

EFFECT OF PREDNISOLONE ON THE PRIMARY IMMUNOLOGIC RESPONSE

L. S. Uteshev, B. V. Pinegin,
A. G. Kalinkovich, and V. V. Lebedev

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Experiments on CBA mice immunized with sheep's erythrocytes showed that prednisolone reduces the number of 19S antibody-forming cells in the spleen if injected before immunization or simultaneously with it. The number of 7S antibody-forming cells fell sharply following administration of prednisolone regardless of when it was injected.

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The use of glucocorticoids to suppress immunologic reactivity of the recipient during transplantation of organs and tissues, and also for the treatment of autoimmune diseases, began a comparatively long time ago [2]. Glucocorticoids, especially cortisone, began to be studied even earlier by cytologists as one cause of reactive inhibition of mitosis during development of the adaptation syndrome [1]. However, until recently there has been no information in the literature concerning the action of corticosteroids on the cellular components of the immunologic response.

The object of the present investigation was to study the action of prednisolone on the number of antibody forming cells synthesizing 19S- and 7S-hemolysins.

EXPERIMENTAL METHOD

Experiments were carried out on CBA mice. The animals were immunized with sheep's erythrocytes (0.2 ml of a 10% suspension intraperitoneally). On the 4th day after immunization the animals were sacrificed, and a cell suspension made from the spleens in Hank's solution (pH 7.5) by squeezing them carefully from an incision in the capsule of the organ. Antibody-forming cells were determined by the method of local hemolysis in agar. Direct, or 19S-plaques, were detected as described in [4]. Indirect cells, forming 7S-antibodies, were identified after incubation for 1 h with rabbit antiserum against mouse 7S-globulins [3].

Prednisolone was injected subcutaneously into the mice as a single dose of 5 mg/kg body weight in series I 24 h before the antigen, in series II together with the antigen, and in series III 24 h after, series IV 48 h, and series V 72 h after the antigen. In series VI the hormone was injected in a dose of 1.25 mg/kg daily for 4 days. The first injection was given simultaneously with the antigen.

Series VII, in which the mice were injected with antigen alone, acted as the control. In each series experiments were carried out on 5 mice.

EXPERIMENTAL RESULTS

On the 4th day, in the spleen of the control mice receiving antigen only, 903.0 ± 19.8 and 389.0 ± 9.6 cells were found, synthesizing 19S- and 7S-antibodies respectively, per million nucleated cells. Under the influence of prednisolone, injected 24 h before or at the same time as immunization, the number of cells synthesizing macroglobulin antibodies fell to 26 and 23.6% respectively of the control level (Fig. 1).

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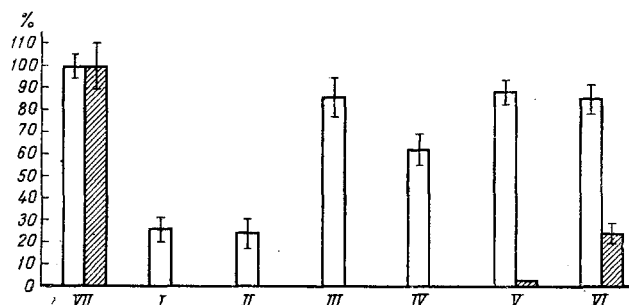


Fig. 1. Effect of prednisolone on number of cells forming 19S- and 7S-antibodies. I, II, III, IV, V, VI, VII) Corresponding series of experiments (times of injection of prednisolone indicated in section "Experimental Method"). Shaded columns correspond to number of cells forming 7S-antibodies; unshaded columns, 19S-antibodies. Number of antibody-forming cells in control (VII) taken as 100%.

4 injections of prednisolone in a dose of 1.25 mg/kg were given, the inhibition of cells forming 7S-antibodies was less marked than after a single injection of the hormone, whereas the number of 19S-cells remained unchanged.

Under the influence of prednisolone, the population of cells forming 7S-antibodies was thus almost totally suppressed regardless of the time of injection of the compound. On the other hand, the times of injection relative to the time of immunization was of great importance for the inhibitory action of the hormone on 19S-cells. Hypoplasia of the lymphoid system of the spleen and the weight of the immunocompetent organs did not correlate with inhibition of the antibody-forming cells (Table 1).

In the modern view, the target organs of glucocorticoids in the body are the lymphoid tissue of the cortical layer of the thymus, lymphocytes of the bone marrow, the germ centers of spleen follicles, and lymph glands. Inhibition of mitosis takes place and, as a result, the population of lymphocytes with a short life span is first reduced. It has been shown that the generation time in a series of antibody-forming cells is 7-8 h. Prednisolone therefore reduces the number of antibody-forming cells to a greater degree than the other lymphoid cells. Some important consequences follow from the strong dependence on time shown in these experiments by the immunodepressive action of prednisolone and the difference in sensitivity of cells forming 19S- and 7S-antibodies to it.

First, cells forming 19S- and 7S-antibodies are evidently not successive stages in the morphogenesis of immunocompetent cells, but different populations of lymphoid tissue cells. Since prednisolone, an anti-mitotic agent, depresses the population of cells forming 7S-antibodies to a rather stronger degree than that forming 19S-antibodies, it can be concluded that an essential stage in the morphogenesis of cells forming 7S-antibodies is mitotic division. Meanwhile, the stage of mitotic division is probably absent in the population of cells forming 19S-antibodies between the receipt of information about the antigen by the cell and the onset of synthesis of the specialized protein (antibodies). A similar conclusion has been reached by other workers [5] who were unable to detect incorporation of thymidine- H^3 into DNA of proliferating cells during synthesis of 19S-hemolysins.

TABLE 1. Effect of Prednisolone on Weight of Immunocompetent Organs, Number of Nucleated Cells in Spleen, and Titers of Circulating Antibodies

Series of experiments	Weight (in mg)		No. of nucleated cells in spleen (in millions)
	thymus	spleen	
I	50,0 \pm 1,2	77,0 \pm 1,9	79,6 \pm 1,4
II	36,2 \pm 1,8	164,0 \pm 2,8	46,9 \pm 0,9
III	34,6 \pm 2,4	88,2 \pm 1,8	74,5 \pm 2,9
IV	36,6 \pm 1,3	91,0 \pm 2,6	59,5 \pm 1,3
V	47,0 \pm 1,1	82,7 \pm 1,2	68,7 \pm 2,1
VI	32,2 \pm 2,1	95,2 \pm 3,4	81,9 \pm 4,2
VII	28,0 \pm 2,1	95,0 \pm 3,1	63,1 \pm 4,2

Meanwhile the cells forming 7S-hemolysins were completely suppressed. In other series, in which a single injection of prednisolone was given, relatively weak inhibition of cells synthesizing 19S-antibodies was found, accompanied by complete inhibition of cells synthesizing 7S-antibodies. In the experiments of series VI, in which

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