Competitive displacement of histones from chromatin by added histones is based on the dynamic character of histone–DNA relations in the chromatin, which has recently been confirmed by experiments similar to those conducted by the present writers previously [2-4], to analyze exchange of chromatin, fragmented by micrococcal nuclease, and exogenous histones [9]. In this connection it can be tentatively suggested that supercooling of DNA loops in the cell is a mechanism of conversion of dynamic DNA–histone relations into static or, in other words, a mechanism of blocking of functional activity of DNA. If, in fact, realization of transcription requires displacement of histones by RNA-polymerase [5], to enable access of this enzyme to the histones it is possible to use destruction of the DNA loops, just as for displacement of H2A and H2B by added histones. The conclusion is in agreement with the view that relaxation of DNA of the minichromosomes of SV-40 is necessary for activation of transcription [10].

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INTERACTION OF MOUSE LYMPH NODE AND SPLENIC LYMPHOCYTES ON INACTIVATION OF ALLOGENEIC HEMATOPOIETIC STEM CELLS

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KEY WORDS: T and B lymphocytes; cellular interaction; inactivation of allogeneic hematopoietic stem cells.

The role of and interaction between subpopulations of T lymphocytes in the phenomenon of inactivation of nonsyngeneic hematopoietic stem cells (HSC), discovered by Petrov and Seslavina in 1967 [7], have been investigated on several occasions [3, 4, 8]. It has been shown that T lymphocytes are effector cells in the inactivation reaction, and comparative characteristics of the inactivating activity of different subpopulations of T lymphocytes, and so on, have been obtained. In a study of interaction between T-lymphocytes subpopulations from the spleen and lymph nodes (LN) of T mice with an artifically created B-cell deficiency, it was concluded that the spleen contains suppressor cells, protecting the stem cells against the inactivating action of allogeneic T-lymphocytes [3]. Meanwhile the attempt to study interaction between intact splenic and LN lymphocytes in this phenomenon proved unsuccessful at this stage because of the complex character of interaction. Later work showed that an important role in the inactivation phenomenon is played not only by T lymphocytes, but also by B lymphocytes of LN. While not possessing an effector function, they have a regulatory influence, reducing or enhancing the inactivating activity of T lymphocytes of LN, depending on the quantitative ratio between them [2, 6].

The aim of this investigation was to study the principles governing interaction of intact LN and splenic lymphocytes from mice during inactivation and discovery of the role of B lymphocytes in this interaction.

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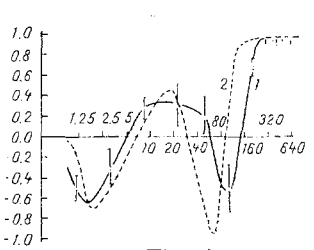

Fig. 1

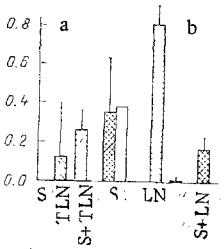

Fig. 2

Fig. 1. Dependence of inactivation index on number of splenic lymphocytes (1) and T lymphocytes of LN injected into recipients (2). Ordinate, inactivation index; abscissa, number of lymphocytes (in thousands). Logarithmic scale.

Fig. 2. Interaction of splenic lymphocytes with T lymphocytes of LN (a) and with intact lymphocytes of LN (b). Columns with oblique shading show inactivation index during action of LN lymphocytes and splenic lymphocytes (S) separately; cross-hatching denotes their combined action; unshaded column shows expected value of inactivation index on assumption of absence of interaction between splenic lymphocytes and T lymphocytes of LN (TLN). Ordinate, inactivation index.

EXPERIMENTAL METHOD

Donors of LN and splenic cells were CBA mice, and donors of bone marrow (BM) cells were C57BL/6 mice. The recipients for the test of suppression of exogenous colony formation were hybrids between them (CBA × C57BL/6) F_1. B and T lymphocytes were obtained from LN by preparative cellular electrophoresis [5], with separation of fractions with low and high electrophoretic mobility [1]. The number of colony-forming units in the recipients' spleen was determined by the method in [9]. Inhibition of colony formation after injection of a mixture of BM and LN cells into the recipients was estimated by determining the inactivation index, as described previously [1]. Animals of the control groups were given an injection of bone marrow, experimental mice received a mixture of bone marrow and lymphocytes. From 10 to 12 recipient mice were used in each group.

The results were subjected to statistical analysis by the usual methods with certain modifications [1].

EXPERIMENTAL RESULTS

Before studying interaction between LN and splenic lymphocytes in the inactivation of allogeneic HSC phenomenon, dependence of the inactivating activity of splenic lymphocytes on their number was obtained. Data showing changes in the inactivation index obtained in three independent experiments are given in Fig. 1. The similar dependence of the inactivation index for T lymphocytes of LN, purified from contamination by B lymphocytes by electrophoresis, obtained previously, is given in the same figure for comparison. The complex relationship between the inactivation index and the number of T cells of LN, including two zones of stimulation and two zones of inactivation, was previously investigated by the writers. It was found that this can be explained by competitive interaction between T_1 and T_2 subpopulations of LN, since the relationship for each of these subpopulations is biphasic in character: a stimulating action on colony formation in the presence of small numbers of lymphocytes and an inactivating action in the presence of large numbers, and superposition of these relationships gives the four-phase curve illustrated in Fig. 1. Evidently the same competitive interaction between T_1 and T_2 subpopulations also is exhibited during a study of the inactivating activity of splenic lymphocytes. With small numbers of splenic lymphocytes, the stimulating action of the T-lymphocytes among them is observed first. With an increase in the number of cells, the T lymphocytes begin to inactivate colony formation. Activity then begins to decline once again, and this is followed by the appearance of a stimulating action of the T_1 lymphocytes. Finally, with large numbers of cells, inactivation rises to the 100% level.

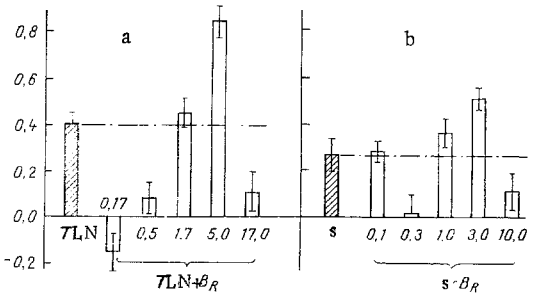

Fig. 3. Regulating effect of B lymphocytes of LN on inactivating activity of T lymphocytes of LN (a) and splenic lymphocytes (b) (right). Ordinate, inactivation index; abscissa, number of cells (in thousands).

It will be clear from Fig. 1 how difficult it is to compare the activating activity of LN lymphocytes and splenic lymphocytes using data from single experiments with a random sample of cell ratios. It is evidently even more difficult to estimate the effect of interaction of these cells.

Results of two experiments to study inactivation of allogeneic HSC by splenic and LN lymphocytes and mixtures of the two are shown in Fig. 2. In all experiments the number of BM cells injected into the recipients was fixed, namely $0.3 \cdot 10^6$ per mouse.

In the first experiment inactivation of stem cells by splenic lymphocytes ($0.5 \cdot 10^6$ per mouse), by T lymphocytes of LN ($0.1 \cdot 10^6$ per mouse) and by their combined action was observed. Within the limits of accuracy of the experiment, no interaction was found between splenic lymphocytes and T lymphocytes from LN. The inactivating action of their mixture was purely additive.

It was shown previously that T lymphocytes from LN are sensitive to the regulating action of B lymphocytes from LN [6]. B lymphocytes from LN, in different numbers, may have either a helper or a suppressor effect. The results of this experiment indicate that among the splenic lymphocytes there are no cells capable of regulating T lymphocytes of LN. Consequently, only B lymphocytes of LN can exert a regulating effect. It is also clear from this experiment that T lymphocytes of LN do not affect the inactivating activity of splenic lymphocytes.

In the second experiment, the results of which also are given in Fig. 2, the question of whether B lymphocytes of LN can regulate the inactivating activity of splenic lymphocytes also was studied. Addition of $0.0005 \cdot 10^6$ LN cells (per mouse) to $0.4 \cdot 10^6$ spleen cells was shown to give marked suppression of inactivation. Since T lymphocytes of LN and splenic lymphocytes do not interact, the B lymphocytes of LN were responsible for the suppressor effect.

The writers showed previously that the regulating action of B lymphocytes of LN on T lymphocytes of LN depends on the number of B lymphocytes, and may be both helper and suppressor. The results of one such experiment are given on the left in Fig. 3a. It follows from Fig. 3b that regulation of activity of splenic lymphocytes by B lymphocytes from LN is similar in character in principle. Suppression with low and high doses of B lymphocytes and a helper effect in the intermediate region are observed.

During interaction between LN lymphocytes and splenic lymphocytes in the inactivation of allogeneic HSC phenomenon differences from additivity are due to the regulating effect of a B lymphocytes of LN which, depending on their number, may give either a helper or a suppressor effect. It can be postulated that in the experiments of Ignat'eva et al. [3], the suppression of inactivation observed by these workers on the addition of a mixture of splenic lymphocytes and lymphocytes from LN into T mice also was connected with the presence of B lymphocytes, even though in only very small numbers, in this mixture because the suppressing action of the latter is very pronounced even when they are present in extremely low concentrations (we recorded a suppressor effect after the addition of only 100 B lymphocytes from LN per mouse).

Just as with regulation of the activity of T lymphocytes from LN, the regulating effect on splenic lymphocytes depends, not on the absolute number of B lymphocytes, but on their ratio to colony-forming units: $\frac{B}{(cfu_S \text{ in control})}$. In six different experiments, with combined injection of splenic lymphocytes and B lymphocytes from LN into recipients, zones of suppression and of helper activity were observed. With values of

$\frac{B}{cfu_S} < 100$ a suppressor effect of the B lymphocytes was observed, but when $100 < \frac{B}{cfu_S} < 400$ a helper effect was observed, and with even higher numbers of B lymphocytes, suppression was again observed. Zones of suppression and helper activity coincide in the case when lymphocytes from LN and spleen are used, and the degree of regulation in both cases, moreover, depends entirely on the ratio between B lymphocytes and cfu_S. This is a further argument in support of our previous hypothesis that allogeneic hematopoietic stem cells are the target for B lymphocytes. By interacting with them, perhaps screening or inducing additional expression of certain receptors through which HSC interact with T lymphocytes, the B lymphocytes evidently exert a regulating effect.

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REACTION OF BIOLOGICALLY ACTIVE POINTS OF THE SKIN TO IMMUNIZATION WITH TYPHUS VACCINE

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KEY WORDS: acupuncture; immune response.

Modern views on immunological reactivity was based on the role of the cellular and humoral factors of immunity, which are functionally linked with the nervous system. The nervous system has been shown to participate in immunological and leukocytic responses of adaptation. Meanwhile attempts to determine correlation between types of higher nervous activity and immunological reactivity have yielded ambiguous results [1, 4].

One of the trends in the study of functions of the autonomic nervous system in recent years is the electrophysiological study of cutaneous zones of increased activity (acupuncture points – APP), in order to evaluate adaptation by method of reflex therapy [6, 9, 12].

There is reason to suppose that adaptive mechanisms, revealed by responses of APP, can be used in addition to other methods of immunodiagnosis and immunocorrection [2, 10, 11]. Research in this direction must include two stages: determination of the principles of correlation between responses of APP and immunological reactivity and the study of the possibility of using methods of action directed toward APP to correct the immune response.

The aim of this investigation was primary evaluation of the response of APP to immunization with typhus vaccine in man.

EXPERIMENTAL METHOD

Combined vaccination was carried out in accordance with the principle of blocking residual virulence of a live vaccine [8] in two stages: primary injection of a chemical vaccine from Rickettsia prowaczeki in a dose of 16 fixation units and secondary (10 days later) injection of live vaccine from rickettsias of subline 288 of

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