

TO THE ACTION MECHANISMS OF BIOPROTECTORS

L.V.Alekseeva, A.A.Kudryavtzeva, V.G.Tyazhlova, I.G.Akoev
 Institute of Biological Physics, Acad.Sci.
 USSR, Pushchino, Mosc Region, USSR,
 142292

The analysis of the data on the action of the means of chemical protection enabled one to propose a general way of realization of the protective action of different radioprotectors (1). On the other hand, a large scatter of natural individual differences in radioresistance of a uniform population of animals (2) made one to search for physiological mechanisms responsible for these differences. To do this, two physiological states of the females markedly differing in their radioresistance were investigated. Mouse, rat and guinea-pig females proved to be more radio-sensitive in the state of active secretion of estrogens and more radioresistant (about two times) in the state of active secretion of progesterone and subliminal secretion of sex hormones (in metestrus and diestrus) (3,4).

The studies of some metabolic and energetic processes in tissues of the females associated with the sex cycle phases have shown that in more resistant states the activity of G-6-P-D increases and the respiration of the mitochondria occurs at a low-energy level that promotes the recovery processes. At the same time the proliferative activity of all regenerating tissues of the organism decreases. The radiosensitive phases of the females have shown a decrease in activity of G-6-P-D, activation of LDH and a transition of the mitochondria to the high-energy state (activation and expenditure of reductive equivalents). At the same time an increase in the proliferating activity of different tissue systems was observed (5).

These metabolic states were modelled by means of adaptogens. It was found that the injection of ginseng and eleuterococcus over prolonged periods (a month) affects the activity of the above enzymes and energy-dependent reaction of mitochondria respiration in opposite directions. On subsequent irradiation the both adaptogens increased the survival by 20-25%. Probably more essential was not the directivity of the activation but the fact itself of activation of glycolysis and Krebs cycle on the one hand, and pentose shunt on the other. The activation of one direction of metabolism is followed by the activation of the other one. Adaptogens exert the protective action only when injected repeatedly over prolonged periods. During this time a gradual development of metabolic and energetic processes enhancing the resistance of the animals occurs.

Progesterone and estrogens responsible for significant changes in the radioresistance of the female organisms associated with the sex cycle were tested as means of chemical protection. The estrogens exert no protecting effect. On the contrary, they cause an increase in the death percentage. Progesterone proved to be a good protector. When irradiating the males 35-40 min after injection of progesterone the survival increased to 90-95% as compared to

48-50% in control. When injected to the mice 10 days before irradiation, estrogen as many other biochemical and pharmacological preparations can exert the protective effect. Despite the fact that in 48 hrs there are no traces in the organism they have time to exert the activating effect on the adaptive system and to decrease the percentage of animal death.

When injecting ACTH - adaptation hormon-15 and 30 min before irradiation, the survival rate of male mice increased to 90% as compared to 50% in control.

Upon injecting ACTH 1, 2 and 24 hrs before irradiation no protection effect was observed, the death of the animals increased. The injection of ACTH 4 hrs before irradiation gave the best result. Here survived 100% mice as compared to 48% in control.

Changes in the radioresistance were modelled also by modifying the intermediates of the Grebs cycle in order to store the energy-rich compounds for the postirradiation repair. As protectors potassium salt of the succinic and glutamic acids was tested. The protection effect did not exceed the values peculiar to bioprotectors - the survival increased to 80% as compared to 50% in control.

Hence, the bioprotectors exerting a general effect on the animal organism such as ACTH and progesteron proved to be most effective. Biological compounds causing particular limited changes of metabolism and cellular energetics such as adaptogens, Crebs cycle modifiers, the compounds activating the ACTH secretion and development of the general nonspecific resistance were found to be less effective.

REFERENCES

- (1) AKOEV, I.G., LACUN, M.A. Radiobiologiya, 6, (1966) 891.
- (2) AKOEV, I.G. "Problems of Postirradiation Repair", M.Atomizdat, (1970).
- (3) ALEKSEEVA, L.V., KUDRYAVTZEVA, A.A. "Peculiarities of the Radiosensitivity associated with the Sex" Radiobiologiya, number 6, v.I4 (1974), 932.
- (4) ALEKSEEVA, L.A., KUDRYAVTZEVA, A.A. "Application of Hormones as Protectors" VINITI N1858-74.
- (5) AKOEV, I.G., ALEKSEEVA, L.V. in "Theoretical Preconditions and Models of Radiation Damage of the Organism", Pushchino (1975) 151-170.