

CONTENT OF LYSOSOMAL CATIONIC PROTEINS IN NEUTROPHILIC
GRANULOCYTES OF RABBITS AND GUINEA PIGS IN THE EARLY
STAGE OF ACUTE RADIATION SICKNESS

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Cationic proteins of neutrophilic granulocytes are recognized as the most active of all bactericidal systems of leukocytes and the most universal with respect to the mechanism of their bactericidal action. These proteins also have the power to increase permeability of cell membranes and to modify the activity of various enzymes, so that they can be classed among the mediators of inflammation. The presence of positively charged atoms in the molecule of cationic proteins is responsible for their electrostatic interaction with physiological polyanions, such as heparin, DNA, and RNA, resulting in a mutual reduction in their biological activity [3].

The wide spectrum of action of the cationic proteins and their participation in physiological processes, signs of disturbance of which are observed in cases of radiation damage (depression of the bactericidal properties of the blood, a decrease in phagocytic activity of the leukocytes, increased permeability, early hypercoagulation, etc.) served as the basis for a study of changes in the content of these proteins in neutrophilic granulocytes in the course of acute radiation sickness.

EXPERIMENTAL METHOD

Experiments were carried out on rabbits weighing 2-2.5 kg and guinea pigs weighing 250-300 g of both sexes. The animals were irradiated on the GUB-200,000 apparatus in doses of 800 and 400 R, respectively (^{60}Co source, dose rate 50 R/min). The content of cationic proteins in the neutrophilic granulocytes was studied by a cytochemical method [1] immediately and 1, 2, 3, 14, and 72 h and 7 days after irradiation. For statistical analysis of the results the mean cytochemical coefficient was calculated by Kaplow's principle and the significance of differences was determined by Student's t-test [2].

EXPERIMENTAL RESULTS

The investigations showed that the content of cationic proteins in leukocytes of irradiated guinea pigs fell during the first day of radiation sickness (Table 1). On the 3rd and 7th days after irradiation a further decrease in the content of cationic proteins in the neutrophilic granulocytes to 64 and 53% of the initial number, respectively, occurred.

The content of cationic proteins in the granulocytes of the irradiated rabbits showed a tendency to fall immediately after irradiation, and after 1 h it differed significantly from the original values. On the 7th day of radiation sickness the level of cationic proteins in the rabbits' leukocytes was reduced on average by almost half of the initial value.

Lysosomal cationic proteins of neutrophilic granulocytes, unlike nuclear histones, can be secreted into the extracellular medium from viable leukocytes. The phenomenon of "leaking" of cationic proteins from azurophilic and specific granules arises regularly during physiological death of neutrophilic granulocytes of the blood and bone marrow [1]. In radiation

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TABLE 1. Dynamics of Mean Cytochemical Coefficient Reflecting Content of Cationic Proteins in Neutrophilic Granulocytes in Guinea Pigs and Rabbits in Early Stage of Acute Radiation Sickness ($M \pm m$)

Time of investigation after irradiation	Guinea pigs (n = 10)	Rabbits (n = 6)
Before irradiation (control)	$1,33 \pm 0,10$	$3,47 \pm 0,05$
First few minutes	$1,55 \pm 0,10$	$3,23 \pm 0,02$
1 h	—	$2,70 \pm 0,04^*$
2 h	$1,64 \pm 0,10$	$2,68 \pm 0,14^*$
3 h	$1,42 \pm 0,02$	$2,74 \pm 0,13^*$
24 h	$0,92 \pm 0,02^*$	$2,80 \pm 0,08^*$
3 days	$0,85 \pm 0,05^*$	$2,26 \pm 0,18^*$
7 days	$0,65 \pm 0,07^*$	$1,84 \pm 0,07^*$

* $P < 0,05$

sickness the number of dying cells in the blood stream increases because of disturbance of the reproductive function of the bone marrow. Accordingly the decrease in the content of cationic proteins in the leukocytes of irradiated animals can be attributed to their "emergency output" or "leakage."

Being highly active compounds with a broad spectrum of biological action, cationic proteins, on entering the general circulation from the cells, may make an important contribution to the mechanism of development of several postradiation reactions. In particular, in the early stage of acute radiation sickness the antiheparin activity of the blood may be raised, hypercoagulation develops, and intravascular platelet aggregation is activated. The results of investigations by the present writers [4, 5] and others [6, 7] show that many compounds with polycationic structure can induce platelet aggregation, inhibit the anti-coagulant heparin, and stimulate the fibrinogen-fibrin reaction and also the process of paracoagulation of fibrin monomers and of fibrinogen-fibrin degradation products. Accordingly the possibility cannot be ruled out that one of the factors leading to elevation of the thrombogenic potential of the blood in the early stages after irradiation is the cationic proteins liberated from granulocytes.

The experiments thus showed that in the early stage of acute radiation sickness in rabbits and guinea pigs the content of cationic proteins in the neutrophilic granulocytes falls, probably as a result of their "output" or "leakage" into the extracellular medium. This may lead, on the one hand, to weakening of the antibacterial function of the leukocytes and, on the other hand, to the appearance of biologically active compounds, involved in the mechanism of development of individual postradiation reactions, in the blood stream.

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