EFFECT OF BLOCKING THE PITUITARY-ADRENAL SYSTEM ON COMPOSITION OF ENDOGENOUS COLONIES OF HEMATOPOIETIC TISSUE IN THE SPLEEN OF IRRADIATED MICE

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Experiments were carried out on CBA mice of both sexes weighing 25-30 g. The pituitary-adrenal system was blocked by intraperitoneal injection of dexamethasone in a dose of 250 μg/100 g body weight in 0.3 ml 0.85% NaCl solution. Three hours after injection of the drug the animals were irradiated with Co^{60} γ rays (800 R, rate 40 R/sec). The composition of the endogenous colonies of hematopoietic tissue in the spleen of the irradiated mice was studied on the 10th day after exposure to ionizing radiation. The number of hematopoietic colonies in the spleen of the mice irradiated after blocking of the pituitary-adrenal system was found to be 3.5 times larger than in the spleen of the control irradiated animals. This difference was caused mainly by the larger absolute number of erythroid, undifferentiated, and megakaryocytic colonies.

Adrenocortical hormones participate in the regulation of the proliferative hematopoietic pool. With an increase in the corticosteroid level in the body, the colony-forming ability of the hematopoietic stem cells is reduced [9, 10]. By contrast, adrenalectomy increases the yield of endogenous and exogenous colonies in the spleen of the irradiated mice [3]. Exposure of the animal to ionizing radiation causes activation of the pituitary-adrenal system.

Summation of the direct and indirect (through the adrenocortical hormones) action of radiation of hematopoiesis can thus take place in the irradiated animal [2, 4, 5].

It is therefore an interesting exercise to study the colony-forming ability of the hematopoietic stem cells in animals irradiated after blocking of the response of the pituitary-adrenocortical system to the action of radiation.

TABLE 1. Composition of Splenic Endocolonies of Hematopoietic Tissue in Mice Irradiated after Pituitary-Adrenal Block (M ± m)

	Irradiation	Pituitary-adrenal block + irradiation
Number of animals in group	26	23
Number of macroscopic endocolonies	0,80±0,2	3,10±0,9+
Number of colonies per section through spleen	1,36±0,3	4,86±0,9+
Morphological composition of colonies:		
erythroid	0,06±0,01	0,87±0,3+
myeloid	0	0,26±0,24
megakaryocytic	0,80±0,2	2,10±0,8+
undifferentiated	0,50±0,2	1,50±0,3+
mixed	0	0,13±0,10

Note. + signifies that differences are significant ($P < 0.05$).

EXPERIMENTAL METHOD

Experiments were carried out on CBA mice of both sexes weighing 25-30 g. The pituitary-adrenal system was blocked by dexamethasone, which has the property of depressing the adrenocortical function of the pituitary and the intensity of steroid production in the adrenal cortex [8, 11]. Dexamethasone was injected intraperitoneally in a dose of 250

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μg/100 g body weight in 0.3 ml of 0.85% sodium chloride solution 3 h before irradiation of the animals with Co^{60} γ rays (800 R, dose rate 40 R/sec). On the 10th day after exposure to ionizing radiation the number of endogenous colonies was counted in the spleens fixed in Bouin's fluid. Histological sections, 5 μ in thickness and stained with hematoxylin-eosin, were used for the morphological analysis of the splenic colonies. Erythroid, myeloid, megakaryocytic, mixed, and undifferentiated colonies were identified [7, 12]. Student's criterion [6] and the χ^2 method [1] were used for the statistical analysis of the results.

The state of the pituitary-adrenal function in the mice after administration of dexamethasone was assessed from the steroid-3β-ol dehydrogenase activity in the adrenal cortex, revealed by a histochemical method.

EXPERIMENTAL RESULTS

The experiments showed that 3 h after administration of dexamethasone the pituitary-adrenal system of the mice was in a state of functional block. This was shown by the sharp decrease in steroid-3β-ol dehydrogenase activity in the adrenal cortex.

As the results in Table 1 show, the number of macroscopic endocolonies and the number of colonies in the histological sections of the spleen of mice irradiated after blocking of the pituitary-adrenal system were on the average 3.5 times greater than in the control irradiated animals. Analysis of the morphological composition of the colonies showed that this difference was due mainly to the larger number of erythroid, megakaryocytic, and undifferentiated colonies. The difference in the number of myeloid and mixed colonies was not statistically significant.

Blocking the pituitary-adrenal system thus promotes the formation of hematopoietic colonies in the spleen after exposure to the harmful action of radiation. The protective effect of the block is exerted to a greater degree on the ability of the hematopoietic stem cells to differentiate into cells of the erythroid series.

These findings do not agree with those of Cittadini and Mancini [9], who observed that dexamethasone, administered before irradiation, reduces the number of splenic endocolonies. However, these workers used a much smaller dose (25 μg/100 g body weight) of dexamethasone than that used in the present experiments, with a correspondingly weaker action on the pituitary-adrenal system [11]. The incomplete blocking of adrenocortical function of the pituitary could perhaps have been reflected in the process of endogenous colony formation in the spleen after irradiation.

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