CHANGES IN BINDING CAPACITY OF CORTICOSTEROID-BINDING PLASMA GLOBULIN IN ACUTE RADIATION SICKNESS

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Within a few hours and on the 4th day after whole-body γ-ray irradiation of rabbits in a dose of 800 R a fraction of free 11-hydroxycorticosteroids, not bound with protein, appears in the blood. Investigation of the binding capacity of the corticosteroid-binding plasma globulin of the blood suggests that the appearance of the free hormone fraction during the first few hours of irradiation is due to a marked increase in the total corticosteroid concentration, whereas dissociation of the protein-steroid complex at the height of radiation sickness is directly associated with a decrease in the binding capacity of the corticosteroid-binding globulin.

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At the height of acute radiation sickness a period of increased glucocorticoid activity is observed, accompanied by an increase in the hormone concentration of the blood [7, 9, 11], which has an adverse effect on the course and outcome of the radiation sickness [2, 8, 15].

Previous investigations showed [1] that a hypercorticoid state can be observed in animals even with a normal blood hormone level as the result of disturbance of the bond between the hormones and plasma proteins, leading to the appearance of a free (biologically active) steroid fraction in the animals' blood.

To study the mechanism of this phenomenon experiments were carried out to determine by a direct method the quantity of hormone which can be bound with the plasma proteins, i.e., to estimate the reserve binding capacity of the corticosteroid-binding globulin (CBG) of the blood plasma in the course of acute radiation sickness.

EXPERIMENTAL METHOD

Experiments were carried out on male chinchilla rabbits weighing 2.5-3 kg. Acute radiation sickness was produced by Co^{60} γ-rays on a type EGO-2 apparatus (dose 800 R, dose rate 600.03 R/min).

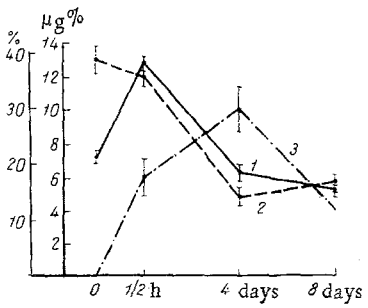

Fig. 1. Concentration of 11-hydroxycorticosteroids and binding capacity of CBG in rabbits' blood in the course of acute radiation sickness. 1) Total hormone level (in μg%); 2) binding capacity of CBG (μg%); 3) free hormone fraction (in %).

All the animals died with manifestations of acute radiation sickness. The concentration of corticosteroids was determined by Guillemin's fluorometric method [10]. The binding capacity of the plasma CBG was studied by the gel-filtration method described by De Moor and co-workers [5].

EXPERIMENTAL RESULTS

In healthy rabbits all the corticosteroids circulating in the blood are bound virtually completely with the plasma proteins. Determination of the binding capacity of the CBG showed (Fig. 1) that the mean normal value of this index is 13.1 μg%. The corticosteroid concentration was elevated 1.5-2 h after irradiation. As previous experiments showed, the free hormone fraction at this period reached on the average 18% of the total content of corticosteroids. Meanwhile the binding capacity of the CBG was almost unchanged from normal (12.1 μg%).

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The appearance of the free hormone fraction was due to an increase in the total level of corticosteroids in the blood 1.5-2 h after irradiation as the result of activation of the function of the pituitary–adrenal system.

In animals exposed to stressors other than radiation (anesthesia, administration of ACTH, cortisone, etc.), the observed activation of adrenal function also is attributable to biologically active steroids [3, 6, 13], the binding capacity of the CBG remaining unchanged [5].

On the 4th day after irradiation definite dissociation of the protein-steroid complex was observed. About 30% of the total content of hormone was in a free state. The appearance of this free hormone fraction was observed against the background of a normal blood steroid concentration, which can probably give rise to a hypercorticoid state. Investigation of the binding capacity of the CBG showed that the appearance of the free steroid fraction was due to a sharp decrease in its binding capacity (4.8 μg%).

On the 8th day after irradiation, the free hormone fraction was reduced (11.7%), and in more than half of the animals no free fraction could be determined. The binding capacity of the CBG at this period remained low (mean 5.7 μg%). Simultaneous determination of the binding capacity of the CBG and the free hormone fraction in the rabbits showed that when the binding capacity of the CBG exceeded the total hormone level in the blood, the free fraction was absent; if the reserves of binding capacity of the CBG were below the total hormone level, a free fraction could be detected. Despite the absence of active hormone in this period of radiation sickness, the reserve capacity of the CBG was lowered below the control level, so that stressor action against this backgound could cause the appearance of the free fraction in considerable quantity.

The possibility is not ruled out that changes in the binding capacity of the CBG observed after irradiation are associated with disturbances of protein metabolism, mainly of glycoprotein metabolism.

In some pathological states (multiple myeloma, nephrotic syndrome, cirrhosis of the liver, exudative enteropathy) the lowering of the binding capacity of the CBG is due, in the opinion of many investigators [4, 5, 14], to a decrease in the α-globulin fraction (the place of localization of the CBG). In radiation sickness, characterized by a disturbance of protein metabolism, an increase in the level of α- and β-globulin is observed [12, 16]. However, the general increase in these fractions is not reflected in changes in the content of CBG.

It is probably most logical to regard the change in the binding capacity of the CBG as the result of structural changes in the protein molecules after exposure to irradiation.

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