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Anhydremia with insulin and water intake.

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Pronounced hypoglycemia due to the injection of large amounts of insulin has been shown by Drabkin and Edwards[1] to be associated with a concentration of the blood. Although this symptom was invariably found, the animals studied fell into two groups: some developed anhydremia rapidly with an acute fall in blood pressure; a larger group exhibited a gradual rise in blood concentration with a well-maintained blood pressure. The clinical observations of Joslin, Gray and Root[2] indicate that desiccation through diarrhea renders patients prone to dangerous insulin hypoglycemia.

The natural outgrowth of the problem was to study the influence of the water intake upon the type of reaction with insulin, especially with reference to the severity of the resulting anhydremia. A more exact statement of the problem was framed in the question: "Will an animal which has been desiccated through water starvation react differently to a large amount of insulin than one which has had plenty of water?"

The procedure was as follows: Unanesthetized dogs (5 to 10 kilograms in weight) were used. The first "control" blood samples were drawn, and the dogs were either thirsted (water starved) or given by stomach-tube an average of 800 cc. of water daily for periods of 3 to 7 days. As an added check upon the results, some of the dogs previously thirsted were also studied under a forced water régime, and vice versa. Just before the administration subcutaneously or intravenously of a large dose of insulin (20 units per kilogram body weight), the second "control" samples were drawn. Blood samples were then taken at suitable intervals following the insulin administration. Each blood sample was analyzed for hemoglobin and dry solids, as

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[1] Drabkin, D. L., and Edwards, D. J., *Am. J. Physiol.*, 1924, lxx, 273.

[2] Joslin, E. P., Gray, H., and Root, H. F., *J. Metab. Research*, 1922, ii, 651.

indices of the amount of blood dehydration, and for sugar. A modified Cohen and Smith[3] technique was employed for the estimation of the hemoglobin, and the method of Schaffer and Hartmann[4] was used for the determination of the sugar. The physical qualities of the blood samples were also noted. A careful record was kept of the symptomatic responses and their nature. Under this head were noted such factors as the presence or absence, type and the time of onset of convulsions, the time of onset of coma, the rapidity and type of recovery if any after the administration, in each case, of resuscitative amounts of glucose (150 to 200 cc. of a 10 per cent solution intraperitoneally).

The experimental results may be summarized as follows: Water starvation for 4 days caused a negligible increase in the concentration of the blood. Thirsting the dogs for longer periods of 5 to 7 days, however, resulted in a moderate concentration (12.8 to 17.4 per cent above the original values).

The response of the blood sugar to insulin was the same in the desiccated dogs as in those which had received water. In each group the fall was rapid and to a low level (from the original values to 30 mg.—0.00 mg. per 100 cc. of blood).

The desiccated animals developed a more profound concentration of the blood than the others. The blood concentration of the water-starved dogs was 36.9 to 64.3 per cent (as determined from the hemoglobin values), 26.9 to 33.5 per cent (as determined by the dry blood solids) in comparison with the corresponding values of 16.7 to 28.0 per cent and 9.7 per cent in the non-desiccated dogs. A graphic record of the hemoglobin concentrations of the two groups showed interesting differences. The curve of concentration of the animals which had no water was steep and continuous; that of the others was more gradual in its ascent, with a tendency for spontaneous return to the normal value during the third hour.

The dogs which had been given water immediately recovered upon the administration of glucose and stayed well. The desiccated animals came out of their coma after the administration of glucose, but were extremely weak, none surviving more than 24 hours. The production of anhydremia on top of desiccation is apparently incompatible with the life of the cells.

[3] Cohen, B., and Smith, A. H., *J. Biol. Chem.*, 1919, xxxix, 489.

[4] Shaffer, P. A., and Hartmann, A. F., *J. Biol. Chem.*, 1920-21, xlv, 365.

The most striking observation, however, was the absence of convulsions in the desiccated dogs, and the presence of severe, spastic convulsions in those with water.

Conclusions:

Dogs, desiccated through water-starvation, when given large doses of insulin developed a more severe anhydremia than the dogs which had water.

Convulsions were not observed in the desiccated animals although they invariably appeared in the others.

Glucose did not prevent the death of the water-starved dogs. The non-desiccated animals immediately recovered after glucose administration.

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The emetic action of strophanthidin in cats with denervated hearts.

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Strophanthidin is a cleavage product derived by hydrolising hispidus or Kombé strophanthin. It can also be obtained from cymarin, an active principle of *Apocynum cannabinum.*[1] Its empirical formula,[2] as lately established, is $C_{23}H_{32}O_6$, $\cdot\frac{1}{2}$ H_2O. Jacobs and Collins have, moreover, thrown much light upon its structural makeup.[3] Pharmacologically, strophanthidin has been but little studied.

As we have already pointed out,[4] this substance has marked emetic properties. It also acts upon the heart in a manner essen-

[1] Windaus and Hermanns, *Ber. der deutsch. chem. Ges.*, 1915,xlviii, 979, 991.

[2] Jacobs and Heidelberger, *J. Biol. Chem.*, 1922,liv, 253; Thoms and Unger, *Zeit. f. angewand, Chem.*, 1924, xxxvii, 721.

[3] Jacobs, *J. Biol. Chem.*, 1923, lvii, 553, 569; Jacobs and Collins, *ibid.*, 1924, lix, 713, and lxiii, 123.

[4] Dresbach and Waddell, *J. Pharm. and Exp. Therap.*, 1924, xxiii, 152.