

ACTION OF HOMOLOGOUS GLOBULIN ON THE PLASMA-CELL REACTION IN THE LYMPH GLANDS

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Few attempts have been made to study how the constant level of the serum globulins is maintained, how the synthesis of these proteins is controlled, and what are the mechanisms of regulation of homeostasis of the cells forming the lymphoid tissue system. Only isolated information is available concerning the stimulation of the plasma-cell reaction by the somatotrophic hormone of the pituitary and its depression by cortisone. The probable stimulation of maturation of the plasma cells by the action of thymus hormone has also been noted [2].

In the present investigation the effect of the serum globulin level on the plasma-cell reaction was studied.

EXPERIMENTAL METHOD

The total globulin fraction was precipitated from rats' serum by 50% saturation and the albumin fraction by 100% saturation with ammonium sulfate. Before they were injected into animals, the preparations of globulin and albumin were made equal in their protein content.

Each experiment was carried out on 3 groups of rats. The animals of group 1 (5 rats) received an injection of globulin, those of group 2 (4 rats) — albumin, and group 3 (4 rats) — physiological saline.

In series I there were 3 experiments (Nos. 1, 3, and 5). The rats received injections of 0.1-0.5 ml of globulin into the right hind limb and 2.4-4.5 ml intraperitoneally. After an interval of 2.5 h, 0.1 ml of Freund's adjuvant was injected into the same limb and 2.5-4.5 ml of globulin was injected intraperitoneally. During the next three days the animals received globulin three times daily by injection into the limb and intraperitoneally. In experiment No. 1 each rat received injections of 505 mg globulin, in experiment No. 3 1012 mg, and in experiment No. 5 884.4 mg globulin. The same scheme was used for the injections of albumin and physiological saline.

In the experiments of series II 0.1 ml of Freund's adjuvant was injected into the right hind limb, and 5 days later globulin was injected into the same limb in doses of 1 ml every 3 h for 2 days. Altogether in experiment No. 2, 197 mg of globulin was injected, and in experiment No. 4 the animals received 277 mg. The rats were sacrificed on the 4th day after the beginning of the experiment in series I and on the 7th day in the experiments of series II. Impression preparations were made from the right and left popliteal lymph glands, and the retroperitoneal and paratracheal lymph glands. The preparations were fixed with methyl alcohol and stained with azure II eosin. In the preparations from each gland the reticulum cells, the total number of blast cells, the plasmablasts, and plasma cells [1] were counted in 30 fields of vision (objective 90, ocular 7). The significance of the results obtained was calculated by Student's method.

EXPERIMENTAL RESULTS

In experiment No. 1, in the rats receiving globulin (505 mg) 28 blast cells and 25 plasmablasts were found in the popliteal lymph gland, while the corresponding figures for the rats receiving albumin were 36 and 30 cells, and for the rats receiving physiological saline 38 and 44 cells. All that can be concluded from the results of this experiment is that there was a tendency for the immature forms of the plasma-cells series to be depressed by the excess of homologous globulin.

In experiment No. 3, the excess of globulin depressed the appearance plasma cells in the stimulated popliteal gland; 62 cells were present in the "globulin" group, 141 in the rats receiving albumin, and 246 cells in the rats receiving physiological saline. The number of plasmablasts and of blast cells was also reduced. The depression of

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Cells	Lymph gland														
	Right popliteal					Retroperitoneal					Paratracheal				
	globu- lin (1st)	albu- min (2nd)	I - P be- tween 1st and 2nd	physiolog- ical saline (3rd)	I - P be- tween 1st and 3rd	globu- lin (1st)	albu- min (2nd)	I - P be- tween 1st and 2nd	physiolog- ical saline (3rd)	I - P be- tween 1st and 3rd	globu- lin (1st)	albu- min (2nd)	I - P be- tween 1st and 2nd	physiolog- ical saline (3rd)	I - P be- tween 1st and 3rd
Reticulum cells	289	316	0.153	320	0.430	263	258	0.796	273	0.602	410	289	0.999	431	0.228
Blast cells	51	21	0.890	22	0.839	42	52	0.602	13	0.986	59	87	0.789	22	0.930
Plasmablasts	17	19	0.368	6	0.789	18	23	0.687	5	0.979	16	40	0.860	9	0.430
Plasma cells	184	367	0.947	277	0.969	287	521	0.987	199	0.816	165	420	0.995	278	0.920

Legend: I – P = criterion of statistical significance of difference between groups (after Student). The difference is statistically significant if $I - P$ is not less than 0.950.

the cells of the plasma-cell series was particularly marked in the paratracheal gland: 39 blasts were present in the "globulin" group and 106 blasts in the "albumin" group, while the number of plasmablasts was 18 and 30, and the number of plasma cells 216 and 458 in the two groups respectively.

In experiment No. 5 a marked decrease was found in the number of plasma cells under the influence of the excess of globulin in all three lymph glands investigated, and a small decrease was observed in the number of blast cells and plasmablasts (see the table).

In experiments Nos. 2 and 3 the globulin, which was injected at the moment of maximal development of the plasma-cell reaction, caused a decrease in the number of cells of the plasma-cell series both in the regional and in the distant lymph glands. In the paratracheal lymph gland of the "globulin" group 21 blast cells,⁴ plasmablasts, and 117 plasma cells were found, with 40, 11, and 407 cells correspondingly in the "albumin" group, and 39, 7, and 247 cells in the group of rats receiving physiological saline.

In experiment No. 2 serum was taken from the rats for estimation of the concentration of globulins and albumin by the method of electrophoresis on paper. Injection of 1012 mg globulin into the rats did not cause hyperproteinemia: it was very quickly removed from the circulating plasma.

Several authors [3-7] have succeeded in suppressing the primary immunological response by the passive injection of specific serum. It was interesting to examine the formation of antibodies in the presence of an excess of homologous globulin. In preliminary experiments a lower titer of antibodies against sheep's erythrocytes was obtained in rats receiving an injection of a large dose of globulin at the same time as the antigen. The difference between the antibody titers in the "globulin" and the control ("albumin") group was statistically significant.

Evidently mechanisms controlling the plasma protein concentration begin to act in rats injected with large doses of globulin, the number of cells producing γ -globulin both in the regional lymph glands for the site of injection and in remote lymph glands is reduced, the rate of synthesis of globulins by the animal itself falls, and an intensified destruction of the injected globulin begins. Whether the injected globulin acts directly on the producing cells or whether it has other methods of action is unknown.

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