ROLE OF THE PITUITARY IN THE REACTION OF THE ADRENAL CORTEX TO IRRADIATION

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As a result of irradiation, during the first few hours the adrenal cortical function is activated, as shown by the liberation of a large amount of corticosteroids into the blood stream. Moreover, the reaction of the adrenals bears a great resemblance to the changes which are observed in response to various stress agents [1, 5, 8, 9].

In most studies of the functional activity of the pituitary during irradiation, the conclusions have been based on changes in the function of the adrenal cortex (the content of cholesterol and ascorbic acid, and so on) [2,11,12]. These investigations do not permit conclusions to be drawn concerning the extent to which the pituitary participates in the reactions of the adrenal cortex. Meanwhile, the information relating to the direct determination of the ACTH concentration in the pituitary and the blood after irradiation is very contradictory [3,4,10].

The object of the present investigation was to study the special features of the course of the reaction of the adrenal cortex to whole-body irradiation in hypophysectomized dogs.

EXPERIMENTAL METHOD

The investigation was conducted on 6 hypophysectomized and 1 control dog. The pituitary was removed suggically through the left temporal bone. The dogs were taken for the experiments 1.5-2 months after the operation. The animals were investigated before whole-body x-ray irradiation and at various stages of radiation sickness. They were exposed to whole-body x-ray irradiation in a lethal dose (600 R) from two type RUM-3 apparatuses.

The criterion of adrenal function was the content of 17-hydroxycorticosteroids and the number of eosinophils in the peripheral blood of the dogs. Blood was taken from the femoral vein 15 min and 1.5 and 3.5 h after irradiation.

At the conclusion of the experiments, the animals were sacrificed and completeness of removal of the pituitary was determined histologically. In all the investigated dogs, the pituitary had, in fact, been completely removed. The 17-hydroxycorticosteroids in the blood were estimated by the method of Silber and Porter, as modified by N. A. Yudaev and Yu. A. Pankov [6].

EXPERIMENTAL RESULTS

The changes in the reaction of the adrenal cortex in the irradiated dog with its pituitary intact (control) are shown in Fig. 1. Phasic changes in the steroid concentration of this type are typical in dogs during irradiation, as demonstrated in the author's laboratory [1].

The reaction of the adrenal cortex to irradiation in two hypophysectomized dogs was just as clearly marked as in the intact animals, although the background concentration of corticosteroids was lowered (Fig. 2, A and B).

Comparison of the results obtained showed that in the hypophysectomized dogs, as in the controls, irradiation caused an increase in the concentration of 17-hydroxycorticosteroids in the blood. However, the dynamics of these changes in the hypophysectomized animals differed to some extent from their pattern in the controls. In the irradiated dogs with an intact pituitary (control) the changes in the content of 17-hydroxycorticosteroids were characterized by two phases of increase: in the early periods and at the height of the radiation sickness. Moreover, the second increase in the corticosteroids before the animal's death acted as a prognostic sign and was dependent on the severity of the disease [8,9].

In contrast to this, in the irradiated hypophysectomized dogs, only one phase of an increase in the steroids in the blood was observed, and in one animal it lasted until death, and in another until the day before death. This

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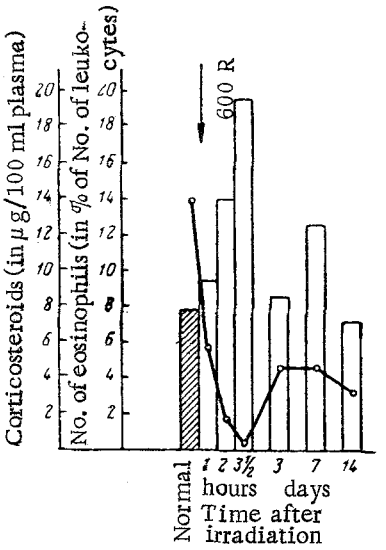

Fig. 1. Effect of whole-body irradiation on concentration of 17-hydroxycorticosteroids and number of eosinophils in the peripheral blood of an intact dog. Columns — corticosteroids; continuous line — eosinophils.

evidently demonstrates that the mechanism responsible for lowering the concentration of the hormone in the blood was disturbed in the hypophysectomized animals. In intact animals, one of the ways of restoring the normal level of corticosteroids is known to be inhibition of the liberation of ACTH from the pituitary. This mechanism evidently plays an important role in the restoration of the normal level of the corticosteroids when disturbed by irradiation. At the same time, the results of the experiments conducted on the hypophysectomized animals showed that stimulation of the adrenal cortex in response to irradiation may also develop in the absence of the pituitary. In all probability, a leading part in the development of this effect was played by the influence of the radiation, not on the pituitary, but on the central link of regulation of the activity of the pituitary-adrenal cortex, namely the subcortical centers. To confirm this hypothesis, the reaction of the adrenal cortex evoked by stimulation of the subcortical regions was studied in hypophysectomized animals.

Experiments were carried out on four hypophysectomized dogs. The subcortical region was stimulated electrically through permanently implanted electrodes. Current from a stimulator generating rectangular pulses of between 1 and 7.5 V in amplitude and of a frequency of 100 cps was used; the duration of stimulation was 3 min. At the end of the experiments, a histological (macro- and microscopic) investigation of the brain was undertaken. This showed that in one dog the electrodes were located in the anterior portion of the hypothalamus, in another in the posterior hypothalamus, and in two dogs in the thalamus.

These experiments showed that a definite increase in the content of corticosteroids and a decrease in the number of eosinophils could be produced in dogs by stimulation of the subcortical formations of the brain even in the absence of the pituitary (Fig. 3). In two hypophysectomized dogs, stimulation of the subcortical regions of the brain led to inversion of the reaction on the day of irradiation and on the third day of radiation sickness.

The results of the experiments on hypophysectomized dogs thus showed that the reaction of the adrenal cortex evoked by electrical stimulation of the brain was considerably modified by irradiation. Since the functional powers

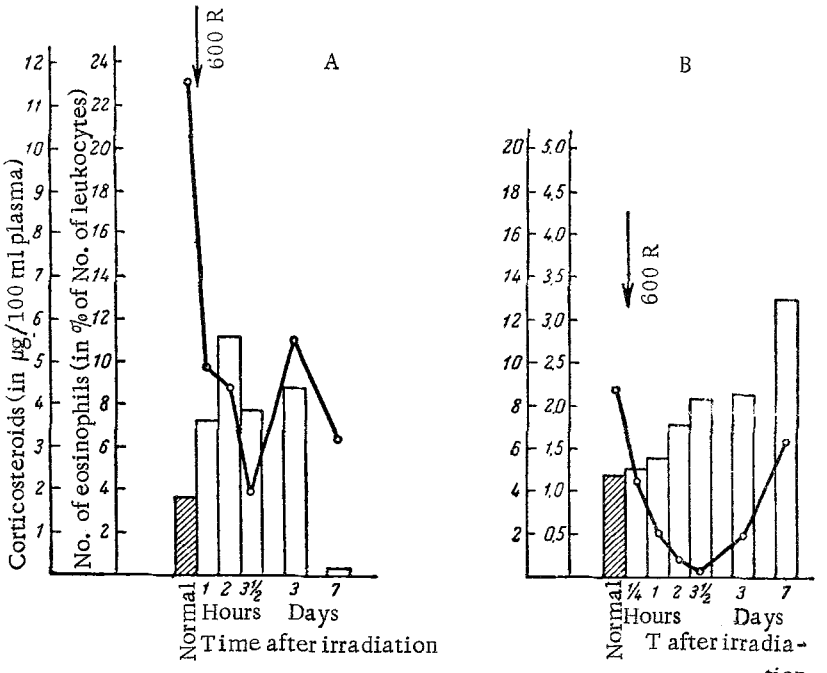

Fig. 2. Effect of whole-body irradiation on concentration of 17-hydroxycorticosteroids and number of eosinophils in the peripheral blood of hypophysectomized dogs. Legend as in Fig. 1.

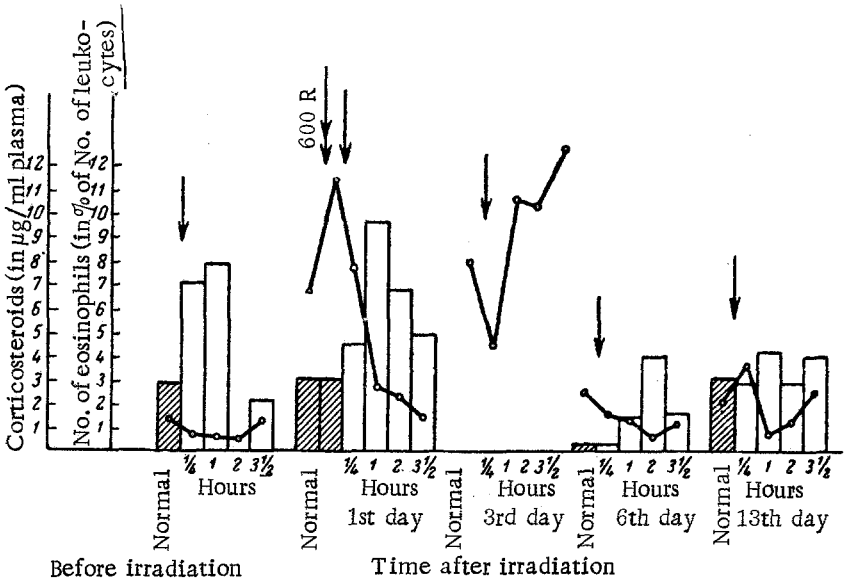

Fig. 3. Changes in the concentration of 17-hydroxycorticosteroids and the number of eosinophils in the peripheral blood in response to electrical stimulation of the reticular nucleus of the thalamus in a hypophysectomized dog before and after irradiation. Arrows pointing downward – stimulation by electric current; double arrow – irradiation. Remainder of legend as in Figs. 1 and 2.

of the adrenal cortex were by no means exhausted immediately after irradiation (as shown by the high level of hormones in the blood, which continued for some time), the phenomena of inversion of the adrenal cortex in response to stimulation of the brain may evidently be explained by changes in the functional state of the subcortical centers. It is interesting that changes of the same type in the reaction to stimulation of the brain have been observed in intact animals under the influence of irradiation [1]. This indicates that they evidently share a common mechanism of origin, contained in the action of ionizing radiation on the subcortical centers.

It may be concluded from the results of these experiments that a factor of great importance in the genesis of the reaction of the adrenal cortex to irradiation is the action of the ionizing radiation on the regulatory subcortical neural centers, and this reaction, moreover, can take place without the pituitary. However, the subsequent reaction of the adrenal cortex in all probability involves the participation of the pituitary, for a marked difference was observed between the dynamics of the reactions in the intact and hypophysectomized animals.

LITERATURE CITED

1. G. Z. Abdullin, V. V. Petelina, V. N. Patalova, et al., in the book: Outlines of the Evolution of Nervous Activity [in Russian], Leningrad (1964), p. 188.
2. É. R. Bagramyan, Probl. Éndokrinol., 3, 19 (1961).
3. M. A. Larina and É. R. Bagramyan, Abstracts of Proceedings of the Annual Scientific Session of the All-Union Institute of Experimental Endocrinology [in Russian], Moscow (1959), p. 31.
4. M. A. Larina, Probl. Éndokrinol, 3, 18 (1960).
5. L. V. Orlova and V. M. Rodionov, Pat. Fiziol., 4, 22 (1957).
6. N. A. Yudaev and Yu. A. Pankov, Probl. Éndokrinol., 2, 35 (1958).
7. É. Betts, Material Relating to the Study of the Endocrine Syndrome Produced by Whole-Body Irradiation of the Organism [in Russian], Moscow (1961).
8. J. Z. Bowers, D. H. Nelson, R. Bay, et al., J. Clin. Endocr., 12, 921 (1952).
9. A. B. French, C. I. Migeon, L. T. Samuels, et al., J. Clin. Endocr., 14, 816 (1954).
10. G. M. Mateyko, A. Edelman, and H. A. Charipper, Am. J. Physiol., 171, 749 (1952).
11. L. F. Nims and E. Sutton, Am. J. Physiol., 177, 51 (1954).
12. H. M. Patt, M. N. Swift, et al., Science, 108, 475 (1948).