COMPARATIVE EFFECT OF ACTINOMYCIN D, IMURAN, AND HYDROCORTISONE ON INTERFERON AND ANTIBODY FORMATION IN MICE

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When actinomycin D was used as an immunodepressant in a dose of 2.5 mg/kg, interferon formation was reduced by 16 times compared with the control and antibody production was completely suppressed. Hydrocortisone, in a dose of 100 mg/kg body weight, also reduced interferon production by 16 times, but antibody formation against Newcastle disease virus was undisturbed. Hydrocortisone affects the formation of antiviral immunity in a similar way to antilymphocytic serum, whereas the action of actinomycin D can be compared with that of x-ray irradiation and imuran, suggesting heterogeneity of the population of interferon-producing cells in the body.

KEY WORDS: immunodepressants; heterogeneity of interferon-producing cells.

In comparative experiments the writers showed previously that the processes of interferon and antibody formation differ in their sensitivity to the action of the same doses of various immunodepressants. For instance, antilymphocytic serum (ALS), while inhibiting interferon formation, did not affect antibody formation [1]. Meanwhile the process of antibody formation proved to be more sensitive to the action of x-ray irradiation and imuran [2, 3] than interferon formation.

In connection with these differences it was decided to study the effect of the same doses of other immunodepressants and to compare then with the effect of imuran on interferon and antibody formation.

Corticosteroids are known to activate virus infections but, at the same time, not to affect specific antibody formation [6]; however, the action of hydrocortisone on interferon and antibody formation has not been compared in the same model.

This paper describes the results of a study of the effect of actinomycin D, hydrocortisone, and imuran on the formation of the factors of antiviral immunity.

EXPERIMENTAL METHOD

Mice weighing 18-20 g were used; Newcastle disease virus (NDV), vaccine strain H, was used to induce interferon and antibody formation. The methods of induction and of determining interferon activity and antibodies were described previously [2, 3]. Actinomycin D was injected intravenously into the mice in a dose of 2.5 mg/kg, in a volume of 0.2 ml, in one injection 2 h before the virus. Hydrocortisone (Roussel) was injected into the mice in a dose of 100 mg/kg, in a volume of 0.35 ml, intraperitoneally 24 h before the virus. Antibodies were determined in the blood serum of the animals that survived until the eighth day of observation Imuran was injected in a dose of 1250 mg/kg, as described previously [3].

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TABLE 1. Comparative Sensitivity of Processes of Interferon and Antibody Formation to the Action of Actinomycin D, Hydrocortisone, and Imuran

Treatment	Interferon titers (in units/ml)	Antibody titers in HIT*
NDV	16 382	80—160
Actinomycin D + NDV	1 024	0
Hydrocortisone + NDV	1 024	80—160
Actinomycin D + hydrocortisone + NDV	512—1024	0
Imuran + NDV	512	0

*Hemagglutination inhibition test.

EXPERIMENTAL RESULTS AND DISCUSSION

The toxic lethal dose of actinomycin D and hydrocortisone for mice was determined in preliminary experiments.

These showed that injection of actinomycin D in a dose of 5 mg/kg into mice caused 100% mortality of the animals by the fourth day of observation, whereas a dose of 2.5 mg/kg caused death of only 25% of the animals by the eighth day of observation. Accordingly, actinomycin D was used in the experiments in a dose of 2.5 mg/kg. Injection of hydrocortisone did not cause death of the mice.

It was interesting to determine the comparative sensitivity of the processes of interferon and antibody formation to the action of the immunodepressant used.

It will be clear from Table 1 that the immunodepressants used in these experiments caused a sharp decrease in interferon production, especially if used in combinations. However, it should be pointed out that there were differences in the action of actinomycin D and hydrocortisone on antibody formation: Hydrocortisone did not affect antibody production whereas actinomycin D suppressed it completely.

These differences could indicate that the points of application of immunodepressive activity and the mechanism of action of the various substances tested are not identical, and also that the processes of interferon formation and antibody formation differ in their sensitivity to the action of the same doses of immunodepressants. In this case it must be pointed out that under the experimental conditions used the action of hydrocortisone was similar to that of ALS, i.e., it reduced interferon production without eliminating it and without affecting antibody formation, whereas the effect of actionomycin D can be compared with the action of x-ray irradiation and of imuran, which completely suppressed antibody formation but affected interferon production to a lesser degree [1, 3]. These experiments thus confirmed the conclusion that the population of interferon-producing cells is heterogeneous [1, 2].

Immunodepressants are widely used at the present time in clinical practice to prevent graft rejection and to suppress specific cellular immunity (imuran, ALS, actinomycin D, corticosteroids, etc.). However, it is no less widely known that all immunodepressants sharply reduce the resistance of the body to viral, bacterial, and fungal infections, and that they activate latent processes induced by the viruses of herpes and cytomegaly and by oncogenic viruses [4, 5, 7]. The results described above indicate that suppression of interferon and antibody production may be one of the factors contributing to the lowered resistance.

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