The results of the present investigation are evidence of the important role of the inducer in the formation of mediators of HDT. On stimulation of interferon formation not only antiviral factor, but also other mediators and, in particular, MMIF, are formed in the tonsillar cells under the influence of the inducer virus. Stimulation of the tonsillar lymphocytes by streptolysin O leading to MMIF formation does not cause the production of antiviral factor, i.e., the inducer virus is a stimulator with a broader spectrum of action, and this must be taken into account when the ability of lymphocytes to produce mediators of HDT is studied.

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EFFECT OF STIMULATION AND INHIBITION OF ERYTHROPOIESIS ON ANTIBODY PRODUCTION AND MIGRATION OF B CELLS FROM THE BONE MARROW AND SPLEEN IN MICE

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The effect of stimulation and inhibition of erythropoiesis on the production of antibody-forming cells (AFC) in the spleen and on the migration of B cells from the bone marrow into the spleen was studied in CBA mice. Stimulation of erythropoiesis was shown to increase the number of AFC in the spleen and migration of B cells from the bone marrow into the spleen sharply 1 and 4 days after blood loss. Inhibition of erythropoiesis led to a very small increase in the number of AFC in the spleen 4 and 7 days after transfusion of syngeneic red cells and inhibited migration of B cells from the bone marrow into the spleen. The possible mechanisms of the effect of stimulation and inhibition of erythropoiesis on antibody formation are discussed.

KEY WORDS: *antibody production; migration of B lymphocytes; blood loss; hypertransfusion.*

It is stated in the literature that stimulation of erythropoiesis is responsible for the increase in the survival rate of animals after subtotal irradiation [2] and activates processes such as the formation of endogenous splenic colonies of hematopoietic cells by polypotent stem cells [9] and the migration of hematopoietic stem cells from the bone marrow into the spleen [10]. Stimulation of erythropoiesis thus leads to considerable changes in the population of hematopoietic stem cells, which are precursors of the mature cells of

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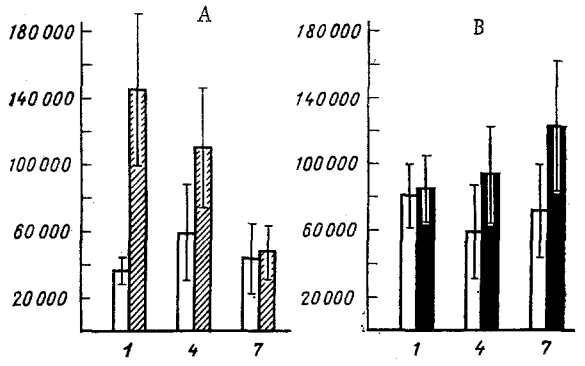

Fig. 1

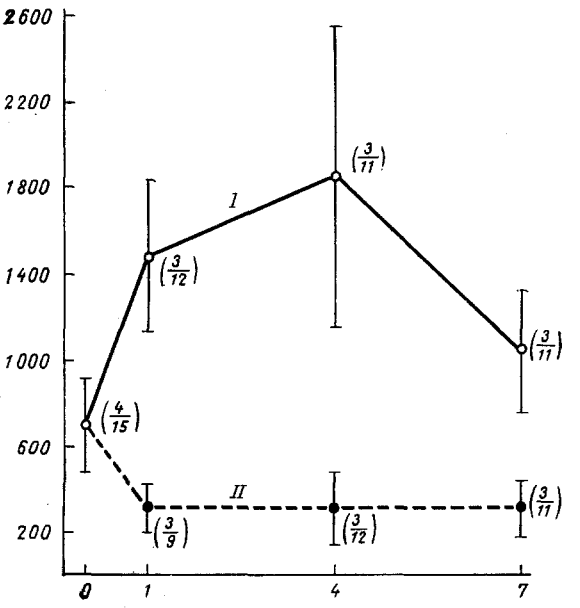

Fig. 2

Fig. 1. Number of AFC in spleen of CBA mice after blood loss (A) and transfusion of syngeneic red cells (B). Unshaded columns, control (intact mice); black columns, transfusion of red cells; obliquely shaded columns, blood loss. Here and in Fig. 2: abscissa, time after blood loss or transfusion of erythrocytes (in days); ordinate, number of AFC in spleen.

Fig. 2. Number of AFC in spleen of CBA mice formed by migration of B cells from bone marrow after blood loss and transfusion of red cells: I) blood loss; II) transfusion of red cells. In parentheses: numerator — number of experiments, denominator — number of animals.

the erythroid, myeloid, and megakaryocytic series, and consequently for immunocompetent cells. However, the data on the effect of stimulation of the erythroid series on the responses of specific immunity are contradictory in character [1, 5, 8].

In the investigation the effect of stimulation and inhibition of erythropoiesis on the production of antibody-forming cells (AFC) and on migration of B cells from the bone marrow into spleen was studied in CBA mice immunized with sheep's red cells.

EXPERIMENTAL METHOD

CBA mice obtained from the "Stolbovaya" nursery of laboratory animals, Academy of Medical Sciences of the USSR, were used. Erythropoiesis was stimulated by bleeding from the orbital sinus in a volume of 0.5-0.75 ml and inhibited by the transfusion of 10^{10} syngeneic red cells 1, 4, and 7 days before immunization or irradiation. The number of AFC in the spleen was counted on the fourth day after immunization by a modified Cunningham's method [7]. Migration of the B cells was determined by the method developed by Petrov et al. [3]. The animals were irradiated on the RUP-150/300-10-1 apparatus at a dose rate of 50 R/min (tube voltage 180 kV, current 10 mA). The results were subjected to statistical analysis by the use of Student's t test.

EXPERIMENTAL RESULTS

The hematocrit index was used to measure the inhibited and stimulated erythropoiesis in these experiments [4]. After transfusion of the red cells it exceeded 71%, after blood loss it was 34-48%, and in the control 51% ($P < 0.05$).

The results of experiments to study the effect of stimulation and inhibition of erythropoiesis on the number of AFC in the spleen are shown in Fig. 1. Inhibition of erythropoiesis led to an increase in the number of AFC on the 4th and 7th days after transfusion of red cells (by 1.6 and 1.7 times, respectively). The number of AFC in the spleen was increased more 1 and 4 days after blood loss (by 4 and 1.9 times, respectively).

The results of experiments to study migration of the B cells after blood loss and transfusion of red cells are illustrated in Fig. 2. In the control CBA mice irradiated with shielding of the region of the bone marrow, the number of AFC determined after injection of thymocytes as a result of migration of B cells from the bone marrow into the spleen was 701± 106. Blood loss caused a sharp increase in the migration of B cells after 1 and 4 days (when the number of AFC in the spleen was 1491 ± 166 and 1872 ± 322, respectively). Hypertransfusion caused inhibition of migration of the B cells when tested 1, 4, and 7 days after injection of syngeneic red cells to virtually the same level (the number of AFC in the spleen was 316 ± 55, 318 ± 83, and 316 ± 65, respectively).

Stimulation of erythropoiesis caused both an increase in the number of AFC in the spleen and an increase in migration of the B cells 1 and 4 days after blood loss, whereas inhibition of erythropoiesis led to an increase in the number of AFC in the spleen on the fourth and seventh days, although by a much lesser degree than blood loss; and it inhibited migration of the B cells from the bone marrow into the spleen.

It is possible that the mechanisms of action of stimulation and inhibition of erythropoiesis on antibody production differ in nature. There is evidence in the literature that inhibition of erythropoiesis by hypertransfusion of red cells leads to increase in the blood antibody titer, whereas no such increase was observed after the injection of erythropoietin into polycythemic mice [6]. The increase in antibody production after inhibition of erythropoiesis by hypertransfusion can evidently be explained by differentiation of the polypotent stem cell predominantly toward lymphopoiesis. Presumably, the sharp increase in the number of AFC in the spleen after stimulation of erythropoiesis was due primarily to increased migration of immunocompetent cells from the bone marrow into the spleen, as the results of the present investigation suggests. This effect may perhaps be mediated through erythropoietin, the level of which rises during stimulation of erythropoiesis.

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