THE MECHANISM OF ACTION OF CORTISONE IN EXPERIMENTAL HYPERSENSITIVITY

II. Hypersensitivity of the Serum Sickness Type*

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Plates 1 and 2

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Several studies have indicated that cortisone and ACTH may inhibit the cardiovascular and renal lesions which ordinarily develop in rabbits following large intravenous injections of foreign protein. Rich and coworkers (1–3) reported a reduction in the incidence of both the cardiovascular and renal lesions in rabbits receiving horse serum and treated with ACTH or cortisone. Seifter and colleagues (4) found that cortisone inhibited the development of the cardiovascular lesions but did not prevent the occurrence of renal lesions in rabbits receiving horse serum. However, Moll and Hawn (5) found that the renal lesions which ordinarily develop in rabbits following the injection of bovine gamma globulin were inhibited by ACTH or cortisone.

At present, the mechanism by which ACTH and cortisone produce these effects is poorly understood. Inhibition of antibody formation, interference with antigen-antibody combination, and suppression of the inflammatory reaction resulting from antigen-antibody combination are possible explanations. In previous studies (6, 7) it was demonstrated that cortisone and ACTH suppress the appearance of circulating antibody in rabbits receiving intracutaneous injections of antigen. Further, it was shown that the inhibition of the Arthus reaction by cortisone, both in rabbits (7) and in guinea pigs (8), depended on the hormonal suppression of circulating antibody.

There is conflicting evidence regarding the ability of cortisone to alter antibody formation following large intravenous injections of foreign protein. Rich and coworkers (1–3) reported that neither cortisone nor ACTH influenced the precipitin titer (antigen dilution method) in rabbits receiving horse serum intravenously. However, Moll and Hawn (5) found that although ACTH did not inhibit antibody formation, cortisone entirely suppressed the appearance of circulating antibody in rabbits receiving an intravenous injection of bovine

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gamma globulin. The studies by Rich and coworkers suggest that the lesions of serum sickness may be inhibited by cortisone or ACTH despite the presence of antibody as measured by the occurrence of both Arthus reactions and circulating precipitins.

Recently it was demonstrated in this laboratory that the administration of crystallized bovine albumin to rabbits produces a consistently large number of cardiovascular, renal, and lymphoid tissue lesions (9). The occurrence of these lesions was correlated with the "immune" phase of antigen elimination. This experimental procedure provided a method by which the relationship between immune response and development of tissue lesions under various conditions could be accurately ascertained. The present paper describes the action of cortisone in modifying the immunological and histological changes in rabbits that had received a single intravenous injection of bovine albumin.

Material and Methods

Crystallized bovine plasma albumin (Armour and Co.) was dissolved in 0.85 per cent saline to form a 10 per cent solution. The pH was brought to 7.4 by the addition of solid sodium bicarbonate.

Cortisone acetate was obtained from Merck and Co., Inc., in a saline suspension containing 25 mg. per ml.

A series of 60 white male rabbits weighing approximately 2 kg. were used as follows: 25 rabbits were injected intravenously with 0.5 gm. of bovine albumin. 25 rabbits were injected intravenously with 0.5 gm. of bovine albumin and were treated with single daily intramuscular injections of 10 mg. of cortisone acetate for 10 days and 5 mg. of cortisone acetate for 2 additional days. 10 rabbits were kept under the same conditions as the above experimental animals but received neither bovine albumin nor cortisone acetate.

Samples of blood of 5 ml. volume were taken from the marginal ear veins of 15 of the 25 control rabbits, 15 of the 25 cortisone-treated rabbits, and 5 of the 10 normal rabbits at 5 minutes and 2, 4, 6, 8, and 10 days after the injection of albumin. The sera from these samples, and others taken at the time of sacrifice, were used to determine the rate of antigen elimination and the time of antibody appearance.

Serum was removed from the specimens of clotted blood within 24 hours after collection and stored in the frozen state at −15°C. until the day of use. The sera from 5 cortisone-treated animals bled on the 12th day were markedly lipemic; the lipid was removed from these by centrifugation at 24,000 *G* for 1 hour. Repeated freezing and thawing of the serum was found to facilitate separation of lipid during centrifugation. This procedure did not affect the antibody or antigen content of non-lipemic sera treated in the same way.

Qualitative tests for the presence of antigen were carried out on each sample of unknown serum. This was done by layering 0.2 ml. of the unknown sample over 0.2 ml. of a pooled antiserum of high titer obtained from rabbits immunized with alum-precipitated crystallized bovine albumin. When this test was positive, a quantitative determination of the antigen concentration in the unknown serum was made by the addition of 1 ml. of an appropriate dilution of the serum to 1 ml. of a pooled antiserum. The resulting precipitate obtained after 48 hours in the cold was washed twice with cold saline and analyzed for nitrogen by the Kjeldahl technique (10). A positive test for excess antibody in the supernatant fluid from the unknown was accepted as proof of complete antigen precipitation. After the nitrogen content of the antigen-antibody precipitate had been determined, the amount of antigen

nitrogen in the precipitate was obtained by reference to a standard precipitin curve of the particular pooled antiserum employed. This curve was constructed from data representing the amounts of precipitate formed by the addition of known quantities of antigen to 1 ml. portions of the pooled antiserum. In every determination, the dilution of the unknown serum was chosen so that the nitrogen content of the precipitate formed by the addition of the pooled antiserum fell on the relatively straight mid-portion of the curve. At this portion of the curve small increments in the amount of antigen are reflected in large increments of total precipitate. The antigen values obtained from the curve were multiplied by the dilution factor of the original sample to obtain the antigen concentration of the unknown serum.

Qualitative tests for the presence of antibody were made by the addition of 4 μg. of antigen N in 0.2 ml. of saline to 0.5 ml. of the unknown serum. When the tests for antibody were positive, quantitative determinations of antibody were performed. Antigen in increments of 2 or 4 μg. of nitrogen was added to 1 ml. of unknown serum until no further precipitation was observed.[1] Antibody nitrogen was calculated by subtraction of the antigen N from total nitrogen found by analysis of the washed precipitate. All serological procedures were carried out at 0–5°C. and were made in duplicate.

One day prior to the day of sacrifice all animals were skin-tested with 1 mg. of antigen in 0.2 ml. of saline. The rabbits were sacrificed by exsanguination and air embolism 12 days after the single intravenous injection of albumin. Histological study included examination of the lungs, heart, thymus, esophagus, thyroid, liver, spleen, pancreas, mesenteric lymph nodes, adrenals, kidneys, testes, intestine, psoas muscle, and skin from the site of the skin test. The kidneys, liver, adrenals, and spleen were weighed. Pieces of tissue were fixed either in 10 per cent formalin or in formalin followed by postchromation in 3 per cent potassium dichromate. Hematoxylin-azure-eosin and hematoxylin-eosin were used for routine staining of tissue sections. Sections of kidneys were stained by the periodic acid–Schiff method in order to study the glomerular basement membranes (11).

EXPERIMENTAL RESULTS

(*a*) *Effect of Cortisone on Allergic Lesions.*—The autopsy findings observed in the bovine albumin–injected controls are detailed elsewhere[2] and are summarized in Table I. These findings consisted of a marked arteritis in 28 per cent (7/25) of the animals; subendothelial leucocytic infiltration in the pulmonary arteries or ascending aorta in 72 per cent (18/25); and endocarditis affecting either the aortic or mitral valves in 54 per cent (13/24); a glomerulonephritis in 80 per cent (20/25); and granulomatous lesions in the spleen and lymph nodes in 83 per cent (20/24) and 50 per cent (8/16) respectively of the rabbits. None of these lesions were present in the normal animals. In 44 per cent (11/25) of the rabbits receiving albumin focal collections of lymphocytes and monocytes were seen in the myocardium. Similar lesions were observed in 10 per cent (1/10) of the normal rabbits.

The cortisone-treated group showed far fewer cardiovascular and renal lesions than the untreated animals. None of the cortisone-treated rabbits developed

[1] The error involved in the precipitation of antibody by successive addition of antigen instead of by the single addition of the required amount of antigen is discussed in reference 6.

[2] Data from this group of animals were included in reference 9. Observations on both the control and treated groups of animals were done at the same time.

arterial lesions. A slight endocarditis was present in 4 per cent (1/23) of the animals and 4 of 23 animals (17 per cent) showed a glomerulonephritis of slight

TABLE I

Immunological and Histological Findings in Rabbits 12 Days after Intravenous Injection of 0.5 Gm. of Bovine Plasma Albumin

Rabbit No.	Antigen or antibody nitrogen, per ml of serum*	Arthus reaction‡	Subendothelial infiltrations	Arteritis	Endocarditis	Glomerulonephritis§	Granulomatous lesion in	
							Spleen§	Lymph node
	μg.							
32	96 At	0	0	0	0	0	0	0
38	68 At	0	0	0	0	0	+	—
49	51 At	0	+	0	0	0	++	0
41	45 At	0	0	0	0	0	0	—
42	43 At	0	+	0	0	++	+++	+
44	43 At	0	0	0	0	+	++	+
45	39 At	0	+	0 (phlebitis of hepatic veins)	0	++	+++	+
46	30 At	0	+	+ stomach, acute	+	++	++	—
29	30 At	0	+	+ lung, acute	+	+++	+++	0
47	26 At	0	+	+ heart, mesentery, acute	+	+	+++	—
50	25 At	0	0	0	0	0	++	+
36	15 At	0	+	0	0	+++	+++	—
34	15 At	0	+	+ lung, acute	+	+++	+++	0
28	12 At	0	+	0	+	+++	++	+
30	8 At	0	+	0	+	+++	+	0
35	5 At	0	+	0	0	+++	+++	+
31	0	0	0	0	—	+++	++	0
26	11 Ab	0	+	0	+	+++	+	0
40	29 Ab	0	0	+ heart, acute	+	+++	+++	—
37	32 Ab	1.2 h	+	+ spleen, heart, peripancreatic, acute	+	+++	++	+
27	35 Ab	3.6 h	+	0	+	+++	0	0
39	75 Ab	4.8 h	+	0	+	+++	0	—
33	86 Ab	1.7 h	+	0	+	++	+	+
48	149 Ab	1.9 h	+	0	0	++	—	—
43	—	—	+	+ heart, acute	+	+++	+++	—
Total...25		5(21%)	18(72%)	7(28%)	13(54%)	20(80%)	20(83%)	8(50%)

* At = antigen; Ab = antibody.

‡ Product of length, width, and height measured in centimeters. h = hemorrhagic.

§ Alterations in kidney and spleen are graded 1+ to 3+.

to moderate severity. One of the 23 animals contained focal accumulations of mononuclear cells in the myocardium. These results are summarized in Table II.

The granulomatous lesions in the spleens were considerably smaller and less abundant in animals receiving cortisone (Fig. 1). However, in contrast to the low incidence of cardiovascular and renal lesions, the percentage of animals

showing some lesion in the spleen was about the same in the treated group as in the controls. The lesions were morphologically similar in the two groups and consisted of an accumulation of epithelioid and occasional giant cells in the

TABLE II

Immunological and Histological Findings in Rabbits Receiving Bovine Plasma Albumin and Treated with Cortisone

Rabbit No.	Antigen or antibody nitrogen per ml. of serum*	Arthus reaction‡	Subendothelial infiltrations	Arteritis	Endocarditis	Glomerulonephritis§	Granulomatous lesion in	
							Spleen§	Lymph node
	μg.							
6	44 At	0	0	0	0	0	+	—
24	44 At	0	0	0	0	0	++	—
11	41 At	0	0	0	0	0	++	—
17	41 At	0	0	0	0	0	++	—
8	39 At	0	0	0	0	0	+	—
4	34 At	0	0	0	0	0	++	—
5	34 At	0	0	0	0	0	++	—
23	34 At	0	0	0	0	0	0	—
20	31 At	0	0	0	0	0	0	—
14	30 At	0	0	0	0	0	++	0
15	27 At	0	0	0	0	0	++	0
2	19 At	0	0	0	0	0	+	0
3	18 At	0	0	0	0	0	+	0
22	18 At	0	0	0	0	0	+	0
1	9 At	0	0	0	0	0	0	0
10	5 At	0	0	0	0	+	+	—
19	2 At	0	0	0	0	0	+	—
25	5 Ab	0.8 p	0	0	0	+	+	—
12	25 Ab	0	0	0	0	+	+	—
16	26 Ab	0	0	0	0	++	0	—
13	30 Ab	0.8 p	0	0	0	0	0	—
21	57 Ab	0.9 h	0	0	+	0	0	—
7	—	—	0	0	0	0	0	—
Total..23			0	0	1(4%)	4(17%)	16(70%)	0

* At = antigen; Ab = antibody.

‡ Product of length, width, and height measured in centimeters. h = hemorrhagic; p = pink.

§ Alterations in kidneys and spleen graded 1+ to 3+.

splenic follicles (Fig. 2). Since the lesions in the spleen are confined to the lymphoid follicles, their smaller size may have been due in part to the cortisone-induced atrophy of the Malpighian follicles. Chiefly as a result of the loss of the lymphoid tissue, the spleens of the untreated animals weighed on the average only one-half as much as those of the control animals (Table V).

In addition to the granulomatous lesions, the change in the lymphoid tissue

which ordinarily appears following exposure to foreign protein (12) was present in both the treated and control groups of animals. This alteration was evidenced by the occurrence of large lymphoblasts and lymphoid cells in mitosis in the splenic follicles and the adjacent pulp (Fig. 3).

TABLE III

Serum Antigen and Antibody Levels in Rabbits Receiving Bovine Albumin

Rabbit No.	Antigen or antibody nitrogen per ml. of serum* at						
	5 min.	2 days	4 days	6 days	8 days	10 days	12 days
	mg.	*mg.*	*mg.*	*mg.*	*mg.*	*mg.*	*mg.*
32	0.840	0.346	0.309	0.220	0.166	0.121	0.096
38	1.06	0.399	0.285	0.208	0.150	0.100	0.068
49							0.051
41							0.045
42							0.043
44							0.043
45							0.039
46							0.030
29	0.885	0.311	0.231	0.170	0.131	0.086	0.030
47							0.026
50							0.025
36	0.890	0.288	0.204	0.150	0.105	0.063	0.015
34	0.940	0.307	0.242	0.179	0.125	0.079	0.015
28	0.710	0.254	0.202	0.143	0.088	0.049	0.012
30	0.750	0.317	0.237	0.151	0.108	0.053	0.008
35	0.750	0.232	0.188	0.141	0.090	0.064	0.005
31	0.650	0.252	0.213	0.138	0.086	0.036	0.000
26	0.950	0.340	0.250	0.181	0.094	0.052	0.011 Ab
40	0.860	0.368	0.242	0.196	0.134	0.076	0.029 Ab
37	1.12	0.304	0.207	0.182	0.101		0.032 Ab
27	0.735	0.284	0.160	0.146	0.043	0.000	0.035 Ab
39	0.775	0.307	0.231	0.171	0.111	0.002	0.075 Ab
33	0.815	0.300	0.206	0.176	0.098	0.036	0.086 Ab
48							0.149 Ab
Median.....	0.840	0.307	0.231	0.171	0.105	0.053	0.015

* Values represent antigen N unless otherwise specified as antibody by abbreviation Ab. Animals are listed in order of decreasing magnitude of serum antigen concentrations or increasing levels of antibody present at time of sacrifice (12 days).

(*b*) *Effect of Cortisone on Antigen Elimination and Development of Antibody.*— The concentration of serum antigen or antibody in each animal at the time of sacrifice is given, together with the histological results, in Tables I and II. In these tables, the animals are arranged in order of decreasing magnitude of serum antigen concentration and increasing levels of serum antibody present at the time of sacrifice, in order to facilitate correlation of the histological and

the immunological findings. The titrations of serum antigen or antibody in 15 control rabbits and 15 cortisone-treated rabbits at various intervals throughout the experimental period are summarized in Tables III and IV, and are

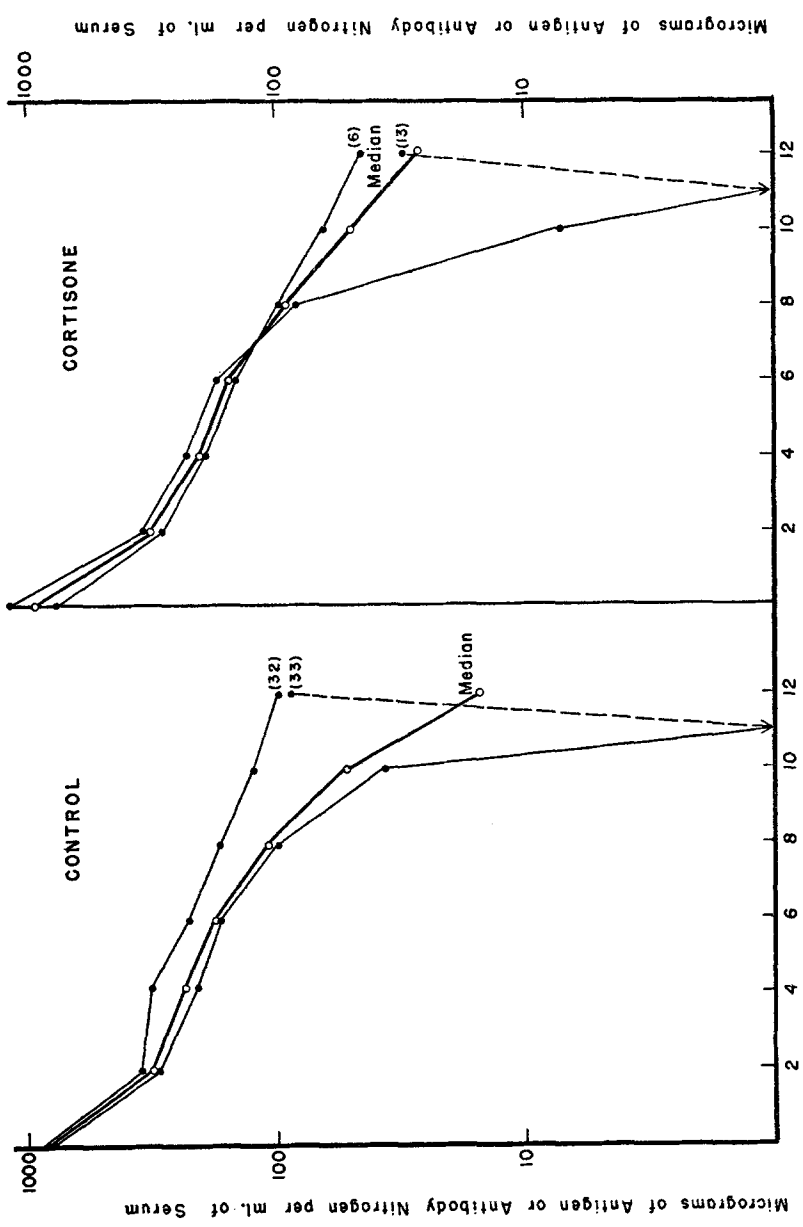
TABLE IV

Serum Antigen and Antibody Levels in Rabbits Receiving Bovine Albumin and Treated with Cortisone

Rabbit No.	Antigen or antibody nitrogen per ml. of serum* at						
	5 min.	2 days	4 days	6 days	8 days	10 days	12 days
	mg.	*mg.*	*mg.*	*mg.*	*mg.*	*mg.*	*mg.*
6	0.750	0.284	0.187	0.141	0.094	0.062	0.044
24							0.044
11	0.975	0.372	0.206	0.163	0.096	0.072	0.041
17							0.041
8	1.00	0.330	0.186	0.160	0.093	0.069	0.039
4	0.775	0.239	0.156	0.122	0.074	0.049	0.034
5	0.925	0.330	0.224	0.143	0.091	0.053	0.034
23							0.034
20							0.031
14	0.975	0.351	0.190	0.155	0.091	0.058	0.030
15	0.850	0.309	0.201	0.198	0.113	0.070	0.027
2	0.665	0.292	0.160	0.121	0.072	0.041	0.019
3	1.18	0.242	0.152	0.088	0.056	0.033	0.018
22							0.018
1	1.13	0.336	0.228	0.138	0.095	0.046	0.009
10	0.775	0.326	0.158	0.111	0.058	0.031	0.005
19							0.001
25							0.005 Ab
12	1.08	0.357	0.234	0.175	0.102	0.026	0.025 Ab
16							0.026 Ab
13	1.23	0.334	0.220	0.167	0.082	0.007	0.030 Ab
21							0.057 Ab
7	0.700	0.246	0.166	0.134	0.073	0.039	D
9	0.800	0.298	0.212	0.158	0.077	D	
18							D
Median.....	0.925	0.326	0.190	0.143	0.091	0.049	0.027

* Values represent antigen N unless otherwise specified as antibody by abbreviation Ab. Animals are listed in order of decreasing magnitude of serum antigen concentrations or increasing levels of antibody present at time of sacrifice (12 days).

presented graphically in Text-fig. 1. In the figure, the median serum antigen concentrations of both the treated and control animals are represented by the middle solid lines. The outer lines are the antigen elimination curves of 2 animals of each group, one showing the highest level of antigen at the time of sacrifice and the other showing the highest level of circulating antibody.



TEXT-FIG. 1. Effect of cortisone on blood clearance of bovine plasma albumin and development of circulating antibody, after data of Tables III and IV. The values for serum antigen (solid line) and for serum antibody (broken line) are plotted semilogarithmically with respect to time after injection of antigen. The median blood clearance of antigen for both the cortisone-treated and control groups of animals is represented by the middle solid line. The curve of the rabbit in each group showing the slowest rate of elimination of antigen (Nos. 32 and 6) and that of the rabbit in each group showing complete elimination of antigen and subsequent development of antibody (Nos. 33 and 13) are also presented. The first phase of antigen elimination represents equilibration of the antigen between the intravascular and extravascular fluid. The second phase between the 2nd and 6th day results from the normal catabolism of antigen by the body, while the third phase beginning after the 6th day, represents increased blood clearance of antigen due to fixation by newly formed antibody (9, 23).

It is evident from an analysis of the tables and the text-figure that the course and rate of antigen elimination were similar in both the treated and untreated animals. In both groups, the disappearance of antigen from the blood showed a characteristic 3 phase pattern consisting of an early phase of rapid antigen loss, a second phase of more gradual antigen disappearance, and a third or so called "immune" phase of accelerated antigen elimination. The presence of a normal third phase of antigen elimination in the cortisone-treated animals is noteworthy since the occurrence of this phase is dependent on antibody production (22, 9). In both groups of animals, there were some animals which eliminated the antigen slowly, probably owing to failure to develop antibody, and others which had eliminated all of the antigen and showed free serum antibody. Approximately equal numbers of animals in each group (7 of 24 controls

TABLE V

Average Weights of Liver, Kidneys, Adrenals, Spleen, and Thymus with Ratios of Each to Average Body Weight

Group	No. of rabbits	Average body weight	Liver		Kidneys		Adrenals		Spleen		Thymus	
			Weight	Organ/Body × 1000 Ratio	Weight	Organ/Body × 1000 Ratio	Weight	Organ/Body × 1000 Ratio	Weight	Organ/Body × 1000 Ratio	Weight	Organ/Body × 1000 Ratio
		kg.	*gm.*		*gm.*		*mg.*		*gm.*		*gm.*	
Cortisone	22	1.62	92±30*	57±18	15.9±2.1	9.8±1.3	104±34	64±21	0.66±0.26	0.41±0.16	0.42±0.16	0.26±0.10
Control	25	2.02	68±13	34± 6	14.0±2.1	6.9±1.0	171±40	85±20	1.65±0.64	0.82±0.32	3.09±0.92	1.53±0.46

* Weight ± S. D.

or 29 per cent and 5 of 22 cortisone-treated animals or 23 per cent) showed free antibody at the time of sacrifice.

(*c*) *A Note on the Anatomic Alterations Produced by Cortisone.*—The anatomic alterations produced by cortisone have been described in a previous publication (13). Similar alterations were encountered in the present experiment. Briefly, these changes consisted of atrophy of the lymphoid tissue of the spleen, mesenteric lymph nodes, and thymus, and marked deposition of glycogen and fat in the liver. These changes were reflected in the average weights of the organs summarized in Table V.

In addition to these changes, a peculiar alteration of the renal glomeruli was noted in some of the cortisone-treated animals. This lesion consisted of marked dilatation and increased tortuosity of some or all of the capillary loops of the glomeruli (Fig. 4). It occurred to a severe degree in 3 animals, to a moderate degree in 7, to a slight degree in 4, and was absent in 9 animals. In the 3 animals with the most severe lesions, several glomeruli in a single section of kidney contained small endocapillary globular masses of homogeneous eosinophilic

and Schiff-positive material, and there were protein casts in the renal tubules. Similar glomerular alterations following treatment with cortisone have been described by Rich and his colleagues (14). It is perhaps pertinent to point out that Cushing noted focal dilatation of cutaneous end-arterioles and capillaries or so called spider telangiectasis in 2 of 12 cases with Cushing's disease (15), and the development of spider telangiectases has been observed following ACTH therapy (16). The mechanism by which these vascular changes occur is not clear. 5 cortisone-treated animals developed a marked lipemia beginning on the 10th day of treatment. There was no apparent relationship between the lipemia and the renal lesions.

DISCUSSION

The results of the present study confirm those of other investigators (1–5) in showing that cortisone may modify the cardiovascular and renal lesions of serum sickness type hypersensitivity which would otherwise develop following the intravenous administration of foreign albumin. Further, the quantitative immunological data clearly demonstrate that cortisone, in the dosage employed, had no effect on the "immune" phase of antigen elimination or on the subsequent appearance of circulating antibody. In previous studies (6, 7) in which sensitization of rabbits was produced by daily intracutaneous injections of small amounts of antigen rather than by a single intravenous injection of a large amount of antigen, cortisone in the same dosages markedly suppressed the appearance of antibody. It is clear that the effect of cortisone depends on the dosage, multiplicity, or route of antigen administration.

It is of interest that cortisone did not reduce the percentage of animals showing the type of granulomatous lesion of the spleen that results from hypersensitivity (9, 23), nor did cortisone suppress the splenic changes which ordinarily develop following exposure to foreign protein (12). The development in the cortisone-treated animals of these splenic alterations which are thought to be indicative of antibody formation is in accord with the immunological findings which indicate that antibody production was unaffected by treatment with cortisone.

Although cortisone inhibited most of the allergic visceral lesions, this hormone had no effect on the development of the Arthus reaction. 5 of 7 control animals (71 per cent) and 3 of 5 cortisone-treated animals (60 per cent) which developed circulating antibody responded with an Arthus reaction to the injection of albumin (Tables I and II). These results corroborate previous work which indicated that suppression of the Arthus reaction by cortisone requires that the appearance of serum antibody be inhibited (6–8).

It is evident that inhibition by cortisone of the cardiovascular and renal lesions in serum sickness type hypersensitivity does not require suppression of antibody production. The mechanism by which cortisone inhibits these visceral allergic lesions is not clear from the present study. It is well known that cortisone

exerts an inhibitory influence on inflammatory reactions produced by a wide variety of stimuli. The possibility exists that inhibition of the lesions of serum sickness may be due to hormonal suppression of allergic inflammation.

Regardless of the mechanism by which cortisone inhibits the visceral allergic lesions, it is clear that the protection is of a limited nature. In previous work from this laboratory (17) it was demonstrated that cortisone markedly suppressed the inflammatory reaction resulting from infection with a slightly virulent pneumococcus, but had no effect on the inflammation produced by a highly virulent strain of this organism. In a comparable way, an inhibition of the allergic inflammatory reaction by cortisone is seen only when the stimulus is small, and is lost when the reaction is severe. Consequently, complete inhibition of the Arthus reaction, in contrast to that of the visceral allergic lesion, requires an additional effect of cortisone, namely a suppression of the appearance of antibody in the serum (7).

In summarizing the action of cortisone on hypersensitivity, it would appear that cortisone may inhibit anaphylactic allergy by two separate means: by suppression of antibody production and by suppression of the damaging effects of antigen-antibody union. In regard to most human allergies, as well as in the case of experimental serum sickness, any therapeutic benefit of cortisone would seem to be derived from the latter mechanism and suppression of antibody production does not seem to play a part (18, 19). On the other hand, in the Arthus reaction and in certain diseases due to immune mechanisms, such as acquired hemolytic anemia and thrombocytopenic purpura, suppression of circulatory antibody by cortisone may be the more important effect (20, 21).

SUMMARY

Cortisone markedly suppressed the cardiovascular and renal lesions of serum sickness type hypersensitivity which ordinarily develop following the intravenous injection of bovine albumin. The inhibitory effect of cortisone on the allergic granulomatous lesions of the spleen was less striking; the lesions were less extensive, but the percentage of animals affected was unchanged.

Cortisone in the dosage employed had no effect on the elimination of antigen following its intravenous administration or on the appearance of circulating antibody. These findings indicate that inhibition of the lesions of serum sickness by cortisone does not depend on the suppression of antibody production. Therefore, it is inferred that cortisone somehow protects the animal from the damaging effects of antigen-antibody union.

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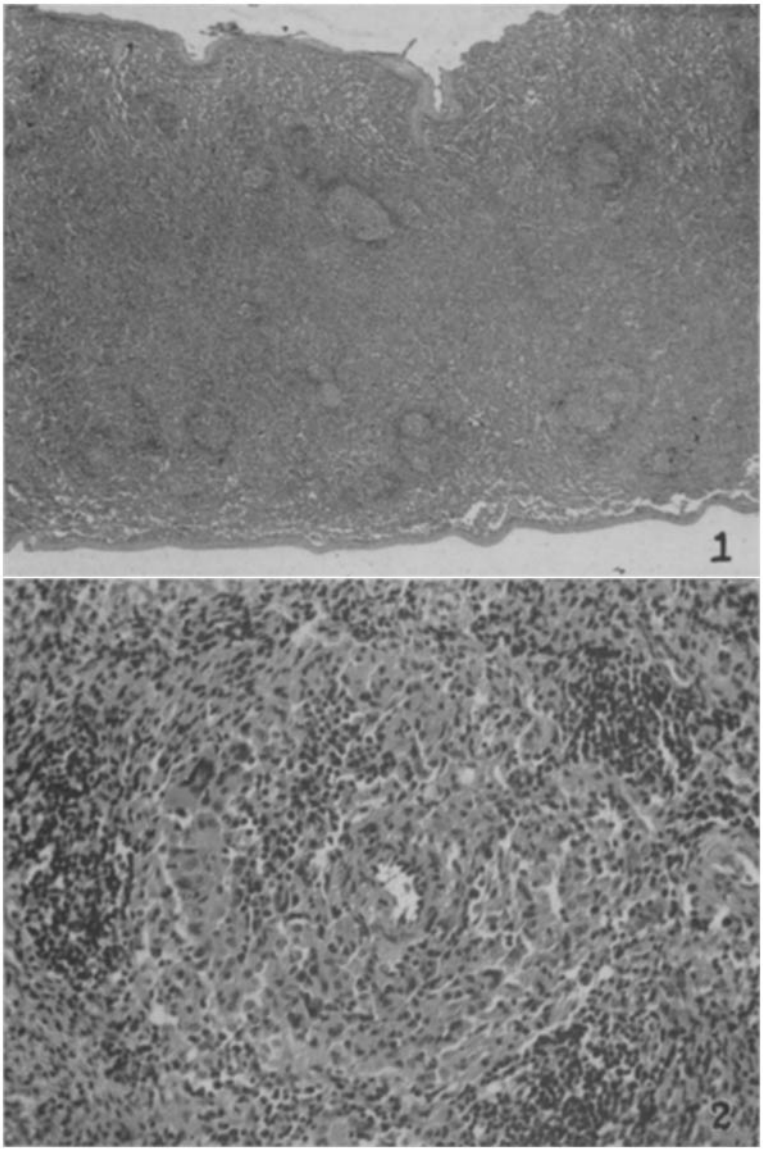
EXPLANATION OF PLATES

Photographs by K. Cramer Lewis, Washington University School of Medicine, St. Louis.

PLATE 1

FIG. 1. Rabbit 24 treated with cortisone. Section of spleen showing decrease in number and size of Malpighian bodies. Hematoxylin and eosin. Low power.

FIG. 2. Rabbit 24 treated with cortisone. Epithelioid and multinucleated giant cells replacing most of the lymphoid tissue of a small splenic follicle. Hematoxylin and eosin. × 200.

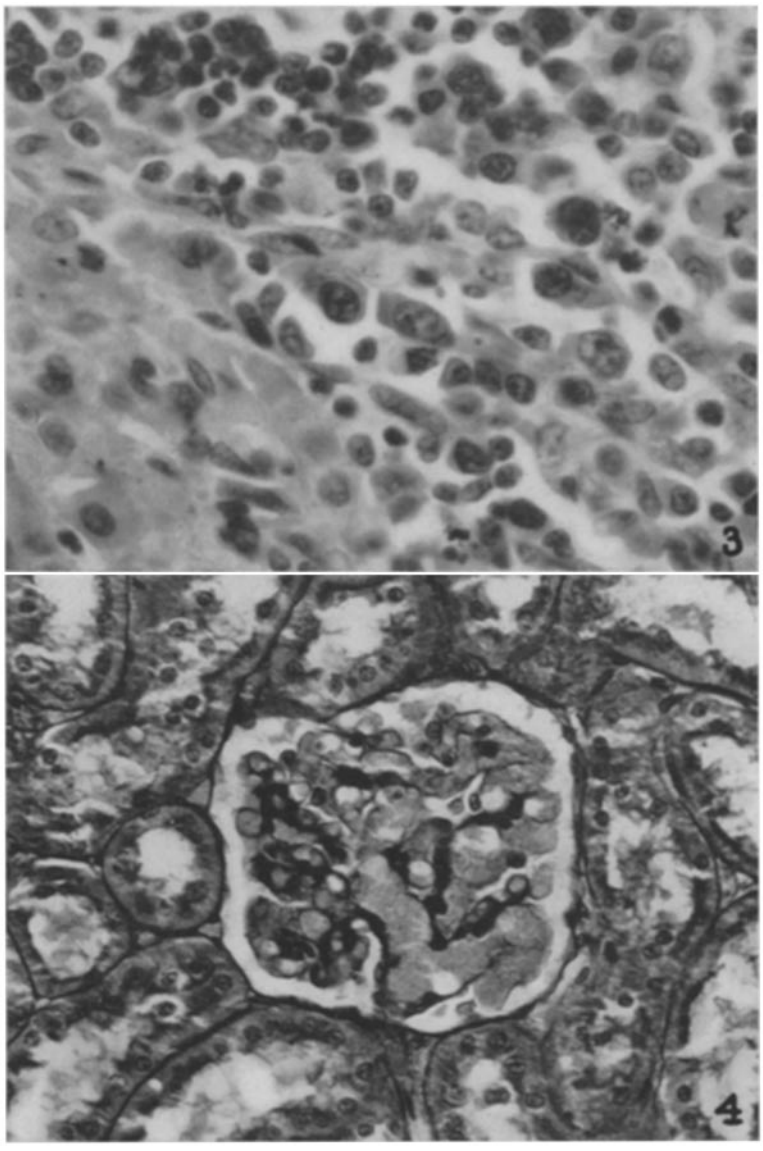


(Germuth: Cortisone in hypersensitivity)

PLATE 2

FIG. 3. Rabbit 24 treated with cortisone. Large lymphoblasts with abundant nuclear chromatin and slight cytoplasm, at periphery of small splenic follicle. Large cells with pale nucleus and abundant cytoplasm are macrophages. Hexatoxylin and eosin. × 950.

FIG. 4. Rabbit 11 treated with cortisone. Glomerulus with normal capillary loops at the extreme left and tremendously dilated loops elsewhere. Periodic acid–Schiff method. × 400.



(Germuth: Cortisone in hypersensitivity)