Effect of Synthetic Lysine Vasopressin on Adrenocortical Secretion

Abstract. By means of direct arterial perfusion of the adrenal glands in the dog it has been shown that synthetic lysine vasopressin stimulates the secretion of hydrocortisone. This effect is not mediated via the adenohypophysis or any other organ but is rather the result of direct stimulation of the adrenal cortex by vasopressin itself.

The relation between the secretion of vasopressin and its effect on adrenocortical activity has not been satisfactorily elucidated. Several workers (*1*) have published data supporting the hypothesis of direct ACTH release induced by vasopressin, whereas other evidence has accumulated which would tend to invalidate this concept (*2*).

In view of certain reciprocal relationships between vasopressin and adrenocortical hormones (*3*), and because the locus or mode of action of vasopressin is not clear, it occurred to us that vasopressin might directly stimulate the adrenal cortex. The adrenal perfusion technique was felt to be an ideal method for studying this problem (*4*).

Dogs, anesthetized with sodium pentobarbital (0.5 mg/kg), were hypophysectomized (*5*), and the adrenals were then prepared for perfusion by the technique of Hilton *et al.* (*6*).

Donor hypophysectomized dogs were bled from a femoral artery the morning of the experiment, and this arterial blood was then perfused by a mechanical pump into the adrenal preparation of the recipient hypophysectomized animal. The recipient animal's heart was then fibrillated to insure noncontamination of the donor blood.

Synthetic lysine vasopressin (*7*) was added to the arterial circuit leading to the adrenal glands at the rate of 1 ml/min for 7 to 10 minutes. The concentrations used varied from 0.2 to 0.3 pressor unit per milliliter (0.7 to 1.0 μg). The blood-flow rate through the glands was kept constant at 10 ml/min throughout each experiment. At the end of each experiment an injection of ACTH at a rate of 1 ml/min for 7 to 10 minutes and at a concentration of 0.5 to 2.5 units per milliliter was given to verify adrenal viability.

The adrenal venous blood was collected in graduated cylinders, the rate of flow was measured, and the concentration of hydrocortisone in the plasma was determined by the method of Peterson *et al.* (*8*). None of the adrenal venous effluent was allowed to return to the recipient animal.

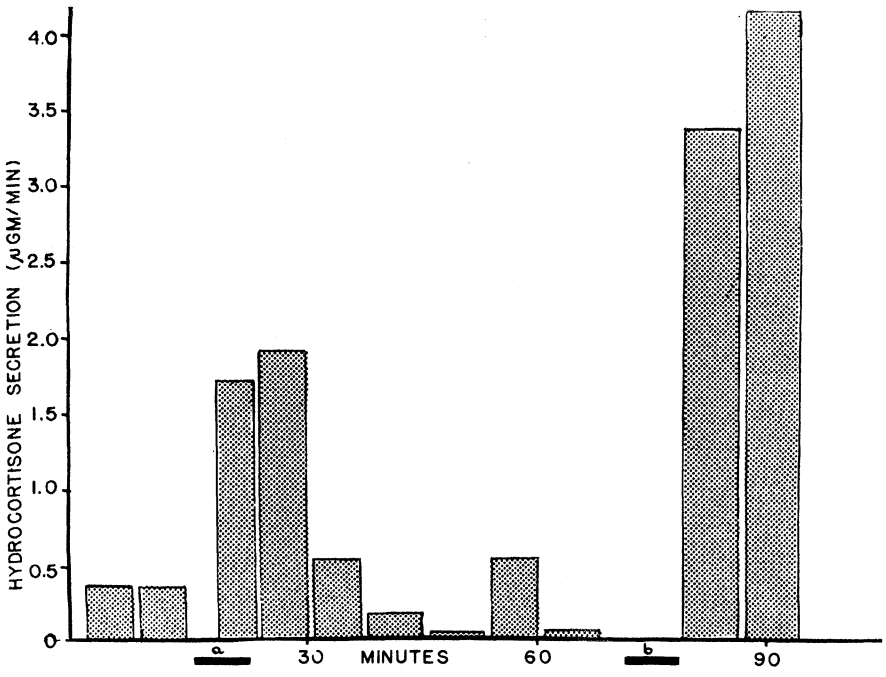

Fig. 1. Following two control periods, at *a*, lysine vasopressin was administered at the rate of 0.3 unit per minute for 7 minutes. At *b*, ACTH was administered at the rate of 1.0 unit per minute for 7 minutes.

Six experiments were performed, and a representative example is shown in Fig. 1. In this experiment, it may be seen, there was a sixfold increase (*9*) in hydrocortisone secretion from the perfused adrenal glands after the administration of vasopressin. The effect was largely dissipated 15 minutes after the end of the injection period. In general, this was the pattern in the six experiments.

It may also be noted from Fig. 1, that following ACTH administration there was a large increment in hydrocortisone secretion. The response to ACTH was greater than that to vasopressin and also indicated satisfactory viability of the preparation. This type of response to ACTH was noted in four of the six experiments; in two experiments the response to vasopressin was greater than that to ACTH.

A mild pressor response within the adrenal arterial circuit was noted in all six experiments, incident to vasopressin administration; the mean rise in blood pressure varied from 10 to 65 mm-Hg, with an average rise of 16 mm.

Our experiments, in which we used the direct perfusion technique, which eliminates any interference from other endocrine glands or organs, indicate that synthetic lysine vasopressin has a direct stimulatory effect on the adrenal glands. These findings raise the question as to whether vasopressin may be an important factor in the "stress" mechanism.

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References and Notes

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4. This work was supported by grants from the New York and American Heart Associations and from the John Polachek Foundation.
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7. The vasopressin used in this study was kindly supplied by Prof. Vincent du Vigneaud's laboratory.
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9. Spectrophotometric analysis showed maximal absorption at a wavelength of 410 mμ.
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