# CHANGES IN NUMBER OF CELLS WITH CHROMOSOMAL ABERRATIONS IN THE BONE MARROW OF IRRADIATED MICE DURING COMBINED TREATMENT WITH COCARBOXYLASE AND TRYPTOPHAN

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Combined treatment with cocarboxylase and tryptophan gave a positive effect during the first 2 h after irradiation, with a decrease in the number of cells with chromosomal aberrations in the bone marrow of mice.

Since the genetic apparatus of cells is damaged by irradiation, the effect of radioprotective substances on the degree of radiation damage to these structures is important.

Experimental investigations have shown that the prophylatic administration of well known protectors such as AET [1, 6, 8], mercamine (2-aminoethanethiol) [3], MEA [2, 12], and 5-methoxytryptamine [6], leads to a decrease in the number of cells with chromosomal aberrations in hematopoietic organs.

Attempts have recently been made to act in specific ways on the biochemical mechanisms of regeneration after irradiation. For instance, the beneficial antiradiation action of ATP [5, 8] on regeneration of the unique genetic structures after irradiation evidently depends on the intensity of oxido-reduction, of ATP synthesis, and of the correlated micro-energy balance. The early disturbance of oxidative phosphorylation after irradiation and the disturbance of ATP synthesis are closely connected with the state of the enzyme system whose reduced activity after irradiation is probably caused by the loss of certain coenzymes by the cell organelles. For example, the decrease in the NAD content in the nuclei [10] could be caused by a disturbance of the metabolism of tryptophan which is required for synthesis of the nicotinamide which is the coenzyme of NAD [13]. A decrease in decarboxylase activity [13] also was observed. As a result of the decrease in enzyme activity during the first 2 h after irradiation, the synthesis of DNA and ATP is brought to a halt, and glycolysis is slowed [11].

In the writers' view, in order to be able to control the energy balance of cells and to restore their normal DNA and ATP synthesis, it is essential in the first place to make an experimental study of the therapeutic effect of combined administration of cocarboxylase and tryptophan, given during the first 2 h after irradiation, on the level of chromosomal aberrations in the bone marrow cells.

## EXPERIMENTAL METHOD

Experiments were carried out on 30 male CC57BR mice weighing 20-22 g. Irradiation was carried out on a $\gamma$-ray apparatus (ÉGO-2) in a dose of 500 R and with a dose rate of 357 R/min. The irradiated animals were divided into three equal groups: 1) control, 2 and 3) mice receiving cocarboxylase and tryptophan: group 2) a single dose 2 h after irradiation; group 3) 30 min and 2 h after irradiation. The preparations were injected intraperitoneally (simultaneously from different syringes): cocarboxylase in a dose of 4 mg and tryptophan in a dose of 8 mg/100 g body weight.

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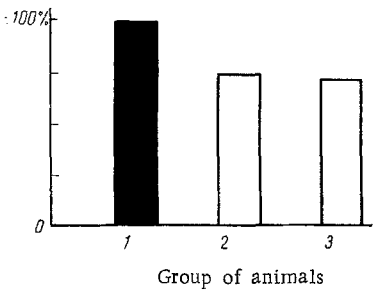


Fig. 1. Number of cells with chromosomal aberrations in the bone marrow of mice 24 h after irradiation and administration of cocarboxylase and tryptophan: 1) control (irradiation); 2) injection of cocarboxylase and tryptophan 2 h after irradiation; 3) injection of cocarboxylase and tryptophan 30 min and 2 h after irradiation.

The animals were decapitated 24 h after irradiation, the bone marrow was extracted from both femora, and the number of cells with chromosomal aberrations in it was counted. Preparations of metaphase plates were made by Ford's method [9] with modifications. Student's criterion was used for statistical analysis.

## EXPERIMENTAL RESULTS

The number of cells with chromosomal aberrations in the bone marrow of the group 1 mice was $90 \pm 2.4$; group 3 mice $72 \pm 3.39$; and group 3 mice $70 \pm 2.02$ (Fig. 1); i.e., it was significantly smaller in the treated animals than in the control ($P < 0.05$).

As was mentioned above, the genetic apparatus of the cell is responsible for its reproductive capacity, which as a whole is intimately linked with the course of cell metabolism [4, 7, 15].

Tryptophan is an essential component in the formation of nicotinic acid, the amide of which is the coenzyme for the enzyme catalyzing the dehydrogenation of the final stage of glycolysis with liberation of energy. Cocarboxylase K (thiamine pyrophosphate) is essential for the action of pyruvate decarboxylase, which catalyzes the decarboxylation of pyruvic acid. Consequently, both cocarboxylase and tryptophan participate in the oxidation of amino acids, fatty acids, and carbohydrates and, consequently, they are essential components for normal metabolism in the cell.

From this standpoint it is probably correct to assess the therapeutic value of administration of a mixture of cocarboxylase and tryptophan as a means of active intervention in the metabolic reactions of the cell which have been disturbed by radiation: oxidative phosphorylation and glycolysis. This leads to the partial repair of chromosome injuries, which in turn leads to an increase in the number of cells, so that hematopoiesis can be restored more rapidly and efficiently.

It must be emphasized in conclusion that the administration of cocarboxylase and tryptophan in the early periods after irradiation (during the first 2 h) leads to a decrease in the number of cells with chromosomal aberrations in the bone marrow of the irradiated mice.

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