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Effect of some Immunomodulators on Hemopoesis

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In recent years convincing data have been obtained on the participation of lymphocytes in the regulation of hemopoesis [8,10], providing a basis for performing goal-directed immunocorrection of disturbances in hemopoesis. This prompted us to investigate the effect of some standard immunomodulators sodium nucleinate, tactivin, and levamisole - on the rehabilitative processes in hemopoetic tissue. Since the effects of these preparations on blood indicators under normal conditions are mainly described [2,6], we carried out our study on a model of experimental iron-deficiency anemia (IDA) in rats, which is characterized by disturbances in erythropoesis, leukopoesis, and immunity [4] accompanied by suppression of the hemopoesis-regulating function of the lymphocytes [3].

MATERIAL AND METHODS

The experiments were carried out on Wistar male rats weighing 120-130 g. IDA was reproduced by the described method [3]. When severe anemia developed, therapy was started with the following preparations: group 1: ferrum-lek (Yugoslavia) in the doses indicated for that preparation (control); group 2: ferrum-lek + sodium nucleinate in a dose of 50 mg/kg five times; group 3: ferrum-lek + tactivin (I. I. Mechnikov Central Scientific-Research Institute of Vaccines and Sera), 0,1 mg/kg one time; group 4: ferrum-lek + levamisole (Hungary) in a dose of 0,5 mg/kg one time. All the preparations were injected intraperitoneally. On day 5 post-injection the animals were killed by decapitation. Using conventional methods, the usual hematological indicators were estimated: the content of leukocytes, erythrocytes, hemoglobin, reticulocytes, and myelokaryocytes in the femur, the leukocyte formula and myelogram were calculated [5], and the cell count of thymus and spleen was determined. DNA synthesis was evaluated according to incorporation of ^{3}H-thymidine in bone marrow cells.

The experimental results were processed by the methods of variational statistics.

TABLE 1. Some Indicators of Hemopoesis for Injection of Immunomodulators into Rats with IDA (M±m)

Indicator	Ferrum-lek, control	Ferrum-lek+		
		sodium nucleinate	tactivin	levamisole
Peripherial blood:				
lymphocytes,	5,8±0,5	9,8±0,8	9,5±0,5	2,9±0,1
reticulocytes	430,0±10,2	364,6±8,1	299,3±4,7	175,5±8,6
Bone marrow:				
myelokarylocytes	60,0±1,2	58,0±2,3	64,0±1,3	39,8±0,9
incorporation of T-thymidine	620,4±3,9	955,3±10,7	640,5±16,7	382,3±3,4

Note. Asterisk: $p<0.05$.

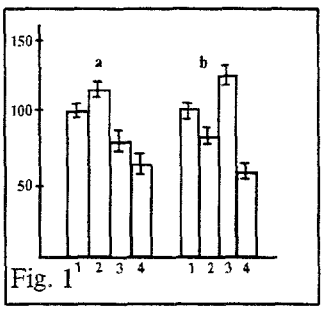

Fig. 1. Effect of immunomodulators on Bone Marrow Cell Composition in Rats. Abscissa: groups of animals; ordinate: % of cell content in relation to control. a) erythroid cells of bone marrow; b) granulocytic cells of bone marrow. 1) ferrum-lek (control); 2) ferrum-lek + sodium nucleinate; 3) ferrum-lek + tactivin; 4) ferrum-lek + levamisole.

RESULTS

The use of the IDA model with iron therapy made it possible to evaluate the effect of the investigated immunomodulators on the characteristics of hemopoesis under the given conditions. It was found that sodium nucleinate stimulated lymphopoesis, evidence of which was seen in the increase of the lymphocyte count in the blood (see Table 1) and of karyocytes in the thymus. This caused the development of slight erythroid hyperplasia in the bone marrow (see Fig. 1), due mainly to basophilic normoblasts.

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However, a reticulocyte reaction was absent, indicating inadequate erythron stimulation and/or a reinforcement of ineffective erythropoesis. Sodium nucleinate is known to be a stimulator of leukopoesis [6], but in the model studied no granulocytopoesis activation was registered in the bone marrow.

The injection of tactivin led to the development of lymphocytosis, an increased cell count in the thymus, and a simultaneous decrease of erythropoesis indicators. At the same time the reaction of granulocytopoesis was revived. This corresponds to data on the effect of the preparation on the bone marrow of untreated rats [2]. The latter probably reflects the phenomena of competitive relationships between immunopoesis and erythropoesis under the influence of tactivin.

The opposite data were obtained in the case of a single injection of the maximal dose of levamisole. This preparation, possessing immunomodulator properties, caused the suppression of all the hemopoesis indicators in the experimental animals, this being one of its known side effects [6].

Thus, use of the immunomodulators resulted in a certain modification of hemopoesis in the animals, vis-a-vis monotherapy with iron. Tactivin caused the activation of granulocytopoesis accompanied by the suppression of erythropoesis, while sodium nucleinate produced another effect, namely a certain erythron stimulation with a slight suppression of leukopoesis in the bone marrow. Levamisole inhibited erythropoesis. Hence, the immunomodulators have a nonuniform effect on the rehabilitative processes in the bone marrow. The mechanisms of such an influence may be diverse: immunological (cell-mediated and antibody-dependent), metabolic, etc. [1,8,9,11]. The data obtained should be taken into account in the pathogenetic substantiation of immunocorrection of hemopoetic disturbances.

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Enchancement of the Oxygen Metabolism of Human Blood Phagocytes under the Influence of Taftsin-like Peptides from a C-Reactive Protein Molecule.

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C-reactive protein (CRP) is one of the main humoral defense factors which have a regulatory effect on cells involved in nonspecific and immune reactions [3,7]. A sharp rise of the serum pentameric CRP (p-CRP) concentration during the first 24-48 h from the beginning of an inflammatory reaction, p-CRP accumulation in the focus followed by disintegration to monomers under acidic conditions in the focus, under the influence of extracellular enzymes, or due to limited proteolysis

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