# PRELIMINARY AND SHORT REPORTS

## EFFECT OF ADRENOCORTICOTROPIC HORMONE (ACTH) AND CORTISONE ON THE SEVERAL VARIETIES OF PEMPHIGUS*

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Since April, 1950, 8 patients with pemphigus have received treatment with adrenocorticotropic hormone (ACTH) or cortisone. Three of the patients had the acute malignant form of pemphigus vulgaris, two had chronic pemphigus vulgaris, one had the vegetative form of the disease (pemphigus vegetans), and two had exfoliative pemphigus (pemphigus foliaceus).

### CLINICAL DATA

*Clinical Response.* Under treatment with ACTH or cortisone, all patients began to improve within 3 to 5 days, provided an effective dose was administered. Continued treatment caused further improvement to such an extent that few if any lesions remained. Maximal improvement was reached within two to five weeks. Improvement was, however, temporary. In most patients, new lesions began to appear approximately two weeks after cessation of therapy; but it took several additional weeks before the number and extent of the lesions became appreciable. In 4 patients a minor exacerbation consisting of papules and vesicles occurred within two or three days after cessation of treatment but subsided spontaneously in a few days. In all 5 patients in whom treatment with ACTH was started more than two months ago a second course of ACTH or cortisone has already been necessary; and to one of these patients, affected with pemphigus foliaceus, even a third course has had to be given. Response on readministration was as good as with the first course. In fact, smaller doses were usually effective, probably because the patients were not allowed to relapse to as severe a state of involvement as had been present on the first administration. The shortest interval between first and second courses of treatment was 23 days. One patient with acute pemphigus vulgaris has now been in remission for over 160 days after having received two courses of ACTH.

No serious side effects developed in any of the patients. In one patient with pemphigus foliaceus, acute glomerulonephritis developed in the interval between a course of ACTH and a course of cortisone. This was probably precipitated by a preceding secondary pyogenic infection of the skin and improved, or at least grew no worse, during the administration of cortisone. No mental disturbances were observed except mild euphoria which occurred in most patients. This was usually followed by mild depression on withdrawal of the drug. Distinct hyperpigmentation of the involved skin appeared with ACTH in 3 patients of Mediterranean stock but diminished following cessation of treatment. A suggestion of "moon face" was present in all patients receiving ACTH or cortisone.

*Dosage.* ACTH was administered in equally divided doses every six hours to 2 patients with acute pemphigus vulgaris, 2 patients with chronic pemphigus vulgaris, 1 patient with pemphigus vegetans, and 2 patients with pemphigus foliaceus. In all patients but one with pemphigus foliaceus a daily dose of 200 mgm. was adequate to cause complete or nearly complete involution of the lesions (Fig. 1). The one patient with pemphigus foliaceus did not improve during 14 days' treatment with 200 mgm. of ACTH per day, but improved within three days when the daily dose was raised to 300 mgm. (Fig. 2). Two patients, one

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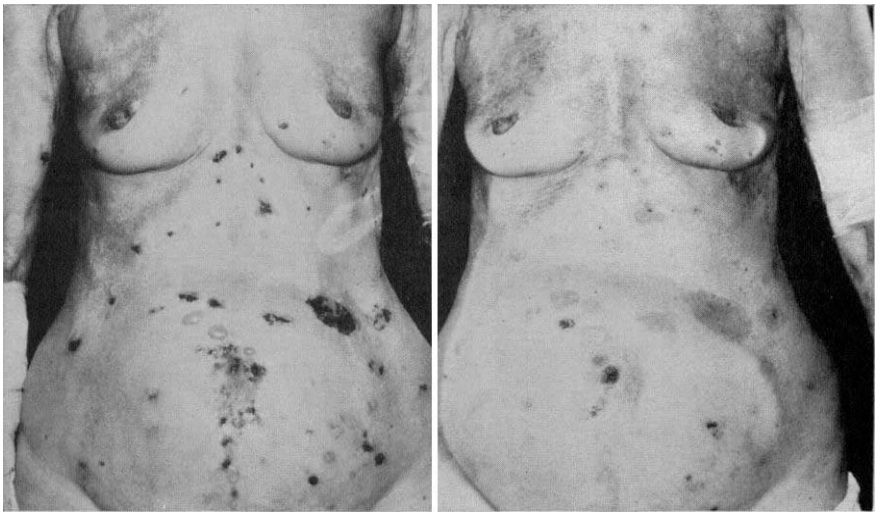

FIG. 1. Condition of the skin of patient E. S. before and after treatment with adrenocorticotropic hormone and cortisone.

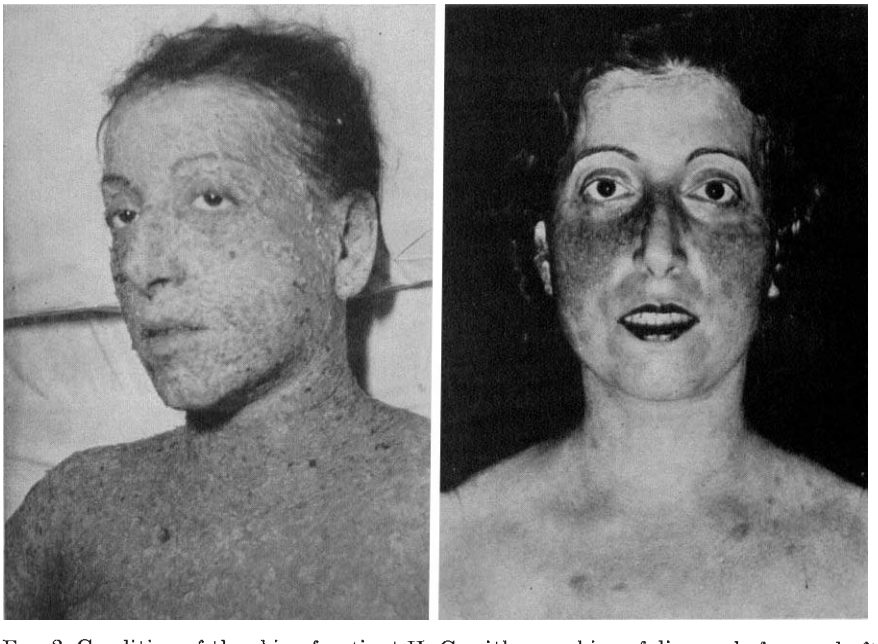

FIG. 2. Condition of the skin of patient H. C. with pemphigus foliaceus before and after treatment with adrenocorticotropic hormone and cortisone.

with acute pemphigus vulgaris and one with chronic pemphigus vulgaris, at first received only 100 mgm. of ACTH daily for one week without clinical improvement, suggesting that as a rule this dose is inadequate.

Cortisone was administered intramuscularly to the 2 patients with pemphigus foliaceus during a relapse and to one new patient with acute pemphigus vulgaris. In the 2 patients

TABLE 1

*Physiological responses of patients with pemphigus treated with adrenocorticotropic hormone (ACTH) or cortisone*

| NAME | DIAGNOSIS | TYPE OF DRUG | ADMINISTRATION | TOTAL AMOUNT GIVEN | DURATION OF COURSE | MAXIMAL CHANGE IN EOSINOPHILS | MAXIMAL CHANGE IN SEDIMENT. RATE | MAXIMAL CHANGE IN WEIGHT | MAXIMAL CHANGE IN 17-KETOSTEROIDS |
|---|---|---|---|---|---|---|---|---|---|
| | | | | *Gms.* | *days* | *per cu. mm.* | *mm. per min.* | *lbs.* | *mgm. per 24 hr. urine* |
| B. A * | Pemphigus vulgaris acutus | ACTH | i.m. | 2.95 | 22 | 917 → 3 | 0.4 → 0.8 | 147 → 155 | 1.4 → 8.0 |
| | | ACTH | i.m. | 1.0 | 5 | 58 → 5 | | 137 → 134 | |
| E. S.† | Pemphigus vulgaris acutus | ACTH | i.m. | 5.7 | 30 | 484 → 0 | 0.8 → 0.1 | 122 → 125 | 0 → 17.6 |
| | | Cort. | p.o. | 3.38 | 16 | 262 → 0 | 0.7 → 0.2 | 123 → 128 | |
| S. A. | Pemphigus vulgaris acutus | Cort. | i.m. | 8.6 | 33 | 2551 → 33 | | 132 → 124 | |
| P. L. | Pemphigus vulgaris chronicus | ACTH | i.m. | 1.38 | 11 | 478 → 6 | | 137 → 140 | 0.4 → 1.8 |
| I. D. | Pemphigus vulgaris chronicus | ACTH | i.m. | 2.6 | 15 | 192 → 2 | 0.35 → 0.2 | 189 → 192 | 10.2 → 19.6 |
| H. S. | Pemphigus vegetans | ACTH | i.m. | 1.38 | 11 | 1837 → 43 | | 195 → 205 | |
| | | ACTH | i.m. | 1.28 | 10 | | | | |
| W. K. | Pemphigus foliaceus | ACTH | i.m. | 5.5 | 33 | 415 → 0 | 0.7 → 0.12 | 131 → 148 | 1.7 → 24.8 |
| | | Cort. | i.m. | 3.25 | 20 | 270 → 94 | 1.2 → 0.35 | 156 → 164 | |
| H. C.‡ | Pemphigus foliaceus | ACTH | i.m. | 8.15 | 46 | 628 → 0 | 1.4 → 0.5 | 117 → 97 | 2.0 → 9.6 |
| | | ACTH | i.m. | 1.25 | 7 | 212 → 4 | 1.7 → 0.7 | | |
| | | Cort. | i.m. | 5.8 | 28 | 282 → 4 | 0.95 → 0.2 | 118 → 112 | |

* See Chart 1.

† See Chart 2 and Fig. 1.

‡ See Fig. 2.

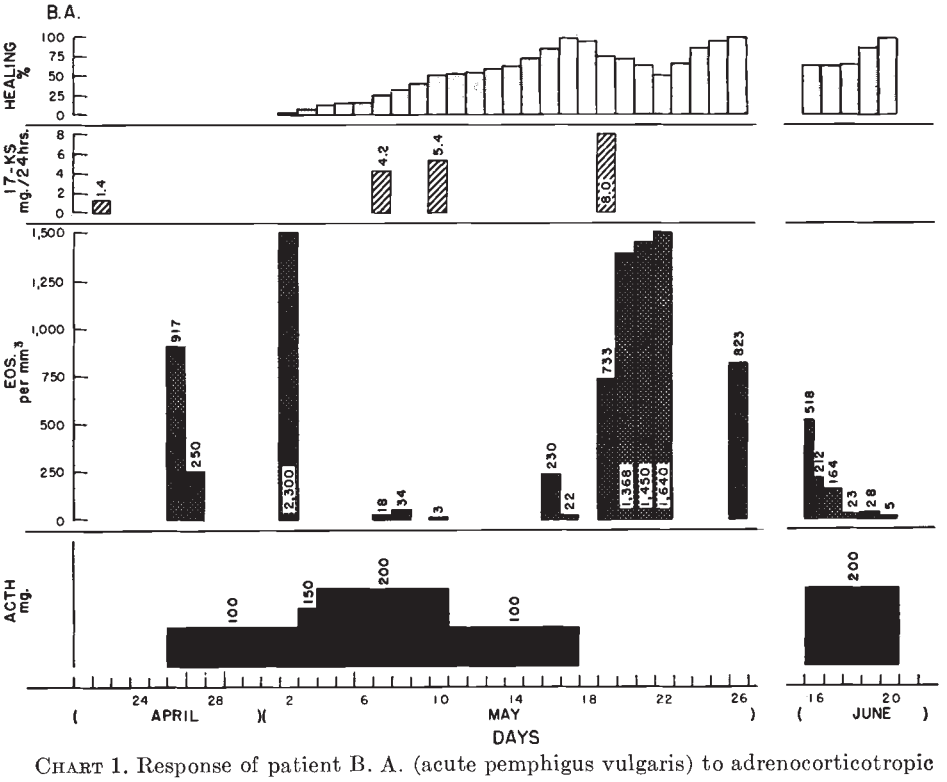


CHART 1. Response of patient B. A. (acute pemphigus vulgaris) to adrenocorticotropic hormone.

with pemphigus foliaceus 300 mgm. per day was found to be effective within two weeks. However, the patient with acute pemphigus vulgaris improved only slightly on 300 mgm. of cortisone per day for twelve days; she became free of new lesions five days after the daily dose was raised to 400 mgm. per day. Cortisone orally in a dose of 300 mgm. per day was given to another patient with acute pemphigus vulgaris during a relapse and improvement began within five days.

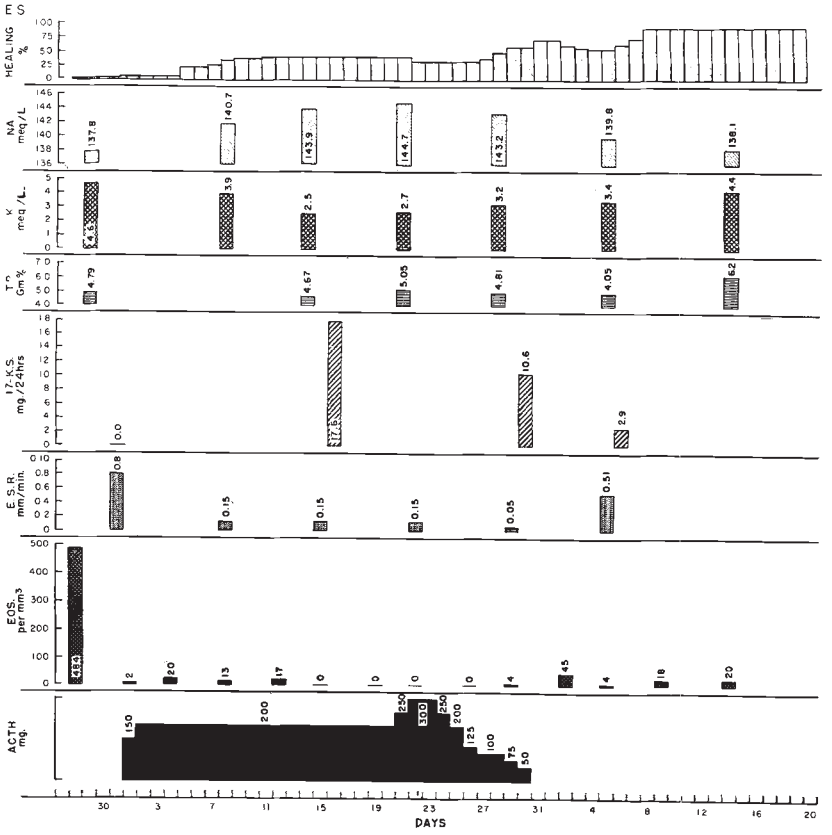


CHART 2. Response of patient E. S. (acute pemphigus vulgaris) to adrenocorticotropic hormone.

### LABORATORY DATA

*Eosinophil Counts.* Blood for eosinophil counts was drawn while the patients were fasting and usually two to three hours after the first dose of ACTH or cortisone of the day. In 6 patients the initial eosinophil count was less than 1,000 per cu. mm. (Table 1). In these patients, with one exception, clinically effective doses of ACTH or cortisone reduced the eosinophil count to values below 10 (Chart 1). In the one exception, the lowest count was 94. In 2 patients the initial eosinophil count was well above 1,000 per cu. mm. In one of them, who had pemphigus vegetans, the count was 1,837 per cu. mm.; it fell to 43 under therapy with 200 mgm. of ACTH per day. In the other patient, who had acute pemphigus vulgaris, the count was 2,551 per cu. mm.; no significant decrease occurred under treatment with 300 mgm. of cortisone intramuscularly per day. However, when the dose was increased to 400 mgm. per day, the count dropped to 33 per cu. mm. In some instances, the

TABLE 2

*Electrophoretic changes in patients under treatment with ACTH or cortisone*

| NAME | DIAGNOSIS | | DATE | TOTAL PROTEIN | RELATIVE ELECTROPHORETIC CONC. | | | | | | ABSOLUTE ELECTROPHORETIC CONC. | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | A | $\alpha-1$ | $\alpha-2$ | $\beta-1$ | $\beta-2$ | $\gamma$ | A | $\alpha-1$ | $\alpha-2$ | $\beta-1$ | $\beta-2$ | $\gamma$ |
| | | | | Gm./ 100 ml. | % of Total Protein | % of Total Protein | % of Total Protein | % of Total Protein | % of Total Protein | % of Total Protein | Gm./ 100 ml. | Gm./ 100 ml. | Gm./ 100 ml. | Gm./ 100 ml. | Gm./ 100 ml. | Gm./ 100 ml. |
| Normal Averages | | | | | | | | | | | | | | | | |
| Serum | | | | 6.80 | 55.0 | 5.0 | 10.0 | 15.0 | 4.0 | 11.0 | 3.74 | .34 | .68 | 1.02 | .27 | .75 |
| Plasma | | | | 7.10 | 53.0 | 5.0 | 10.0 | 14.0 | 8.0 | 10.0 | 3.76 | .36 | .71 | .99 | .57* | .71 |
| Patients with Pemphigus | | | | | | | | | | | | | | | | |
| B. A. | P. v. ac. | Before | 4–22–50 | 4.96 | 37.0 | 9.8 | 12.5 | 17.0 | 11.3* | 12.4 | 1.84 | .48 | .62 | .84 | .56* | .62 |
| | | After | 5–17–50 | 5.11 | 42.1 | 10.1 | 9.5 | 17.1 | 7.2* | 14.1 | 2.15 | .52 | .49 | .87 | .37* | .72 |
| E. S. | P. v. ac. | Before | 7– 2–50 | 5.02 | 37.5 | 11.4 | 15.6 | 17.5 | 4.3 | 14.0 | 1.88 | .57 | .78 | .88 | .22 | .70 |
| | | After | 8–22–50 | 5.33 | 47.6 | 8.1 | 14.0 | 19.6 | 2.7 | 8.1 | 2.54 | .43 | .75 | 1.04 | .14 | .43 |
| | | Before | 11– 9–50 | 5.33 | 44.3 | 8.7 | 10.8 | 15.6 | 9.0* | 11.7 | 2.36 | .46 | .58 | .83 | .48* | .62 |
| | | After | 11–20–50 | 5.54 | 49.1 | 7.5 | 13.5 | 14.6 | 6.0* | 9.3 | 2.72 | .42 | .75 | .81 | .33* | .52 |
| S. A. | P. v. ac. | Before | 10– 2–50 | 5.45 | 43.5 | 7.8 | 11.4 | 14.5 | 11.2* | 11.8 | 2.37 | .43 | .62 | .79 | .61* | .64 |
| | | During | 10–16–50 | 5.62 | 32.1 | 10.5 | 12.0 | 14.9 | 9.6* | 20.8 | 1.80 | .59 | .67 | .84 | .54* | 1.17 |
| | | After | 10–30–50 | 6.04 | 48.3 | 6.1 | 8.9 | 17.5 | 6.9* | 12.3 | 2.92 | .37 | .54 | 1.06 | .42* | .74 |
| H. S. | P. veg. | Before | 5–22–50 | 6.59 | 47.4 | 8.0 | 11.0 | 13.9 | 3.4 | 16.5 | 3.12 | .53 | .72 | .92 | .22 | 1.09 |
| | | After | 6–12–50 | 7.00 | 57.0 | 5.8 | 5.0 | 5.8 | 4.4 | 22.1 | 3.99 | .41 | .35 | .41 | .31 | 1.55 |
| W. K. | P. fol. | Before | 7–19–50 | 6.25 | 38.6 | 9.6 | 12.1 | 12.2 | 12.9* | 14.8 | 2.41 | .60 | .76 | .76 | .81* | .93 |
| | | After | 8–19–50 | 6.34 | 54.2 | 8.1 | 8.3 | 14.9 | 3.4 | 11.2 | 3.44 | .51 | .53 | .94 | .22 | .71 |
| | | Before† | 10– 9–50 | 5.58 | 39.0 | 9.7 | 13.3 | 9.5 | 12.9* | 15.6 | 2.18 | .54 | .74 | .53 | .72* | .87 |
| | | After† | 11–20–50 | 5.96 | 34.5 | 9.1 | 15.4 | 17.3 | 13.6* | 10.3 | 2.06 | .54 | .92 | 1.03 | .81* | .61 |

* Value includes fibrinogen.

† The electrophoretic data were obtained while the patient had glomerulonephritis.

eosinophil counts rose to pretreatment levels two or three days after omission of the drugs (Chart 1). The impression was gained that adequate clinical improvement occurred only with doses of ACTH or cortisone sufficiently large to cause a considerable decrease in the number of eosinophils.

*Erythrocyte Sedimentation Rate.* Serial determinations of the sedimentation rate were made on 5 patients. The rate was elevated in all (Table 1). In 4 patients the rate decreased to normal as clinical improvement occurred (Chart 2). The rate remained elevated in one patient in whom some oral lesions persisted after the cutaneous lesions had healed. It is felt that the sedimentation rate represents a fairly accurate indicator of the response of the patient with pemphigus to ACTH or cortisone.

*Urinary Excretion of 17-ketosteroids.* The excretion of the 17-ketosteroids per 24 hours in the urine was determined in 6 patients before and after treatment with ACTH. In all, a rise in excretion was noted after treatment (Table 1).

*Serum Electrolytes.* In 2 patients a significant decrease in the amount of serum potassium occurred during treatment with ACTH, namely from 4.3 to 3.0 mEq./L. in one patient, and from 4.6 to 2.5 mEq./L. in the other. In both patients electrocardiographic changes consistent with hypokalemia were noted. These changes reverted to normal with the oral administration of 3 to 4 Gm. of potassium chloride per day. In several patients potassium chloride was given orally as a prophylactic measure.

*Plasma Proteins.* A moderate to marked decrease in total plasma proteins to values below 5.6 Gm./100 ml. was observed in 6 patients. Two patients, one with chronic pemphigus vulgaris and one with pemphigus vegetans, had values within the normal range. Clinical improvement under therapy was associated with a rise in the total protein. Electrophoretic analyses before and after therapy were carried out in 5 patients (Table 2). Before therapy the albumin was lowered in all instances, whereas the alpha-1, alpha-2 and gamma globulins were elevated. As a rule, the electrophoretic patterns changed toward normal without, however, becoming entirely normal.

*Water Balance.* Water retention, reflected by a gain in weight amounting to 8 pounds or more was noted in 3 of the patients (Table 1).

*Blood Pressure.* No significant increase in blood pressure was observed in any of the patients.

*Blood Sugar.* No rise in the fasting blood sugar was observed nor was there any significant renal excretion of glucose.