State of the Hematopoietic System in Rats Subjected to Emotional Stress after Low-Dose Chronic Irradiation

Yu. B. Deshevoi, B. B. Moroz, K. V. Sudakov, E. A. Yumatov, and R. M. Salieva

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Examination of processes occurring in the hematopoietic system of rats subjected to emotional stress shortly after 30-day exposure to low-dose γ-radiation revealed the inhibitory influence of radiation exposure on the development of adaptive reactions by this system in the stressed animals.

Key Words: *radiation exposure; stress; bone marrow; thymus; spleen; peripheral blood*

Major nuclear accidents generate an array of serious psychological and social reactions, and therefore research into the health effects of exposure to low radiation doses and the consequent emotional stress acquires special importance. If the exposure to a stressor is excessive and/or long-lasting or if some component of the adaptation system is defective, impairments at the level of somatic functions may occur and the sequelae of stress may well become a main factor in the pathogenesis of various diseases, including those associated with disorders of the immune and hematopoietic systems [2,5-7,9].

The aftermath of the Chernobyl accident has highlighted the need for exploring the effects of prolonged emotional tension following chronic exposure to low-dose ionizing radiation. The purpose of the present investigation was to examine how the blood system of animals chronically exposed to low-dose radiation would respond to a situation of aggressive conflict.

MATERIALS AND METHODS

A total of 98 random-bred male rats weighing 160-180 g were used. One day after their 30-day exposure to γ-quanta from ^{137}Cs in a dose of 90 rad at a rate of 3 rad/day, the test rats were placed under emotional stress that resulted from behavior characterized by aggressive conflict. Stress was induced by fixing the rats securely by the tail in openings of the walls of vivarium cages that each contained several rats at short distances apart so that they could easily come in direct contact with each other; the rats remained thus fixed 5 h daily for up to 4 days [10]. Nonirradiated rats subjected to emotional stress as described above served as controls. Animals in all groups were of the same age.

At 10, 24, 48, and 96 h after the start of stress exposure, rats were decapitated. Cell counts in the femoral bone marrow, thymus, and spleen were estimated; differential counts of cells in impression smears of bone marrow were made [2]; erythrocytes, reticulocytes, and platelets as well as leukocytes of different subsets were counted in peripheral blood samples [8]. The numerical data were subjected to statistical analysis using Student's *t* test to estimate the significance of differences.

RESULTS

When the state of hematopoiesis was studied in the rats after their chronic low-dose irradiation before stressing, the number of erythroid cells in the bone

Laboratory of Radiation Pathophysiology, Institute of Biophysics, Ministry of Health of Russia; Anokhin Institute of Normal Physiology, Moscow

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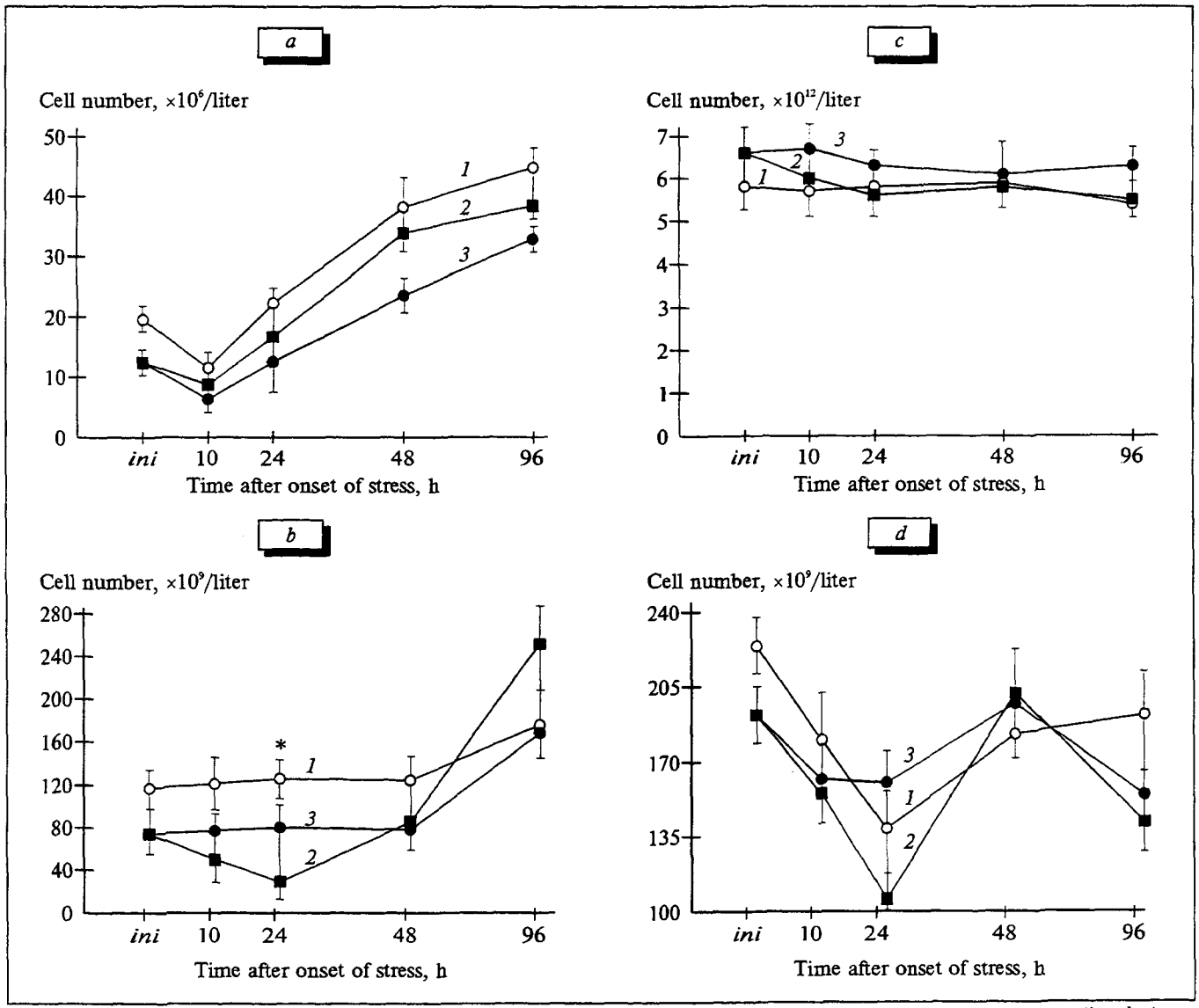

Fig. 1. Cell counts in the bone marrow and peripheral blood at different times after the start of exposure to emotional stress. *a*) marrow erythroid cells; *b*) blood reticulocytes; *c*) blood erythrocytes; *d*) blood platelets. Here and in Figs. 2 and 3: *ini* = initial cell count before stress exposure; *1*) cell count in nonirradiated stressed rats; *2*) cell count in rats subjected to both chronic irradiation and stress; *3*) cell count in rats subjected to chronic irradiation only. The data are means±standard error of the mean (each point represents 7 animals). *$p<0.05$ in relation to the group subjected to both chronic irradiation and stress.

marrow was found to have dropped by 37% (as compared to nonirradiated controls), along with a fall in the number of peripheral blood reticulocytes (Fig. 1). Other cell populations in the bone marrow and blood were not affected, nor was the cell count in the spleen (Figs. 1-3), whereas the thymus was markedly depleted of cells, whose number amounted to 64% of the normal level (Fig. 2). (It should be noted that both erythropoiesis in the bone marrow and lymphopoiesis in the thymus virtually returned to normal 2-4 days after the 30-day radiation exposure - data not shown.) In this setting, the response of the blood system to prolonged emotional stress was examined and two stages of the general adaptation syndrome were identified.

The mobilization stage of this syndrome, observed within the first 24 h after the onset of stressful exposure, is characterized by cell depletion of the thymus and spleen (mainly as a result of lymphocyte migration), elevated lymphoid cell counts in the bone marrow, release of mature neutrophils from the marrow into the blood, and neutrophilia, lymphopenia, and eosinopenia in the peripheral blood [2,4,7]. During the first stage, therefore, there occurs massive migration and inter-organ redistribution of various populations of lymphoid cells and of the mature granulocytes. This reaction, elaborated in the process of evolution, is a preventive measure against possible infection, and it also constitutes a basis for subse-

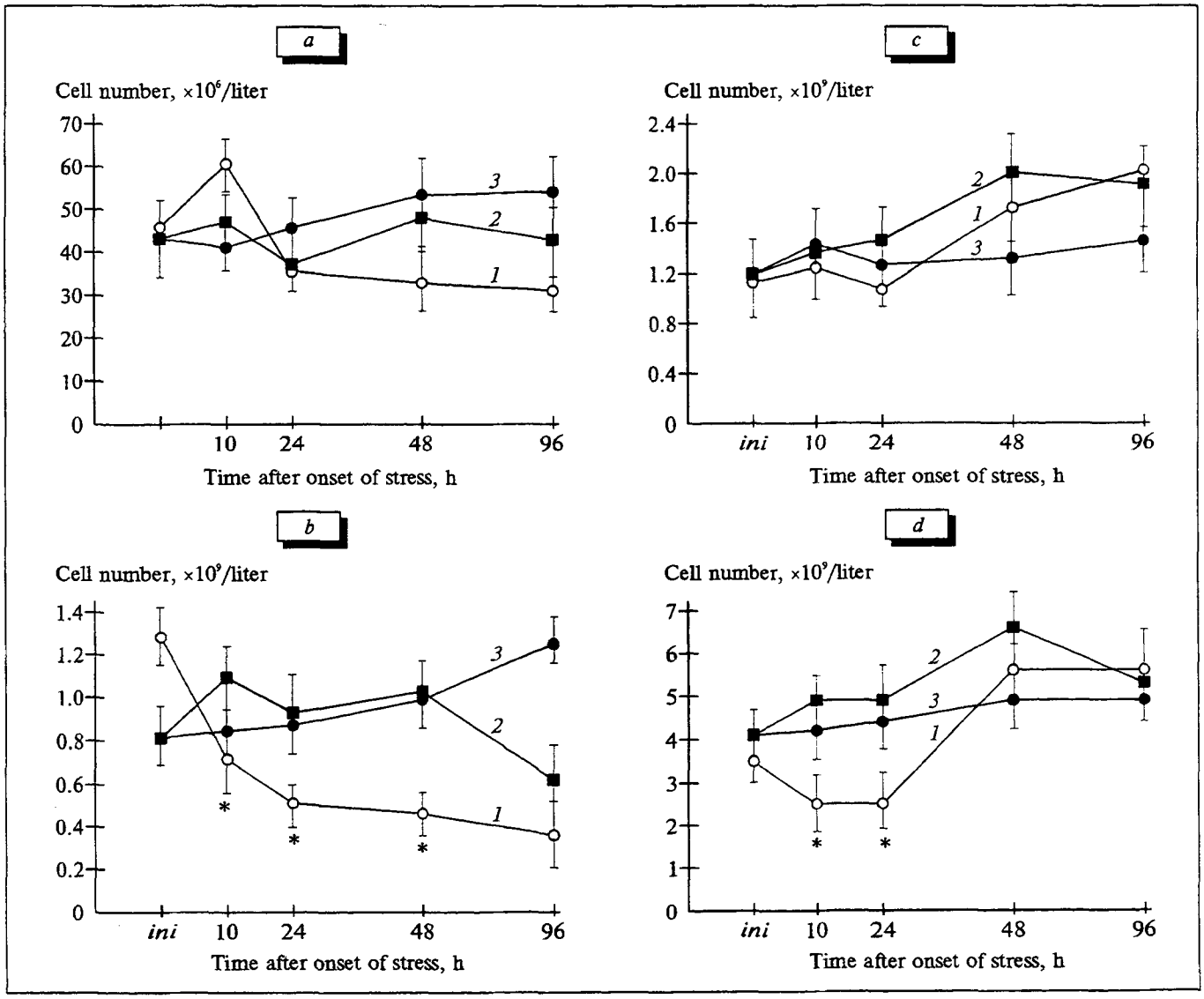

Fig. 2. Counts of lymphoid cells in the bone marrow (*a*), thymus (*b*), spleen (*c*), and blood (*d*).

quent changes in the blood system that take place during the stage of resistance, whose hallmark is activation of bone marrow hematopoiesis [1-4].

At 10 h after the start of the first 5-h fixation (during the mobilization stage), the number of thymic cells in the nonirradiated rats was only 44% of its initial level, and the thymuses of these rats remained depleted up to 96 h after the start of stressing. In contrast, cell counts in the thymuses of irradiated rats did not decrease appreciably until after 96 h of stress (Fig. 2). The spleens of irradiated rats responded to the emotional stress in the same manner as did those of nonirradiated (control) animals (Fig. 2). The bone marrow of nonirradiated stressed rats showed a 132% rise above normal in lymphocyte numbers by 10 h ("lymphoid cell peak") followed by falls at later times. No lymphoid cell peak was observed in the marrows of irradiated rats. In the marrows of control animals, the increase in the lymphocyte population occurred concomitantly with a decline in cells of the myeloid series. By 10 h after the start of stressing, the counts of band and segmented cells in the marrows of nonirradiated rats had decreased to 43% of their initial level; no release of mature neutrophils from the marrow into the blood was detectable in the irradiated stressed animals (Fig. 3).

Neutrophilia developed in the peripheral blood of both groups during the first 10 h of stress exposure, but was less strongly marked in the irradiated rats (neutrophil numbers in these reached 173% of their initial level *vs.* 270% in nonirradiated rats), apparently on account of limited neutrophil migration from the bone marrow. Lymphopenia shortly after the start of stressing was observed in the blood of nonirradiated rats only (Fig. 2).

Between 48 and 96 h after the onset of stress exposure, nonirradiated rats developed bone marrow hyperplasia, which resulted from the stimulation of both erythropoiesis and neutrophil production. During that period the number of erythroid cells and the total number of myeloid cells in the bone marrow reached 230% and 134% of the initial level, respectively (Figs. 1 and 3). As already noted, such changes are characteristic of the stage of resistance, which is the second stage of the general adaptation syndrome. In the irradiated stressed rats, in contrast to nonirradiated controls, only erythropoiesis was activated in the bone marrow at 48 h and 96 h, along with elevation of reticulocyte numbers in the blood; neutrophil production was not activated (Figs. 1 and 3).

The results presented above indicate that the substantial changes in nonspecific reactions of the blood system observed in irradiated rats at the mobilization stage of the general adaptation syndrome (absence of cell depletion in the thymus, of a "lymphoid cell peak" in the bone marrow, and of the release of mature neutrophils from the latter) led subsequently to an inadequate hematopoietic response at the resistance stage. This was manifested, in particular, in the failure of neutrophilopoiesis to be activated in the bone marrow. Taken together, the findings from this study suggest that chronic irradiation adversely affects the development of adaptive reactions in the blood system during emotional stress.

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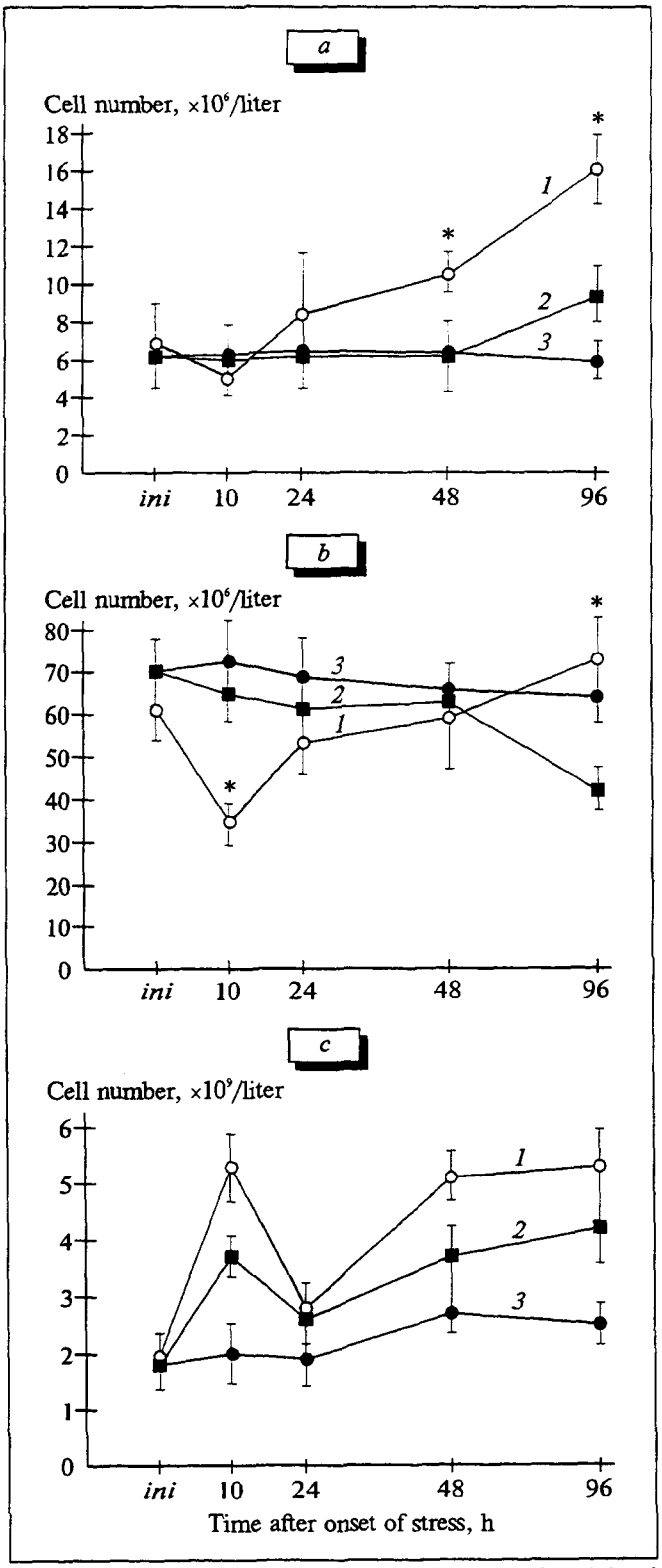

Fig. 3. Neutrophil counts in the bone marrow and peripheral blood. *a*) young cells (myeloblasts — myelocytes) in marrow; *b*) band cells+segmented cells in marrow; *c*) blood neutrophils.