( 5 ) | .25 (.16–.37) | .17 (.11–.22) |
| 16 | 6 | 139 (128–151) | 6 (4.2 –7.7) | .45 (.37–.5 ) | .22 (.14–.28) |
| 17 | 0 | | | | |

* Three day pretreatment values for 24 hamsters in the group. During treatment, ECGs and heart punctures were made on 8 hamsters every other day.

tion of this ion or of lithium in the extracellular environment results in a depolarization of the cell(7,8).

Since vasoconstriction resulting from cortisone administration was not accompanied by significant alterations in either electrolyte levels or electrocardiograms, hyperpotassemia is not implicated as the cause. Our negative findings in the hamster differ from those of Overman who reported an increased plasma potassium in cortisone-treated dogs(9). After adrenalectomy, we found significant electrolyte and corresponding electrocardiographic changes in the absence of vasoconstriction. However, this does not obviate the possible role of hyperpotassemia during the terminal phase of adrenalectomy when compensatory vasoconstriction may be present. Important in this respect is the report by Katz and Lindner(3) that increased potassium concentrations in the dog produce sustained coronary constriction almost to the point of complete occlusion. However, it has been reported that a decrease in the plasma pH, bicarbonate ion, and sodium concentration will produce electrocardiographic alterations similar to those found during increased potassium concentrations (10).

*Summary.* Adrenalectomized hamsters exhibit an increase in the concentration of serum potassium and a decrease in serum sodium. These alterations in electrolyte levels are accompanied by changes in the electrocardiogram. The most significant modifications are bradycardia, a depressed T wave which in severe hyperpotassemia may be completely reversed, and an increased QT interval. Vasoconstriction in the cheek pouch does not necessarily accompany the hyperpotassemia of adrenal insufficiency. Moreover, cortisone-treated hamsters exhibited definite vasoconstriction, although there were no significant changes in the serum electrolyte levels or electrocardiograms.

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Received July 9, 1953. P.S.E.B.M., 1953, v84.