# OBSERVATIONS ON THE EFFECT OF CORTISONE IN ACNE VULGARIS*

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It is generally accepted that androgenic hormones play an important role in the pathogenesis of acne vulgaris. Various studies have indicated that there is an increase in the androgen-estrogen ratio in patients with the disease (1), and Hamilton (2) has shown that administration of testosterone to male castrates will produce acne in many of them. It also is well known that testosterone will produce acne (along with masculinizing effects) when given to normal females. The source of androgen in the female is considered to be the adrenal cortex primarily, and in males a significant proportion of androgen is derived from the adrenal, although the testis is the more important source.

The development of knowledge concerning the suppressive effect of cortisone on adrenal cortical function was, therefore, of interest because of its possible application to an understanding of the problem of acne.

Cortisone in therapeutic doses is known to temporarily suppress the activity of the adrenal cortex by inhibiting pituitary adrenocorticotropin (ACTH) output in patients receiving the hormone (3). More recently it has been shown by Wilkins and co-workers (4) and by others that amounts of cortisone smaller than the usual therapeutic doses will reduce the abnormally high output of 17-ketosteroids in patients with congenital adrenal hyperplasia and will suppress or reverse the clinical signs of virilism seen in these patients. The virilization and the abnormal hormone excretion are considered due to excess production of androgenic hormone by the adrenal cortex. Cortisone in amounts ranging from 25 to 50 or more milligrams daily (in adults) will cause the 17-ketosteroid excretion to return to levels found in normal individuals and apparently will not interfere with the normal adrenal response to stress.

Because of the facts cited above, a brief clinical study into the effect of small doses of cortisone in patients with acne was undertaken. No facilities were available for determinations of hormone blood levels or excretion.

## DETAILS OF THE STUDY

Nine females, with ages ranging between 18 and 34 years, and eight males between 16 and 21 years of age with papular and comedone types of acne were given cortisone. The average dose was 25 mg. daily, although four patients received 50 mg. daily for the first two days of their course; two others received 50 mg. daily for their entire course of six and 14 days respectively. One of the latter patients was especially heavy, weighing 225 pounds. Two of the 17 patients received part

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of their course by the intramuscular route, 50 mg. at intervals of two or three days. The remaining patients took the hormone orally. Periods of administration varied from six to 28 days, but the majority were of ten to 14 days' duration. Four patients received more than one course of the hormone.

Evaluation of results was on the basis of clinical appraisal and on changes noted by the patients. In many of the patients no other treatment was given during the time of cortisone administration; some continued to use routine local therapy with sulfur-resorcin lotion previously prescribed. In seven patients, including two males, estrogen had been administered for varying periods of time (premenstrually in the females) prior to cortisone; in three of these the hormone was started immediately after discontinuance of the estrogen, and in four the cortisone was given one to six weeks after the last dose of estrogen.

## RESULTS

Seventeen patients (eight males and nine females) received cortisone. Five of these, including one male, showed a discernible effect. These cases are presented in detail.

*Case 1*—Seventeen year old male with moderate numbers of deep, cystic comedones and a few inflammatory papules. Ethinyl estradiol* 0.05 mg., had been given daily for 24 days, with slight breast tenderness noted on the 22nd day. One week after the end of this course, cortisone was given, 50 mg. daily during the first two days, then 25 mg. daily for eight days. At the end of this time there was a 50 per cent reduction in the number of cystic comedones and a slight reduction in the number of inflammatory papules. No other changes were noted. The patient returned three months later for observation. At this time he still had fewer comedones than were present initially, but he had a mild increase in the number of inflammatory papules. Cortisone was again given on the same schedule. At the end of eight days there was no appreciable change. There was no follow-up. No estrogen was administered prior to the second course of cortisone.

*Case 2*—Twenty-three year old single female with many deep, cystic comedones on face, oily skin, and a moderate number of inflammatory papules. The response to local therapy, terramycin orally, acne surgery, and premenstrual administration of ethinyl estradiol for four months had been very poor. The estrogen was given in increasing doses, finally reaching 0.1 mg. daily for six days immediately prior to cortisone. The latter was given for 14 days at the rate of 25 mg. daily. At the end of the course there was an estimated 80 per cent reduction in the number of cystic comedones, and the patient thought the skin was less oily. At the next menstrual period the usual flare did not occur, and the improvement was maintained for four months. Eight months after cortisone the patient returned, having had a gradual increase in comedones and papules for three and one-half months, but the skin was not as bad as it had been originally. Cortisone was again given, 25 mg. daily for 28 days. The response this time was less marked. Comedones were moderately reduced, but inflammatory papules were not affected. No estrogen was given prior to the second course.

*Case 3*—Twenty-eight year old single female who had had acne for 12 or 14 years. She showed an oily skin, numerous small scars, and a moderate number of medium-sized inflammatory papules and occasional pustules. She also suffered from mild bronchiectasis. She was treated with a sulfur-containing liquid locally, and by premenstrual estrogen for six months. The hormone produced a definite reduction in oiliness and a moderate reduction in the papules on a schedule of 0.04 mg. of ethinyl estradiol daily for 14 days before each menstrual period. During the last two months on this schedule, she also was given terra-

*Estinyl, Schering Corporation, Bloomfield, N. J.

mycin with marked improvement in the inflammatory papules. Prior to the menstrual period at the seventh month, after having had no estrogen for two and one-half weeks (during which time the oiliness had returned), she was given cortisone, 50 mg. daily for two days, then 50 mg. every second day to a total of ten days just before the menstrual period. Terramycin also was given for three or four days just prior to the menstrual period. The patient noted the same reduction in oiliness of the skin while on cortisone that she had experienced with the estrogen, and the change was noted prior to addition of the terramycin. Cortisone was repeated in the following month, again for ten days prior to menstruation, with the same effect. During this time the patient experienced an exacerbation of her chronic chest infection, with a tight cough, for which she took potassium iodide for three days. This was accompanied by a considerable exacerbation in the papular element of her acne for a few days during the period of cortisone administration.

*Case 4*—Thirty-four year old single female who had experienced mild adolescent acne, followed by occasional papules for several years. In the two months prior to her examination she had noted a number of lesions on the chin and inferior to the anterior portions of the mandibles. These lesions consisted of shallow, relatively small inflammatory papules and scattered, deep, cystic type comedones. The skin was not excessively oily. Estrogen therapy was contemplated, and later used, but first she was given cortisone for ten days. The dose was 50 mg. daily for two days, then 50 mg. every second day for four more doses. There was a reduction of about 50 per cent in the number of deep comedones but no change in the inflammatory papules. Although her skin was not especially oily, the patient stated that while on the cortisone (and also when on ethinyl estradiol later) she was able to use less face powder than usual because the skin was less oily, smoother, and the powder remained in place for a longer time. This change was noted after five days of therapy with either hormone. No objective change in the texture of the skin was discernible, however. Subsequently the patient took ethinyl estradiol premenstrually for several months with almost complete clearing of the lesions.

*Case 5*—Eighteen year old girl with severe acne of four or five years duration. She had received six x-ray treatment of 75 r each in 1950 and six in 1951 with temporary improvement. Six months after the second series of treatments she had many comedones over the entire face and scattered inflammatory papules. During 1952 she received considerable treatment, including various local remedies, premenstrual estrogen therapy, terramycin, vitamin A, and desiccated thyroid. There was temporary improvement from the estrogen but the effect was not maintained upon further therapy during eight menstrual cycles. Six weeks after the last estrogen administration, cortisone was given at the rate of 25 mg. daily for ten days, during which time she failed to have the usual menstrual flare. At the end of the course there was a moderate but definite reduction in the comedones and papules, but a relapse to the previous condition occurred within three days. A second course of cortisone was started two weeks prior to the next menstrual period, 25 mg. daily for the first week, and 25 mg. every second day during the second week. Initial improvement was again noted, but before the dose was reduced there was a mild relapse, which increased on the lower dosage. Two weeks later she was worse than before the cortisone was given. Subsequently diethylstilbestrol was applied in a shake lotion and erythromycin was given orally without effect. Vitamin A in aqueous solution* was started at a dose of 100,000 units daily. Two weeks later the patient was again given cortisone, 25 mg. daily, plus ethinyl estradiol, 0.02 mg. daily for two weeks. There was a mild improvement in the skin, so both hormones were again given, but the dose of estrogen was increased to 0.04 mg. daily and the administration was started at the end of the menstrual period and given for 18 days, presumably producing an anovulatory cycle. At the end of this time there was a further slight improvement. The same schedule was repeated and the patient returned six weeks after its completion. At this time the skin was markedly improved, both as to comedones and papules, appearing better than at any

* Aquasol A., 50,000 unit capsules, U. S. Vitamin Corporation, 250 East 43rd Street, New York City 17, New York.

time in 18 months. The patient stated that the improvement began during the third course of combined estrogen and cortisone, and the improvement was maintained during the ensuing six weeks. She was still taking Vitamin A, which had previously been given 18 months earlier without effect.

The remaining 12 patients showed no significant effect. Eight of these received no estrogen at any time prior to the cortisone; two had taken ethinyl estradiol for 14 days immediately preceding the cortisone; and two others had had estrogen therapy terminated six weeks and 11 weeks before cortisone (the former was a female on premenstrual estrogen for five months and the latter a male who received a single course for 21 days). Several of these patients had moderate to marked oiliness of the skin which was unaffected by the hormone. Two of the females in the failure group received the cortisone by intramuscular injection at the rate of 50 mg. every two or three days.

## DISCUSSION

It is seen that four of the five improved cases had received estrogen, either during, immediately before, or within six weeks of the cortisone administration, whereas only two of the failure cases had had previous estrogen. In three of the improved cases who received more than one course of cortisone, it appeared that the courses given after estrogen administration were more effective than those given at a more remote time after estrogen. The explanation for this apparent potentiating effect of estrogen, if it is valid, is not known.

It is also interesting to note that the most severe patient (Case 5) in the improved group, who had previously had little effect from all types of therapy, including estrogen, was remarkably improved by cortisone combined with estrogen, the latter being given on an ovulation suppressing schedule.

An additional factor of interest is the fact that in some of the patients the effect on the oiliness of the skin which was noted after cortisone was identical to that which was produced at a separate time by estrogen.

Since 70 per cent of the patients showed no discernible effect from cortisone, doubt is cast on the validity of one or both of the original premises; namely, that adrenal androgen influences acne, and that cortisone in small amounts reduces adrenal androgen in patients with acne. Since the termination of the observations, a report has been published by Gardner (5) in which he noted a reduction of slightly elevated 17-ketosteroid excretion in women with idiopathic hirsutism when relatively small amounts of cortisone were administered. As part of his control, cortisone was given to two normal women and there was no effect on their 17-ketosteroid excretion. This would give weight to the belief that the adrenal suppressive effect desired in the acne patients studied actually was not produced.

Still to be explained, however, are the five patients (30 per cent of the total) who noted a definite beneficial effect from the cortisone. It is felt that these changes were not due to chance or to factors other than cortisone, since the effect was sharp and was lost shortly after the cortisone was stopped in three of the

cases. Other treatment factors were unaltered or had previously been shown to produce no effect prior to the cortisone.

The mechanism of this effect of cortisone could be explained on the assumption that in a small percentage of acne patients the adrenal production of androgen is higher than normal and is reduced by cortisone. Other possibilities undoubtedly exist, but exact explanations will await more complete studies. It is believed that cortisone may be a useful tool in helping to clarify some of the endocrine problems concerned in acne vulgaris.

SUMMARY

1) Seventeen patients with acne vulgaris (eight males and nine females) were given one or more courses of cortisone in doses averaging 25 mg. daily for periods of ten to 28 days in an attempt to benefit the skin by the known adrenal suppressive effect of the hormone.

2) The patients were evaluated on a purely clinical basis as follows. Four females and one male noted mild to moderate suppression of oiliness and reduction in the number of comedones. This effect was temporary in two females and in the male. Two other females noted a prolonged suppression of comedone and papule formation after stopping cortisone, for three months in one and for more than six weeks in the other.

3) Twelve patients noted no effect from the cortisone.

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