EFFECT OF ADRENOTROPIC AGENTS ON REPRODUCTION OF ANAPHYLACTIC REACTION OF ISOLATED HUMAN SMOOTH-MUSCLE ORGANS

G. V. Poryadin and A. P. Baranov

UDC 616-056.3-092.9-085.217.22

Passive sensitization of the human lungs, bronchi, and small and large intestine by the blood serum of patients sensitive to ragweed pollen was compared. Passive sensitization and the subsequent anaphylactic contraction were constantly reproduced in the isolated human bronchi, lungs, and ileum. The development of this reaction was less constant in the large intestine, jejunum, and appendix. The magnitude of the anaphylactic reaction of human smooth muscle was substantially altered after treatment of the muscle with substances acting selectively on the β-adrenergic receptors of these organs.

Key words: passive anaphylaxis; smooth-muscle organs; adrenotropic agents.

The study of the latent mechanisms of formation of allergic reactions is an important problem in modern experimental allergology. This is particularly true of investigation of the sensitization of smooth-muscle organs, the basis for the development of widespread manifestations of allergy in animals and man [2, 4].

The investigation described below is a continuation of others carried out in the laboratory directed by Academician of the Academy of Medical Sciences of the USSR A. D. Ado to study the mechanisms of the anaphylactic reaction of isolated human smooth-muscle organs [3, 6]. Reproduction of passive sensitization and the anaphylactic reaction of human smooth-muscle organs (lungs, bronchi, small intestine, appendix, large intestine, and rectum) was studied by the use of blood serum from pollinosis patients containing allergic antibodies (reagins).

EXPERIMENTAL METHOD

Passive sensitization of the smooth muscles was induced with the reagin-containing serum in a dilution of 1:10 (in isotonic sucrose solution) for 2 h at 37°C and with constant aeration. The anaphylactic reaction was reproduced in a bath for isolated organs (volume 20 ml) at 37°C by the addition of extract of ragweed pollen (30 μg/ml). The degree of the anaphylactic reaction of the lung tissue was assessed from the output of histamine, the concentration of which was determined by a biological method on the atropinized guinea pig ileum. The amplitude of the anaphylactic contraction of the smooth muscles was estimated as a percentage of the reaction of these organs to a standard dose of acetylcholine (2 μg/ml). Contractions of the muscle were recorded under isometric conditions. Details of the method were described previously [5, 6, 7].

EXPERIMENTAL RESULTS

The output of histamine from the passively sensitized lung tissue on the addition of ragweed extract (0.2 μg/ml) averaged (12 experiments) 2.3 μg/g tissue.

Passive sensitization and subsequent anaphylactic contraction were successfully reproduced in isolated segments of the human lobar and segmental bronchi. The mean amplitude of the anaphylactic contrac-

Allergologic Research Laboratory, Academy of Medical Sciences of the USSR, Moscow. (Presented by Academician of the Academy of Medical Sciences of the USSR A. D. Ado.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 79, No. 3, pp. 76-79, March, 1975. Original article submitted April 22, 1974.

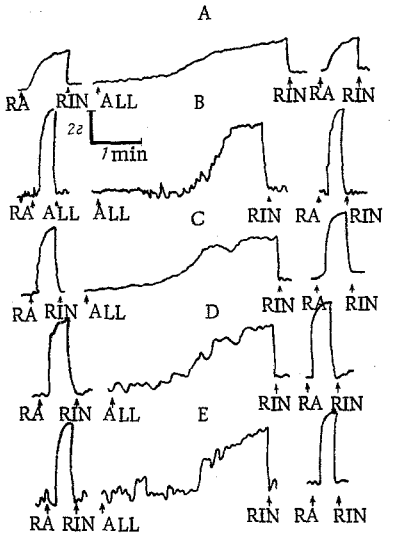

Fig. 1

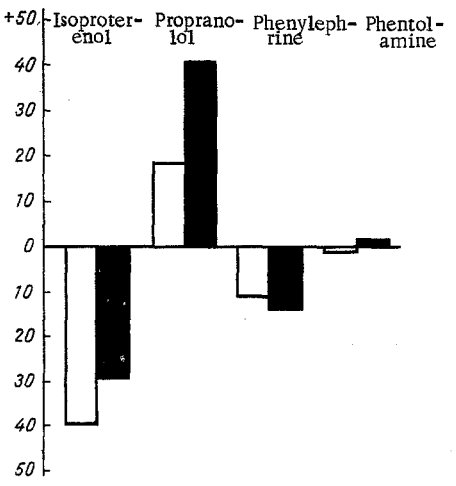

Fig. 2

Fig. 1. Character of anaphylactic contraction on isolated segments of human smooth muscles previously sensitized with serum of untreated patients sensitive to ragweed. A) Bronchi; B) ileum; C) appendix; D) large intestine; E) rectum. RA) Reaction to addition of acetylcholine (2 μg/ml); ALL) addition of specific allergen (extract of ragweed pollen, 30 μg as nitrogen per ml); RIN) rinsing organ with Krebs' solution for 10 min.

Fig. 2. Liberation of histamine by human lungs and anaphylactic reaction of small intestine in the presence of adrenotropic agents. Unshaded columns – "immunologic" liberation of histamine from lung tissue; shaded columns – anaphylactic reaction of ileum. Ordinate, deviation from initial level, in %.

tion of the bronchi (relative to that to 0.3 μg/ml acetylcholine) was 130.0 ± 11.3%. The latent period of the maximal anaphylactic contraction of the bronchi, in 20 experiments, was 104.5 ± 2.4 sec and the time of increase of the anaphylactic contraction up to the maximum was 106.0 ± 2.2 sec (Fig. 1A).

To compare the sensitizing ability of the sera of patients sensitive to ragweed pollen toward various parts of the human intestine, segments of the appendix, ileum, jejunum, large intestine, and rectum were sensitized with serum from the same patient. The patients' sera were found to possess extremely low sensitizing activity toward the segments of jejunum. In that case passive sensitization was reproduced in only 2 of 8 cases.

Active patients' sera constantly sensitized strips of small intestine from the ileocecal region. The character of the maximal anaphylactic response of the ileum was basically similar to that of the isolated segment of human bronchi (Fig. 1B). The duration of the latent period and of the increase in muscle contraction in this case, based on the results of 27 experiments, was 104.3 ± 0.8 and 105.2 ± 0.9 sec respectively. The maximal strength of anaphylactic contraction was 65.6 ± 1.6%.

Smooth-muscle preparations of the large intestine (87.5%) and rectum (90.3%) were somewhat less active as regards producing passive sensitization. The mean values of the anaphylactic contraction obtained on the large intestine (67.8 ± 3.1%) and on the rectum (70.4 ± 7.6%) did not differ significantly from each other ($P > 0.5$). The latent period and the rise time of the anaphylactic contraction of the sensitized segments of human large intestine were 100.1 ± 1.8 and 96.4 ± 1.6 sec respectively, and of the rectum 103.5 ± 2.1 and 94.8 ± 3.2 sec respectively.

Passive sensitization of the human appendix was possible in 75% of cases. The amplitude of the anaphylactic contraction in this case was 56.1 ± 3.1%.

Recent investigations [1, 8] have shown that a disturbance of the balance between two types of adrenergic effector systems (α- and β-receptors) may play a role in the mechanism of development of allergic manifestations in man and animals. To obtain proof of the participation of this system in anaphylaxis the effect of adrenotropic agents on the anaphylactic reaction of human smooth muscles and lung tissue was

studied. The concentration of histamine liberated from passively sensitized lung tissue in response to the addition of antigen and the amplitude of the anaphylactic contraction of the human ileum were taken as 100%. The change in the liberation of mediator and in the anaphylactic reaction of the jejunum in the presence of the adrenotropic agents was expressed as a percentage of these basic values.

Incubation of sensitized fragments of human lungs with 4 μg/ml isoproterenol, which selectively stimulates β-adrenergic receptors, for 20 min at 37°C before the addition of ragweed extract was shown to inhibit the liberation of histamine by 44.7 ± 1.3% (Fig. 2). Perfusion of segments of human small intestine with isoproterenol also reduced the amplitude of the subsequent anaphylactic contraction – by 29.5 ± 2.7%.

Blocking the β-receptors of sensitized lung fragments or segments of ileum with 20 μg/ml propranolol (for 20 min) increased the liberation of histamine by the lungs or the anaphylactic reaction of the smooth-muscle segments by 17.2 ± 2.1 and 41.7 ± 4.6% respectively (Fig. 2).

The effect of stimulation of the α-receptors on anaphylaxis of the lungs and small intestine was investigated by perfusing the isolated organ for 20 min with phenylephrine (2.5 μg/ml). This treatment of the lung fragments inhibited the liberation of histamine by only 12.0 ± 1.6%. Perfusion of segments of intestine with phenylephrine also was accompanied by some inhibition (by 14.8 ± 3.2%) of the anaphylactic reaction of the organ (Fig. 2).

Preliminary treatment of the lung tissue and segments of small intestine with 40 μg/ml phentolamine, which blocks α-receptors, did not affect the subsequent liberation of histamine or the anaphylactic reaction of the human ileum (Fig. 2).

These experiments yielded evidence, first, that passive sensitization and subsequent anaphylactic reactions can be reproduced in the human lungs, bronchi, and ileum and that these phenomena can be used as an experimental model with which to study the mechanisms of allergic reactions of human smooth-muscle organs. The development of this reaction was less constant in the human jejunum, large intestine, and appendix.

The experiments also show that disturbance of the equilibrium between α- and β-adrenergic receptors may be one of the factors that increases the severity of allergic reactions in persons with various manifestations of allergy of immediate (anaphylactic) type.

LITERATURE CITED

1. V. N. Abrosimov, in: The Pollinoses [in Russian], Krasnodar (1973), p. 3.
2. A. D. Ado, General Allergology [in Russian], Moscow (1970).
3. A. D. Ado, J. E. Bermont, I. S. Gushchin (Guchin), et al., Allergie u. Asthma, 15, 235 (1969).
4. A. D. Ado, L. M. Ishimova, and A. A. Pol'ner, Vestn. Akad. Med. Nauk SSSR, No. 4, 8 (1963).
5. I. S. Gushchin, Farmakol. i Toksikol., No. 2, 209 (1965).
6. G. V. Poryadin, "Passive sensitization of human smooth-muscle organs," Candidate's Dissertation, Moscow (1969).
7. A. Csapo, Am. J. Physiol., 177, 348 (1954).
8. R. P. Orange, M. A. Kaliner, P. J. Laraia, et al., Fed. Proc., 30, 1725 (1971).