STIMULATION OF THE FORMATION OF POST-VACCINATION ANTIBODIES BY BLOOD LETTING

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In an earlier paper [1] we presented material dealing with the stimulation of normal anti-dysentery antibodies in donors and rabbits using blood letting. It was of interest to elucidate the stimulating effect of blood letting on antibody formation in vaccinated animals [2-5].

METHODS

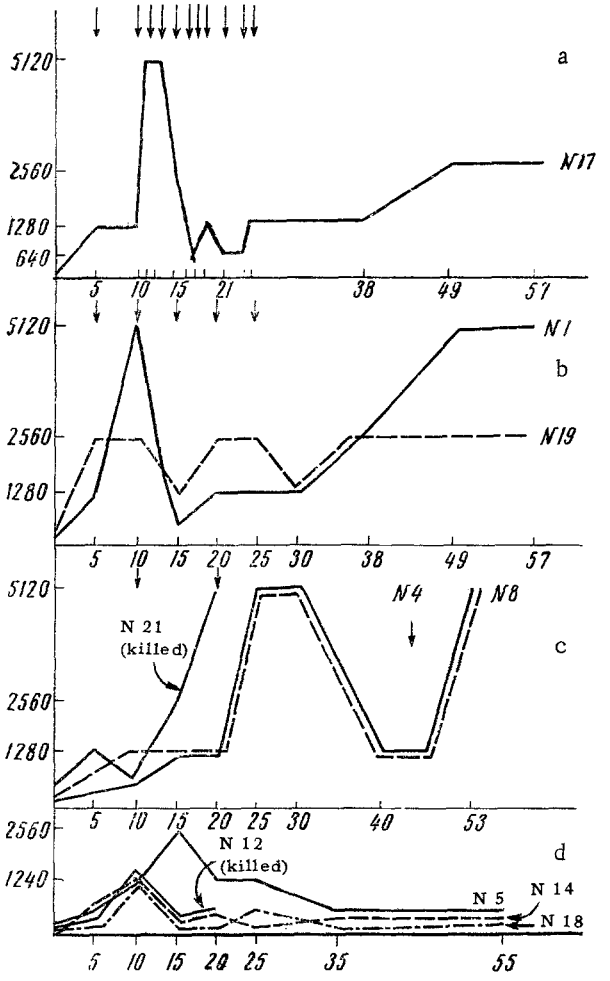
Ten nonpedigreed rabbits of different colors and weighing from 2050 to 2520 grams were used. After establishing in them the normal anti-dysentery agglutinins, they were injected subcutaneously in the right retroscapular space with 10⁹ killed vaccine from the Flexner bacillus in a volume of one milliliter. Then, six of these underwent blood letting; four animals from which no blood was taken served as controls. The venesection schedule, antibody titers, composition of the serum, weight of the spleen and four subcutaneous lymph nodes, their plasmoblasts and plasmocytes were studied by methods described in the previous communication.

RESULTS

A summary of the data concerning the stimulatory effect of blood letting on the formation of post-vaccination antibodies in experimental and control rabbits is presented in the figure. In rabbits No. 17 (Figure, a) and No. 1 (Fig., b) the antibody titer reached 1 : 5120 after five days post venesection. At that same time in the control animals No. 5, 12, 14, 18 (Fig., d) for the same period the antibody titer was 1 : 1280. Consequently, a single venesection raised the agglutinin titer in experimental animals four times above the controls. Subsequent 10 venesections over 15 days in rabbit No. 14 and four venesections with a five day interval in rabbit No. 1 led to a lowering of the agglutinin titer. However, after a 14-day rest in the former case and a five-day rest in the latter the agglutinin titer in these animals began to rise without continued stimulation by venesection and after 10 days, in rabbit No. 17, and 20 days, in rabbit No. 1 (observation period), reached the levels of 1 : 2560 and 1 : 5120, respectively. In rabbit No. 19 after the first venesection the antibody titer did not rise, after the second, it fell, after the third, it rose to a maximum (1 : 2560), after the fourth, it did not change, after the fifth, it again fell; after eight days the titer rose to 1 : 2560 and remained at that level without venesection for 19 days (observation period).

In control animals the quantity of agglutinins, with slight variations, decreased at the 55th day after the start of the experiment almost had reached the original level. Animal No. 12 at the time of the antibody rise at the twentieth day was killed for study of the lymph node and spleen reaction. In rabbit No. 5 the agglutinin concentration continued to rise even after 10 days post-immunization, reaching a titer of 1 : 2560 on the fifteenth day and then, as in rabbit No. 14 and 18, decreasing over the 40 days following almost to the initial values.

Stimulation of antibody formation was observed also in rabbit No. 4, 8, and 21 (Fig., c), from which blood was taken once in 10 days. The antibodies in rabbit No. 21 and 4 continued to rise after the first venesection, performed on the 10th day after the start of immunization. Agglutinins in rabbit No. 21 reached a dilution of 1:5120 ten days after this and exceeded the titer in control animals at this time by 2, 4, and 8 times. Rabbit No. 21 was killed at this stage for study of the spleen and lymph node reaction. Rabbit No. 4 and 8 received their second blood letting ten days after the first and the agglutinin titer rose over the succeeding five days. It continued at that level



Dynamics of post-vaccination antibody formation in rabbits undergoing blood letting and in control rabbits. Vertical numbers—serum dilutions; horizontal numbers—day of observation; numbers on the curves—number of the rabbit. Arrows indicate blood letting.

for five days, then decreased, but after the third venesection, performed five days after the antibody concentration declined, rose to its maximal level (1 : 5120).

Analysis of these data indicates a general regularity in the changes in antibody formation.

In controls, vaccinated a single time and not subjected to venesection, the quantity of agglutinins rose to maximal value by the 10-15th day and then smoothly decreased, almost reaching the initial value by the 55th day. In five out of six of the singly vaccinated rabbits the first blood letting led to an increase in antibody titer, exceeding that of the control animals by two to four times. Subsequent blood letting—daily and once in five days—were accompanied by a decrease in the agglutinin concentration in the experimental animals.

Almost the same picture was observed in rabbits from which blood was taken once in ten days. Increase in antibody titer after its decrease was evoked by the next blood letting.

Thus, the features of stimulation of post-vaccination and normal antibodies by blood letting seemed identical in our experiments. At the same time it must be emphasized that the schedule and doses of blood letting which we selected may not be the best, since other approaches to the given problem have not been studied.

In studies on two experimental and two control animals, triple intravenous injection of killed Flexner's bacillus following blood letting produced in one experimental animal (No. 23) an antibody titer of 1 : 20,000 on the tenth day, and 1 : 40,000 in the other animal (No. 24). After two similar venesections with the subsequent introduction of antigen in rabbit No. 23 the antibody titer fell to 1 : 10,000 and in rabbit No. 24, to 1 : 20,000. After two weeks the next venesection was performed without further introduction of antigen. The antibody titer at the fifth day after this rose in rabbit No. 23 to 1 : 20,000 and in rabbit No. 24 to 1 : 80,000. The titer in control animals did not exceed 1 : 10,000. The preventive properties of the serum of vaccinated and bled animal No. 21, studied in experiments with white mice, appeared stronger in comparison with the properties of the serum from similarly vaccinated control animal No. 12.

It is seen from the data in the table that the morphological indices of immunity are considerably more pronounced in the experimental rabbit than in the control. These data are in full agreement with the data concerning agglutinin titers and preventive properties of the serum presented earlier. And here, as in the experiments with normal antibodies, the stimulating effect of blood letting on antibody production is extremely clearly expressed.

Thus, blood letting in rabbits, performed after inoculating with killed Flexner's bacilli, invariably produce an increase in the titer of agglutinins, an increase in the preventive properties of the serum, a rise in spleen weight of lymph nodes, the number of plasmoblasts and plasmocytes in the nodes as compared with the similar indices in control animals. The stimulatory effect on antibody production is clearly marked after one blood letting of 15-20 ml (0.6-0.8% of body weight of rabbit) performed five days after immunization or in other animals five days after the second blood letting performed once in 10 days after vaccination. Four subsequent venesections at intervals of five days or less and multiple venesections lead to a decrease in antibody titer and, probably, to temporary exhaustion of the antibody production. After the animals are permitted a brief rest this function is restored; the antibody titer

Spleen and Lymph Node Reaction to Blood Letting

Rabbit	Weight of rabbit (in g)	Spleen weight (in mg)	Lymph node weight (in mg)				Total weight of lymph nodes	Number of plasmoblasts (numerator) and plasmocytes (denominator)					
			Right	Left	Right axillary	Left axillary		In spleen	In lymph nodes				
									Right	Left	Right axillary	Left axillary	Total
Control No. 12	2,400	1,290	70	60	70	50	250	9/8	26/15	19/36	18/11	7/33	70/95
Experimental No. 21	2,480	1,420	100	100	70	70	340	51/9	131/15	97/30	115/10	96/34	439/89

rises without further blood letting. In rabbits from which blood was taken twice in a 10-day interval it was necessary to make a third, supplementary, venesection in order to achieve a similar effect. In order to maintain the antibody titer at the level reached by the vaccinated animals using blood letting it is probably advisable to make the next venesection only after the titer begins to fall.

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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.
