# ROLE OF THE PITUITARY IN EXPERIMENTAL HYPERTENSION PRODUCED BY CONFLICT OF BASIC CORTICAL PROCESSES

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The reasons for examining the part played by the pituitary in the hypertension associated with experimentally produced neurosis were the similarity of the condition to hypertensive disease in man and the generally recognized importance of the pituitary-adrenal system in the genesis and development of the latter condition.

The only information available on the problem is contained in references to increased ACTH activity in dogs with conditioned reflex hypertension produced by the Makarychev and Kurtsin' method [3] and changes in adrenal hormone activity in experimental hypertension induced by conflict of cortical processes [2].

## METHOD

The experiments were carried out with two pairs of male dogs, the animals in each pair being similar in respect on conditioned reflex activity, blood pressure, age and weight.

Blood pressure was measured in the femoral artery by the Korotkov method and oscillographically in a setting quite unconnected with conditioned reflex stimulation.

Positive and differential conditioned reflexes were elaborated to two electric bells of different tone by the classical food-conditioned method of Pavlov.

When the conditioned reflexes were firmly established (the paired stimuli had been applied at least 300 times) and the dogs' blood pressure levels had been determined, the main experiments were carried out in two series on each experimental pair. In the first series transbuccal hypophysectomy [13] was performed on one dog from each pair, and the other was kept as control. When, in the surgically treated animals, blood pressure had become stabilized and conditioned reflex activity was again normal, three "conflicts" were produced at intervals of a day in all four dogs to induce hypertension, the development of which was studied carefully.

The experiments of the second series were undertaken when blood pressure was again at or close to its original level and—this was an essential condition—conditioned reflex activity was again normal. The roles of the animals were reversed: hypertension was produced in the same way in the already hypophysectomized dogs which, however, were given repeated injections of ACTH and pituitrin (and so became controls) and in the now hypophysectomized animals which had previously served as controls (and now became the experimental animals).

ACTH was injected intramuscularly in dosage corresponding to that administered to man (1·2 U/kg).

The sodium, potassium, calcium, cholesterol and lecithin contents of the dogs' sera were estimated in the course of the experiments.

## RESULTS AND DISCUSSION

Hypophysectomy was followed by considerable leukocytosis with a three-fold increase in the number of eosinophils present. The ACTH dosage selected proved adequate in that it led to restoration of the original leukocyte count and original blood pressure levels.

Degree of Hypertension after "Conflict" in Hypophysectomized and Control (intact and hypophysectomized dogs given ACTH and pituitrin) Dogs

| Dog | Blood pressure (mm Hg) | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Systolic | | | | | | Diastolic | | | | | |
| | hypophysectomized dogs | | | controls | | | hypophysectomized dogs | | | controls | | |
| | initial | maximum | difference | initial | maximum | difference | initial | maximum | difference | initial | maximum | difference |
| Losik | 149 ± 4 | 163 | 44 | 148 ± 2 | 230 | 82* | 54 ± 1 | 87 | 33 | 55 ± 1 | 121 | 66 |
| Listik | 154 ± 2 | 213 | 59 | 154 ± 4 | 238 | 84* | 56 ± 2 | 110 | 54 | 56 ± 2 | 123 | 67 |
| Dzhul'ka | 148 ± 3 | 205 | 57 | 161 ± 2 | 226 | 65 | 51 ± 2 | 85 | 34 | 58 ± 1 | 140 | 82 |
| Reks | 172 ± 2 | 219 | 47 | 182 ± 1 | 245 | 63 | 61 ± 2 | 123 | 62 | 67 ± 2 | 140 | 73 |
| M | 51.75 ± 3.68 | | | 73.50 ± 5.50 | | | 45.75 ± 7.26 | | | 72.00 ± 3.67 | | |
| P | < 0.05 | | | | | | < 0.05 | | | | | |

*Hypophysectomized dogs given ACTH and pituitrin.

Table 1 shows that the "conflicts" produced a greater degree of hypertension in the control than in the control than in the hypophysectomized animals.

The differences between experimental and control animals in respect of the degree of hypertension became even more convincing when progressive blood pressure changes were studied. The results of observations on one pair of dogs (the other pair yielded similar results)* are shown graphically in Fig. 1 and 2. Fig. 1 makes it clear that there was a significant increase of blood pressure (by 23-44 mm Hg) for 11 days after the first "conflict" and that pressure was back to its original level four days later.

In the control animal the increase of blood pressure was more constant and more prolonged. Pressure was considerably increased (by 35-69 mm Hg) for more than 20 days in this dog. It was still increased 33-35 days after "conflict."

Derangement of the animals' higher nervous activity, associated with a fresh increase of blood pressure, was again produced in the second series of experiments. The features of the development of hypertension were now, however, the reverse of those observed in the first series of experiments (Fig. 2). Hypertension was now greater, more constant and more persistent in the hypophysectomized dogs given pituitary hormones than in the newly hypophysectomized dogs not receiving replacement therapy.

The cholesterol and lecithin contents of the serum were virtually unchanged after hypophysectomy and increase of blood pressure.

Serum calcium was slightly increased but sodium and potassium contents were practically unchanged after hypophysectomy. Serum calcium was increased at the height of the hypertensive phase in the first series and reduced at the corresponding time in the second series of experiments. In most instances serum sodium was increased and serum potassium reduced at the commencement of the hypertensive phase; the reverse was the case later, sodium being reduced and potassium increased. A considerable increase of sodium and reduction of potassium throughout the period of hypertension was observed in one case (a hypophysectomized dog receiving hormones).

These results may be interpreted in the following way. As "conflicts" between basic cortical processes led to the development of hypertension in hypophysectomized animals, it may be concluded that the pituitary gland is not essential to the development of this form of experimental hypertension. Yet, absence of the pituitary still has a

*Changes in systolic pressure only are shown. Changes in diastolic pressure were essentially similar.

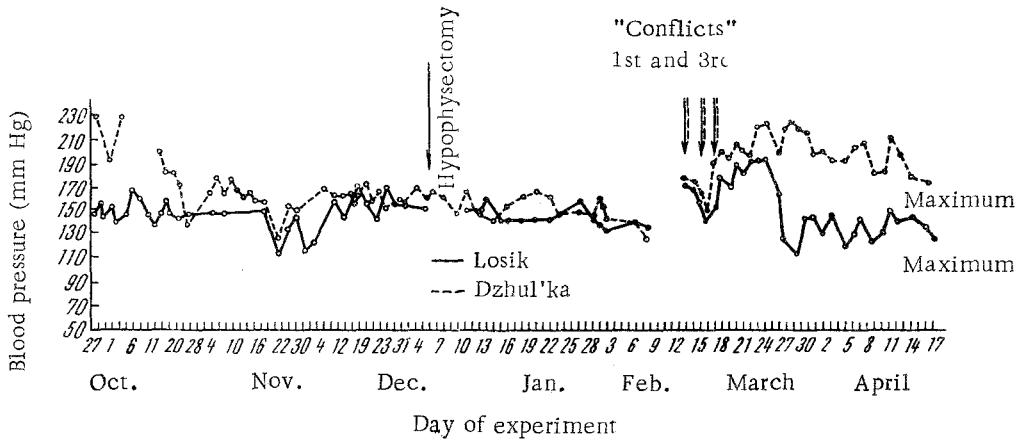


Fig. 1. Development of experimental hypertension induced by conflict of cortical processes in hypophysectomized (Losik) and control (Dzhul'ka) dogs (first series of experiments).

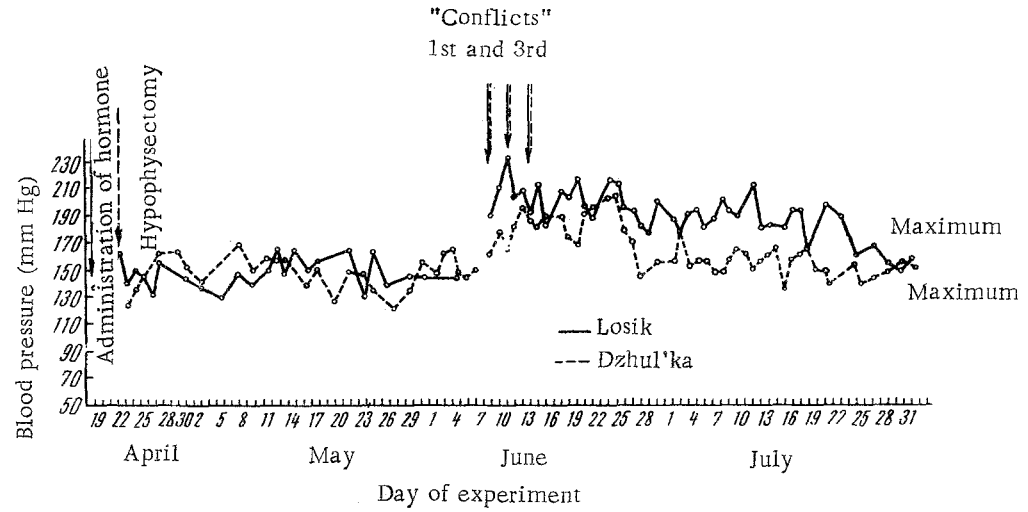


Fig. 2. Development of experimental neurotic hypertension after hypophysectomy in Dzhul'ka and during hormone replacement therapy in the hypophysectomized dog Losik (second series of experiments).

definite effect on the course of hypertension: it was less persistent and less constant in the hypophysectomized animals. The pituitary can therefore be regarded as playing some part in the production of this form of experimental hypertension.

Some indication of the mechanism of its participation is afforded by the second series of experiments in which "conflicts" led to the production of more constant and more prolonged hypertension in the hypophysectomized animals given ACTH and pituitrin. The pituitary would therefore appear to influence the degree of hypertension through these hormones.

These results are in essential agreement with other published findings on the part played by the pituitary in the pathogenesis of renal [6, 9, 10] and reflexogenic [5] hypertension and with our earlier observations on the importance of the pituitary in the pathogenesis of experimental postcommotional hypertension [4].

The pressor effect of ACTH is known to depend on its action on cortex and adrenals. There are also reports that this hormone is concerned in the production of hypertensinogen and renin [7]. This evidence, together with the fact that postpituitary secretion is intensified by renal ischemia, affords grounds for suggesting that the influence of the pituitary on the development of hypertension in association with experimental neurosis is largely indirect through adrenal and renal mechanisms.

It is very probable that adrenocortical function can be activated and the secretion of mineralocorticoids in-

creased in some degree in hypophysectomized animals. It is known that the atrophic changes seen in the adrenal cortex after hypophysectomy do not involve the zona glomerulosa, which is credited with the secretion of aldosterone, the most active of the mineralocorticoids [5]. There is other evidence that ACTH is responsible for the secretion of less than 50% of aldosterone [10]. It has been suggested that the secretion of this hormone is controlled by the hypothalamus through the secretion of an active hormonal substance, glomerulotropin [14].

Although, therefore, adrenal stimulation is still possible after hypophysectomy, optimum activation of the adrenals requires the presence of the pituitary.

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**All abbreviations of periodicals in the above bibliography are letter-by-letter transliterations of the abbreviations as given in the original Russian journal. *Some or all of this periodical literature may well be available in English translation.* A complete list of the cover-to-cover English translations appears at the back of this issue.**

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