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A COMPARISON OF THE ACTION OF TOTAL X-IRRADIATION AND
ADRENOCORTICOTROPIC HORMONE (ACTH) ON CORTICOSTEROID
SECRETION IN RABBITS

- USSR -

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A COMPARISON OF THE ACTION OF TOTAL X-IRRADIATION AND
ADRENOCORTICOTROPIC HORMONE (ACTH) ON CORTICOSTEROID
SECRETION IN RABBITS

[This is a translation of an article written by
L. V. Orlova, V. M. Rodionov, and L. I. Tuul'
of the Institute of Biological and Medical
Chemistry, Academy of Medical Sciences USSR,
in Problemy Endokrinologii i Gormonoterapii
(Problems of Endocrinology and Hormonotherapy),
Vol VI, No 1, Moscow, 1960, pages 33-37.]

We established in a previous work [1] that general irradiation of rabbits induces an essential reorganization of the function of the adrenals in these animals. In the venous adrenal blood of irradiated rabbits, as compared with the control animals, there was noted a decreased content of corticosterone (compound B) and an increased content of hydrocortisone (compound F) and of an unidentified compound X. The change of the correlation of concentration of corticosteroids in the adrenal blood of rabbits was noted before and under other types of states of stress. Thus, Kass and Hechter [4] observed a sharp increase of the F/B ratio in rabbits after prolonged introduction to them of ACTH. N. A. Yudayev, Yu. A. Pankov and N. P. Surikova [2] obtained analogous data in rabbits that were subjected to the action of cold and aseptic infection. However, in the works of these authors there were no indications of a considerable increase in the blood of experimental animals of concentrations of any corticosteroids, except the compounds F and B. It was interesting to clarify to what extent the increase of the speed of secretion of compound X observed by us is a specific consequence of the irradiation of animals. For the solution of this problem, this work conducts a comparative study of the adrenal function in rabbits which received ACTH and in rabbits which were subjected to irradiation.

The Method.

Rabbits were taken for investigation. In animals on which a laparotomy was performed under hexanal narsosis, the venous blood drawn off from the adrenal was collected through a tube tied into the renal vein. Before collection of blood, heparin was introduced to the rabbits. In the adrenal blood of animals, the content of corticosterone, hydrocortizone and a not completely identified substance, which was conditionally marked by us as compound S, was determined by means of the method of N. A. Yudayev, Yu. A. Pankov and K. V. Druzhinina [3]. The separation of the investigated compounds was performed by means of the method of chromatography on paper in the B₅ system of Bush.

The experimental animals were divided into four groups. The first group included rabbits to which, for the duration of 20-21 days, 15 units each of ACTH was introduced daily according to the method of Kass and Hechter in the form of a suspension in peach oil, which contained 2% of wax [2]. The rabbits of the second group were irradiated with X-rays at a dose of 800-1100 r with a voltage of 195 kV, current intensity 15 mA, filter 1 mm Al + 0.5 Cu, skin focus distance 60 cm and dose power of 11.5 r/min. The blood of this group of rabbits was analyzed on the second day after irradiation, since we have shown before that during this time the greatest changes of the adrenal function in irradiated rabbits are observed. A group of control animals corresponded to each experimental group of animals. To rabbits which received ACTH, animals into which peach oil with wax was introduced intramuscularly during the same period of time served as control; to irradiated animals, normal rabbits served as control.

The Results.

In Fig. 1 the summary concentration of corticosteroids in gamma per 100 ml. of adrenal blood is represented.

As is seen from Fig. 1, the concentration of corticosteroids in both experimental groups, as compared with the corresponding control groups, decreased somewhat; especially in the group of animals which received ACTH.

This can apparently be related to the increase of the velocity of blood flow through the enlarged adrenal glands of experimental animals. In introduction of ACTH as well as in irradiation, the adrenals of rabbits enlarge in weight and in size, which is seen in Fig. 2. In

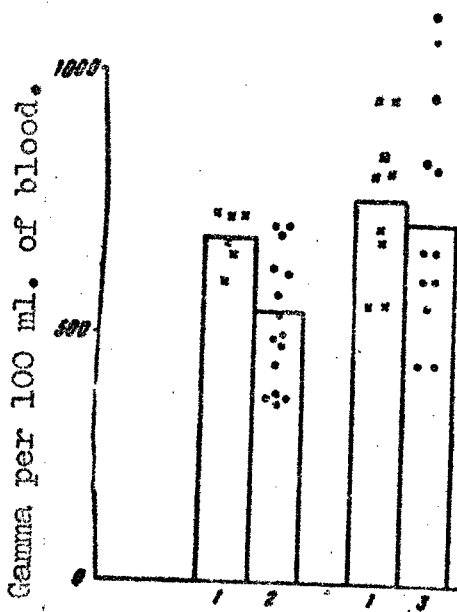


Fig. 1. Summary concentration of corticosteroids in the adrenal blood of rabbits.

The columns characterize the average summary concentration. Individual data for experimental groups of animals (2-ACTH, 3-irradiation) are marked with dots; with crosses for control groups (1).

both experimental groups, except for compounds F and B, it was possible to see considerable amounts of a compound

irradiated animals the weight of the adrenal increases to 178% with respect to the weight of the adrenal of control animals, and, in those receiving ACTH, to 143%. It would be possible to expect that such an increase of the gland would lead to a sharp increase of the amount of hormones secreted by it.

However, this was not observed (Fig. 3). The amount of steroids secreted by adrenals during a unit of time, does not change on the average in rabbits which received ACTH, and, in irradiated animals, increases only by 29%. On chromatograms obtained after the processing blood collected from rabbits of

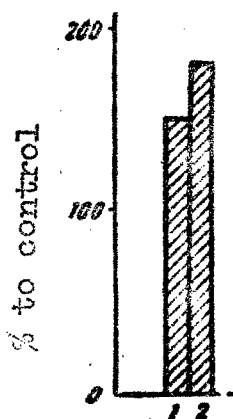


Fig. 2. Average weight of adrenals in percent with respect to control. 1-L-ACTH; 2-irradiation.

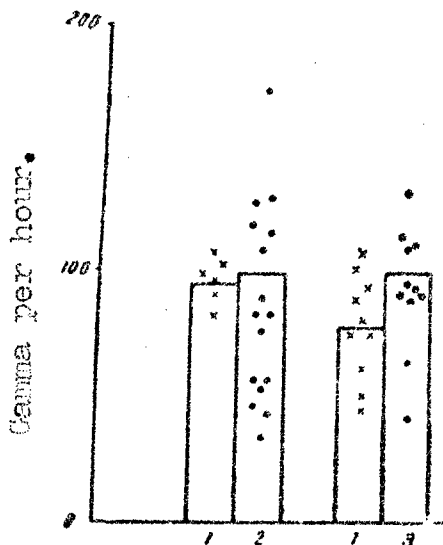


Fig. 3. Summary velocity of corticosteroid secretion. Symbols are the same as in Fig. 1.

which absorbed ultraviolet rays and which is located in the zone of cortisone. In control animals, the amounts of this compound were insignificant. In previous work, the compound located in this place was designated by us as compound X. Insofar as compounds of various structure may possess the same chromatographic motility, we attempted first of all to clarify, by means of the methods available to us, whether this compound is general for all groups of animals investigated by us. The data cited in the table evidence that in all cases (in control animals, in animals which received ACTH, and in irradiated animals) we dealt with one and the same substance. On the basis of this data, certain preliminary conclusions may be reached regarding the structure of this compound. For conducting the reactions indicated in the table, substance X was subjected to additional purification by means of rechromatographing in the same system of solvents.

The comparison of compound X obtained from rabbits that were normal, receiving ACTH, or irradiated

Rabbits	Chromogens, maximum of absorption gamma in m μ	Reaction				Maximum in ultraviolet gamma in m μ
		with ortho-phosphoric acid	with methanol alkali	with tri-phenyl-tetra-zole	with phenylhydrazine benzole	
Normal	275	Weakly blue-violet	blue luminescence	Weakly positive	negative	250-252
Normal with ACTH Irradiated	275 275	the same "	the same "	the same "	the same "	230-232 230-232

On the basis of the chromogene spectrum and reaction with methanol alkali, it is possible to assume that compound X possesses a Δ^4 -3-ketogroup in the A ring. A negative reaction with m-dinitrobenzole argues that the given compound is not a ketosteroid. The reaction with triphenyltetrazole chloride and silver nitrate testifies to the presence of an alpha-ketole side chain. The absence of an oxygroup with a carbon 17 atom is evidenced by the negative reaction with phenylhydrazine. For final identification of compound X, additional investigations are necessary.

Thus, it was not possible for us to note essential differences either in the summary quantity or in the qualitative composition of steroid hormones secreted by the adrenals of irradiated rabbits as well as of those receiving ACTH. It was possible to note a difference between the action of irradiation and prolonged introduction of ACTH only in the change of the speed of secretion of separate compounds.

In Fig. 4, the speed of secretion of corticosterone is given in gamma/hour per unit of weight of the adrenal. It is seen that the speed of secretion

of corticosterone decreases sharply in rabbits which received ACTH and considerably less sharply in irradiated animals.

The speed of secretion of hydrocortisone per unit of weight of the tissue of the gland (Fig. 5) increases by a factor of 6 after introduction of ACTH. In irradiated animals, the increase of secretion of hydrocortisone is expressed less sharply.

The inverse ratio may be seen in comparison of the speeds of secretion of compound X (Fig. 6). The speed of secretion of this compound increases in animals of both experimental groups; however, in the group of irradiated rabbits, it is expressed more sharply.

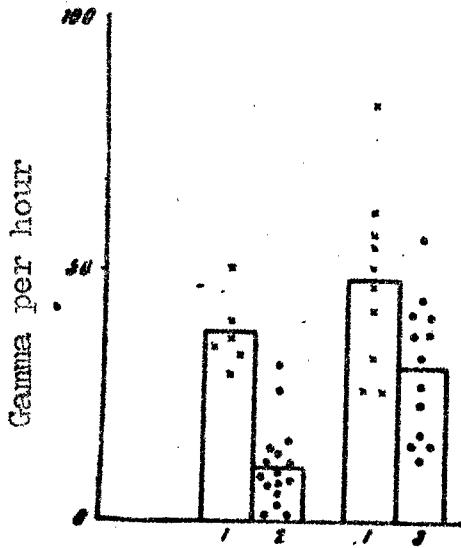


Fig. 4. The speed of secretion of corticosterone per 100 mg of tissue of the adrenal. Symbols are the same as in Fig. 1.

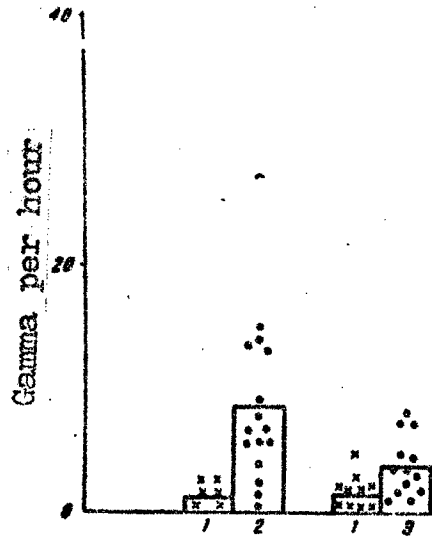


Fig. 5. The speed of secretion of hydrocortisone per 100 mg. of the tissue of adrenal. Symbols are the same as in Fig. 1.

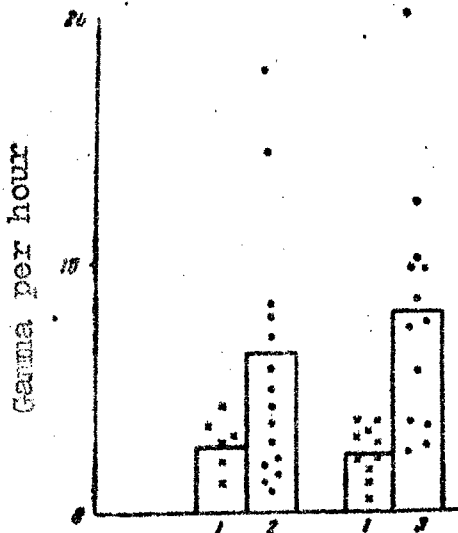


Fig. 6. The speed of secretion of compound X per 100 mg. of adrenal tissue. Symbols are the same as in Fig. 1

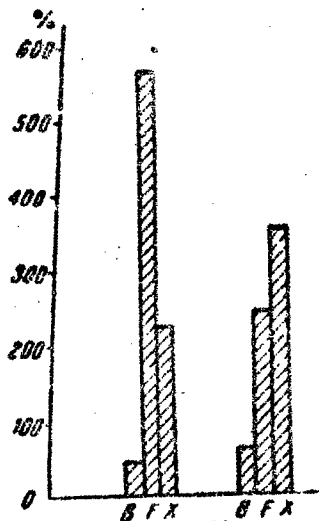


Fig. 7. The speed of secretion of corticosteroids per 100 mg. of the adrenal tissue in percent with respect to control. Three left columns - introduction of ACTH; three right columns - irradiation

The relative changes of the speeds of secretion of separate corticosteroids in irradiated rabbits and in those receiving ACTH are summarized in Fig. 7, from which it is seen that under the given conditions of experiment the introduction of ACTH induced a sharp increase of the speed of hydrozortisone secretion, a less significant increase of the speed of secretion of compound X and a decrease of the speed of secretion of corticosterone. In irradiated rabbits a sharp increase of the speed of secretion of compound X and one less significant of hydrocortisone. The decrease of the speed of secretion of corticosterone was insignificant.

The cited data testifies that the adrenals of rabbits which were irradiated with a lethal dose of X-Rays do not secrete, at least in considerable quantities, any steroids which differ from hormones which are produced by the cortical layer of these glands after their prolonged stimulation with ACTH.

The difference in the action of adrenocorticotrophic hormone and irradiation is manifested only in a comparison of the change of speeds of secretion of separate corticoids in irradiated rabbits and in those receiving ACTH.

However, the difference in the methods of conducting the experiments - single irradiation and prolonged introduction of ACTH - does not allow us to speak of the specificity of these changes. It is possible that with a change of the duration of the introduction or dosage of ACTH, these differences may become less noticeable.

For further study of this problem, a comparison of the function of adrenals of irradiated animals and animals which are under the influence of stimuli of another type would be interesting.

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