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Concentrating Capacity of the Kidney as Revealed by Injection of Posterior Pituitary Extract.*

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Although it has not been clearly established that there is a "ceiling concentration" representing the maximum concentrating capacity of the kidney tubules,[1] the ability of the kidney to secrete a concentrated urine is used as a clinical test of the functional capacity of this organ. The effect of posterior pituitary extract in retarding the excretion of water and at the same time increasing the output of solids is well known. It has been shown by Nelson and Woods that in mice the increase in solids (chlorides) may be great enough to break through the inhibitory effect on the elimination of water.[2] This simultaneous reduction in water and increase in chloride output might at some point give a urine which represented the maximum concentration possible for the given conditions. The present report presents the results obtained when the degree of concentration obtained by moderate restriction of food and water is compared with the concentration resulting from such restriction combined with the effect of posterior pituitary extract.

Experimental: Bladder fistula dogs were trained to stand in stocks for 3-hour collection periods. Prior to use food and water were withdrawn for 18 hours. Collections were made at 10-minute intervals while the animals were in the stocks. Urine concentrations were determined by specific gravity determinations (weighing in a 1 cc pyknometer), and by chloride determinations (using a modified Volhard-Arnold method). When posterior pituitary extract was given, one international unit as contained in a commercial preparation was given intramuscularly, in a volume of one cubic centimeter. Smith has commented adversely on the use of a mixture of pressor and antidiuretic hormones in such studies,[1] but we are not aware of satisfactory evidence against the generally accepted view that the

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† The data are taken from the thesis presented by William Gosnell Paine in partial fulfillment of the requirements for the degree of Master of Science.

1 Smith, Homer W., *The Physiology of the Kidney,* Oxford Medical Publications, 1937.

2 Nelson, Erwin E., and Woods, G. G., *J. Pharm. Exp. Ther.,* 1934, **50**, 241.

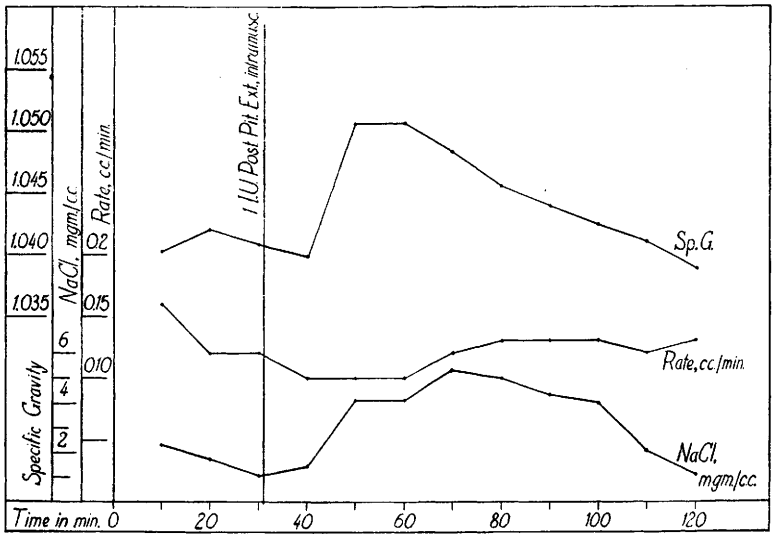

FIG. 1.

The effect of injection of 1 unit of posterior pituitary extract intramuscularly, on urine rate, urine chlorides and urine specific gravity, in a bladder fistula dog after 18 hours' withdrawal of food and water.

pressor and antidiuretic activities are resident in the same fraction.[3] Control experiments differed only in the failure to administer pituitary extract.

Fig. 1 gives the results of a typical experiment in which pituitary was given. Although the urine resulting from restriction was quite concentrated, (sp. gr. 1.043), after pituitary it rose in 20 minutes to appreciably higher values (sp. gr. 1.051). Similarly the chloride content increased from approximately 1 mg per cc to over 5 mg per cc. In different experiments the rate either rose slightly, remained constant, or as here fell slightly. It should be emphasized that until the animals have been adequately trained, it is difficult to get uniform rates of secretion during the control period. All experimental findings have been in the same direction as those shown in this figure. Ten controls in which only restriction was used, are in fact supplemented by the control periods prior to injection of pituitary in the 16 experiments in which this was given. The average rate in the controls was 0.11 cc per minute, specific gravity 1.038 and chloride content 2.2 mg per cc (as NaCl). After pituitary the average maximum specific gravity reached was 1.049 and the average maximum chloride 7 mg per cc. The rate changes have been mentioned. These chloride concentrations are by no means high, since in other

3 Van Dyke, H. B., *The Physiology and Pharmacology of the Pituitary Body*, University of Chicago Press, 1936, p. 325.

experiments administration of extra chloride resulted in concentrations up to 20 mg per cc. Reference to the figure reveals that the specific gravity reached its maximum somewhat earlier than did the chlorides. This failure of the two peaks to coincide in time was a finding in every experiment. It may possibly be explained by the observation of Stehle that there is a greater increase in potassium than sodium in the urine formed under pituitary.[4] A change in the K:Na ratio would of course modify the specific gravity. Determinations of this ratio were not made. In a few experiments, however, it was found that the changes in urea concentration were not significant, and did not serve to explain the phenomenon.

Summary. In dogs, placed under conditions similar to those employed clinically for revealing the concentration capacity of the kidney, that is, under restriction of food and water, the administration of posterior pituitary extract results in the formation of a more concentrated urine than follows from restriction alone.

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Effect of Rabbit Adenocarcinoma Material on Brown-Pearce Rabbit Epithelioma.

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A material[1, 2, 3] which always has been present in primary and metastatic tissue obtained from the Brown-Pearce tumor of the rabbit has been shown to be filtrable through a Berkefeld "V" candle, desiccable, thermolabile (56°C) and different from the Duran-Reynals factor. It has consistently influenced the growth and spread of this particular strain of malignant cells *in vivo,* and when injected intratesticularly or intracutaneously into rabbits, in a dosage com-

[4] Stehle, R. L., *Am. J. Physiol.,* 1927, **79**, 289.

[1] Casey, A. E., PROC. SOC. EXP. BIOL. AND MED., 1932, **29**, 816; 1933, **30**, 674, 1025; 1934, **31**, 663, 666; 1936, **34**, 111; 1939, **40**, 223, 228, 230; *Am. J. Cancer,* 1934, **21**, 760, 776; **22**, 665; 1936, **26**, 276; 1937, **31**, 446; *Arch. Path.,* 1935, **20**, 156; 1936, **22**, 275; 1937, **23**, 741; 1938, **25**, 754; 1939, **27**; *Proc. III Internat. Cancer Congress,* Atlantic City, Sept., 1939.

[2] Casey, A. E., and Moragues, G. V., *Arch. Path.,* 1939, **27**; *Am. J. Cancer,* in press.

[3] Erös, G., *Proc. III Internat. Cancer Congress,* Atlantic City, Sept., 1939.