Effect of Antibodies to Histamine in Ultralow Doses on Production of Allergen-Specific Antibodies

V. I. Agafonov, N. V. Bel'skaya, M. G. Danilets, Yu. B. Bel'skii, E. S. Trofimova, Yu. L. Dugina*, and O. I. Epstein*

We studied the effects of potentiated antibodies to histamine on production of IgE and IgG1 in response to 3-fold immunization of mice with ovalbumin in doses of 0.5, 10, and 100 μg. The course of treatment with antibodies to histamine suppressed production of allergen-specific IgE and IgG1 in mice 2-fold immunized with ovalbumin in doses of 100 and 0.5 μg, respectively. In mice immunized 3 times with ovalbumin in various doses the preparation suppressed production of IgE and IgG1.

Key Words: *immunoglobulins; antibodies to histamine; ultralow doses*

Our previous studies showed that administration of affinely purified potentiated antibodies to histamine (PAB-H) relieves anaphylactic shock [1]. Histamine acts as the inflammatory mediator and immunomodulator [2-4]. This substance promotes allergic reactions to antigens in the initial stage of the immune response [5-8]. Histamine intensifies secretion of IgE and IgG1 by stimulating interleukin-4 synthesis [7]. Here we studied the effect of PAB-H on production of allergen-specific IgE and IgG1 under various regimens of immunization.

MATERIALS AND METHODS

The potentiated preparation contained PAB-H in homeopathic dilutions (equivalent concentration 10^{-24} wt %) and distilled water (DW). Experiments were performed on 135 CBF_1 mice (class I conventional strain) aging 2-4 months and weighing 18-20 g. The concentrations of IgG1 and IgE were determined by the method of passive skin anaphylaxis. The measurements were performed with 10 outbred albino mice (18-20 g) and 10 outbred rats (180-250 g) obtained from the Institute of Pharmacology.

Production of IgE and IgG1 was induced by intraperitoneal administration of ovalbumin (OVA, ICN) and adjuvant ($Al(OH)_3$, ICN). The mice were immunized with 0.5 μg OVA and 0.5 mg adjuvant, 10 μg OVA and 5 mg adjuvant, or 100 μg OVA and 5 mg adjuvant.

Institute of Pharmacology, Tomsk Research Center, Siberian Division of the Russian Academy of Medical Sciences; "Materia Medica Holding" Research-and-Production Company, Moscow

Immunization with the antigen and adjuvant was performed 1, 2, and 3 times at 3-week intervals.

PAB-H and DW were given perorally in a single dose of 0.2 ml for 10 days (1 time a day). In experiments with single immunization PAB-H and DW were given for 5 days before and 5 days after treatment. In animals immunized 2 or 3 times PAB-H and DW were administered over 10 days after treatment.

Blood plasma was taken 5 days after the first immunization and 3 days after the second and third immunizations to measure the concentration of immunoglobulins.

To estimate IgG1 level the plasma from immunized mice (30 ml, dilutions 1:4, 1:8, and 1:16) was injected intracutaneously on the back of mice. OVA in a permissible dose of 0.5 mg in 0.2 ml 0.5% Evans blue was administered into the retroorbital sinus 2 h after injection of the plasma. To measure IgE level the plasma from immunized mice (30 ml, dilutions 1:4, 1:8, and 1:16) was injected intracutaneously on the abdomen of rats. OVA in a permissible dose of 100 mg/100 g in 1 ml 0.5% Evans blue was administered into the caudal vein 24 h after passive immunization. The reaction was determined by staining of the skin after 30 min. The animals were killed, and the skin was dissected. We evaluated maximum dilution of the plasma that stained the inner skin surface.

RESULTS

PAB-H suppressed IgE production after 3-fold immunization with the antigen in various doses (Fig. 1). This effect of PAB-H was observed after the second

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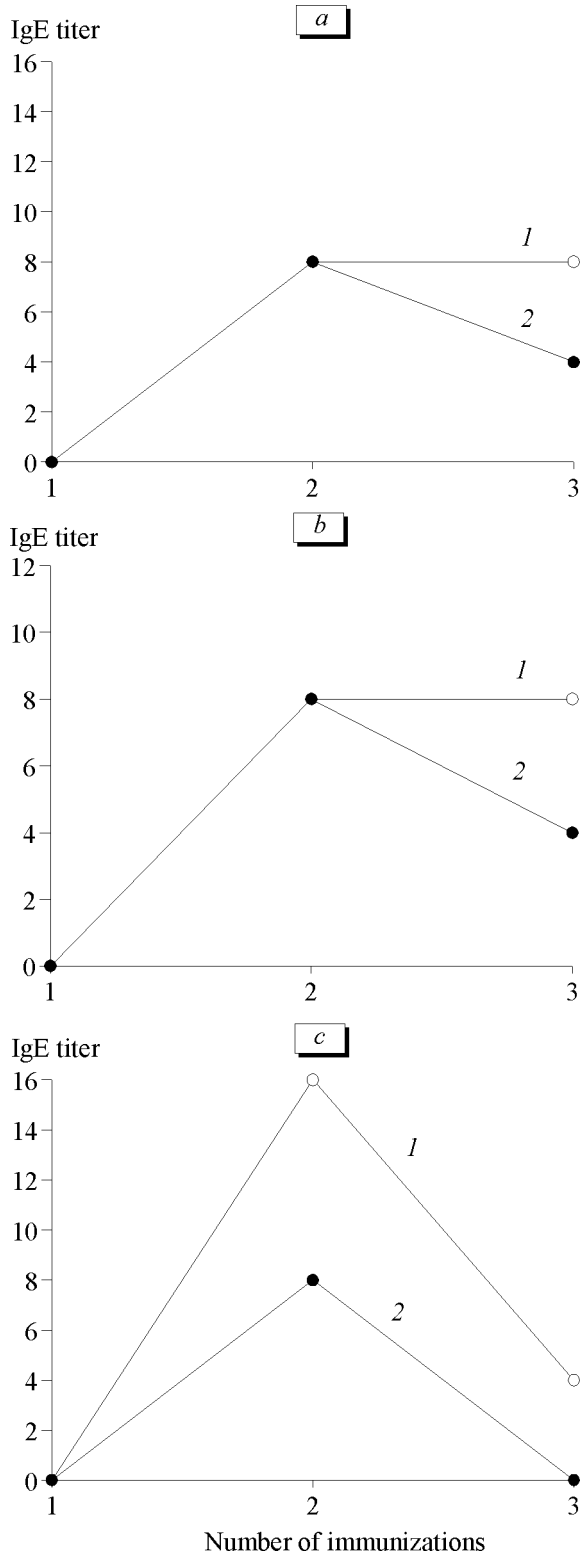

Fig. 1. Effect of potentiated antibodies to histamine (PAB-H) on IgE production induced by immunization of mice with ovalbumin in doses of 0.5 (*a*), 10 (*b*), and 100 μg (*c*). Here and in Fig. 2: distilled water (control, *1*) and PAB-H (*b*).

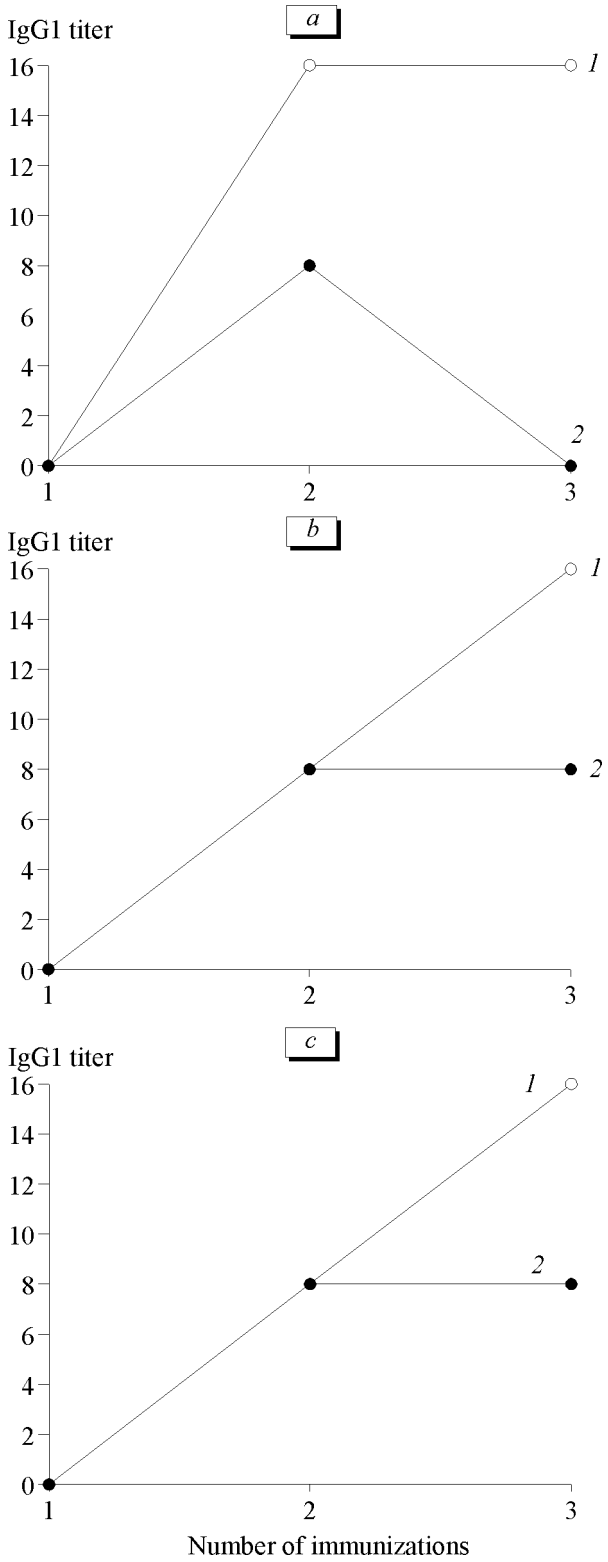

Fig. 2. Effect of PAB-H on IgG1 production induced by immunization of mice with ovalbumin in doses of 0.5 (*a*), 10 (*b*), and 100 μg (*c*).

immunization of animals with the antigen in a dose of 100 mg (Fig. 1, *c*).

The course of treatment with PAB-H suppressed production of OVA-specific IgG1 in mice 3-fold immunized with the antigen in various doses (Fig. 2). In animals receiving the antigen in a dose of 0.5 mg, PAB-H inhibited IgG1 production after the second immunization (Fig. 2, *a*).

Our results indicate that administration of PAB-H to experimental animals suppresses production of OVA-specific IgG1 and IgE. These data suggest that anti-anaphylactic activity of PAB-H is associated with their ability to suppress production of allergen-specific antibodies.

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