DEGRANULATION OF BASOPHILS AS AN INDICATOR OF STRESS

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Regular appearance of degranulation of basophilic blood leukocytes was shown to occur not only during the development of allergic inflammation in a joint and in the skin, but also during experimental acute and chronic blood loss, burn trauma, and acute radiation sickness. The degranulation reaction reflects stress developing in response to stress situations.

KEY WORDS: basophils; degranulation; allergy; stress situation.

Liberation of biologically active substances from cells during allergic reactions *in vivo* has been widely discussed in the literature. The reaction of degranulation of basophilic leukocytes and mast cells is the most interesting phenomenon from this respect.

The object of the investigation was to study the state of the blood basophils of animals in situations leading to considerable functional stress, when liberation of biologically active substances can take place from cells.

METHODS

Degranulation of the basophils by Shelley's method [12] and the number of basophils per cubic millimeter blood [7] were studied in the initial state and in the course of development of allergic arthritis (series 1, 60 rabbits), and the Arthus (17 animals, antigen normal horse serum 1 : 100) and Schwartzmann (2nd series, 15 animals) phenomena. In addition the nonspecific reaction of the basophils was studied in 10 rabbits with acute blood loss (removal of 17.5% of the blood volume in one stage), in 10 animals with chronic blood loss (repeated bleeding of an amount equal to 55.6% of the total blood volume) (series 3), in 10 animals (series 4) with experimental radiation sickness (a single irradiation from the dorsal side; target-skin distance 30 cm, filter 0.5 mm Cu + 1 mm Al, 180 kW, 10 A, field 8/10 cm, dose rate 93 R over a period of 9 min 30 sec, dose 790 R), and in 10 animals (series 5) with burn trauma produced by application of a flame for 3 min. In the experiments of series 5, to detect the degree of autosensitization of the animals Hoigne's method was used (using

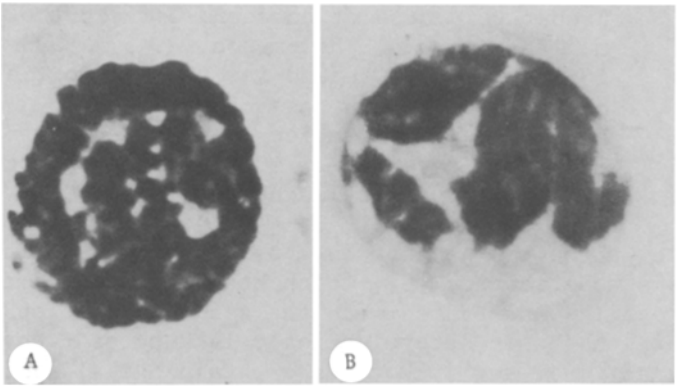

Fig. 1. Basophilic leukocytes from perpheral blood of rabbits with allergic arthritis. A) Normal basophil, B) degranulated basophil after contact with specific antigen. Stained with neutral red, 3500 ×.

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TABLE 1. Number of Basophilic Leukocytes in 1 mm^3 Blood and Their Degranulation during Development of Allergic Arthritis in Rabbits (M ± m)

Determination	Initial data	Sensitizing injection of antigen		Reacting injection of antigen	Height of manifestation of arthritis	Next observations made after	
		I	III			10 days	20 days
Number of basophils	133±6	208±6	243±7	318±20	306±13	228±17	150±7
P		<0,001	<0,001	<0,001	<0,001	<0,001	0,05
Percent of changes		56	82	139	130	71	12
		<0,001	<0,001	<0,001	<0,001	<0,001	0,05
Percent of degranulation – basic determination	2±2	18±4	22±4	46±5	39±5	38±5	29±4
P		<0,001	<0,001	<0,001	<0,001	<0,001	<0,001
1st Control determination	4±2	13±4	12±3	28±4	30±5	24±4	19±4
P		<0,01	<0,01	<0,001	<0,001	<0,001	<0,001
2nd Control determination	1±1	12±3	17±4	35±4	31±5	30±5	21±4
		<0,01	<0,001	<0,001	<0,001	<0,001	<0,01

Note. Data analyzed by V. S. Genes' method [4]. Values of M ± m given (m denotes mean error, in %); P relative to initial data in all cases.

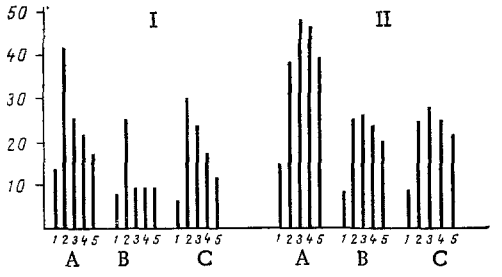

Fig. 2. Degranulation of basophils in Schwartzmann and Arthüs phenomena. I) Schwartzmann phenomenon, II) Arthüs phenomenon. A) Basic determination, B) 1st control, C) 2nd control determination. Legend for I: 1) initial data, 2) 1 h after preparatory dose of antigen, 3) height of manifestation of phenomenon, 4, 5) 5 and 10 days later. Legend for II: 1) initial data, 2) after 3rd dose of antigen, 3) height of manifestation of phenomenon, 4, 5) 10 and 20 days later. Ordinate, % of degranulated basophilic leukocytes.

a lysate of autologous erythrocytes as antigen, positive results with dilution of antigen 1 : 240) in Klemparskaya's modification [3], which has been adopted in clinical practice [4]. The reaction of the basophils was studied with the animals' own leukocytes in three variants: leukocytes + serum + antigen (basic determination), leukocytes + physiological saline + antigen (1st control determination), and leukocytes + physiological saline + serum (2nd control determination). The necessary ingredients were used in equal volume [5]. In series 3-5 the nonspecific reaction of the basophils was studied without addition of antigen, so that it was possible to detect the "vulnerability" of the basophils *in vivo* [6].

RESULTS

The results of the experiments of series 1 are given in Table 1. The highest percentage of degranulation was found after reacting injection of the antigen and at the height of development of allergic arthritis (Fig. 1). At these times the number of basophils was considerably increased and the percentage of degranulated basophils in the control determination

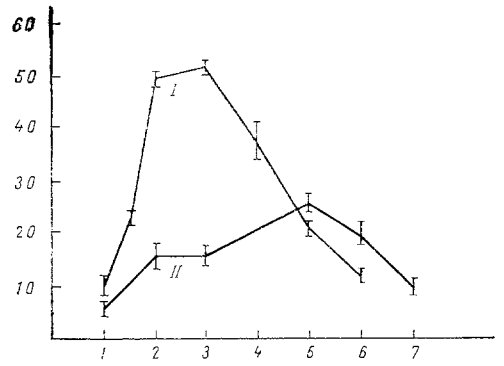

Fig. 3. Degranulation of basophils after flame burn and in acute radiation sickness. I) Flame burn, II) acute radiation sickness. 1) Initial data, 2) 24 h later, 3-7) 7, 14, 21, 30, and 42 days later respectively. Intermediate division on curve I immediately after burning. Abscissa, times of observation; ordinate, % of degranulated basophilic leukocytes.

was higher. In the experiments of series 2 similar results were obtained (Fig. 2). In series 3 a nonspecific reaction of the basophils appeared immediately after blood loss. More marked changes were observed after acute blood loss ($P < 0.001$). The results of the experiments of series 4 and 5 are given in Fig. 3. In the experiments of series 5 no correlation was found between the presence of autoantibodies in the blood and the nonspecific reaction of the basophils ($P = 0.2$).

It was first shown in Ado's laboratory [2] that the state of the basophils during an anaphylaxic reaction which was assessed as degranulation was not due to true injury to the target cells, but is the result of their activation, followed by a state of relative rest. The absence of cell destruction is shown by preservation of the membrane potential of the cells during the action of antigen-antibody complexes on them and their ability to give active movements within a few hours after completion of the allergic reaction [8].

In the stress reaction during blood loss, irradiation, and burn trauma conditions facilitating the release of biologically active substances from the granules of the basophils are evidently created, with the result that the impression of degranulation is obtained. The possibility cannot be ruled out that the sensitivity of the basophils to environmental conditions is increased. This suggestion is indirectly supported by data on labilization of the cell membranes under the influence of hypoxia, x-ray irradiation, and other factors, as a result of which the release of biologically active substances into the external medium is facilitated [11]. The experiments showed that activation of basophils can arise in response to the action of various strong stimuli on the body. The appearance of degranulation in stress situations can be regarded as a physiological process linked with the release of biologically active substances.

The results thus confirm once again the appearance of a response of the basophils as the result of a specific antigen—antibody reaction in experimental animals with allergic inflammation (series 1 and 2), but they also showed the possibility of appearance of a nonspecific response of the basophils to the stress factor (series 3-5). In accordance with I. V. Davydovskii's general pathological views the reaction of the basophils can be regarded as an extreme manifestation of the action of definite mechanisms which are usually balanced under physiological conditions.

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ROLE OF THE HYPOTHALAMUS IN THE RESPONSE OF THE RAT PITUITARY AND TESTIS TO INJECTION OF THE ANTIANDROGEN 4-NITRO-3-TRIFLUOROMETHYLISOBUTYRANILIDE

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The effect of the antiandrogen 4-nitro-3-trifluoromethylisobutyranilide (flutamide, NFBA) on the plasma FSH, LH, and testosterone levels and on activity of steroid-Δ^5-3β-ol dehydrogenase activity in the testes was studied in intact male rats and rats with destruction of the median eminence of the hypothalamus. In rats undergoing a mock operation and with the hypothalamus intact, NFBA increased the LH, FSH, and testosterone levels by five, two, and four times respectively, and enzyme activity by three to four times. After destruction of the median eminence the secretion of FSH was unchanged by NFBA, and the LH and testosterone levels and enzyme activity were increased by only 1.5-2 times, i.e., much less than in animals undergoing the mock operation. The results of these experiments indicate a leading role of the hypothalamus in the response of the pituitary and testis to the antiandrogen.

KEY WORDS: antiandrogens; median eminence of hypothalamus; lutinizing hormone (LH); follicle-stimulating hormone (FSH).

During a study of the effect of the peripheral nonsteroid antiandrogen 4-nitro-3-trifluoromethylisobutyranilide (NFBA, niftolid, flutamide, Sch-13521) on the reproductive system of male rats a phenomenon of activation of the pituitary—testicular complex was observed, manifested by increased secretion of LH and testosterone [2]. The writers postulated that the primary link in the chain of these changes was the blocking action of antiandrogen on feedback receptors in the hypothalamic centers regulating gonadotropin secretion [2].

The obtaining of experimental data confirming this hypothesis is of great importance for establishment of a theoretical basis for the use of NFBA in order to study the functional reserves of the hypothalamic—pituitary—testicular system [1]. The object of the present investigation was to compare the response of the pituitary and testis of rats, both intact and with destruction of the median eminence (ME) of the hypothalamus, to injection of NFBA.

METHODS

Experiments were carried out on male Wistar rats weighing 200-250 g. Electrolytic destruction of ME of the hypothalamus was carried out on the animals by application of an anodal

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