EFFECT OF PENTOXYL ON ANTIBODY FORMATION IN THE SPLEEN OF ALBINO MICE IN AN IMMUNODEPRESSIVE STATE

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The effect of pentoxyl on a number of antibody-forming cells in the spleen was investigated in experiments on immunized noninbred albino mice after the production of an artificial immunodepressive state in the animals by a single injection of the sodium salt of 2-mercaptobenzthiazole (2-MBT). Administration of pentoxyl was accompanied by a definite stimulation of antibody formation in the spleen of the immunized animals treated with the immunodepressant. This effect was most marked in the period of maximal inhibition of antibody formation. During weakening of the immunodepressive action of 2-MBT the effectiveness of pentoxyl as a stimulator of immunogenesis was reduced.

The use of pyrimidine derivatives to stimulate the defensive forces of the organism is attracting the attention of clinicians [1, 5, 9, 10, 14] as a result of experimental evidence that pentoxyl, methyluracil, and other preparations of this series can increase the resistance of the organism and, in particular, its immunological reactivity [2-4, 6-8, 15, 17]. However, there are only isolated reports in the literature of the effect of pentoxyl on immunogenesis when immunological reactivity is depressed [3, 16].

An essential role in the mechanism of action of 2-mercaptobenzthiazole (2-MBT) is ascribed to its antimetabolite effect [12, 13].

In this investigation the effect of pentoxyl on antibody formation in the spleen was studied in albino rats in an immunodepressive state induced by administration of the sodium salt of 2-MBT, which has a wide spectrum of inhibitory action on various biological objects as well as a teratogenic [12, 13] and mutagenic [11] effect.

EXPERIMENTAL METHOD

Five series of experiments were carried out on 94 sexually mature noninbred mice of both sexes weighing 18-23 g.

The number of antibody-forming cells in the spleen of the animals was counted by the method of local hemolysis in gel [18].

In series I the number of antibody-forming cells was determined in the spleen of intact animals; in series II in the spleen of albino mice on the 4th, 7th, 14th, and 21st days after immunization with 0.5 ml of a 5% suspension of sheep's erythrocytes; in series III a single subcutaneous injection of 2-MBT in a dose of 5 mg/kg was given to the mice 48 h after immunization. Antibody-forming cells in the spleen were counted at the same times as in series II.

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TABLE 1. Effect of Pentoxyl on Antibody Formation in the Spleen of Albino Mice

Series of expts.	No. of antibody-forming cells in the spleen per million of the cell population at various times after immunization			
	4 days	7 days	14 days	21 days
II	94±17,7	37±6,1	7±2,8	5±1,7
III	14±3,3	12±2,2	19±6,4	25±4,3
IV	128±39	48±7,7	—	—
V	—	—	69±14,2	33±3,2

In series IV a single injection of 2-MBT (5 mg/kg, subcutaneously) was given 48 h after immunization of the animals, and pentoxyl was injected as a 0.1% aqueous solution in a dose of 20 mg/kg subcutaneously 4, 8, 24, 32, and 36 h after the injection of 2-MBT. The mice were killed 4 and 7 days after immunization.

In series V the animals were immunized, 48 h later they received a single injection of 2-MBT (5 mg/kg), and another 4 h later they started to receive injections of pentoxyl (0.1% solution, 20 mg/kg, subcutaneously) which continued twice a day for 12 days. The antibody-forming cells were counted 14 and 21 days after immunization.

The numerical results were subjected to statistical analysis. Differences for which $P < 0.05$ were regarded as significant.

EXPERIMENTAL RESULTS

The results of these experiments are summarized in Table 1. The number of antibody-forming cells in the spleen of the intact animals was extremely small. In two of the five animals it was 3 and 5 per million of the cell population, respectively. In three animals no antibody-forming cells could be found in the spleen.

In the animals used in the experiments of series II the number of antibody-forming cells 4 days after immunization was considerably higher than in the intact animals. By the end of the second and, in particular, of the third week the number of antibody-forming cells was hardly different from the number of cells in the intact animals.

An immunodepressive effect clearly appeared 4 and 7 days after immunization (series III). The number of antibody-forming cells in the animals of series III was 80% lower ($P < 0.001$) 4 days and 68% lower ($P < 0.01$) 7 days after immunization than in the animals of series II. On the 14th day after immunization the difference in the number of antibody-forming cells in the spleen between series II and III was no longer statistically significant ($P > 0.1$). On the 21st day the number of antibody-forming cells in animals receiving 2-MBT not only was not reduced but, on the contrary, it was significantly ($P < 0.001$) higher than the corresponding value in the animals of series II.

In the animals of series IV receiving pentoxyl and 2-MBT the number of antibody-forming cells in the spleen on the 4th day after immunization was significantly higher than if the immunodepressant alone was given ($P < 0.001$), and it was indistinguishable from the number of antibody-forming cells in the immunized animals ($P > 0.5$). A similar picture was observed on the 7th day.

To judge from the results of the experiments of series V the number of antibody-forming cells after the end of the course of pentoxyl therapy (14 days after immunization) was significantly greater than their number in the animals treated with the immunodepressant alone ($P < 0.05$) and significantly higher ($P < 0.001$) than the number of antibody-forming cells in the immunized animals. One week after the end of the course of treatment (21 days after immunization) the number of antibody-forming cells corresponded to the level observed in the animals of series III ($P > 0.25$) and was significantly higher ($P < 0.001$) than in the immunized animals of series II.

These investigations thus yielded direct proof that pentoxyl stimulates antibody formation in the spleen of immunized animals treated with an immunodepressant.

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