EFFECTIVENESS OF ACTH IN THE PROPHYLAXIS OF ACUTE RADIATION SICKNESS

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Intravenous injection of ACTH into rats (and, to a lesser degree, into mice and dogs) before irradiation has a protective action, reducing mortality and causing a less severe leukopenia. During the first few hours after irradiation the content of 11-hydroxycorticosteroids in the animals receiving ACTH was higher than in the controls.

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The discovery of periodic changes in activity of the pituitary – adrenal system in acute radiation sickness [2, 7] stimulated studies of the possibility of using ACTH in this disease. However, the many investigations of the effectiveness of prophylactic hormone administration yielded conflicting results [1, 3, 4, 5]. Stimulation of steroid production can be achieved most rapidly by intravenous injection of the hormone. Accordingly, an investigation was carried out in which single intravenous injections of ACTH were given immediately before irradiation.

EXPERIMENTAL METHOD

Experiments were carried out on mice, rats, and dogs. The animals were irradiated on the EGO-2 apparatus with Co^{60} γ-rays in doses of 300 R for dogs, 600 R for rats, and 700 R for mice, at a dose rate of 586.9-725 R/min. ACTH was injected into the mice and rats 15 min before irradiation, and into the dogs 30 min before irradiation, in a dose of 1 unit/kg body weight for rats and dogs and 10 units/kg body weight for mice. The effectiveness of ACTH was judged from the clinical course of the disease, changes in the blood morphology, and the survival rate of the animals.

The level of 11-hydroxycorticosteroids (11-HC) in the blood was determined by a fluorometric method [6] before injection of ACTH, and before and at various times after irradiation.

EXPERIMENTAL RESULTS

Injection of ACTH reduced the mortality of the experimental animals by half. In the control group 10 of the 58 mice (17.7%) survived, compared with 12 of 35 mice (34.3%) in the experimental group. However, the difference between these mean values is not statistically significant.

The prophylactic administration of ACTH was much more effective in rats: none of the 12 animals receiving the hormone died, whereas, in the control group, only 28 of the 53 rats survived (52.7%, $P < 0.001$).

No data concerning the prophylactic use of ACTH against radiation sickness in dogs could be found in the accessible literature. In the present experiments 5 of the 6 dogs receiving ACTH survived (compared with 9 of the 16 control animals).

The dynamics of changes in the leukocyte count in the period after irradiation was similar in the experimental and control animals, but as a rule the leukocyte count was higher in animals receiving ACTH than in the control (Table 1).

Preliminary administration of ACTH prevented the development of severe leukopenia, especially in the first two weeks after irradiation.

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TABLE 1. Changes in Leukocyte Count in Blood (thousands/mm^3) of Irradiated Animals

Animals	Group	Intact	Days after irradiation					
			3-rd	7-th	12-th	20-th	30-th	45-th
Rats	Control	10,4±0,35 (31)	1,0±0,6 (8)	2,0±0,5 (17)	3,0±0,3 (19)	8,5±4,9 (19)	7,1±0,6 (18)	—
	Experimental		2,9±0,2* (6)	5,1±0,4* (6)	6,1±0,7* (6)	18,1±1,6 (6)	9,2±0,7 (6)	—
Dogs	Control	10,1±0,8 (16)	5,7±0,3 (16)	3,6±0,4 (16)	1,6±0,2 (16)	1,2±0,3 (11)	3,1±0,6 (9)	7,6±0,8 (9)
	Experimental		5,1±0,6 (6)	3,9±0,6 (6)	2,7±0,3* (6)	2,4±0,6 (5)	3,1±0,9 (5)	7,0±0,8 (5)

Note: Number of animals shown in parentheses. Asterisk indicates that difference from control is significant ($P < 0.05$).

The blood 11-HC level in the dogs receiving ACTH 1-2 h after irradiation was higher (18-19 μg%) than in the controls (8-8.5 μg%). No significant difference between the 11-HC concentration in the blood of the experimental and control dogs was found 1, 3, 7, 12, and 20 days after irradiation.

If ACTH was given by daily intramuscular injection (1 unit/kg body weight) during the week before irradiation, the protective effect of the hormone was less marked: two of the four animals died, i.e., the mortality was identical in the control and experimental groups.

It can be concluded from analysis of the results that a single stimulation of steroid production immediately before irradiation has a definite protective action. It is probable that an excess of glucocorticoids in the body at the time of irradiation and for the first few hours thereafter plays a definite role in the mechanism of the prophylactic effect of ACTH.

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