# THE EFFECT OF DIPHENHYDRAMINE HYDROCHLORIDE ON SPECIFIC IMMUNOLOGICAL REACTIONS IN ANAPHYLACTIC SHOCK (EXPERIMENTS IN VITRO)

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V. K. Kozlov

Division of Immunology (Head, Active Member AMN SSSR N. N. Zhukov-Verezhnikov), Institute of Experimental Biology (Director, Professor I. N. Maiskii), of the AMN SSSR, Moscow
(Presented by Active Member AMN SSSR N. N. Zhukov-Verezhnikov)
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In the study of the mechanisms of allergic reactions investigations of considerable value may be carried out with the use of antihistamines—synthetic antihistamine drugs capable, not only of depressing the toxic action of histamine on the tissues, but also of inhibiting the development of allergic reactions.

The mechanism of the protective action of this group of drugs in anaphylactic shock has so far received little study. The investigation of the action of antihistamines on specific immunological reactions, in particular, is far from complete. The data given in the literature are extremely contradictory. Some workers [2, 5] have found experimentally that antihistamine drugs prevent the reaction between antigen and antibody. Others found that these drugs had no effect whatever on the reactions of immunity [3, 4]. It has also been demonstrated [1] that the antihistamine drug diphenhydramine hydrochloride (dimedrol) has a powerful inhibitory action on the Arthus phenomenon while not affecting the process of antibody production.

The object of the present investigation was to study the effect of dimedrol on the specific immunological reactions of the organism. Attempts were made to determine the action of dimedrol on the complementary activity of the sera and on the antibody titer in vivo, and also to study the action of this drug on the antigen—antibody reaction and on the fall in the titer of antibodies and complement in the blood of the animal associated with this reaction.

## EXPERIMENTAL METHOD

Experiments were carried out on male rabbits weighing 2.5-3 kg. The animals were sensitized intravenously with normal horse serum in the form of 3 injections, each of 1 ml, over a period of 7 days. Eight days after the last injection of antigen the antibody titer was determined. In nearly all the animals a high titer of precipitins (1:1000-1:10,000) was observed in the blood at this time.

After this preliminary experiment all the sensitized animals were divided into 3 groups. In the experiments with the 1st group of rabbits (8 animals) the action of dimedrol was studied on the complement level and the antibody titer in the blood, and in the experiments with the 2nd group of rabbits (24 animals) its action was studied on antigen—antibody reaction taking place in vivo; the 3rd group (19 animals) acted as controls. Accordingly, the rabbits of the 1st group received only dimedrol, those of the 2nd group—dimedrol and antigen (horse serum), and those of the 3rd group—antigen only. Dimedrol was injected subcutaneously into the abdominal wall in a dose of 20-40 mg/kg. The antigen was injected in a dose of 1.0-1.5 ml/kg. In one series of experiments intraperitoneal injection of horse serum was combined with its intravenous injection.

The titers of antigen and complement in the rabbits' serum were determined before and 30 min, 2 h, and 3 h after injection of dimedrol or antigen into the animal. Blood for obtaining serum was taken from the heart. In all the experiments the ring-precipitation reaction was used to determine antibodies. Complement was titrated by the usual method on the day of the experiment.

Changes in Titer of Complement and Precipitins in Blood of Sensitized Rabbits after Injection of Antigen and Dimedrol

| Group of animals | Number of animals | | | | | | |
|---|---|---|---|---|---|---|---|
| | Total | With complement titer | | With precipitin titer | | | |
| | | Reduced to zero | Unchanged | Reduced to zero | Reduced by 90-99% | Reduced by 50-67% | Unchanged |
| 1 | 8 | — | 8 | — | — | — | 8 |
| 2 | 24 | 19 | 5 | 11 | 3 | 3 | 7 |
| 3 | 19 | 15 | 4 | 11 | 1 | 1 | 6 |

## EXPERIMENTAL RESULTS

Injection of dimedrol had no significant effect on the complement level or the precipitin titer. Both indices remained unchanged throughout the period of observation, i.e., for 3 h from the moment of injection of the drug (see table).

The object of the next series of experiments was to determine whether the antianaphylactic action of dimedrol is associated with its activity against specific immunological reactions and, in particular, with its inhibitory effect on the antigen–antibody reaction. For this purpose, the dynamics of the changes in the titers of precipitins and complement was studied in the course of ordinary anaphylactic shock (control determinations) in the first place, and the same immunological indices were then studied in anaphylactic shock occurring after the preliminary injection of dimedrol into the animal.

The observations showed that in the course of ordinary anaphylactic shock caused by intraperitoneal injection of horse serum into the animal, the titers of precipitins and complement in most cases fell. This fall subsequently presented a convenient model for studying and comparing the effect of dimedrol on the character of the changes in complement and precipitins caused by injection of the specific antigen (see table).

The fall in the titers of complement and precipitins was observed in approximately the same percentage of cases in the group of rabbits receiving injections of antigen alone and in the group receiving dimedrol in addition to antigen. The difference between the values obtained in the experimental and control groups was not statistically significant. These facts demonstrate that the drug does not affect the reaction developing in vivo between antibodies and an injected exogenous antigen, i. e., it neither depresses nor inhibits this reaction.

## LITERATURE CITED


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