Experiences With ACTH and Cortisone in Selected Dermatoses

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SUMMARY

Fifty patients with various kinds of skin diseases who were not adequately relieved by conventional therapy were treated with ACTH or cortisone given systemically.

Almost all patients with disseminated neurodermatitis had dramatic initial response, but in only about half the cases was improvement maintained when use of the drugs was discontinued.

It appeared that in other skin diseases, such as lupus erythematosus, scleroderma, psoriasis, dermatomyositis and pemphigus, while improvement may be noted for a time, relapse to the original state occurs after the treatment is stopped.

In four cases of chronic discoid lupus erythematosus, although some improvement was observed when steroid therapy was given, the histologic pattern of biopsy material taken from the lesions after treatment still was characteristic of the disease.

ADRENOCORTICOTROPIC hormone (ACTH) and cortisone were used systemically in the treatment of 50 selected patients with skin diseases. In most cases the dermatosis was recalcitrant to conventional therapy.

In the present report, *disseminated neurodermatitis* and *atopic dermatitis* are used as synonymous terms; and by *eczema*, as the term is used here, is meant dyshidrotic or asteatotic pruritic non-specific dermatosis characterized by erythematous papulovesicular eruption.

Of the 50 patients, 22 had atopic dermatitis, four chronic lupus erythematosus, four acrosclerotic scleroderma, eight "drug eruptions," two psoriasis, two pemphigus, two eczema, two pruritus due to systemic disease, one Kaposi's idiopathic multiple hemorrhagic sarcoma, one idiopathic urticaria, one urticaria due to food sensitivity, and one infectious eczematoid dermatitis.

Steroid therapy was not instituted until after sufficient trial of other methods had failed. All patients treated were observed for the initial eosinophil response to adrenal cortical stimulation or to cortisone, and the weight and blood pressure of all patients was recorded daily. If extended treatment was necessary, electrolyte studies were done at regular intervals.

Improvement was graded as slight, moderate, or great, and the grade was determined by the degree of reduction in the objective symptoms in the skin (such as erythema, lichenification, edema and scaling) and of decrease in the subjective symptoms such as burning and itching.

ACTH was given intramuscularly and cortisone intramuscularly and orally in daily divided doses. It was usual to give 100 to 120 mg. of ACTH per day for the first three or four days and then reduce the amount gradually to 40 to 60 mg. per day. The schedule for cortisone usually consisted of 300 mg., 200 mg., and 100 mg. on successive days and then 100 mg. per day until further gradual reduction was decided upon.

Atopic Dermatitis

Of the 22 patients with atopic dermatitis treated with ACTH or cortisone (Table 1), 13 had dramatic improvement, with reduction in the erythema, resolution of the weeping and lessening of the itching within 48 hours (Figure 1). Nine others improved appreciably in four to five days. Therapy was continued after clinical improvement at a maintenance dose with the idea that the longer the itch-scratch reflex was blocked, the longer the healing time and the less likelihood of relapse. At the time of this report 12 of the 22 patients had complete relapse. In seven cases there was continued improvement, but the longest follow-up was only five months. Two patients had initial improvement but did not return for further observation. One patient had partial relapse and at the time of report had remained in that condition for five months.

Drug Eruptions

Eight patients with "drug eruptions" were treated with ACTH or cortisone. Two patients who had eczematous eruption from gold therapy responded promptly to cortisone, and there was no relapse. One patient with blotchy erythema that had developed when Terramycin® was given systemically for infection of the urinary tract was given cortisone orally. The skin lesions cleared up immediately but recurred three times at the same sites. ACTH then was given and the skin cleared and remained clear. One case of exfoliative dermatitis in a man who had been given sulfamerazine for infection of the urinary tract was treated with cortisone by mouth. The dermatitis cleared rapidly and did not recur. Another patient with a morbilliform eruption due to mersalyl had dramatic response to cortisone given

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orally, and the skin remained clear. Three patients with acute urticaria owing to sensitivity to penicillin were treated. In two patients the results were very good, but in one the effect was equivocal.

Miscellaneous Dermatoses

Four patients with chronic discoid lupus erythematosus were treated with cortisone. The longest period of treatment was three and one-half months and the shortest was one month. All four patients previously had had adequate courses of gold and bismuth with no response. Three of the patients had moderate response and one a slight response to cortisone therapy, but in all cases there were relapses to the former state when treatment was discontinued.

Four patients with acrosclerosis received ACTH or cortisone. Three were not relieved. One had moderate improvement with softening and increased mobility of the skin. While the patient was undergoing steroid therapy, however, visceral scleroderma changes developed.

Cortisone was used in two cases of pemphigus vulgaris. One of the patients, a 54-year-old man seriously ill with acute fulminating pemphigus, had dramatic response, and six months after therapy still was free of lesions (Figure 2). The other patient had pemphigus foliaceus of several years' duration. There was slight response to cortisone, and immediate relapse when therapy was discontinued. ACTH was tried and the result was equally disappointing.

Two patients with dyshidrotic eczema involving the hands and arms and complicated by overtreatment had no response to adequate trial of steroid therapy. One was given cortisone by mouth for two weeks and the other received ACTH followed by a course of cortisone.

Cortisone was given orally in two cases of severe pruritus associated with systemic disease—Hodgkin's disease in one case and biliary cirrhosis with xanthomatosis in the other—and the pruritus in both cases was relieved but it recurred immediately when the hormone was discontinued or even when the dose was reduced. The skin xanthomata were not

TABLE 1.—*Disseminated Neurodermatitis (Atopic Dermatitis) Treated with ACTH and Cortisone*

	Age and Sex	Duration of Illness	ACTH	Cortisone	Length of Treatment (days)	Total Dose (mg.)	Initial Improvement	Follow-up
1.	14 mo. M	11 months	.....	syst.	7	400	great	Slight relapse followed by improvement. No follow-up.
2.	17 mo. F	14 months	.....	syst.	7	450	great	Great improvement. Followed for three months.
3.	14 yr. F	History of infantile eczema	.....	syst.	14	2000	great	Complete relapse.
4.	18 yr. M	Present attack 2 years. History of infantile eczema	.....	syst.	11	720	great	Complete relapse.
5.	21 yr. F	Recurrent since infancy	.....	syst.	12	1300	great	Complete relapse.
6.	23 yr. F	Recurrent since infancy	.....	syst.	14	1400	great	Great improvement. Followed for four months.
7.	23 yr. M	Present attack 6 months. History of infantile eczema	.....	oral	11	1200	great	Slight relapse followed by great improvement. Followed for two months.
8.	27 yr. F	6 months	.....	oral	28	3300	great	Slight relapse followed by great improvement. Followed for four months.
9.	29 yr. F	Recurrent 1 year	yes	.....	9	720	great	No follow-up. Patient did not return.
10.	30 yr. M	Recurrent since infancy	.....	syst.	12	1300	great	Complete relapse.
11.	30 yr. M	Recurrent since infancy	yes	.....	11	1000	great	Complete relapse.
12.	40 yr. M	Recurrent 15 years	.....	syst.	14	1200	moderate	Complete relapse.
13.	41 yr. M	2 months	yes	.....	11	600	great	Complete relapse.
14.	42 yr. M	2 month	.....	oral	21	3000	great	Slight relapse followed by moderate improvement. Followed for three months.
15.	52 yr. M	Recurrent 6 years	..... yes	syst.	5 5	700 500	moderate great	Complete relapse. .....
16.	54 yr. M	8 months	yes	.....	7	400	moderate	Continued improvement. Followed for two months.
17.	55 yr. F	1 year	yes	..... syst.	25 21	2000 2500	great	Relapse, but not complete. .....
18.	61 yr. M	4 months	yes	.....	9	550	moderate	Great improvement. Followed for five months.
19.	62 yr. M	Recurrent 6 years	yes	.....	14	1240	great	Complete relapse.
20.	64 yr. M	Recurrent 8 years	yes	.....	30	2025	great	Complete relapse.
21.	66 yr. M	Recurrent 4 years	yes	.....	9	575	great	Complete relapse.
22.	80 yr. M	6 months	.....	oral	7	900	great	Complete relapse.

affected and the depth of jaundice remained about the same.

One patient with generalized psoriasis without arthritis was given cortisone by mouth for one month with no improvement. Another, who had severe rheumatoid arthritis and psoriasis, had no cutaneous improvement after three months of cortisone therapy (100 mg. daily), but subsequently a course of ACTH was given and in two weeks of therapy improvement occurred in more than half of the lesions. A nine-year-old girl with sensitization dermatitis and secondary infection, involving the face, neck and extremities, that had developed after a plastic operation on the face, was given cortisone, and within 48 hours the lesions were almost cleared (Figure 3). Treatment was given for one week, and there was no relapse after three months.

One patient with chronic idiopathic urticaria, possibly psychogenic, became worse while ACTH therapy was being carried out, while another patient with the disease, which might have been caused by allergic sensitivity to a food, had immediate clearing and no recurrence.

In a case of Kaposi's multiple idiopathic hemorrhagic sarcoma, no improvement was noted after ten days of therapy with cortisone, and new lesions continued to develop.

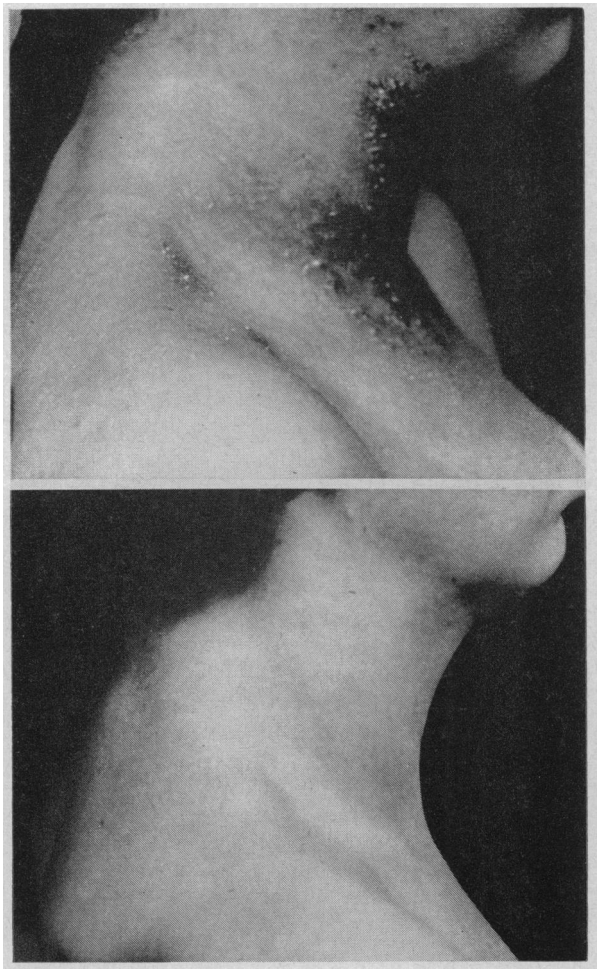

Figure 1.—Severe atopic dermatitis, before and six days after treatment with cortisone.

DISCUSSION

It is interesting to consider the rationale for the use of ACTH and cortisone in certain dermatoses. Adrenocorticotropin used systemically and adrenal cortical extract and cortisone applied locally have effects on the skin of rats.[1, 12, 13] After prolonged treatment these effects consist of a thinning of the epidermis both in number of cells and in cell area in the prickle layer, reduction of collagen bundles with increased compactness of collagen, reduction in size of sebaceous glands and hair follicles, and blanching of the skin. These observations are not necessarily applicable to human skin, but if they were it would seem reasonable to use the drugs either locally or systemically for treatment of any skin diseases associated with hyperkeratosis, increased dermal fibrosis and seborrhea. Unfortunately, prolonged systemic use of ACTH and cortisone produces acne and hirsutism,[9] thereby encouraging the seborrheic state.

Both hormones are said to inhibit the formation of granulation tissue,[7] but healing of this type does not take place in dermatitis and superficial dermatoses. Recent reports suggest that burns[2] heal more rapidly when ACTH or cortisone is given and that skin grafts may have a higher percentage of "takes" when these drugs are used.[22]

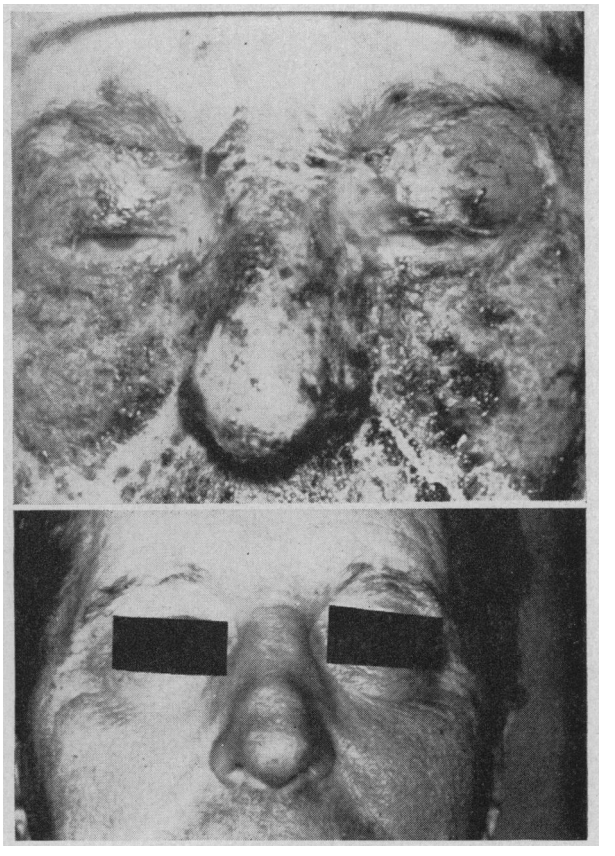

Figure 2.—Pemphigus vulgaris, before and one month after treatment with cortisone.

Experimentally ACTH and cortisone have been found to inhibit the anaphylactoid reaction[8] and the production of the Arthus phenomenon,[4] possibly by the prevention of the formation of antibodies. Also, ACTH and cortisone have been used successfully in treatment of a variety of allergic disorders.[6, 10] Use of the hormones in treating atopic dermatitis, infantile eczema and allergic drug eruptions, as well as the numerous types of sensitization dermatosis, would thus seem reasonable.

Both ACTH and cortisone usually cause pronounced euphoria and psychological uplifts. This effect must be considered when reviewing the results of therapy in dermatoses that are aggravated or caused by emotional disturbances. The euphoric effect of the steroids may be important in the relief of itching. However, these hormones may have a direct antipruritic effect. It is in treating pruritic dermatoses that these hormones appear to be of the greatest value. It must be kept in mind that a transitory depression may occur after use of the drugs is discontinued.

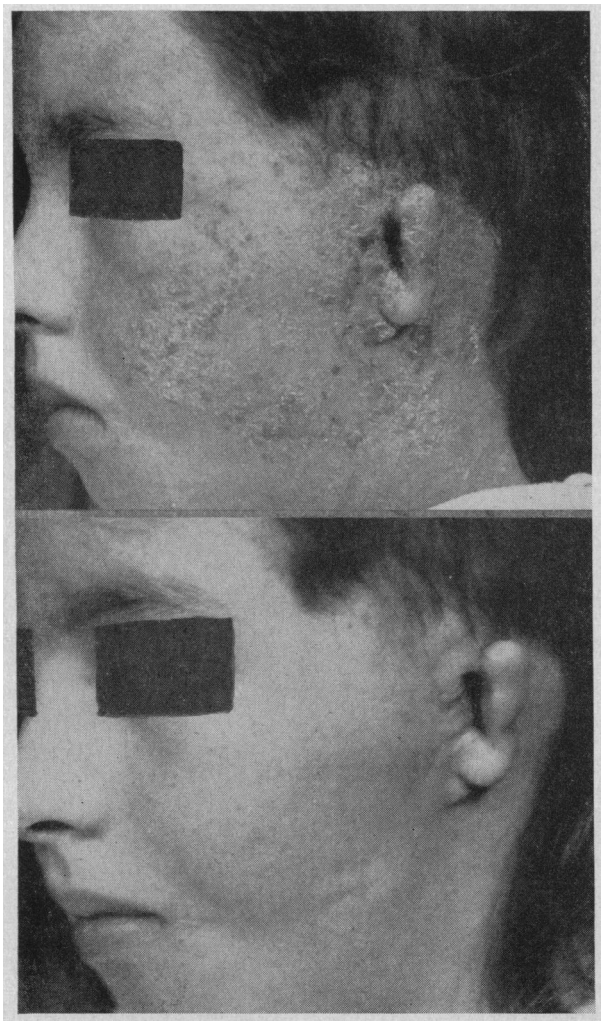

Figure 3.—Infectious eczematoid dermatitis, before and four days after treatment with cortisone.

COMMENT

The results of therapy with ACTH and cortisone in skin diseases have not measured up to the hopes for them. The drugs have been sufficiently studied to permit the conclusion that the disease process is seldom if ever reversed. The symptoms and external evidence of the disease become obscured only to reappear when the drugs are discontinued. The fact that a small number of patients with atopic dermatitis have relapse when steroid treatment is discontinued, and then recover, may be due to the fact that while ACTH or cortisone is being given the anterior pituitary and the adrenal cortex become temporarily inhibited. Then, when the exogenous hormones are cut off, there is a temporary delay in the endogenous production of ACTH and glucocorticoid hormones[9] with the result that the itching and skin eruptions reappear until the anterior pituitary or adrenal cortex starts secreting normally again. Therefore, the period immediately following discontinuance of hormonal therapy may be a critical one, for it may be decided then whether or not there will be complete relapse.

In biopsy of material taken from patients in the four cases of chronic discoid lupus erythematosus in the present series, pathologic changes characteristic of the disease were noted following treatment. In the cases of atopic dermatitis, striking histologic resolution was noted following therapy (Figure 4).

Severe complications occasionally occur with the use of these hormones. They are edema, hypochloremic hypokalemic alkalosis, hypertension, hyperglycemia, acne, hirsutism, striae atrophicae, keratosis pilaris, amenorrhea, the "moon face" and fat distribution associated with Cushing's disease, osteoporosis, and psychic changes.[8, 11] Although these are reversible changes and the more serious ones occur only after prolonged treatment, they indicate the need for caution in deciding to use these drugs for dermatitis which can be treated successfully by other methods. However, in such critical conditions as pemphigus vulgaris, ACTH and cortisone may be the only effective therapeutic agents available. Because of certain complications which occurred during treatment of one patient with atopic dermatitis, the following case is reported.

CASE REPORT

A white American housewife, 55 years of age, was admitted to hospital with complaint of extensive itching eruption of nine months' duration. Conservative therapy had not been effective. A diagnosis of atopic dermatitis was made. ACTH was given and within three days the skin was almost clear. Crusting impetigo of the face caused by coagulase-positive staphylococci and hemolytic streptococci, both sensitive to aureomycin and chloramphenicol, then developed. When the impetigo did not abate after four days of antibiotic therapy—aureomycin locally and chloramphenicol by mouth—ACTH was discontinued and the lesions cleared in the next 24 hours. Then, however, there was a slight relapse in the neurodermatitis. ACTH therapy was resumed and rapid improvement again was noted. The patient was discharged with prescription of a maintenance dose of corti-

sone. Two days later she was readmitted in a state of severe confusion and mania. Paranoid schizophrenia (previously existing) was diagnosed. While the patient was completely out of touch with reality, the skin was clear but the eruption gradually recurred as the mental status improved. When last observed, seven months after hospitalization, the patient was in a vastly better psychic state and the condition of the skin was slightly improved.

In this case there were two complications of ACTH and cortisone therapy. The first was pyogenic infection which would not heal while ACTH was being given, possibly due to the inhibition by the hormone of the immunizing reactions of the tissues or to an alteration of the powers of the circulating leukocytes.[3] The rapid improvement following the withdrawal of the hormone points to some interference in tissue reaction to infection. It is well known that ACTH and cortisone do have certain psychic effects. Euphoria is by far the most common, but depressive states do occur and possibly other aberrant psychic states can develop. The opinion of Hoffer and Glaser[5] is that ACTH and cortisone do not cause psychosis but merely bring to light a condition that was already present. In the case reported herein, the schizophrenic state had been present previously.

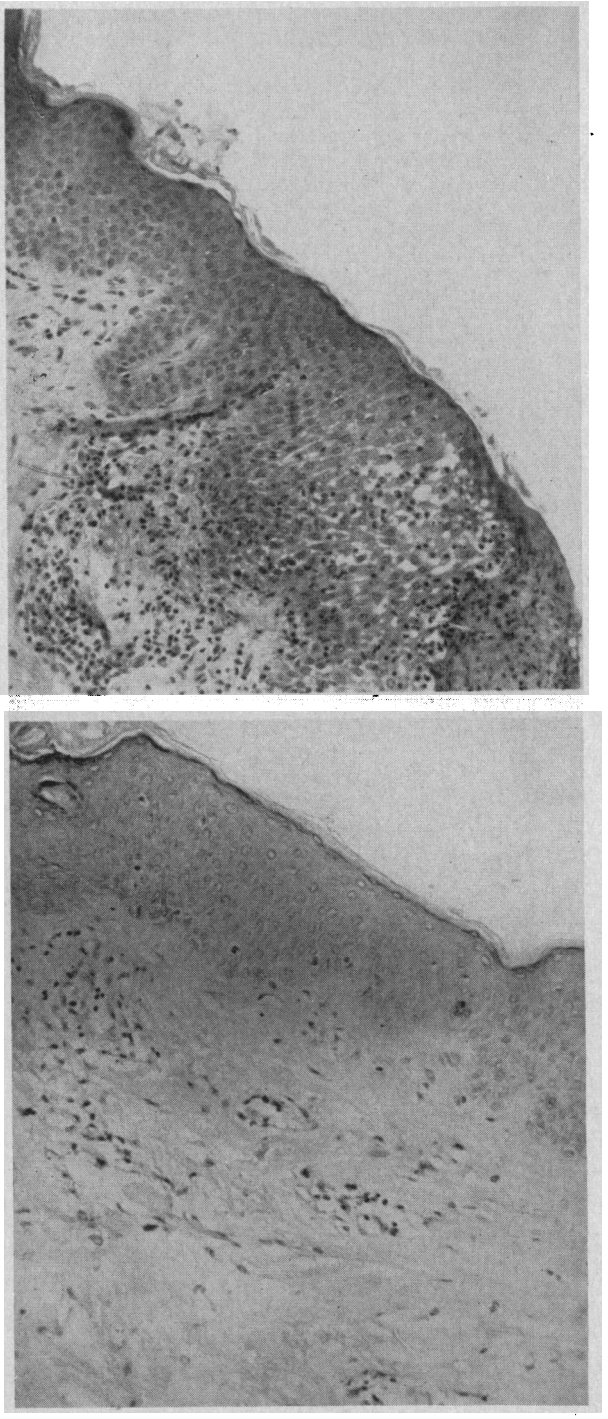

Figure 4.—Skin, arm, atopic dermatitis, before treatment and at eighth day of cortisone treatment.

ACTH or cortisone therapy is indicated in atopic dermatitis if the condition has been present for a long time and is refractory to all other methods of therapy. Use of the steroids may break a vicious cycle and shorten an already long drawn-out disease, but this cannot be a firm conclusion until reports of longer follow-up periods are available. These agents should be used until a maximum effect is reached and then reduced gradually to a maintenance level. Bland topical therapy with sedation should be instituted at the same time, and if the ACTH or cortisone is gradually withdrawn, a rebound relapse may thereby be prevented.

In cases of atopic dermatitis in which there is a strong emotional element, psychotherapy might well be begun when treatment with ACTH or cortisone is started because of the euphoric state which seems to make the patient a more willing subject. Three patients in the present series were treated in that way and after three months of follow-up the results were very encouraging.

CONCLUSIONS

Cortisone and ACTH therapy should not be used indiscriminately in patients with diseases of the skin. In all dermatoses, except those which are usually of a temporary nature, results with ACTH and cortisone are disappointing. At present it cannot be said that any of the patients in the series here reported upon were cured. Although in seven of 22 cases of atopic dermatitis there were remissions of from two to five months at the time of report, this is not a long enough time to permit conclusion that cortisone or ACTH will break the cycle of periodic relapses in such cases.

Results of studies by the authors and by other investigators would appear to indicate a definite place for the use of ACTH or cortisone in treating "drug eruptions" and long-standing cases of atopic dermatitis where other methods have failed.

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