EXPERIMENTAL REPRODUCTION OF THE PHENOMENON OF IMMUNOLOGICAL UNRESPONSIVENESS TO FORMALDEHYDE, A RELATIVELY WEAK CHEMICAL ALLERGEN

L. A. Dueva

UDC 612.017.1:612.015

The phenomenon of tolerance and suppression of sensitization to formaldehyde was reproduced in experiments on adult guinea pigs by injecting the pure hapten or its conjugation products with homologous and heterologous serum proteins into the heart. A narrow range of doses of formaldehyde was shown to induce the opposite effect: resensitization in a dose of 500 μg, tolerance in a dose of 1000 μg, a weak tolerogenic effect with a predominantly toxic action in a dose of 3000 μg.

Because of current interest in the question of specific hyposensitization to chemical allergens experiments were carried out on 190 adult guinea pigs to reproduce the phenomenon of tolerance and suppression of sensitization to formaldehyde, using the pure hapten and its conjugation products with protein as the inducing agent.

EXPERIMENTAL METHOD AND RESULTS

The experimentally developed optimal scheme for the reproduction of tolerance to formaldehyde consisted of a single injection of the agent into the heart, followed (8-14 days later) by sensitization of the animals by 20 epicutaneous applications of a 4% solution of formaldehyde. The effect was read on the 34th day of the experiment. Conjugation products of formaldehyde with homologous and heterologous proteins were prepared by adding the hapten ex tempore to dilute guinea pig complement and to fresh rabbit serum in the ratio of 1:100 (sufficient to bind the whole of the hapten). The doses for injection into the guinea pig's heart were 500, 1000, 3000, and 15,000 μg for formaldehyde and 500 and 1000 μg (as formaldehyde) for the conjugation products. The phenomenon of suppression of sensitization was reproduced in animals previously sensitized by epicutaneous application of formaldehyde and by a single injection of the hapten into the heart in doses of 500 and 1000 μg. The degree of allergy was determined by skin tests with one drop of 1% formaldehyde solution and by specially devised tests for this hapten based on lysis of leukocytes in vitro [2] and from changes in the optical density of the plasma [1].

Animals sensitized by a similar cycle or receiving an injection of formaldehyde into the heart, together with intact animals, were used as the control.

The optimal tolerogenic effect was observed after intracardiac injection of the hapten in a dose of 1000 μg: absence of reaction of contact hypersensitivity (assessed at 2.4 points in the sensitized control animals), an intensity of lysis of leukocytes not exceeding the nonspecific reaction of the intact animals (9.1 and 9.2%), complete suppression of antibody formation (with the appearance of antihapten antibodies in the sensitized animals (45% of cases). An increase in the dose of formaldehyde to 3000 μg weakened the tolerogenic effect and led to a progressive increase in the intensity of the toxic action with an increase in the dose (to 15,000 μg): contact hypersensitivity assessed at 1.2 points, intensity of lysis of leukocytes 18%, antihapten antibodies in 16% of the animals. Meanwhile injection of 500 μg hapten caused transient but sig-

Immunological Laboratory, Institute of Work Hygiene and Occupational Diseases, 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. 77, No. 2, pp. 67-69, February, 1974. Original article submitted June 29, 1972.

nificant resensitization: contact hypersensitivity 3.55 points, lysis of leukocytes 37%, antihapten antibodies in 60% of animals. The use of conjugation products of the hapten with serum proteins as the agent evoked an effect similar to that of the corresponding doses of the pure hapten: suppression of development of sensitization (in a dose of 1000 μg) or resensitization (in a dose of 500 μg). The facts that the protein conjugation products and the hapten were equivalent in their action and that the character of the protein carrier did not influence the degree of the effect can most likely be explained by loss of species-specificity of the proteins because of the high reaction-inducing activity of formaldehyde. In the experiments to suppress sensitization, 6 h after its administration, formaldehyde in a dose of 1000 μg caused complete, and in a dose of 500 μg it caused partial (1.4 points) suppression of contact hypersensitivity, followed by a gradual increase to 24 h (to 1 and 1.8 points, respectively). No antihapten antibodies were detected regardless of the time of action or dose of the tolerogenic agent.

The narrow range of doses of formaldehyde inducing opposite effects (resensitization in a dose of 500 μg, tolerance in a dose of 1000 μg, manifestation of toxicity in doses above 3000 μG) is linked with the high toxicity and relatively weak allergenic activity of this hapten. Comparison of the results with those of the control experiments (sensitization and intracardiac injection of different doses of formaldehyde) suggests that the phenomenon of immunological unresponsiveness is one of immunological paralysis or overloading as a result of the action of the hapten in doses close to the threshold of its toxic action.

LITERATURE CITED

1. R. Hoigne, Schweiz, Med. Wschr., 91, 1148 (1961).
2. H. Pettit, H. Sullivan, and E. Hurt, J. Allergy, 31, 30 (1961).