10. J. R. Oehler, R. D. Herberman, D. A. Campbell, et al., Cell. Immunol., 29, 238 (1977).
11. D. B. Wilson, J. C. Howard, and P. C. Nowell, Transplant Rev., 12, 3 (1972).

CHANGES IN ACTIVITY OF SOME MECHANISMS OF SPECIFIC AND NONSPECIFIC IMMUNITY IN VITAMIN B_1 DEFICIENCY

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The effect of thiamine deficiency on the immune response and activity of certain mechanisms of natural immunity was studied in adult rats. Thiamine deficiency was simulated experimentally by a single injection of hydroxythiamine, a vitamin B_1 antagonist. Administration of hydroxythiamine caused a marked decrease in complement activity, phagocytic activity of the peripheral blood leukocytes, bactericidal activity of the serum, and antibody production in response to immunization with sheep's red blood cells. Conversely, lysozyme activity increased. In vitamin B_1 deficiency the intensity of incorporation of [^{14}C]leucine into liver protein synthesis was reduced.

KEY WORDS: thiamine deficiency; hydroxythiamine; factors of natural immunity; immune response.

Data in the literature on the effect of vitamin B_1 deficiency on the activity of mechanisms of specific and nonspecific immunity are few in number and contradictory in nature [1]. One reason for this is the difficulty encountered by research workers when attempting to simulate alimentary avitaminosis B_1. A considerable period of time elapses between exclusion of thiamine from the diet and the appearance of any marked metabolic disturbances, and during that time various compensatory reactions disturbing the purity of the biochemical changes are able to develop. These defects are overcome by the nowadays widespread method of administration of thiamine antimetabolites in order to obtain B_1 avitaminosis in a short time [2, 3].

The object of this investigation was to study the effect of vitamin B_1 insufficiency caused by administration of hydroxythiamine (HT), a powerful thiamine antimetabolite, which has no vitamin activity, on certain mechanisms of specific and nonspecific immunity.

EXPERIMENTAL METHOD

Experiments were carried out on 60 noninbred male rats weighing 250-300 g. Acute thiamine insufficiency was produced by a single subcutaneous injection of HT in a dose of 400 mg/kg. HT synthesized in the Department of Regulation of Metabolism, Academy of Sciences of the Belorussian SSR, was used. The compound was kindly presented by A. N. Martinchik. To study the state of nonspecific immunity, blood was taken from the animals before and 48 h after injection of HT. According to the literature data, the biochemical changes reflecting B_1 avitaminosis reach their maximum at this time, but compensatory changes are still insignificant [2]. The serum bactericidal activity was studied by a nephelometric method, using *Staphylococcus aureus* (strain Zhaev) as the test organism; complement activity was determined relative to 50% hemolysis. The serum lysozyme content was determined by Dorofeichuk's method. The phagocytic activity of peripheral blood neutrophils relative to *Staph. aureus*, strain Zhaev, was determined by the usual method, by counting the total number of phagocytic cells and calculating the phagocytic index. To study the effect of thiamine insufficiency on antibody production, 48 h after injection of HT the animals were immunized intraperitoneally with 2 ml of a 10% suspension of sheep's red blood cells. The antibody titer was determined in the usual way by the passive hemagglutination test. Activity of the protein synthesizing function was judged from the intensity of incorporation of [^{14}C]leucine into liver protein metabolism. The radioactive amino acid was injected intraperitoneally two days after injec-

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TABLE 1. Changes in Activity of Mechanisms of Natural Immunity in Acute Vitamin B_1 Deficiency (M±m)

Index of nonspecific immunity	Time of observation		P
	before injection of HT	48 h after injection	
Bactericidal activity of serum	62,8±4,1%	18,2±2,6%	<0,001
Phagocytic number	70,2±3,3%	21,5±1,1%	<0,001
Phagocytic index	3,5±0,14	1,8±0,03	<0,05
Complement	50,3±1,99 units	30,6±1,05 units	<0,01
Lysozyme	27,2±0,9 units	36,6±1,4 units	<0,05

TABLE 2. Changes in Level of Hemagglutinating Antibodies in Acute Vitamin B_1 Deficiency (M±m)

Group of animals	No. of animals in group	Antibody level expressed in log units after various times			
		7 days	14 days	21 days	28 days
Experimental	10	2,44±0,07	3,23±0,06	2,86±0,1	2,4±0,1
Control	10	2,92±0,12	3,66±0,14	3,11±0,09	2,7±0,1
P		<0,05	<0,01	<0,01	<0,01

tion of HT. The animals were killed 1, 3, and 6 h after injection of the label, the liver was removed and homogenized, and the homogenate treated by Sarkar's method [6], after which the radioactivity was counted on a Nuclear Chicago scintillation counter and expressed in cpm/mg protein. The severity of the vitamin B_1 deficiency was judged from changes in transketolase activity in the rats' red blood cells 48 h after injection of HT [5].

EXPERIMENTAL RESULTS

The first signs of marked vitamin B_1 deficiency were observed in the experimental animals 48 h after injection of HT, namely a decrease, on average by 50%, in the transketolase activity in the red cells. Marked disturbances of responses of natural immunity also developed by this time. Results of observations on 22 animals are summarized in Table 1. Clearly thiamine deficiency had on the whole an unfavorable effect on nonspecific immunologic mechanisms. The phagocytic activity of the polymorphs and bactericidal activity of the serum were reduced by HT by more than two-thirds of their initial levels and the complement titer also was significantly lowered. Meanwhile the serum lysozyme level rose.

Vitamin B_1 deficiency depressed antibody production. Table 2 gives the mean values of antibody titers expressed in log units. At all times of observation the hemagglutinin level was significantly lower in the experimental animals receiving HT than in the control.

Acute avitaminosis B_1 led to a disturbance of protein synthesis, reflected in the intensity of incorporation of label during liver protein synthesis (observations of 18 rats). Activity in the control group 1 h after injection of [^{14}C]leucine was 2367±104 cmp/min•mg protein, and in the experimental group 1592±181 cpm/min•mg ($P<0.01$); the corresponding values 3 h after injection were 2203±84 and 1568±111 cpm/min•mg ($P<0.01$). The differences were still significant 6 h after injection of [^{14}C]leucine (activity in the control was 1682±149 and in the experimental group 1004±67 cpm/min•mg).

The experiments thus showed that acute avitaminosis B_1 has an unfavorable effect on the activity of the mechanisms of specific and nonspecific immunity. Depression of antibody production, lowering of the complement level, and inhibition of nonspecific bactericidal activity, which is largely dependent on the serum complement level, perhaps reflect disturbances in the system of protein synthesis which develop, as the present writers and others [4] have shown,

in experimental thiamine deficiency. During analysis of the mechanism of disturbance of an energy-dependent process such as phagocytosis, the very important role of vitamin B_1 in the supply of energy to the cell must be recalled in the first place. Thiamine is known to participate through pyruvate dehydrogenase in the oxidative decarboxylation of pyruvic acid and through α-ketoglutarase dehydrogenase in the oxidative decarboxylation of α-ketoglutaric acid [4]. Inhibition of the activity of the above enzymes leads to disturbance of the basis of the energy economy of the cell.

It is difficult at present to specify the causes of the increase in the serum lysozyme concentration which was found. Administration of HT may perhaps lead to increased permeability of the subcellular and plasma membranes of the leukocytes, with the liberation of lysozyme, a lysosomal enzyme, into the blood stream.

LITERATURE CITED

1. N. B. Lutsyuk and A. K. Morozova, Vopr. Pitan., No. 5, 56 (1975).
2. Yu. M. Ostrovskii, Active Centers and Groups in the Thiamine Molecule [in Russian], Minsk (1975).
3. A. N. Razumovich, "Energy metabolism during aging in tissues with different functional specialization," Author's Abstract of Doctoral Dissertation, Vilnius (1971).
4. V. B. Spirichev, in: The Molecular Basis of Pathology [in Russian], Moscow (1966), p. 244.
5. E. F. Rogers, Methods Enzymol., 18A, 245 (1970).
6. N. K. Sarkar, Int. J. Biochem., 6, 423 (1975).

CYTOPHILIC IMMUNOGLOBULINS ON THE SURFACE OF POLYMORPHS IN MICE IMMUNIZED PERORALLY WITH LIVE VACCINE FROM SUPPRESSOR REVERTANT *Salmonella typhimurium* Rev 8

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The spleen cell migration inhibition test in the presence of monospecific antisera against mouse immunoglobulins of the G, A, and M classes was used to detect cytophilic antibodies on the surface of mouse granulocytes. Peroral administration of live vaccine from suppressor reverant *Salmonella typhimurium* Rev 8 to AKR mice protected the animals against infection with a virulent strain of *S. typhimurium*. An increase in the number of cytophilic IgG on the surface of the polymorphs was observed in the immunized mice.

KEY WORDS: cytophilic antibodies; neutrophil granulocytes (polymorphs); mouse typhus; antisera against mouse immunoglobulins; enteral immunization.

The nature of the resistance developing after immunization with live *Salmonella* vaccines, especially those prepared from *Salmonella typhimurium*, has been inadequately explained [5]. Definite importance is attached to antibodies which are cytophilic for phagocytic cells [4], [8-10]. The object of the present investigation was to study immunoglobulins on the surface of neutrophilic granulocytes (polymorphs) of mice immunized with *S. typhimurium* vaccine and at the same time, to evaluate postvaccinal resistance, circulating antibodies, and cellular immunity.

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