Management of Atopic Dermatitis

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■ *Fourteen patients with severe atopic dermatitis of long duration, requiring long term systemic corticosteroid therapy were managed with a treatment program designed to preserve the natural lipid surface film, avoid controllable stimuli to sweating, control skin infection, modify existing keratoderma and utilize active topical corticosteroid therapy in non-lipid vehicles. Substantial healing of the skin occurred in all cases even with discontinuance of systemic administration of steroids.*

COMPLETELY SUCCESSFUL treatment of severe atopic dermatitis is yet to be achieved, and management of the patient with a skin disease of this order is a major challenge to the therapist. Long-term systemic steroid therapy brings about good control for many patients, but has serious, undesirable metabolic complications. Topical corticosteroid therapy by surface depot (occlusive) therapy,[2,3,6] effective in many kinds of inflammatory dermatosis, cannot be used in most atopic patients because of the sweat retention factor. A treatment regimen which could control the skin lesion without using systemic corticosteroids, and obtain optimal effects from the highly active topical corticosteroids now available, is desirable.

Beginning in December, 1962, I began using a treatment regimen[4] which has proved superior to any in my previous experience. The program is designed to cope with the skin lesion itself, and does not alter the many constitutional, humoral, physiologic and psychologic factors known to be present and operative in the constellation of atopic clinical manifestations. It appears to be a more satisfactory means of managing the atopic skin, achieving patient comfort and bringing about a considerable degree of healing of the dermatitis.

Although the treatment regimen is one of which I find no previously published report, it is made up of a combination of measures that have been used by many therapists in the past. The experiences reported here are empirical clinical observations in the form of case reports, and no conclusions are drawn or implied relative to the basic nature and cause of atopic disease.

Objectives of Treatment

That xeroderma, keratoderma and sweat retention are commonly present in the atopic skin is widely recognized in the literature.[1,2,6]

The treatment regimen here presented has the following objectives:

1. Preservation of whatever natural lipid surface film is present in the patient. In this respect the management is analogous to that of any patient

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with "dry skin eczema," asteatotic skin or xeroderma.

2. Avoidance of all controllable factors which induce exacerbation such as (a) stimulus to sweating by the conventional hot bath, medicated or otherwise; (b) all greases, ointments and lipid emulsions; (c) any topical medication which may possibly produce irritation of any kind.

3. Healing of the active dermatitis with topical corticosteroids.

4. Control of bacterial infection in the skin when present.

5. Correction of keratoderma if possible.

Clinical Material

Since December 1962, 30 consecutive patients with atopic dermatitis seen in private practice have been managed by this program. The results have been most encouraging in all patients, and no patient has been lost from observation. The patients of most significance and the subject of this report were 14 adults with severe intractable dermatitis of many years' duration, with only minor remissions that usually were induced by systemic corticosteroid therapy. Eleven patients had received corticosteroid therapy for long terms either continuously or intermittently, and attempts to withdraw systemic corticosteroids had resulted in prompt exacerbation. All had been under competent dermatologic management, some of them at major medical institutions. Six patients were referred by other dermatologists for inclusion in this study. Five patients had been under my care on systemic corticosteroid therapy for four years or more before the present treatment was begun. Of the 14 patients, 13 have asthma, and five have cataracts. The essential data on these patients is summarized in Table 1. There was only one case in which the disease began in adult life and the diagnosis might be questionable (Case 1). In the others, the disease had commenced in early childhood or infancy and continued throughout life, with brief periods of relative freedom during the period age four to ten years.

This group of patients therefore might be considered to be a stern trial for any treatment. Sulzberger[5] said: "Cases persisting or beginning after the middle twenties are the most difficult to manage, usually have little tendency to spontaneous cure, and fortunately are relatively rare . . ." Obermayer[1] agreed that in patients whose disease has persisted into the third decade of life, spontaneous remission is unusual and the disease is chronic and recalcitrant and the prognosis poor.

For comparison of evidence as to the efficacy of a method of treatment, it is sometimes important to know what therapeutic measures were *not* em-

TABLE 1.—*Clinical Data on 14 Patients with Atopic Dermatitis Treated by Method Described.*

Patient	Age and Sex	Duration of Atopic Dermatitis	Associated Atopic Disease	Cataracts Present	Last Previous Major Remission	Previous Systemic Steroid Therapy		Severity at Start of Present Treatment	Present Treatment Initiated	Duration of Control Without Relapse (Months)
						Maintenance Dose	Duration			
1.	54F	11 years	asthma	posterior subcapsular	1954	8 mg. Medrol®†	6 years continuous	moderate*	12/28/62	14
2.	33F	continuous since infancy 29 years	asthma, hay fever	.....	none in past 19 years	unknown	10 years intermittent	very severe	1/22/63	13
3.	27F	26 years recurrent	asthma	.....	1960	unknown	2 years intermittent	moderate	2/28/63	12
4.	25F	25 years	hay fever	.....	1958	15 mg prednisone	2 years intermittent	moderate*‡	4/ 3/63	11
5.	18F	15 years	hay fever	.....	1957	10 to 15 mg prednisone	5 years continuous	moderate*‡	4/ 9/63	11
6.	27M	age 1-3, 14-26	hay fever	.....	1956	2 to 4 mg Medrol®†	4 years continuous	controlled*‡	6/18/63	8
7.	28M	28 years continuous	asthma, hay fever	.....	1951	4 to 6 mg Medrol®†	8 years intermittent	moderate*	7/ 2/63	7
8.	26F	24 years continuous	asthma	.....	none since onset	.....	none in past 4 years	moderate	7/12/63	7
9.	60F	59 years	asthma, hay fever	.....	1952	4 to 8 mg triamcinolone	4 years intermittent	moderate	9/ 6/63	5
10.	37M	33 years	asthma, hay fever	posterior subcapsular	1955	4 to 6 mg Medrol®†	8 years continuous	severe*‡	9/20/63	4
11.	27F	26 years	asthma, hay fever	posterior subcapsular	1960	8 to 12 mg triamcinolone	3 years continuous	severe*‡	10/26/63	4
12.	32M	32 years continuous	asthma, hay fever	.....	none since onset	10 mg prednisone	8 years continuous	very severe*‡	10/29/63	4
13.	43M	42 years	asthma	posterior subcapsular	1938	8 mg Medrol®†	7 years intermittent	moderate*	11/ 1/63	4
14.	48M	since infancy, severe since age 22	asthma	bizarre cataract —atopic type	1951	5 to 10 mg prednisone	10 years continuous	moderate*‡	11/15/63	3

*on systemic steroids. †Methylprednisolone. ‡—Cushingoid.

ployed and what possibly influential factors were *not* present. A pertinent list for the present series follows:

- Patients were not put in hospitals.
- Diet was not controlled in any way.
- Daily routine activities were not changed. Working and professional people remained on their jobs, college students continued in school, housewives continued all routine activities.
- Psychological factors were not discussed. One patient (Case 4) had been under psychiatric treatment for one year without benefit on the skin, and this treatment was not interrupted.
- Sedatives and tranquilizers were not routinely used.
- There was no change of marital status in any patient.
- There was no recent change in environment. All had lived in California for at least three years.
- The patients were not told not to scratch.

Treatment Regimen

The regimen of treatment in this series entailed the following items:

- Systemic use of corticosteroids was discontinued.
- Bathing or washing, medicated or otherwise, was prohibited (except as indicated below), since this might remove what natural lipid surface film was present. In addition, hot baths were forbidden, since they are a stimulus to sweating. (Ocean swimming, however, usually is well tolerated.)
- The skin was "cleansed" daily with a lipid-free lotion (Cetaphil®, Texas Pharmacal). This was applied once or more daily and was gently wiped off or left to dry. Soap and water cleansing of the fingers and toes, axillary, inguinal-crural and perianal areas, is permitted if not involved with dermatitis. This program was esthetically acceptable to all patients.
- Greasy and lipid lubricants were not permitted. (Although lubrication might be desirable, I have not found a "lubricant" which does not cause heating and itching of the atopic skin.)
- Acutely inflamed areas were assumed to be infected with bacteria, and in such cases systemic antibiotics were used for 10 to 12 days when indicated. Triacetyloleandomycin was used for this purpose except when other drugs were indicated by culture and sensitivity studies.
- Corticosteroid topical therapy. The measures noted above are essential if maximum benefit is to be derived from active topical medication such as corticosteroids. Conversely, it can be said that much of the benefit from topical corticosteroids can be lost if concomitant local measures have adversary effect. In this series fluocinolone acetonide 0.01 per cent in propylene glycol was used as the major steroid. However, triamcinolone acetonide and flurandrenolone acetonide should be effective provided they are applied in lipid-free vehicles.
- Vitamin A, 50,000 units daily in adults, was given for at least six months.
- Thyroid extract USP, 30 to 60 mg, was administered daily unless contraindicated. Protein-bound iodine (PBI) and other thyroid function tests were not routinely done in this group of patients. However, my experience has been that there is no consistent laboratory evidence of significant hypothyroidism in patients with atopic dermatitis, the PBI being in the range of 4 to 5 micrograms per 100 ml. Hence giving thyroid extract routinely is open to criticism in these circumstances. I have given it, as I do routinely with patients with keratoderma, with the idea that it may potentiate the effect of the vitamin A.
- Phenobarbital, antihistaminics and ataractics were given in the early phases when pruritus was still present. None of the 14 patients in the present series required such medication for more than a few days at the beginning of treatment.
- Exercise and exposure to the sun were permitted only after decided improvement had occurred and the patient noted sweat on the surface of the skin.

Each patient was given copies of written instructions, reassurances and explanations of the reasons for various aspects of the regimen, as follows:

1. Until your skin has become more "normal," the treatment will be more effective if the skin is not washed. *Therefore soap and water baths and showers are to be discontinued until further notice.* Washing under the arms, in the groin, the genitals and around the anal area, and the hands and feet is permitted provided these areas are not involved with the dermatitis.

Regardless of what you may put into the water, *the hot bath or shower which you use to try to get relief from itching is especially bad for your skin. Use the Cetaphil lotion instead—as often as you feel the need. Rub in gently and wipe off the excess. This is the substitute for the bath or shower both for cleansing and for relief of symptoms.*

2. Even though your skin is dry, there is reason to believe that *greases and oils aggravate your skin problem.* So, until further notice, *do not apply any lubricant or skin softener.* In the early period of your treatment, the skin will be scaly and will look rough—but resist the temptation to wash it off or to grease it.

3. In applying your steroid medication, be certain that it is rubbed in completely so that none remains on the surface.

4. As the skin begins to improve, those areas that have been thickened and leathery may show many *small* hard "lumps." These are *not a complication,* but probably have been present for a long time. They become visible as the skin around them begins to be less swollen. *They will gradually and completely disappear as the treatment continues.*

5. It is not expected that you can refrain from scratching when the itching is severe.

6. *Do not apply anything to your skin except what has been specifically prescribed.*

Results of Treatment

The results of treatment were as follows:

- Patient comfort, usually some degree of subjective improvement, was obtained in less than two weeks.
- All patients remained controlled without return to systemic steroids.
- Major but not complete healing of the skin in from two to six months, including disappearance of areas of heavy lichenification in some areas, return of the skin toward normality, decrease of keratoderma and apparent return of "more normal" lipid surface film.
- Return of more normal sweating in three patients.
- Disappearance of white dermographism. (Three patients volunteered this observation.)

The short-term results of treatment have been good, but the ultimate evaluation must await long term observation and treatment of many more patients. In this group the longest period of control was 14 months in two patients, and the shortest was three months in one patient.

Discussion

The treatment program here described, which effectively controlled the dermatitis in the 14 patients in the present series, has been used in 16 other cases of less severe disease with equally good results.

The observations are purely empirical. The results have not been subjected to statistical analysis, and it is possible they are a coincidence. It should be noted that this study involves no comparisons with other forms of treatment except my own past experience and the previous experience of the patients included in the study. It is possible that there are other forms of treatment which are superior, but which have not come to my attention. The program is presented as what thus far has been a highly successful management of the skin in patients with atopic dermatitis. It is not put forward as a "cure."

Evaluation of Measures Used

Under the conditions of this study, there is no basis for accurately evaluating the relative importance of the several therapeutic measures used, and it may be that some of them, for example the administration of vitamin A and thyroid extract, are unnecessary and contribute nothing important to the results. However, it is clear to me that at least five measures are essential to success, namely, (1) abstention from washing the skin; (2) avoidance of greases and oils; (3) control of bacterial infection in the skin; (4) use of active topical corticosteroid in vehicles free of, or low in, lipids; (5) avoidance of all other topical agents which have any potential for irritation.

Certain limited evaluations have been done as follows: Patients who use the corticosteroid solution but who do not comply with the no-bathing, no-greasing restrictions, do not get good results, and continue to have exacerbations. On the other hand, patients who do comply with the no-bathing, no-greasing restrictions, but use a propylene glycol vehicle alone in limited areas, obtain little or no healing of the skin even though the areas may be reasonably comfortable.

In one patient, the entire program was carried out except that the only local application to the right arm was a lubricating oil which she had used and preferred for several years. In four weeks all other areas were decidedly improved and comfortable, whereas the right arm still showed a highly active, lichenified, erythematous dermatitis and was very pruritic.

Topical Corticosteroid Therapy

No attempt was made to evaluate the relative activity of various topical corticosteroids, and no implications are intended. Good results could be expected with other active corticosteroids such as triamcinolone acetonide and flurandrenolone, but these were not available to me in propylene glycol.

Fluocinolone acetonide in propylene glycol was the major steroid preparation used in this group of patients and it was well tolerated by all of them. All patients preferred the propylene glycol vehicle to any cream vehicle insofar as comfort after application was concerned. From the standpoint of therapeutic effectiveness, excellent results were obtained in limited test areas with fluocinolone acetonide cream and triamcinolone acetonide cream.

Resolution and healing of areas of dermatitis can be hastened by the use of higher concentration of

TABLE 2.—*Amounts of Topically Applied Corticosteroid*

Patient	Per Cent Body Surface Area Involved (Approximate)	Average Daily Dose (in mg) Fluocinolone Acetonide	
		First 60 Days	First 180 Days
1.	50	0.57	0.34
2.	95	1.75	1.80
3.	15	0.27	0.13
4.	20	0.50	0.30
5.	30	0.55	0.64
6.	80	0.90	0.43
7.	30	0.25	0.15
8.	20	not accurately recorded	
9.	35	0.62	0.56 (150 days)
10.	90	not accurately recorded	
11.	95	0.82	0.52 (120 days)
12.	98	not accurately recorded (3 mg +)	
13.	95	1.30	0.75 (120 days)
14.	20	0.39	0.19 (90 days)

topical corticosteroids, and this was demonstrated in limited areas treated with triamcinolone acetonide cream 0.5 per cent, and fluocinolone acetonide cream and solution 0.2 per cent. However, since application of these high concentrations to large areas of skin raises the question of systemic absorption, and since the objective of this treatment is to get results without appreciable systemic corticosteroid effect, the major part of the treatment was carried through with the 0.01 per cent solution. This entire question needs further elucidation.

The average daily amount of fluocinolone acetonide solution (0.01 per cent) at the initiation of treatment was 15 ml (equivalent of 1.5 mg of the active drug) usually applied in two to three applications, with less being used as the involved area decreased. The solution is dropped onto the skin surface with a dropper and spread with the fingers —one drop covering about 25 square centimeters if the skin surface is reasonably intact. The solution should be rubbed gently until it seems to be rubbed in. An uncomfortable sticky sensation results if excess material remains on the skin surface. When applied to denuded and fissured areas, a burning and stinging sensation occurs which is rarely severe enough to interfere with treatment.

In this group of patients the amount of topical steroid used was far below the amount of systemic steroid required to produce equivalent results in the skin (Table 2). Three patients were studied for pituitary adrenal function after they had been on the program a minimum of four months, and off systemic steroids for this period. There was no evidence of impaired pituitary adrenal function as measured by response to metyrapone in two patients and to intravenous ACTH and metyrapone in one.*

*The details of these studies will be published in a separate report.

(Unfortunately these tests were not done immediately after withdrawal of systemic corticosteroid therapy. If impaired function had been found after the present topical therapy, it would have been impossible to determine whether the impairment was due to the present therapy or was a consequence of the long-term systemic steroid therapy plus the extensive topical steroid therapy previously administered.)

Seven of the patients had signs of hypercorticism (Cushingoid) at the time systemic steroid therapy was withdrawn. In all seven these signs disappeared completely on the present program.

In one instance (Case 5) systemic steroid therapy had been abruptly withdrawn one week before the patient was referred to me for inclusion in this study. She was having exacerbation of the dermal disease and was Cushingoid. Improvement began in less than two weeks of the present program, and since improvement continued it was not necessary to reinstitute systemic steroids at any time. In other patients systemic steroids had been continued up to the start of this present treatment and were withdrawn gradually over a period of two to four weeks. In no instance was it necessary to reinstitute systemic corticosteroid therapy for control of the dermatitis.

Dosage of Topical Steroid

To a degree, the maximum daily dosage was arbitrarily limited since the patients were asked to try to limit the amount to 15 or 20 ml of solution daily. However, one patient (Case 12, Table 2) who had severe universal dermatitis with heavy lichenification of large areas, used considerably more. In the average patient with involvement of scalp, face and neck, cubital and popliteal areas, 15 ml will provide adequate application twice daily. As improvement occurs, the amount needed decreases, as noted in the averages for the six-month treatment period (Table 2).

Role of the Vehicle

Avoidance of greases and oils requires that any active medication be applied in a suitable vehicle free of, or very low in, lipid content. Propylene glycol, a higher alcohol, is non-toxic, non-irritating, non-sensitizing and especially well tolerated by atopic patients (and in other sweat retention syndromes). It is strongly hygrosocopic, and this may possibly explain its usefulness in atopic patients if imbibition of sweat pores is a factor in sweat retention (Sulzberger[5]). Propylene glycol is also demulcent and tends to form a protective coating on abraded surfaces. It is a vehicle of wide applicability with few disadvantages and is especially useful in intertriginous areas and in the scalp and

external ear. I have used it for more than ten years in several thousand patients, as a vehicle for a variety of agents, and have never observed a reaction to the vehicle if properly used.

Time Factors

Symptomatic improvement occurred within two weeks in all patients, but significant healing of the skin lesions took longer, depending upon the severity of the lesions at the beginning of treatment. Areas of decidedly thickened, lichenified, leathery skin required four to six months, and in some areas complete return to normal was not achieved with fluocinolone acetonide 0.01 per cent solution. In these limited resistant areas, treatment with 0.5 per cent triamcinolone acetonide cream and 0.25 per cent fluocinolone acetonide cream were used with success. Large areas of moderate severity did clear with the 0.01 per cent solution, usually in periods of one to four months.

Sweat Function

Of particular interest was that three patients (Cases 2, 4 and 5) with lifetime disease, after pronounced improvement in the dermatitis, volunteered the observation that they were conscious of sweating for the first time in many years. Previously when under conditions of high environmental temperature and humidity, they felt uncomfortable, the skin feeling "sticky" but not moist, and they were not conscious of sweating in the usual sense.

Role of the Patient

Since this treatment is carried out entirely by the patient, conscientious cooperation and attention to detail is crucial to any success which might be achieved. However, patients who have suffered the misery of this disease for many years are strongly motivated to cooperate and carry through any program which offers help. I have stressed to them that even though some relief of symptoms can be obtained in a few weeks, real progress can only come with many months of application of the program. Since virtually all patients with chronic, severe atopic dermatitis are addicted to long hot baths or showers, and also to generous and frequent use of greases and oils, careful explanation by the physician at the beginning of treatment is necessary to wean them from these practices. They must be warned that at times the skin may be dry and peeling, and that they must resist the temptation to soak the scales off in a hot tub or to apply oils and greases.

Reactions and Complications

The treatment regimen herein described has been remarkably free of significant reactions and complications. The question of greatest importance is the possibility of systemic corticosteroid effect through percutaneous absorption. However, as indicated in Table 2, the amounts applied to the skin daily have been below that which could produce systemic effect even if the absorption approached 100 per cent of the applied dose.

In one female patient, folliculitis of the face occurred after nine months of this program. It was assumed that this was the result of "no-washing" and was in the nature of acneform or rosacea-like folliculitis. This is supported by the facts that cultures revealed no pathogenic organisms, there was no response to antibiotics systemically and locally, and there appeared to be response in several weeks to washing once daily with Lowila® cake* and water. After three weeks of washing, the patient noted that the skin had become uncomfortably dry and itching, and preferred to return to the Cetaphil cleansing. The folliculitis did not recur.

If this patient is excluded, there was no suggestion that the regimen—specifically the topical steroid—promoted infection or reduced resistance to infection of any kind. Furunculosis did not occur.

In two patients under conditions of extremely high humidity and heat, "heat rash" occurred. However, this would not be unexpected in atopic patients and should not be considered a complication of treatment. As a matter of fact, treatment was continued and appeared to have a beneficial effect, the eruptions clearing in less than one week.

Probably the most important complication was the exacerbation of asthma in three patients in this group. In two, this did not occur until they had been on the program for many months and the skin lesions had become completely clear or nearly so. The third patient (Case 14) had been receiving systemic steroids continuously for 12 years and when systemic administration was discontinued gradually over a period of four weeks, severe asthma developed for the first time since treatment by that means had been begun. This occurred about a week after the last oral dose of prednisone. At the time of the attack of asthma, the skin had become about 90 per cent clear and the lesions flared only slightly with the return of asthma. The patient was referred to an allergist who was of the opinion that resumption of systemic steroids was necessary, at least temporarily, for the control of the asthma. In the other two patients, the asthma was controlled with inhalation therapy and an occasional single oral dose (4 mg) of triamcinolone. Over a period of one month the asthma gradually subsided and both patients thereafter remained free of it.

Ten other patients who had had asthma in the

*Lauryl sulfoacetate in a corn dextrin base.

past, had no major exacerbation during the present period of observation.

The impression is strong that the patient with atopic dermatitis aggravates the condition by the bathing and showering which he does either for the supposed healing effect or for relief of symptoms. Often on his own or encouraged by a physician, he takes long hot baths (medicated or otherwise) and showers, sometimes two or three times daily, and immediately afterward greases or oils the skin. It is apparent that both these measures are directly deleterious, and when they are discontinued there is almost immediate (within a few days) relief from itching and a sudden definite decrease in the inflammation and swelling of the skin. The symptomatic response is apparent in a few days and some objective changes are evident in one to two weeks—long before much actual healing can be obtained with topical steroids. This effect was observed in all the 14 patients in the present series.

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ADDENDUM: This series now totals 63 patients, ages ranging from 2 to 60 years, and includes 6 additional severe cases, with continuing satisfactory results. An additional 12 months has been added to the period of control without the use of systemic corticosteroids in this group of patients.

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