EFFECT OF IMMUNOSYMPATHECTOMY ON IMMUNOLOGICAL REACTIVITY

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The role of the sympathetic nervous system in the regulation of immunoallergic processes was studied on immunosympathectomized BALB mice. Antibody formation against normal horse serum and crystalline bovine albumin was sharply inhibited in the sympathectomized mice. Meanwhile no increase in specific leukocytolysis was observed. The course of anaphylactic shock was more severe in the sympathectomized mice, if the antibodies circulated in their blood before the reacting dose of antigen was injected. Animals with a zero antibody titer did not develop shock.

Levi-Montalcini and co-workers suggested a new method of desympathization known as immunosympathectomy [10, 11]. In this case desympathization is carried out by injecting antibodies specifically inhibiting growth and development of sympathetic neurons. Animals treated in this way constitute a very convenient model with which to study the role of the sympathetic nervous system in the regulation of various functions, including the function of specific immunity.

This paper gives the results of a study of the effect of immunosympathectomy on antibody production and on the course of anaphylactic shock.

EXPERIMENTAL METHOD

Male BALB mice were used. The sympathetic nervous system was destroyed by parenteral injection of antibodies against nerve tissue growth factor into newborn mice [10]. At the age of 2-2.5 months the mice were immunized with normal horse serum or crystalline bovine albumin. The antigen was injected subcutaneously into the inguinal region three times on alternate days: 0.25 ml serum or 7% albumin solution at each injection. The immune reaction was assessed from the antibody titer, the degree of specific leukocytolysis, and the severity of anaphylactic shock. The antibody titer in the blood serum was determined by the ring-precipitation test in microtest tubes. Specific leukocytolysis was studied by luminescence microscopy in the modification [3]. Anaphylactic shock was produced on the 21st-24th day of sensitization. The reacting dose of antigen (0.05 ml horse serum or 7% bovine albumin solution) was injected intravenously. The severity of the anaphylactic shock was estimated from the drop in blood pressure measured in the common carotid artery by an electromanometer (Orion).

EXPERIMENTAL RESULTS

In mice receiving antibodies against nerve tissue growth factor, 7-8% of the neurons still remained in the stellate ganglion [2], in agreement with observations made by other workers [7]. The catecholamine concentration in the organs of the desympathized animals was sharply reduced. The response of the cardiovascular system to exogenous noradrenalin was considerably increased but its response to asphyxia

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TABLE 1. Antibody Formation and Course of Anaphylactic Shock in Intact and Immunosympathectomized Mice (M ± m)

Group of animals	Type of antibodies (in $\log_2$)	Blood pressure (in mm Hg)		Time taken to reach minimal pressure (in min)
		before shock	after shock	
Intact mice	n=11 10,1±0,84	n=9 94±4,5	n=9 76±5,7	n=5 29±5,6
Immunosympathectomized mice	n=10 5,20±1,13 P<0,01	A. n=4 74±3,6 P<0,01 B. n=2 70±18,0	A. n=4 18±11,2 P<0,001 B. n=2 65±9,0	n=5 15±2,0 P<0,05 —

Legend to Tables 1 and 2: n) number of animals; P) significance of difference between mean values in experimental (ISA) and control (intact mice) series; A) first group of ISA, B) second group of ISA (explanation in text).

TABLE 2. Dynamics of Antibody Formation and Specific Leukocytolysis in Intact and Immunosympathectomized Mice at Various Times after Immunization with Crystalline Bovine Albumin (M ± m)

Group of animals	Before immunization	Seventh day after immunization		14th day after immunization		21st day after immunization	
	leukocytolysis (in %)	titer of antibod. (in $\log_2$)	leukocytolysis (in %)	titer of antibod. (in $\log_2$)	leukocytolysis (in %)	titer of antibod. (in $\log_2$)	leukocytolysis (in %)
Intact mice	n=6 7,6±1,51	n=5 9,8±0,85	n=6 20,7±4,58	n=6 13,2±0,98	n=5 24,1±3,90	n=6 11,4±0,85	n=6 12,4±1,76
Immunosympathectomized mice	n=6 12,2±0,84 P<0,05	n=6 5,2±0,73 P<0,01	n=6 12,0±0,85 P<0,01	n=6 6,3±0,86 P<0,001	n=5 12,5±5,61 P<0,1	n=6 5,4±0,80 P<0,001	n=5 9,5±4,12

was reversed: the pressor effect was changed to depressor [2]. In the immunosympathectomized animals (ISA), organs with an adrenergic innervation (nictitating membrane, atrium, blood vessels) did not react to stimulation of the degenerated sympathetic fibers [6, 13].

These results demonstrate the effectiveness of the immunological method of desympathization. It was interesting to discover whether the immunological reactivity of the ISA was modified.

For the experiments of series I, 11 control animals and 10 ISA were used. The antigen was horse serum. Antibodies were determined on the 11th day after immunization. The process of antibody formation in the ISA was sharply inhibited (Table 1). No antibodies whatsoever were found in the serum of four experimental mice and in another four they were found in minimal titers. No decrease in antibody production was observed in only two ISA.

In the experiments of series II antibody formation against crystalline bovine albumin was studied in the ISA at various times after injection of the antigen, and the pattern was compared with the specific leukocytolysis test. As in series I, results indicating sharp inhibition of antibody formation in the ISA were obtained in these experiments also. Antibody production was lowered at all periods of the immune response. In addition, whereas a high antibody titer in the control animals correlated with a marked increase in specific leukocytolysis, in the ISA the decrease in antibody production coincided with the absence of increase in specific alteration of leukocytes (Table 2). The absence of increase in leukocytolysis in the ISA was further evidence of the weakening of their immunological reactivity [1].

The ISA differed from the intact animals not only in the character of their immune response but also in the course of anaphylactic shock. Considering the definite correlation between the intensity of allergic responses and the antibody titer, on the one hand, and of the state of the adrenergic control mechanisms on the other [4, 5, 8], two alternative types of course of shock could be expected in the ISA: an increase in its

severity in those animals which preserved to some extent the ability to form antibodies and its weakening in animals which had completely lost this ability. Anaphylactic shock was studied in nine intact animals and six ISA. The latter were divided into two groups. Group A consisted of four mice with a positive precipitin titer and group B of two mice with a zero antibody titer (Table 1). In the initial state the blood pressure was lower in the ISA. Injection of the reacting dose of antigen caused definite shock to develop only in those ISA whose ability to produce antibodies, although disturbed, was still present (Table 1). Anaphylactic shock was weak in nearly all the control animals, while in the two experimental animals with well-defined immunoareactivity it was virtually absent (Table 1). All the nine control mice survived, but of the four experimental animals of group A, two died.

These results indicate that the sympathetic nervous system plays an important role in the formation of the animal's response to an antigenic stimulus. After injection of an antigen it participates in the regulation of antibody formation (it has a positive immunotropic action), while after injection of the reacting dose of antigen it helps to mobilize the defensive reactions aimed at ensuring the animal's survival. According to data in the literature ISA differ from intact animals only in the reduction of their sympathetic nervous system. The other regulatory systems, such as the parasympathetic, are undisturbed [2, 9]. Consequently, the weakening of the immunological reactivity of the animal in these experiments was due chiefly to one factor alone – to desympathization, i.e., to a decrease in the intensity of sympathetic regularity influences acting on the effector organs, including the immune system. This means that the character of the animal's response to an antigenic stimulus is largely determined by the functional state of the adrenergic mechanism. Data in the literature showing the direct effect of adrenalin on immunocompetent cells [12] are another powerful argument in support of this view.

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