The immunostimulating activity of panangin, which has been successfully used in clinical practice to normalize intracellular metabolism of potassium and magnesium ions, is an interesting fact. Activation of immunogenetic processes by this substance, connected with T cell function, suggests that panangin may be not only an active regulator of intracellular ion metabolism, but also an effective activator of the T system of the body.

The immunologic activity of the oligopeptides with different functions confirms the hypothesis [8] that common functional blocks exist in different systems, and that the immunologic activity of individual amino acids, most of which enter the body after enzymic degradation of proteins in the gastrointestinal trace, is evidence of the important role of the digestive system in processes of immunogenesis.

LITERATURE CITED

1. G. A. Belokrylov, Zh. Mikrobiol., No. 4, 23 (1976).
2. G. A. Belokrylov and N. P. Kunevich, Immunologiya, No. 5, 19 (1980).
3. N. A. Belokrylov, V. G. Morozov, and V. Kh. Khavinson, Immunologiya, No. 6, 63 (1982).
4. R. N. Glebov and G. N. Kryzhanovskii, The Functional Biochemistry of Synapses [in Russian], Moscow (1978), pp. 278-302.
5. I. M. Kiselev and G. A. Belokrylov, Byull. Éksp. Biol. Med., No. 10, 15 (1982).
6. A. K. Klimov, Peptides and the Digestive System [in Russian], Leningrad (1983), p. 126.
7. E. N. Kochina, Neurohormonal Regulation of Digestion [in Russian], Moscow (1983), pp. 257-276.
8. A. M. Ugolev, Zh. Évol. Biokhim. Fiziol., No. 1, 11 (1982).
9. R. S. Basch and G. Goldstein, Proc. Natl. Acad. Sci. USA, 71, 1474 (1974).
10. G. Goldstein, M. P. Scheid, E. A. Boysse, et al., Science, 204, 1309 (1979).
11. N. K. Jerne and A. A. Nordin, Science, 140, 405 (1963).
12. N. P. Plotnikoff and G. C. Miller, Int. J. Immunopharmacol., 5, 437 (1983).
13. J. P. Tischio, J. E. Patrick, H. S. Weintraub, et al., Int. J. Peptide Protein Res., 14, 479 (1979).

SUPPRESSOR CELL HYPERACTIVITY RELATIVE TO ALLOGENEIC LYMPHOCYTE PROLIFERATION AS A MANIFESTATION OF DEFECTIVE T–T-CELL INTERACTIONS IN SYSTEMIC LUPUS ERYTHEMATOSUS

M. A. Stenina, A. A. Potapova, A. V. Biryukov, A. Yu. Skripnik, and A. N. Cheredeev

UDC 616.5-002.525.2-07: 616.155.32-097

KEY WORDS: systemic lupus erythematosus; T suppressor cells; theophylline.

In the contemporary literature there is much factual evidence of the varied manifestations of disturbances of the immune response in patients with systemic lupus erythematosus (SLE). The development of these disturbances is in good agreement with the view that in SLE there is a state of B-cell hyperactivity, caused by an uncertain etiologic factor and arising against the background of major disorders of immunoregulation [4], which are due to a quantitative and functional defect among immunoreulatory lymphocyte subpopulations, and also, perhaps, to an internal defect of the immunoregularoty cells (IRC) themselves and (or) of the cells controlled by them. This last factor, which has received less study, suggests an important role of disturbance of intercellular interactions in the pathogenesis of the immune changes in SLE.

The aim of this investigation was to study the state of immunoregulatory processes in SLE at the T–T-cell interaction level, and to test the possibility of their pharmacologic modulation.

Department of Immunology, N. I. Pirogov Second Moscow Medical Institute. (Presented by Academician of the Academy of Medical Sciences of the USSR, R. V. Petrov.)

Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 102, No. 8, pp. 215-217, August, 1986. Original article submitted July 19, 1985.

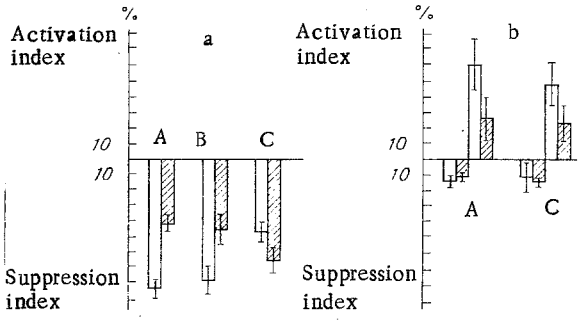

Fig. 1

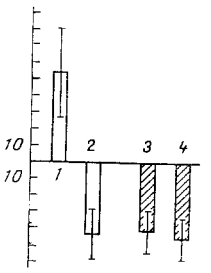

Fig. 2

Fig. 1. Immunoregulatory activity of blood MNC from patients with SLE and normal subjects when lymphocytes from normal subjects (a) and patients with SLE (b) were used as proliferating target cells. Here and in Figs. 2 and 3: above abscissa, activation index (in %); below abscissa, suppression index; unshaded columns, patients with SLE; shaded, normal subjects. Immunoregulatory activity induced by treatment of cells with con A (A), theophyllin ($5 \cdot 10^{-5}$ M) (B), con A in the presence of $5 \cdot 10^{-5}$ M theophylline (C).

Fig. 2. Effect of theophylline on con A-induced immunoregulatory activity of blood MNC from patients with SLE and normal subjects, when proliferating cells from patients with SLE were used as target cells. 1, 3) Without addition of theophylline; 2, 4) theophylline ($5 \cdot 10^{-5}$ M) added in the phase of estimation of immunoregulatory activity.

EXPERIMENTAL METHOD

Mononuclear cells (MNC) from the blood of 10 patients with SLE, with the II-III degree of clinical activity of the disease, and receiving corticosteroid therapy, were used as the test object. The mean daily dose of hormones given was 18.3 ± 8 mg. The control group consisted of 30 healthy blood donors.

Proliferative activity of MNC was assessed by measuring incorporation of ^{3}H-thymidine into cultures stimulated for 72 h by mitogens: phytohemagglutinin (PHA, 10 µg/ml, from Difco, USA) and concanavalin A (con A, 30 µg/ml, from Serva, West Germany). To study the effect of theophylline on mitogen-induced MNC proliferation it was added to the cultures in doses of $5 \cdot 10^{-5}$ and $5 \cdot 10^{-3}$ M. The results were expressed as a logarithmic index of stimulation [1].

Immunoregulatory activity of MNC induced by con A (30 µg/ml, 72 h) was assessed as inhibition of proliferation of target cells stimulated by PHA (10 µg/ml, 72 h). Freshly isolated MNC from healthy blood donors or from patients with SLE were used for this purpose.

The effect of theophylline on induction of immunoregulatory activity of MNC and of perception of their action by target cells was estimated. Theophylline ($5 \cdot 10^{-5}$ M) was added to the cultures in the phase of induction of immunoregulatory activity or in the phase of assessment of the action of IRC. In the first case, the MNC to be tested were cultured for 72 h in the presence of theophylline and con A (or without it), treated with mitomycin C, and used as IRC during action on proliferating target cells. In the second case, induced IRC were incubated for 72 h with the target cells in the presence of theophylline ($5 \cdot 10^{-5}$ M). The regulation index (RI) was calculated by the usual equation: $RI = (1 - A/B) \times 100$, where A stands for incorporation of isotopes into cultures with added cells, B for the same but without addition of IRC.

EXPERIMENTAL RESULTS

Data on con A-induced immunoregulatory activity of MNC from patients with SLE and from healthy blood donors, when proliferating cells from healthy donors were used as target cells, are given in Fig. 1A. The patients' MNC inhibited proliferation of normal target cells. Moreover, the suppressor action of IRC from patients with SLE was significantly greater than the action of normal human IRC.

Incubation of MNC for normal subjects and patients for 72 h with theophylline induced the appearance of immunoregulatory activity in them. The degree of inhibition of prolifera-

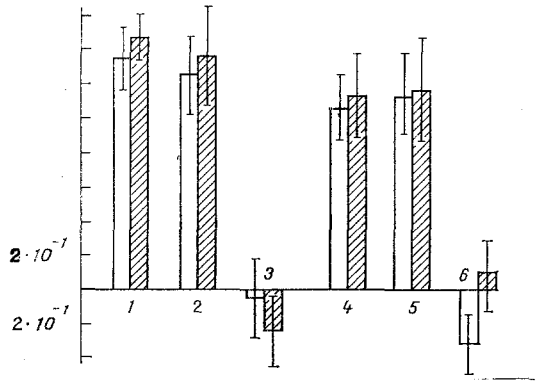

Fig. 3. Comparison of proliferative activity of blood MNC from patients with SLE and normal subjects, induced by PHA and con A (1, 4), by PHA and con A in the presence of $5 \cdot 10^{-5}$ M theophylline (2, 5), and by PHA and con A in the presence of $5 \cdot 10^{-3}$ M theophylline (3, 6).

tion of normal lymphocytes by IRC induced by theophylline was indistinguishable from the intensity of con A-induced suppression.

If theophylline was added to the cultures in the phase of induction of immunoregulatory activity together with con A, the suppressor action of the patients' MNC was significantly weaker than that of con A or theophylline. Conversely, normal lymphocytes treated with con A in the presence of theophylline inhibited proliferation of normal target cells more strongly than cells treated with theophylline alone or with con A alone.

The results of estimation of con A-induced immunoregulatory activity of MNC from patients with SLE and normal subjects, when proliferating cells from patients with SLE were used as target cells, are given in Fig. 1B. Unlike in the experiments conducted on normal target cells, two types of effects are recorded: very weak suppression and strong activation of lymphocyte proliferation. Indices of suppression of proliferation of "SLE" target cells by IRC from patients and normal subjects did not differ significantly. The activation index was significantly higher when IRC from the patients was used than with normal cells. Neither under normal nor under pathological conditions did theophylline, added to the culture in the phase of induction of immunoregulatory activity, significantly change the degree of suppression or activation of proliferation of target cells from patients with SLE.

Results of experiments in which IRC induced beforehand by con A were cultured with target cells from patients with SLE in the presence of theophylline are given in Fig. 2. Whereas without theophylline IRC activated proliferation, in its presence marked suppression was observed. Theophylline did not change the action of IRC on proliferation of normal lymphocytes.

When the effect of theophylline was studied on mitogen-induced MNC proliferation no difference was found in the proliferative activity of intact MNC of normal subjects and patients. Theophylline, in a dose of $5 \cdot 10^{-5}$ M, did not affect proliferation, but inhibited it in a dose of $5 \cdot 10^{-3}$ M. The results of determination of the number of T cells with receptors for the Fc-fragment of IgG in SLE and normal subjects are given in Table 1. No significant differences were found in their relative number.

The discovery of hyperactivity of MNC in the con A-induced suppression test (Fig. 1a) contradicts the widely held view of a quantitative and functional suppressor subpopulation, typical of SLE. However, there are conflicting data in the literature on the absence of a deficiency of cells with the suppressor phenotype, and even of a tendency for their number to increase [2, 5]. In our patients we likewise found no change in the relative number of T cells with a receptor for the Fc-fragment of IgG (T_γ cells).

We considered that the results of analysis of immunoregulatory activity depends on the state of each of the components used for its assessment: the IRC and the proliferating target cells perceiving its action. By combining IRC and target cells which we knew to be normal

TABLE 1. Number of T Lymphocytes with Receptor for Fc-Fragment of IgG in SLE

Group of subjects	Number of T cells		Number of T_γ cells	
	%	in 1 μl	%	in 1 μl
Patients with SLE	30,4±4	636±128	22±3	157±31
Healthy blood donors	70,4±4	1100±300	18±7	250±70

with IRC and target cells from patients, we showed that perception of the action of IRC by target cells from patients with SLE is disturbed. Besides a low suppression index, this was also shown by manifestation of an activating effect on IRC under these experimental conditions (Fig. 1b). The ability of the patients' target cells to undergo mitogen-induced proliferation did not differ from that of normal subjects (Fig. 3). The fact that perception of the action of immunoregulatory T lymphocytes by proliferating T cells and, evidently, the suppressor cell hyperactivity due to this, recorded during their action on normal target cells, are abnormal thus suggests that the disturbance of T–T-cell interactions is another possible cause of the disturbance of immunoregulation in SLE. We found that this defect can be corrected by adding theophylline to the cultures in the phase of evaluation of immunoregulatory activity (Fig. 2). In concentrations not affecting target cell proliferation. The choice of theophylline was determined by information on the important role of purine compounds as immunomodulators [6]. Theophylline, added to the culture in the phase of induction of immunoregulatory activity by itself caused the appearance of suppressor activity in MNC (Fig. 1A). This is in agreement with data in the literature on the ability of methylxanthines to induce the appearance of suppressor properties in the lymphocyte [3, 7].

One other matter must be mentioned. The opposite action of con A-induced IRC of patients with SLE on proliferation of "SLE" and normal target cells assumes that in the intact organism IRC may have an activating action on the function of some cell populations and may inhibit the same function in other cells. This may explain the combination of defenselessness against infectious agents with the distinct features of autoaggression frequency found in SLE.

LITERATURE CITED

1. A. A. Potapova, A. N. Cheredeev, M. A. Stenina, and N. V. Mel'nikov, Lab. Delo, No. 10, 625 (1985).
2. L. Chatenoud and M. A. Bach, Kidney Int., 20, 267 (1981).
3. S. C. Cheung, J. Allergy, 69, No. 1, 120 (1982).
4. A. S. Faucci, J. Allergy, 66, 5 (1980).
5. C. Gattinger, H. Huber, G. Michlmaur, and H. Breunsteiner, Immunobiology, 163, 46 (1982).
6. J. W. Hadden, P. Cornaglia-Ferraris, and R. G. Coffen, Prog. Immunol., 5, 1393 (1984).
7. B. Schohat, Z. Shpira, H. Joshua, et al., in: International Conference on Lymphatic Tissues and Germinal Centers in Immune Reactions. Proceedings, New York (1982), p. 687.

IMMUNOBIOLOGICAL EFFECT OF BITEMPORAL EXPOSURE OF RABBITS TO MICROWAVES

V. M. Bogolyubov, S. B. Pershin, I. D. Frenkel', V. D. Sidorov, A. I. Galenchik, Yu. T. Ponomarev,* A. S. Bobkova, S. N. Kuz'min, I. Ya. Moshiashvili, N. N. Kozlova, E. G. Korovkina, and Yu. V. Agibalov

UDC 612.017.1-06:[612.826.4+612.432].014.426

KEY WORDS: microwaves; thyroid function; glucocorticoids; immunodepressive effect.

The part played by the higher autonomic centers of the hypothalamus and pituitary in the regulation of immune functions has now been established. The writers previously showed that secretion of endogenous hormones can be subjected to the influence of high-frequency electromagnetic field energy [1, 3].

The aim of this investigation was to study the immunobiological effect of electromagnetic waves in the decimeter band (DMW; microwaves) applied to the temporo-parietal region of the head.

*Deceased.

Laboratory of Clinical Biochemistry and Immunology, Central Scientific-Research Institute of Balneology and Physiotherapy, Ministry Public Health of the USSR, Moscow. I. I. Mechnikov Moscow Scientific-Research Institute of Vaccines and Sera, Ministry of Public Health of the USSR.

(Presented by Academician of the Academy of Medical Sciences of the USSR P. N. Kosyakov.) Translated from Byulleten' Eksperimental'noi Biologii i Meditsiny, Vol. 102, No. 8, pp. 217-219, August, 1986. Original article submitted May 31, 1985.

0007-4888/86/0008- 1118$12.50