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**Revival from Insufficiency and Maintenance of Adrenalectomized Dogs with Low Serum Sodium and Chloride Levels.**

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In a previous publication<sup>1</sup> attention was called to the fact that the dog prostrate from adrenal insufficiency, with greatly diminished volume of circulating fluid, low arterial pressure, marked hemoconcentration and exhibiting symptoms of severe dehydration and shock, retains large quantities of fluid apparently immobilized within the tissues. This tissue fluid was shown to be sufficient in quantity, when mobilized and shifted to the blood stream under the influence of cortical hormone, to revive the animal from collapse to the point where all symptoms disappear and activity, vigor and appetite return to normal.

The present communication is concerned with the relation of this internal fluid shift to serum sodium and chloride changes.

The dog exhibiting symptoms of adrenal insufficiency is unable to dilute its blood, *i. e.*, shift the tissue fluids to the blood stream to bolster up a failing circulation. However, within a few hours following hormone administration blood dilution occurs, the hemoconcentration decreases along with a rise in arterial pressure, all symptoms disappear and activity and vigor return. Accompanying these changes is a marked diuresis with outpouring of a large volume of urine.

We assumed on the basis of the experiments of Loeb, *et al.*,<sup>2</sup> and Harrop, *et al.*,<sup>3</sup> that the cortical hormone probably mobilized and redistributed sodium and chloride along with the tissue fluids. Investigation of this point, however, reveals that following hormone administration to dogs in severe insufficiency the shift of fluid from tissues to blood stream occurs despite no elevation of the serum sodium and chloride levels. On the contrary, these electrolytes may even decrease. The essential data obtained from a representative experiment are given in Table I. When given adequate hormone

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<sup>1</sup> Swingle, W. W., Piffner, J. J., Vars, H. M., and Parkins, W. M., *Am. J. Physiol.*, 1934, **108**, 144.

<sup>2</sup> Loeb, R. F., Atchley, D. W., Benedict, E. W., and Leland, J., *J. Exp. Med.*, 1933, **57**, 775.

<sup>3</sup> Harrop, G. A., Soffer, L. J., Ellsworth, K., and Trescher, J., *J. Exp. Med.*, 1933, **58**, 17.

TABLE I.  
 Changes in Hemococentration (Dilution) in the Dog Revived from Adrenal Insufficiency and Maintained Free from Symptoms at Low Serum Sodium and Chloride Levels.

| Date     | Wt. Kg.* | Pulse per min. | B.P. mm. Hg. | Serum Na m-eq. | Serum Cl m-eq. | Hb. gm./100 cc. | Hemat. vol. % | R.B.C. millions | Blood urea mg. % | Blood glucose mg. % | Remarks                                  |
|----------|----------|----------------|--------------|----------------|----------------|-----------------|---------------|-----------------|------------------|---------------------|--|
| 11/6/35  | 7.6      | 68             | 102          | 140.8          | 114.2          | 11.5            | 38.2          | 5,29            | 33.3             | 80                  | Normal health. Extract discontinued.     |
| 11/16/35 | 7.3      | 64             | 46           | 122.9          | 96.4           | 18.4            | 53.4          | 8,88            | 86.9             | 73                  | Severe insufficiency. Extract injected.† |
| 11/20/35 | 6.9      | 128            | 106          | 120.7          | 93.0           | 14.9            | 44.8          | 6,76            | 26.6             | 78                  | Normal, no symptoms, active, vigorous.‡  |

\*This animal had been bilaterally adrenalectomized 4 months previous to use in these experiments and maintained in normal health by daily injections of cortical hormone.

†Dog given free access to water but all food withheld for 4 days. This animal was maintained free from symptoms for 14 days with low sodium and chloride levels and used in another experiment.

‡Cortical hormone (3 cc. per kg.) injected intravenously. Thereafter similar amounts of hormone given daily intraperitoneally in divided doses.

such animals can be returned to normal health and vigor and maintained so for considerable periods (*e. g.*, 2 weeks) with negligible change of the serum sodium and chloride from their low pre-injection levels.† If the dog is to be maintained in normal condition at low serum sodium and chloride concentrations the animals should be allowed free access to water and fed a diet relatively free of these electrolytes.

Results similar to those described above for adrenal insufficiency have been obtained in adrenalectomized dogs which have had their sodium and chloride depleted by intraperitoneal injections of isotonic glucose according to the method of Darrow and Yannet,<sup>4</sup> and Gilman.<sup>5</sup> Using such animals it is possible by withholding hormone, to shift body fluids from the blood to the tissues, and by injection of adequate hormone to shift the fluid back to the blood stream despite the fact that throughout the experiment the serum sodium and chloride are at all times extremely low.

*Summary.* (1) The clinical condition of the adrenalectomized dog revived from severe insufficiency is independent of the serum sodium and chloride levels. (2) Such animals can be maintained in apparently normal condition for 2 weeks or longer with the serum sodium and chloride at the levels observed when the animal is verging on death from insufficiency. (3) The disappearance of symptoms is largely due to the effect of the cortical hormone on the mobilization and shift of tissue fluids to the blood stream. This shift occurs in the face of low serum sodium and chloride concentration. (4) The serum sodium and chloride levels remain unaffected by repeated large injections of cortical hormone if all food is withheld or a salt-free diet fed.

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† Animals maintained free from symptoms, with serum sodium below 120 m-eq per liter and chloride below 95 m-eq, can be run through the complete cycle of adrenal insufficiency and recovery by withholding and injecting hormone. The electrolytes remain unchanged.

<sup>4</sup> Darrow, D. C., and Yannet, H., *J. Clin. Invest.*, 1935, **14**, 266.

<sup>5</sup> Gilman, A., *Am. J. Physiol.*, 1934, **108**, 662.