

THE INFLUENCE OF NOVOCAINE ON IMMUNOGENESIS

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The successful application of novocaine in radiation sickness therapy [7, 8, 10, 11] and its desensitizing influence in animal experiments [3-6, 12] demonstrate the power of this preparation to change immune responses. Considering the great significance of the phenomena of autosensitization in the pathogenesis of radiation sickness [8, 9] we may suppose that the effectiveness of novocaine therapy depends in this case on its ability to suppress the development of allergy. In the reports available to us we have found none concerning the nature of the action of novocaine on the production of antibodies, which must be present in any immunobiological reaction. I. M. Vol'pe [1, 2] has shown that the reaction is weakened after vaccination, and that the titer of agglutinins was unaffected when 0.2 ml of a 10% novocaine solution was added to the injected dose of vaccine.

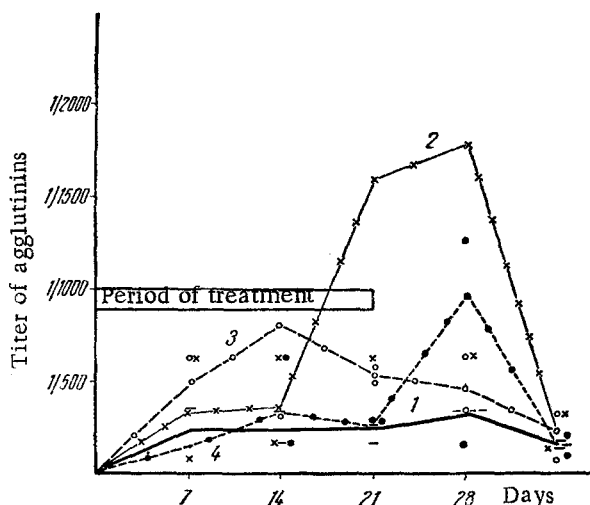
EXPERIMENTAL METHOD

To study the influence of novocaine on immunogenesis we carried out experiments on 33 male rabbits weighing 2.5-2.8 kg, and on 570 male white mice weighing 18-20 g. The rabbits received 10 ml of a 1% novocaine solution subcutaneously, or 20 ml of a 0.5% solution by mouth; the novocaine was given daily in the morning on an empty stomach for 16 days. Treatment was begun two days before immunization with the minimum dose of Breslau vaccine (25 million microbial cells intravenously). The titers of the agglutinins before the vaccination lay between 0 and 1:10. After vaccination measurements of the titers were made on the 7, 14, 21, 28, and 33rd day.

EXPERIMENTAL RESULTS

An analysis of the results obtained is shown in Fig. 1 for 23 rabbits; it can be seen that injection of novocaine suppressed antibody formation. This conclusion was confirmed by a statistical treatment of the results for the 14th day (period of maximum titer in the control animals). The subcutaneous injection induced a more intense and prolonged suppression of immunogenesis than its introduction by mouth, when the reduction in the titer of the antibodies occurred only during treatment, and subsequently in four out of the eight rabbits it was found to be temporarily increased even more than it was in the controls. It was interesting that if oral novocaine treatment was started 3 days after the vaccination its suppressive influence was much more marked (see figure).

The suppressive influence of novocaine on immunogenesis was observed not only in experiments in which antimicrobial agglutinins were produced but also when six rabbits were immunized with boar erythrocytes or four with horse serum. Half of these animals were treated. The mean titer of the hemolysins seven days after the intravenous injection of a large dose of erythrocytes (2 ml of a 3% suspension) rose to 1:11510 in the control rabbits,



Change in the production of agglutinins in rabbits from the results of one of the experiments (three rabbits in each arrangement). 1) Subcutaneous injection of novocaine; 2) novocaine given by mouth; 3) control; 4) novocaine given by mouth from the third day after vaccination.

TABLE 2. Influence of Novocaine Treatment on the Condition of the Anti-Infection Immunity in Nonirradiated and Irradiated Mice Receiving a Single Subcutaneous Injection of 0.25 ml of Tetravaccine on the Third Day after Irradiation

Date of experiment	Method of treatment	Total mice	Nonirradiated mice						Irradiated mice					
			Vaccinated			LD ₅₀ of untreated animals			Vaccinated			LD ₅₀ untreated		
			Treated		Untreated	Untreated		LD ₅₀ of untreated animals	Treated		Untreated	Treated		LD ₅₀ untreated
			LD ₅₀	IR	LD ₅₀	LD ₅₀	IR	LD ₅₀ of untreated animals	LD ₅₀	IR	LD ₅₀	LD ₅₀	IR	LD ₅₀ untreated
March 6, 1962	0.2 ml of 0.5% solution given by mouth from the 1st day of irradiation onwards	144	230	10.9	225		10.6	21	41	1.6	75		2.7	27
	0.1-1% of solution given subcutaneously at the same time.	142	98	4.1					47	1.7				
Aug. 7, 1962	By mouth, same program	144	200	8	150		6	25	38	1.2	62		2	30
	Subcutaneously, same program	140	75	3					36	1.2				

Note. IR is the index of resistance (ratio LD₅₀ vaccinated to LD₅₀ unvaccinated).

but in those treated with subcutaneous injections of 10 ml of a 1% novocaine solution the figure was 1:2160, i.e., 5.3 times smaller. A single intravenous injection of a large dose (3 ml) of horse serum into the control rabbits caused precipitins to appear as early as the seventh day; the titers were 1:100-1:1000, and were maintained up to the 21st day. In the treated rabbits the production of precipitins was suppressed. There was only a temporary appearance of a weak positive reaction in one rabbit for a dilution of 1:100, and it occurred on the seventh day; in the second rabbit it did not occur until the 21st day.

We have also studied the influence on immunity of novocaine given subcutaneously or by mouth in experiments on white mice either x-irradiated with 300 r, or nonirradiated (Table 2). In the latter group the reduction of the index of resistance was doubled when the novocaine was given subcutaneously, while in the irradiated animals novocaine either by mouth or by injection depressed immunogenesis.

In our opinion the results given here may be of importance in the study of the mechanism of novocaine in radiation sickness. It would be advantageous to study the possibility of using this drug in cases when it was required to suppress the immune reaction, for example in autoimmune diseases, in tissue transplantation, or in the development of tumors.

SUMMARY

Experiments were carried out on 33 rabbits and 570 mice. It was shown that novocaine injected subcutaneously or given by mouth daily depressed immunogenesis, i.e., depressed the production of agglutinins, hemolysins and precipitins.

The depression of antibody production was most marked and prolonged when the novocaine was given by subcutaneous injection; it then persisted after the treatment had been discontinued. When the novocaine was given by mouth antibody production was depressed only during the period of treatment; in some animals the antibodies were formed after the end of the treatment. In mice immunity to typhoid bacillus was depressed after subcutaneous administration of novocaine. After mice had been irradiated with 300 r, immunogenesis was depressed whichever way the novocaine was given. The results obtained may be important in relation to the depression of the immune response in treatment of radiation sickness, in tissue transplantation, and in tumor development.

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All abbreviations of periodicals in the above bibliography are letter-by-letter transliterations of the abbreviations as given in the original Russian journal. Some or all of this periodical literature may well be available in English translation. A complete list of the cover-to-cover English translations appears at the back of this issue.
