STIMULATION OF CELLULAR IMMUNITY AND IMMUNOLOGIC MEMORY BY SOMATOTROPIC HORMONE

T. G. Shemerovskaya and I. G. Kovaleva

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The role of somatotropic hormone (STH) in the development of hypersensitivity of delayed type (HDT) and immunologic memory was demonstrated in guinea pigs. Injection of human STH (in doses of 0.25 and 1 mg per guinea pig) in the period of sensitization and formation of HDT stimulated the development of cutaneous hypersensitivity. Inhibition of endogenous STH by means of antiserum against guinea pig STH protected the animal against the development of hypersensitivity in the period both of sensitization and of reaction. HDT was restored after the action of the antiserum ceased. Experiments with a model of immunologic memory showed that the sensitization period is the most sensitive, whereas the period of preservation of immunologic memory remained resistant.

KEY WORDS: somatotropic hormone; hypersensitivity of delayed type; sensitization; immunologic memory.

Somatotropin is regarded as the hormone that stimulates immunogenesis. However, the factual material on which this conclusion is based is very limited in amount, especially with respect to cellular immunity. It deals mainly with the role of the hormone in the evolution of the immune system [4, 8, 9] and stimulation of the lymphoid organs and plasma-cell response [1, 2, 7, 11]. A few investigations have dealt with the effect of STH on antibody formation [1, 3, 5, 6]. Some workers describe a stimulant action of STH [3], other deny that the hormone has any effect on antibody formation [5, 6], whereas a third group consider that somatotropin has a marked action only on the prepared organism [1].

The object of the present investigation was to study the effect of STH on the development of hypersensitivity of delayed type (HDT) and on immunologic memory in guinea pigs.

EXPERIMENTAL METHOD

Experiments were carried out on female guinea pigs weighing 200-250 g. STH was obtained from human pituitary glands by Raben's method [10] or from guinea pig pituitary glands by the writers' modification of the same method. Antiserum against STH was prepared by injecting guinea pig STH subcutaneously into rabbits into the plantar pads together with Fruend's adjuvant three times at intervals of three weeks.

During the experiments STH was injected subcutaneously in different doses and at different times relative to sensitization.

Antiserum was injected in a dose of 2 ml subcutaneously four times on alternate days. To reproduce HDT, a suspension of killed Mycobacterium tuberculosis cells in physiological saline was used in doses of 0.1 mg (in the experiments to create and detect immunologic memory), 0.5 mg (to obtain a moderate HDT), and 5 mg per guinea pig (to create a marked degree of hypersensitivity). HDT was evaluated by intradermal injection of 0.1 ml of standard dry tuberculin in dilutions of 1:10 and 1:100. A positive reaction consisted of erythema more than 10 mm in diameter. The skin tests were carried out 10, 14, 20, 32, and 50 days after sensitization. The statistical analysis of the results was carried out by the χ^2 method.

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TABLE 1. Effect of STH on Development of HDT in Guinea Pigs

Group of animals	Daily dose of STH (in mg)	Days of injection	Total dose (in mg)	Number of positive skin reactions	
				10th day	20th day
1	1	—8+2	11	9/9	7/9
2	1	+2+12	11	5/6	4/6
3	0,25	—8+2	2,75	6/6	6/6
4	0,25	+2+12	2,75	4/6	3/6
Control	—	—	—	4/10	0/9

Legend: Numerator gives number of animals with positive reactions to tuberculin 1 : 100; denominator gives number of animals in group. Here and in Table 2, – and + denote injection of STH before and after sensitization respectively.

TABLE 2. Effect of STH on Immunologic Memory

Group of animals	Daily dose of STH (in mg)	Days of injection	Dilution of tuberculin 1 : 10		Dilution of tuberculin 1 : 100		
			15–20 mm	>20 mm	<15 mm	15–20 mm	>20 mm
1	0,25	—8+2	0/5	5/5	0/5	2/5	3/5
2	0,25	+12+22	4/5	0/5	2/4	2/4	0/4
3	0,25	+32+42	1/5	4/5	2/5	3/5	0/5
Control	—	—	4/4	0/4	1/4	3/4	0/4

Legend: Numerator gives number of animals with a particular size of reaction; denominator gives number of animals in group.

EXPERIMENTAL RESULTS

In the experiments of series I, the effect of somatotropin on HDT was studied. Guinea pigs received a subcutaneous injection of STH in a dose of 0.25 mg daily for 11 days (Table 1). In some cases injection of the hormone began eight days before sensitization, in others on the second day after sensitization. The animals were sensitized with 0.5 mg of dried M. tuberculosis cells per guinea pig, and this led to the development of sensitivity to tuberculin by the 10th day in four of the 10 control guinea pigs, whereas by the 20th day sensitivity to tuberculin in these animals had disappeared. A marked increase in the number of positive reactions was observed in the guinea pigs receiving STH injections. The greatest stimulation of HDT was observed when STH was injected eight days before sensitization (groups 1 and 3). By the 10th day all the animals (15 of 15) had positive skin tests (whether receiving STH in a dose of 1 mg or 0.25 mg per guinea pig). The hormone gave a smaller, but statistically significant, effect when injected from the second day after sensitization.

In the experiments of series II, the effect of STH on immunologic memory was studied (Table 2). The guinea pigs received two injections of subsensitizing doses of M. tuberculosis cells with an interval of 40 days (0.1 mg per guinea pig). This resulted in positive skin tests on the 50th day after the first injection of antigen in all the animals tested. After the total dose (0.2 mg) had been given to the guinea pigs in a single injection, sensitization was not observed. The animals were divided into groups which received STH injections starting two days before the first sensitization, in the period between injection of the antigen, and two days before the second sensitization. The most sensitive period was found to be the period of development of the state of sensitization, whereas the period of pereservation of immunologic memory was virtually resistant to the action of STH in this dose.

To study the effect of endogenous STH on the development of hypersensitivity, antiserum against homologous STH was injected into the guinea pigs. The animals were sensitized with a large dose (5 mg) of M. tuberculosis cells, equivalent to not less than 10 minimal sensitizing doses. The antiserum was injected in order to act on the periods of sensitization and of production of HDT. One group of animals received antiserum with effect from two days before sensitization the second group from the sixth day after sensi-

tization. The control animals were divided into two subgroups: those receiving normal rabbit serum and those receiving antiserum from rabbits immunized with Freund's adjuvant. In the first group, of eight skin tests with tuberculin carried out 12 days after sensitization, seven were negative, compared with all eight in the second case. All 16 tests on the control animals were positive. On the 24th day, the second time that the skin tests were carried out, suppression of hypersensitivity in the animals receiving antiserum was no longer observed, and five of the eight tests in the first group and six of the six tests in the second group were positive, whereas in the control group all tests were positive.

The fact of suppression of hypersensitivity in the period of injection of antiserum against endogenous STH into animals shows that this hormone is an essential factor for the development of cellular hypersensitivity. Restoration of HDT followed cessation of the action of antiserum. The action of STH could be linked both with provision for energy metabolism in immunogenesis and with direct affinity for the lymphoid system.

Injection of exogenous STH stimulated the development of HDT, but the endogenous hormone under normal conditions can also evidently lead to adequate development of the immune process. In those of the experiments described above in which large, highly immunogenic doses of M. tuberculosis cells were used for sensitization, it will be noted that STH had no marked effect.

These results may explain some aspects of the role of STH in immunogenesis.

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