demographic structure, formed in the course of long-term adaptation to arctic conditions of life. It is important that information of this kind be collected on a large scale for other circumpolar populations and compared with the corresponding information for populations living in other climato-geographic regions.

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EXPERIMENTAL STUDY OF THE IMMUNOSUPPRESSIVE PROPERTIES OF VITAMIN D

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Vitamin D is widely and universally used for the prevention and treatment of vitamin D deficiency in children. Nevertheless, until very recently there was no information whatever in the literature on the effect of additional vitamin intake on activity of the immune system.

In 1982 the present authors showed for the first time in experiments on rats that vitamin D, in massive doses, causes atrophy of the thymus, inhibits the development of the delayed-

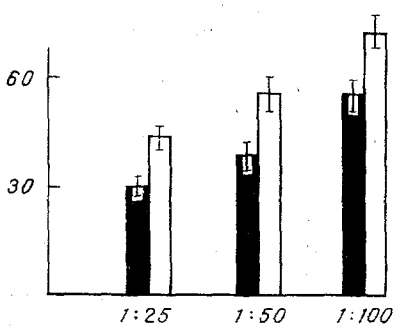

Fig. 1. Effect of vitamin D on NKC activity in mice. Abscissa, ratio of effector to target; ordinate, cytotoxicity index (in %). Unshaded columns — control; shaded — experiment.

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TABLE 1. Effect of Vitamin D on Number of Leukocytes and Lymphocytes in Guinea Pigs' Peripheral Blood

Parameter	Before administration of vitamin D	After administration of vitamin D
Leukocytes (in 1 mm^3 blood)	5727±693	3889±840
Lymphocytes %	72,3±3,0*	58,3±1,2
abs. (in 1 mm^3 blood)	4095±450*	2300±528
T-lymphocytes %	37,5±4,0*	14,1±2,5
abs. (in 1 mm^3 blood)	1591±318*	372±129
B-lymphocytes %	31,1±7,0	29,6±6,6
abs. (in 1 mm^3 blood)	1244±203*	668±167

Legend. Asterisk indicates statistically significant differences between parameters.

type hypersensitivity reaction, weakens the mitogenic response of lymphocytes to their stimulation by phytohemagglutinin (PHA), and inhibits the immune response to T-dependent antigen strongly, and to T-independent antigen less so [1]. Later these data were mainly confirmed by investigators in other countries, who used active vitamin D metabolites (chiefly 1,25-dihydroxyvitamin D_3), through which the biological functions of vitamin D are realized [9, 11, 12, 14].

The aim of the present investigation was to study quite different aspects of the action of vitamin D on immunity, not previously examined: its effect on the number of T- and B-lymphocytes in the peripheral blood, on activity of natural killer cells (NKC), and on the intensity of transplantation immunity.

EXPERIMENTAL METHOD

Male guinea pigs weighing 250-300 g (n = 20) and male CBA mice weighing 16-18 g (n = 140) were used. For 5 days the animals received an oily solution of vitamin D_2 (ergocalciferol) per os in a daily dose of 160,000-320,000 IU/kg body weight. Animals of the control groups received the oily solvent only, by the same scheme.

To determine the number of T- and B-lymphocytes in the peripheral blood of the guinea pigs blood was taken from the animals by cardiac puncture before the experiment began and 24 h after completion of the course of vitaminization. T-lymphocytes were identifed by the rosette-formation test with rabbit's erythrocytes [16] and B-lymphocytes by EAC-rosette formation [8]. NKC activity was determined by measuring the release of ^{51}Cr from GAC-1 target cells after incubation for 4 h with mouse splenocytes [2]. The level of transplantation immunity was judged by the rate of rejection of an EL-3 ascites tumor after allografting from C57Bl/6 into CBA mice. Under the conditions used rejection of the tumor is a model of graft rejection and obeys the same immunologic rules. The CBA mice were given an intraperitoneal injection of $3 \cdot 10^7$ ascites tumor cells 24 h after the final dose of vitamin D. Preliminary experiments showed that rejection of the tumor when allografted into CBA mice occurs 10-12 days after transplantation. Starting with the 8th day after transplantation of the tumor, therefore, some animals were killed and their peritoneal exudate was examined for the presence of tumor cells. Animals were killed every 2 days until no more tumor cells could be detected in mice of the experimental and control groups.

EXPERIMENTAL RESULTS

Data on the effect of vitamin D on the number of leukocytes and lymphocytes in the peripheral blood of the guinea pigs are given in Table 1. Clearly, vitamin D caused leukopenia and absolute and relative lymphocytopenia. T-lymphocytes were affected particularly badly, for their number was reduced to 25-40% of the original value. Expressed as a percentage, the number of B-lymphocytes was unchanged, but because of the total lymphocytopenia, the absolute number of B-lymphocytes was appreciably reduced.

The effect of vitamin D on NKC activity in CBA mice is shown in Fig. 1. Whatever the ratio of target to effector, vitamin D significantly depressed natural killing.

Another section of the work showed that vitamin D inhibits rejection of the transplanted tumor. In the control group the graft was rejected 10.8 ± 0.4 days after transplantation, compared with 17.1 ± 0.3 days in mice receiving vitamin D ($p < 0.001$).

Analysis of the mechanisms of the immunosuppressive action of vitamin D demands consideration of several factors and, in particular, data obtained earlier [1] on elevation by vitamin D of the plasma level of 11-hydroxycorticosteroids, which possess immunosuppressive properties. Effects such as atrophy of the thymus and T-lymphocytopenia are characteristic of the action of corticosteroids [4]. Inhibition of NKC activity may also be the result of the direct action of glucocorticoids, of which there is evidence in the literature [13], or it may be mediated through the thymus, which plays an essential role in the regulation of NKC activity [5]. Recent data on inhibition of interleukin-2 production by active forms of vitamin D [14], which may be a direct cause of weakened killer activity, must also be taken into account. In this connection there are interesting data to show that glucocorticoids also inhibit interleukin-2 production [6, 10]. The inhibitory action of vitamin D on the interleukin-2 system may thus be both direct and indirect in character. So far as transplantation immunity is concerned, the effect of vitamin D on it may have a very simple and convincing explanation. The principal effector cells which participate in graft rejection, as we know, are T-lymphocytes [3, 7]. The important role of NKC in this process has been proved recently [4, 15]. Since vitamin D, as a previous [1] and the present investigations showed, depresses the activity of both immunologic systems, the delaying of graft rejection is a natural consequence of these processes.

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