in the stools of 13 other patients in this epidemic, we believe that the failure to detect poliomyelitis virus in the stools of a paralytic patient excreting C virus should be regarded as a technical difficulty, and should not necessarily be regarded as an indication that C virus caused the lesion resulting in paralysis. For the present, and until it is proved otherwise, the patient's paralytic manifestations should be considered to result from CNS infection with poliomyelitis virus. However, the finding of dual infections in poliomyelitis appears to occur too frequently to be regarded merely as coincidence. Is it possible that infection with poliomyelitis virus would have been a mild affair in these patients had not C virus infection been superimposed on the poliomyelitis infection? Consideration is being given to the possibility that C virus infection may be one of the predisposing factors which may turn a nonparalytic into a paralytic case.

Summary. Both poliomyelitis virus and Coxsackie virus (C virus) were isolated from the acute phase stools of several paralytic patients during an epidemic of poliomyelitis which occurred in Easton, Pa., in 1949. In 2 such cases, neutralizing antibody tests were carried out with acute and convalescent serum reacting with a suspension of virus obtained directly from acute phase stools. It was found that both patients responded to their illness by simultaneously developing antibodies both to poliomyelitis virus and to C virus.

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Effect of 17-Hydroxy-11-Dehydrocorticosterone (Compound E) and of ACTH on Arthus Reaction and Antibody Formation in the Rabbit. (18058)

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Hench and his coworkers(1) reported the beneficial effects of adrenal cortical hormone, compound E, and the adrenocorticotropic hormone in patients with rheumatoid arthritis. Subsequently, encouraging therapeutic results were obtained with these hormones in the treatment of the acute phase of rheumatic fever(2,4), periarteritis nodosa(3) and disseminated lupus erythematosus(4). These 4 diseases have in common numerous clinical manifestations and similar basic pathological alterations consisting of focal necrosis of collagen and damage to the cardiovascular system(5). Rich and Gregory(6,7) have demonstrated that hypersensitivity of the Arthus type can produce periarteritis nodosa as well as cardiovascular lesions in the rabbit resembling those of rheumatic fever. Since these observations suggest that anaphylactic hypersensitivity may play a role in the pathogenesis of this group of diseases, a study of the effect of compound E and ACTH on the development of the Arthus state in the rabbit

1. Hench, P. S., Kendall, E. C., Slocumb, C. H., and Polley, H. F., *Proc. Staff Meetings Mayo Clin.*, 1949, v24, 181.

2. Hench, P. S., Slocumb, C. H., Barnes, A. R., Smith, H. L., Polley, H. F., and Kendall, E. C., *Proc. Staff Meetings Mayo Clin.*, 1949, v24, 277.

3. Shick, R. M., Baggenstoss, A. H., and Polley, H. F., *Proc. Staff Meetings Mayo Clin.*, 1950, v25, 135.

4. Hench, P. S., Kendall, E. C., Slocumb, C. H., and Polley, H. F., *Arch. Int. Med.*, 1950, v85, 545.

5. Rich, A. R., *Harvey Lectures*, 1946-47, v42, 106.

6. Rich, A. R., and Gregory, J. E., *Bull. Johns Hopkins Hosp.*, 1943, v72, 65.

7. Rich, A. R., and Gregory, J. E., *Bull. Johns Hopkins Hosp.*, 1943, v73, 239.

was undertaken.

Methods and materials. The ACTH, obtained from Armour and Co. in the form of unsterile powder was administered to the animals in saline solution containing an equivalent of 10 mg of standard ACTH LA-1-A per ml.

Compound E was obtained as cortisone acetate from Merck and Co., Inc. in the form of unsterile crystals.* After solution in warm anhydrous acetone, these crystals were suspended in saline and most of the acetone removed by evacuation. Finally, the suspension was made up to a volume such that 1 ml of the suspension contained 10 mg of compound E.

Crystalline hen's egg albumin, the antigen employed in this study, was prepared according to the method of Kekwick and Cannan(8).

For sensitization, 24 male albino rabbits weighing approximately 2 kg each were injected intracutaneously every day for 18 days with 0.2 ml of a crystalline egg albumin solution containing 4.2 mg of egg albumin nitrogen per ml. Beginning with the first sensitizing injection, and with each succeeding one, 8 of these animals were injected intramuscularly with one dose per day of 10 mg of compound E and another 8 animals were injected intramuscularly with 10 mg of ACTH per day given in 4 doses of 2.5 mg each every 6 hours. This treatment was maintained throughout the experiment. These total daily dosages of 5 mg/kg are approximately 3.5 times those generally employed in the treatment of man (100 mg per 70 kg of body weight). The site of each inoculation of egg albumin was observed 24 hours (in some instances at shorter intervals) after injection and every reaction was measured and recorded. All of the rabbits were weighed and bled for 2-3 ml of blood from the marginal ear vein at the commencement of the experiment and on the 4, 7, 9, 11, 14 and 16th days.

The antibody content of the serum for crystalline egg albumin was determined as follows: Egg albumin was added to 0.5 ml of serum in increments of 1 or 2 μg of nitrogen until a final addition of antigen produced no further precipitation. After each addition of antigen, the sera were incubated at 37°C for 1 hour and usually allowed to remain overnight at 0-5°C and then centrifuged. Finally, after 3 to 5 days at 0-5°C, the precipitates were collected by centrifugation in the cold and washed twice with cold saline (9). The washed precipitates were dissolved in 4.0 ml of 0.1 N sodium hydroxide and the absorption determined in a 1 cm quartz cell at a wavelength of 280 millimicrons with a Beckman spectrophotometer. At this wavelength the absorption of such a solution is proportional to its antibody-antigen nitrogen content. The resulting optical densities were therefore converted into precipitate nitrogen from a standard reference curve. Since complement is not present in aged sera,† the antibody nitrogen was obtained by subtraction of antigen nitrogen from the total value. Tests on the supernatant sera were all positive for slight excess antigen. Duplicate determinations were done wherever possible. These agreed usually within $\pm$ 5% when the antibody content was above 100 μg per ml.‡

* Since there are no apparent differences in the physiologic effects of cortisone (Compound E) and cortisone acetate, the latter compound is referred to throughout as compound E.

8. Kekwick, R. A., and Cannan, R. K., *Biochem. J.*, 1936, v30, 227.

9. Heidelberger, M., and Kendall, F. E., *J. Exp. Med.*, 1935, v62, 697.

10. Sayers, G., and Sayers, M. A., *Ann. New York Acad. Sci.*, 1949, v50, 522.

† None of the sera tested exhibited complement activity.

‡ Only small volumes of sera were taken for analysis, to avoid possible stress on the pituitary-adrenal system(10). Therefore the standard precipitin method as devised by Heidelberger and Kendall(9) was not employed. The present method is not a precise measure of antibody content; for example, with the serial addition of antigen, "univalent antibody might remain undetected. To determine the magnitude of this error, several of the sera obtained on the final bleeding were tested by both methods. It was found that only with sera of high antibody content was there disagreement, in which case the values obtained with the standard method were substantially higher because of the coprecipitation of "univalent"

TABLE I.

Effect of Compound E and ACTH on Production of Arthus State in Rabbits Receiving Daily Intracutaneous Injections of Egg Albumin. (Figures presented below represent the product of the height, width and length of the 24-hr skin reactions measured in centimeters).

Rabbit No.	Treatment	Magnitude and appearance of 24-hr skin reactions observed on the following days:													
		5	6	7	8	9	10	11	12	13	14	15	16	17	18
1	None														
	Control	0	0	3.9*	18 *	10 *	6.7†	—	16 ‡	—	18 ‡	7.6‡	7.4‡	14 ‡	—
2	”	0	.3*	.3*	.7*	3.0*	2.9*	4.2*	7.6*	5.7*	4.6*	4.8*	4.7*	2.7*	2.8*
3	”	.3*	—	.3*	.2*	1.2*	1.2*	2.1*	2.2*	4.9*	2.2*	2.2*	1.0*	2.8*	2.9*
4	”	.3*	0	.2*	.2*	2.1*	6.6‡	22 ‡	23 ‡	—	19 ‡	9.6‡	2.6‡	12 ‡	—
5	”	0	.6*	.7*	.9*	3.0*	13 *	14 *	30 ‡	24 ‡	33 ‡	33 ‡	31 ‡	25 ‡	24 ‡
6	”	.4*	0	.3*	.7*	.3*	0.4*	1.4*§	4.1*§	10 ‡§	Dead				
7	”	0	0	.6*	0	.7*	10 *	12 ‡	6.0‡	9.9‡	23 ‡	17 ‡	25 ‡	12 ‡	12 ‡
8	”	0	0	0	.5*	.7*	47 *	68 ‡	37 ‡	39 ‡	51 ‡	32 ‡	43 ‡	40 ‡	61 ‡
9	Compound E	0	0	0	0	0	0	0	.4*	0	.2*	.6*	.4*	.2*	.7*
10	”	0	0	0	0	0	0	0 §	.3*§	0 §	.3*	.4*	.3*	.5*	.4*
11	”	0	0	0	0	0	.1*	0	0	0	.1*	.1*	.1*	.1*	.4*
12	”	0	0	0	0	.1*	0	0	0	0	0	.1*	0	.1*§	.1*§
13	”	0	0	0	0	0	0	.3*	.2*	.1*	0	.4*	.2*	0	.2*
14	”	0	0	0 §	0 §	0	0 §	0 §	0 §	.1*§	0 §	.2*§	Dead		
15	”	0	0	0	0	0	0	0 §	.1*	0 §	0 §	.1*§	0 §	Dead	
16	”	0	0	0	0	0	0	0 §	0 §	0	0	0	0	Dead	
17	ACTH	0	0	0	0	4.4*	4.7*	7.2*	9.7*	7.2*	7.8*	3.5*	3.5*	1.9*	.4*
18	”	0	0	.6*	3.1*	6.1*	8.7‡	12 ‡	25 ‡	15 ‡	25 ‡	15 ‡	14 ‡	11 ‡	13 ‡
19	”	0	0	0	0	0.1*	0	0	0	0	.3*	.3*	.2*	.4*	.1*
21	”	0 §	0 §	0 §	0 §	0 §	0 §	0 §	0 §	.6*§	2.0*§	Killed			
22	”	0	0	0	.9*	3.8*	10 *	8.4†	5.1‡	8.8‡	22 ‡	34 ‡	10 ‡	19 ‡	15 ‡
23	”	0	0	0	0	3.4*	6.7†	9.2‡	8.4‡	3.0‡	10 ‡	12 ‡	7 ‡	8 ‡	6 ‡
24	”	0	0	0	0	4.2*	.9*	5.6*	.8*	0	3.3*	.9*	1.1*	.5*	1.9*

* Pink. † Red. ‡ Hemorrhagic. § Diarrhea.

Most of the sera obtained from the animals treated with compound E were lipemic. Because of the possibility that this alteration might in some manner affect the reactivity of the antibody with antigen, the ability of the serum to passively sensitize guinea pigs was determined. Guinea pigs weighing approximately 250 g were injected intravenously using the hind leg vein with varying amounts of rabbit serum obtained from the final bleeding. Two days later, these animals were challenged with a shocking dose of egg albumin (1 mg in 1 ml saline) and their reactions noted.

On the 18th day, *passive* Arthus reactions were induced in all of the animals(11). The rabbits were injected intracutaneously at two different sites with 0.4 ml of antipneumococcus type II rabbit antiserum representing 1 mg and 0.5 mg of antibody nitrogen respectively. One-half hour later, 1 mg of pneumococcus type II polysaccharide was injected into each site. Skin lesions were observed and recorded 8 and 24 hours later. Neither the antiserum nor the polysaccharide control gave an appreciable skin reaction.

Eighteen days after the first injection of egg albumin, all the animals were bled from the heart and killed. The autopsy findings will be discussed in a subsequent paper.

Experimental results. A. *The effect of compound E and ACTH on the Development of the Active Arthus State.* In Table I are recorded the size and appearance of the 24-hour skin lesions of each animal produced by the injections of egg albumin throughout the experimental period. The numbers presented in the columns are the product of the height,

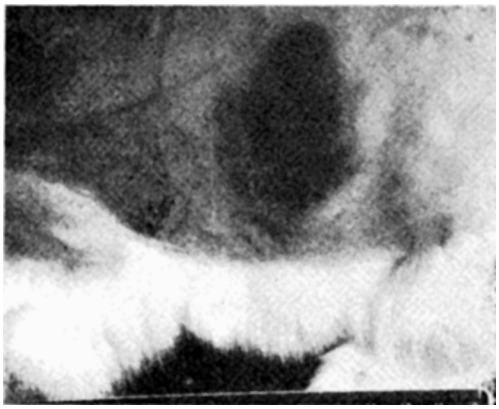

FIG. 1, 2, 3—Twenty-four hour old skin lesions in rabbits produced by the 15th daily intracutaneous injection of egg albumin.
FIG. 1. Control rabbit No. 7 with edematous and hemorrhagic Arthus reaction.

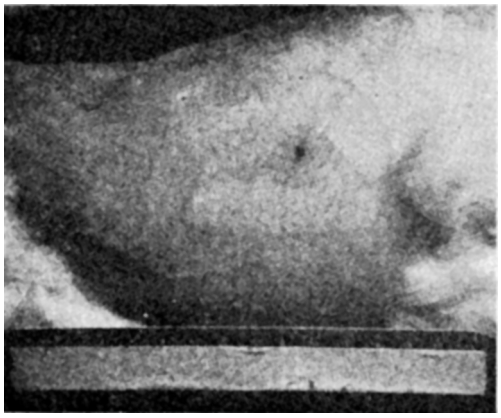

FIG. 2. Compound E-treated rabbit No. 13 with small, pale pink skin reaction. The black spot is made by gentian violet marking the site of injection. This lesion represents the largest ever obtained in the 8 Compound E-treated rabbits.

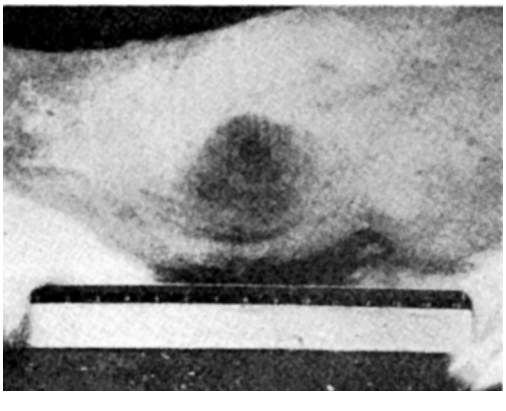

FIG. 3. ACTH-treated rabbit No. 23 with edematous and hemorrhagic Arthus reaction.

antibody. With the low titered sera there was close agreement. Thus if the standard precipitin method had been employed the differences observed between the low titered sera of most of the treated animals and the high titered sera of the controls would be even greater.

11. Fischel, E. E., and Kabat, E. A., *J. Immunol.*, 1947, v55, 337.

§ The height of the lesion was obtained by measuring the thickness of a doubled layer of skin at the site of greatest swelling, subtracting the thickness of a fold of normal skin and dividing by 2 to obtain the thickness of a single layer.

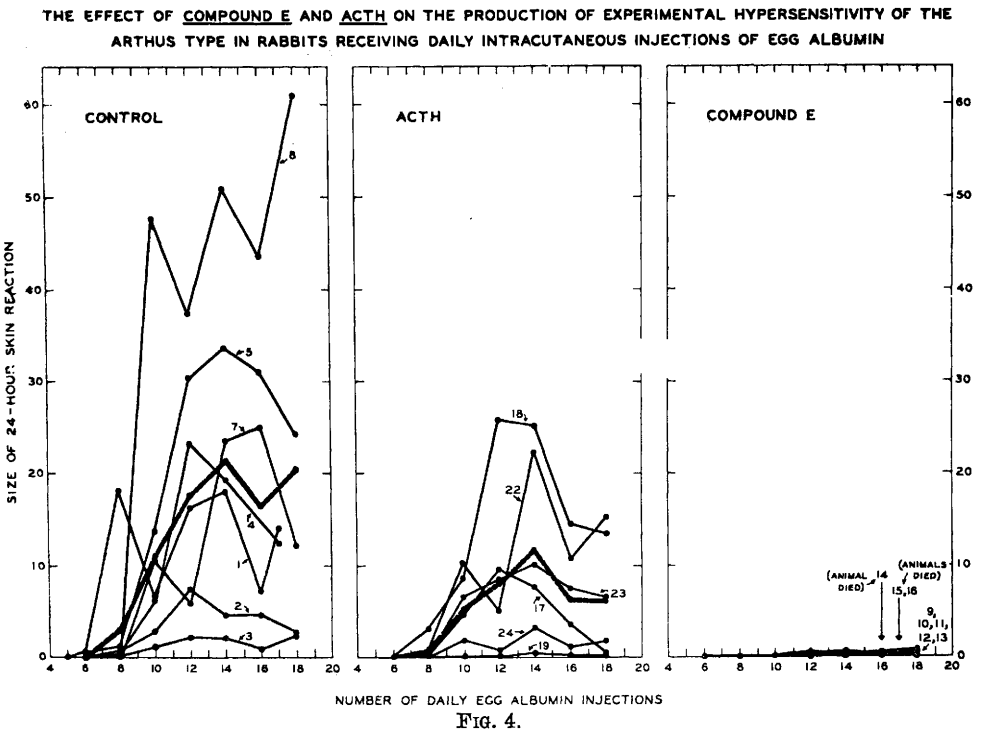

FIG. 4.

width, and length of these lesions.§ The results in Table I are graphically illustrated in Fig. 4 where the abscissa represent the number of the daily injections and the ordinate the magnitude of the lesion.

As shown in Table I and Fig. 1, 3 of the 8 control animals showed definite but small wheals on the 5th injection of egg albumin. On the 7th injection, wheals were produced in all of the 8 control animals and by the 13th injection, all of the 8 control animals had developed large Arthus reactions. In 6 of the 8 animals, in addition to extensive pink or red edema, the lesions contained large hemorrhagic and necrotic centers. In 2 of these animals (No. 5 and No. 8) the skin reactions were of such size that they occupied a large portion of the animal's side. These hemorrhagic and necrotic lesions often reached their greatest size after 48 hours, and healed with black scab formation.

In contrast, the 8 animals treated daily with 10 mg of compound E gave only slight or no skin reactions to egg albumin. The very slight reactions observed developed only after a much longer period of sensitization and consisted of flat, poorly defined pale pink areas in the skin. No extensive edema, hemorrhage or necrosis was seen.

Treatment with ACTH inhibited the production of the Arthus reaction but not nearly to such a marked degree as did treatment with compound E. As shown in Table I, 2 animals gave slight reactions, 2 animals gave moderate reactions and in only 3 out of the 7 were there hemorrhage and necrosis. One of the 8 ACTH animals (No. 20 not presented in the table) died on the 5th day.

B. *The effect of compound E and ACTH on antibody production.* Since, in the active Arthus reaction, antibody production is essential to the development of the reactive state, the possibility presented itself that the inhibition of reactivity by compound E and ACTH may have been due to the inability of animals under treatment to produce sufficient antibody.

In Table II are presented the anti-egg albumin antibody nitrogen content of 1 ml of serum from blood obtained from each animal

TABLE II.

Antibody Content of Sera from Rabbits Sensitized by Daily Intracutaneous Injections of Egg Albumin and Treated with ACTH or Compound E. (All sera were negative for anti-egg-albumin antibody on 0, 4 and 7 days).

Rabbit No.	Treatment	Antibody nitrogen content of serum, (μg/ml) on following days after first sensitizing injection of egg albumin				
		9	11	14	16	18
1	None, control	24	—	146	212	325
2	"	0	0	—	24	24
3	"	0	20	18	—	18
4	"	24	—	220	311	207
5	"	16	56	86	148	214
6	"	0	20	Dead		
7	"	8	24	84	180	200
8	"	8	44	90	236	304
Avg		10	27	107	185	185
9	Compound E	0	0	12	—	0
10	"	0	4	7	0	0
11	"	8	8	11	6	0
12	"	0	0	2	—	—
13	"	0	0	0	6	0
14	"	0	0	0	Dead	
15	"	0	0	3	0	Dead
16	"	0	4	0	0	Dead
Avg		1	2	4	2	0
17	ACTH	0	12	3	8	—
18	"	20	40	45	130	212
19	"	0	8	—	5	45
20	"	—	16	Killed		
22	"	8	24	46	76	82
23	"	20	28	64	118	130
24	"	0	8	8	6	7
Avg		8	19	33	57	95

at varying intervals as previously described. These results are presented graphically in Fig. 5. As is shown there, the sera of 5 of 7 control animals tested contained at least 200 μg of antibody nitrogen per ml at the termination of the experiment. The sera of the two other control animals contained 20 and 24 μg of antibody N per ml and these two animals gave the poorest Arthus reactions of the group (compare Fig. 4 and 5).

It is obvious from the table and figure that treatment with ACTH decreased the ability of the rabbits to produce antibody. Considering only the sera obtained from the final bleeding, ACTH suppressed antibody formation by an average of 50%. Only one of the sera of the 7 animals tested ever contained more than 200 micrograms of antibody N per ml. Again the 3 poorest skin reactors (Rabbits 17, 19, 24) had produced the smallest amount of antibody.

The effect of compound E on antibody production was more marked than that obtained with ACTH. None of the sera from the 8 animals receiving compound E ever contained more than 12 μg of antibody N per ml. At the end of the experiment, none of the sera of the 4 animals tested contained any detectable antibody by the technic employed.

As a confirmation of the precipitin reaction, the ability of the sera obtained by cardiac puncture at the termination of the experiment to produce passive anaphylaxis in guinea pigs was determined as shown in Table III. All of the sera tested from the control and ACTH-treated animals were able to passively sensitize guinea pigs to a shocking injection of egg albumin antigen. With serum from rabbit No. 6, 0.25 ml or less was sufficient to produce fatal sensitization. However, even 2.0 ml of serum from the compound E treated animals failed to sensitize the guinea pigs to even the slightest degree. It should be pointed out that as little as 32 μg of anti-egg albumin antibody nitrogen are required to produce fatal sensitization in 100% of the guinea pigs

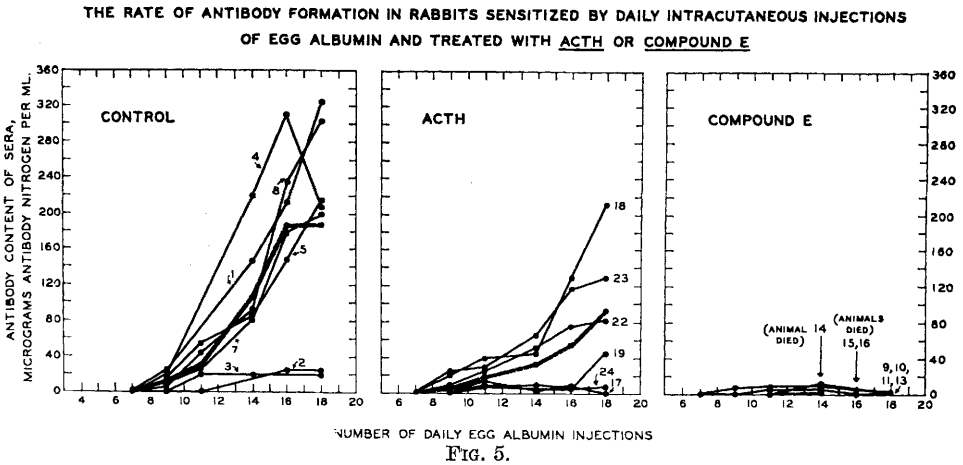

FIG. 5.

tested in this manner(12).

C. *The effect of compound E and ACTH on the passive Arthus reaction.* Although the suppression of antibody formation by treatment with compound E or ACTH could in itself fully explain the inhibitory effect of these two substances on the production of the allergic state, there was a further possibility that the animal's skin reactivity may have been altered by treatment. All of the animals were therefore tested for their ability to exhibit a passive Arthus reaction, when given antibody. Each rabbit was injected intracutaneously at two different skin sites with 1 mg and 0.5 mg respectively of rabbit antipneumococcus II antibody nitrogen contained in 0.4 ml of serum. Thirty minutes later, 1 mg of pneumococcus II polysaccharide was injected into each site. In columns 1 and 2 of Table IV are recorded the reactions observed 8 hours after the injection of the antigen. As is shown there, all of the rabbits both treated and controls, regardless of their ability to react actively to injections of egg albumin, produced a similar response to the intracutaneously injected antibody and antigen.

Discussion. The experimental data indicate that compound E and to a lesser extent, ACTH, suppress the development of the allergic state ordinarily produced in the rabbit by repeated intracutaneous injections of crystalline egg albumin. While 6 out of 8 control animals demonstrated large hemorrhagic and necrotic skin reactions following a preliminary period of sensitization, only 3 out of 7 of the ACTH-treated animals and none of the 8 rabbits receiving compound E produced lesions of similar severity. In all 3 groups of animals, there was a close correlation between the antibody nitrogen content of the sera and the severity of the skin reaction. The data show that the inhibitory effect of compound E and ACTH on the development of the Arthus state results from the ability of these hormones to suppress antibody formation, a prerequisite for the production of the active Arthus reaction(13).

Of particular interest is the fact that treatment with compound E and ACTH did not alter the animal's ability to produce the Arthus reaction when antibody was injected intracutaneously. During the passive Arthus reaction, all of the animals reacted in a similar manner and to the same degree regardless of treatment. This is particularly pertinent in view of the present emphasis on the general increased resistance to stress supposedly produced by treatment with these substances.

The mechanism by which ACTH and compound E suppress antibody formation is not apparent. The marked lymphoid atrophy and gluconeogenesis observed in these animals, which will be reported later, may in some way be related to the lack of antibody production.

12. Kabat, E. A., and Landow, H., *J. Immunol.*, 1942, v44, 69.

13. Culbertson, J. T., *J. Immunol.*, 1935, v29, 29.

TABLE III.

Relative Ability of Sera Obtained from Rabbits Sensitized by Repeated Intracutaneous Injections of Crystalline Egg Albumin and Treated with Compound E or ACTH to Passively Sensitized Guinea Pigs.

No. of rabbit from which serum was obtained	Treatment received	Volume of serum injected into guinea pig, ml	Reaction of guinea pig to 1 mg of egg albumin injected 48 hr later
1	None, control	.5	Dead, 5 min.
2	"	1.0	" 2 "
3	"	1.0	Moderate reaction
4	"	.5	Dead, 3 min.
5	"	.5	" 3 "
7	"	.5	" 3 "
8	"	.5	" 2 "
	"	.25	" 2 "
	"	.25	" 2 "
9	Compound E	2.0	None
10	"	2.0	"
11	"	2.0	"
13	"	2.0	"
18	ACTH	1.0	Dead, 2 min.
19	"	2.0	" 2 "
22	"	.5	" 3 "
23	"	.5	" 1 "
24	"	1.0	Moderate reaction

The lymphocyte has been suggested as the site of antibody formation. It is conceivable gluconeogenesis might decrease antibody formation by promoting the breakdown of the amino acids necessary for antibody protein synthesis.

Whether the therapeutic effects of compound E and ACTH in the rheumatic diseases are due to the suppression of antibody formation is a particularly interesting possibility in view of the evidence of an allergic mechanism in this group of diseases. Mirick(14), however, has reported that in man antibody to pneumococcal polysaccharides was produced as promptly and in as high titer in patients receiving ACTH or cortisone as in controls.

In the present experiment, ACTH suppressed antibody formation and the allergic state to a much less degree than did compound E. Since the effects of ACTH are produced through the adrenal cortex, the question is therefore raised as to whether under the conditions of the present experiment, the rabbits were able to produce large quantities of compound E-like substances in response to ACTH stimulation.

The presence of diarrhea, possibly of an infectious nature, in a large number of the compound E-treated animals should be noted. Diarrhea was observed in 5 of the 8 compound E-treated animals but only in 1 each of the 7 ACTH-treated animals and the 8 controls. The question may be raised as to whether the presence of diarrhea in the compound E-treated animals might account for their failure to respond to antigenic stimulation. However, diarrhea appeared in these rabbits after the controls had reacted to a marked degree to the egg albumin. Furthermore, 3 animals without diarrhea behaved in all respects similar to those in which diarrhea occurred. If the suppression of antibody response to crystalline egg albumin by compound E represents a specific case of a generalized phenomenon, the apparent increased susceptibility of compound E treated animals to diarrheal infection might be explained as failure to develop protective antibodies. In this regard, Antopol(15) has reported spontaneous

14. Mirick, G. S., Abstracts, 42nd Ann. Meeting, Am. Soc. Clin. Invest., 1950, 46.

TABLE IV.
Failure of Compound E and ACTH to Inhibit Passive Arthus Reaction in Rabbits. (To be contrasted to their striking effect on development of the Active Arthus Reaction).

Rabbit No.	Treatment	Size of skin wheal, cm, with	
		1 mg antibody N	0.5 mg antibody N
1	None, control	2.2 × 2.2 × 0.2 p.pk.	2.7 × 2.3 × 0.25 p.pk.
2	"	3.2 × 2.2 × 0.2 pk.	3.0 × 3.2 × 0.3 pk.
3	"	3.1 × 2.8 × 0.3 p.pk.	4.0 × 2.5 × 0.3 p.pk.
4	"	2.4 × 2.2 × 0.3 p.pk.	3.5 × 2.1 × 0.25 p.pk.
5	"	3.1 × 1.2 × 0.3 p.pk.	3.9 × 2.5 × 0.3 p.pk.
7	"	3.5 × 2.8 × 0.25 pk.	4.0 × 2.7 × 0.3 pk.
8	"	2.7 × 2.3 × 0.2 p.	2.7 × 2.8 × 0.25 p.pk.
9	Compound E	3.8 × 3.0 × 0.35 pk.	3.3 × 2.5 × 0.25 pk.
10	"	2.5 × 2.5 × 0.3 pk.	2.6 × 2.1 × 0.25 pk.
11	"	2.7 × 2.4 × 0.25 p.pk.	3.1 × 2.6 × 0.2 p.pk.
12	"	2.5 × 2.0 × 0.15 p.pk.	2.0 × 3.1 × 0.15 p.pk.
13	"	2.8 × 2.6 × 0.3 pk.	2.5 × 2.5 × 0.35 pk.
17	ACTH	3.3 × 2.3 × 0.35 pk.	2.5 × 1.7 × 0.25 pk.
18	"	3.1 × 2.2 × 0.25 pk.	3.0 × 2.2 × 0.3 pk.
19	"	2.8 × 1.7 × 0.3 p.	3.0 × 2.1 × 0.25 p.
22	"	2.3 × 2.0 × 0.2 p.	3.3 × 2.4 × 0.25 p.
23	"	2.1 × 2.1 × 0.25 pk.	2.9 × 2.7 × 0.2 pk.
24	"	2.4 × 2.3 × 0.2 pk.	2.9 × 2.1 × 0.25 pk.

p = Pale. pk. = Pink.
The rabbits which had been receiving daily injections of egg albumin were passively sensitized at 2 different skin sites by the intracutaneous injection of 1 mg and 0.5 mg of rabbit anti-pneumococcus II antibody nitrogen, each contained in 0.4 ml of serum. Thirty minutes later, 1 mg of pneumococcus II polysaccharide was injected into each site. The 8-hour readings are recorded above. Neither the serum nor the polysaccharide control produced a skin reaction.

Corynebacterium pseudotuberculosis murium infection in mice under treatment with compound E while untreated controls remained uninfected.

Summary. 1. The effects of compound E and ACTH on experimental hypersensitivity of the Arthus type and on antibody production in the rabbit are described. Both compound E and ACTH inhibited sensitization to repeated intracutaneous injections of crystalline egg albumin. Moreover the inhibition produced by compound E was much greater than that obtained with ACTH; with compound E sensitization was almost completely prevented in all of the 8 animals tested.

2. The data indicate that the inhibitory effect of compound E and ACTH on the development of the Arthus state results from the ability of these hormones to suppress antibody formation. As shown by antibody nitrogen determinations, compound E and ACTH suppressed antibody formation by an average of 100 and 50% respectively.

3. In contrast to their striking effect on the production of the active Arthus reaction, compound E and ACTH had no effect on the passive local Arthus reaction, when antibody is supplied to the animal. Thus, the capacity of the animal to react to antibody-antigen combination in the tissues is not altered by treatment.

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