

The present case indicates that the known adverse effects such as dryness of the skin and scaling also may be seen in the ear, and that in predisposed persons this irritative condition may cause excessive cerumen production and otitis externa.

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## Transepidermal Water Loss and Sweat Gland Response in Lamellar Ichthyosis before and during Treatment with Etretinate: Report of Three Cases

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**Abstract.** Despite its desquamative effect, oral etretinate had no normalizing effect on the increased basal transepidermal water loss in 3 patients with lamellar ichthyosis. Neither was any improvement achieved during treatment in the defective sweat gland function as measured after stimulation by intracutaneously injected methacholine chloride solution.

**Key words:** Etretinate; Transepidermal water loss; Sweat gland function; Evaporimetry

An increased transepidermal water loss (TWL) has been demonstrated in lamellar ichthyosis and other ichthyoses (4, 5). Furthermore, in lamel-

lar ichthyosis there is a failure in normal sweating which may cause hyperpyrexia in warm weather or during exercise. So far the mechanisms of these disturbances are not known.

Because of its desquamative effect, oral etretinate (an aromatic retinoid, Ro 10-9359) has proved useful in the treatment of various hyperkeratotic dermatoses including lamellar ichthyosis (for reviews, see 2, 7). In the present paper we report the effect of this treatment on TWL and on the activity of sweat glands in 3 adult patients with lamellar ichthyosis.

## MATERIAL AND METHODS

### *Patients and treatment*

Three adult patients with congenital lamellar ichthyosis were studied. Histological biopsies confirmed the clinical diagnosis. Three healthy persons served as controls. Age and sex distributions are presented in Table 1. The patients were given etretinate at an initial dose of 0.75–1.00 mg/kg/day. The dose was later reduced to a maintenance level of 0.50–0.90 mg/kg according to the clinical response.

### *Measurement of transepidermal water loss (TWL) and sweat gland function*

Basal TWL and peak sweat response after stimulation were measured before and during treatment, using an evaporimeter (8) (Evaporimeter EP 1, Servomed, Stockholm) to record sweating, as described previously (9).

Sweat gland function was evaluated by injecting 0.1 ml of methacholine chloride (Mecholyt®, Sigma) in saline, 1:10<sup>3</sup> dilution, intracutaneously in symmetrical sites of the upper back skin of the patients. This concentration has been used to reveal absence of active sweat glands (10). In healthy controls the dilution 1:10<sup>7</sup> was used, since in normal skin high concentrations exceeded the measuring capacity of the apparatus.

The temperature of the test area was measured with an YSI 408 thermistor and was recorded on a Telco recorder. The local mean skin temperature in the patients was 33.3 (SD ±0.6)°C and in the control subjects 33.6 (SD ±0.3)°C. The temperature of the test room ranged from 20 to 23°C, and the relative humidity from 15 to 40%.

## RESULTS

The results of TWL and sweat rate measurements in patients and controls are presented in Table 1. The basal TWL in ichthyotic patients was almost 3-fold compared with that in controls. A slight increase in TWL was observed during treatment. Methacholine stimulation with a 1:10<sup>3</sup> dilution had virtually no effect on total cutaneous water loss in

Table 1. Basal TWL and methacholine-induced sweat response in 3 patients with lamellar ichthyosis before and during treatment with etretinate, and in 3 control subjects

Patient	Age (years)	Sex	Duration of treatment (months)	Basal TWL	Peak sweat response g/m <sup>2</sup> h Methacholine stimulation	
					1: 10 <sup>3</sup>	1: 10 <sup>7</sup>
PM	52	m	0	10	11	—
			1	12	13	—
			2	10	12	—
			4	13	17	—
			5	13	22	—
			10	15	19	—
			12	18	26	—
KJ	19	m	0	18	24	—
			3	18	18	—
			11	22	23	—
LL	27	f	0	10	16	—
			7	16	20	—
			11	17	24	—
Controls						
YJ	48	m	—	5	—	76
JV	20	m	—	8	—	57
MH	22	f	—	7	—	59

patients with lamellar ichthyosis, whereas in controls the highly diluted test substance produced a nearly 10-fold increase.

## DISCUSSION

In agreement with the previous reports (4, 5) our results show that the transepidermal water loss is increased in lamellar ichthyosis. This is compatible with the findings of Elias et al. (3) who reported that properties other than thickness of the stratum corneum determine its barrier capacity. So far it is not certain whether the increased water loss in lamellar ichthyosis represents a disturbance of the barrier function of the horny layer or is a result of surface irregularities or cracks in the epidermis (1). Recently, the horny cells in lamellar ichthyosis were reported to have a defective marginal band (6), but the relation of this finding to the barrier function is obscure. Treatment with etretinate had no normalizing effect on the increased TWL. Instead, a slight tendency to an increase in TWL was seen. This may be related to the desquamation produced by etretinate.

The sweat glands of our patients appeared histologically normal and no poral occlusion was observed. However, no sweat gland activity could be demonstrated by methacholine stimulation before

or during etretinate treatment. In search for an explanation we tested the effect of successive stripping until glistening, but observed no increase in sweat response in the methacholine-pretreated skin. This may indicate that the cause of sweat gland inactivity does not reside entirely in the massive horny layer and may suggest a defect in the intra-epidermal sweat duct or in the dermal sweat gland components. In our study etretinate was not able to normalize this defect. Nevertheless, the subjective feeling of discomfort in warm weather abated in all our patients.

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## Comparison of Two Application Schedules for Clobetasol 17 Propionate

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**Abstract.** In a double-blind trial, intermittent treatment of psoriasis, designed to take advantage of the tachyphylaxis phenomenon and consisting of 3 days of twice daily application of 0.05% clobetasol-17-propionate ointment alternating with 4 days of the base alone, gave results that were no better than obtained with continuous treatment. In 10 patients, a weekly treatment consisting of 3 successive days with as little as 8 g 0.05% clobetasol-17-propionate ointment (24 g a week) followed by 4 days of bland ointment, sufficed to reduce the desquamation to 'hardly any' and the erythema/infiltration to 'slight'. This might be attributable to the drug reservoir in the stratum corneum, as postulated by Vickers.

Little is known about the optimal frequency for the application of topical corticosteroids. Some authors advise four inunctions a day, but a larger group recommends two a day. Observations on corticosteroid-induced tachyphylaxis (1) suggest that for corticosteroid-responsive dermatoses, intermittent treatment with corticosteroids would give better results than daily treatment.

## MATERIAL AND METHODS

To test this hypothesis, the following double-blind trial was carried out in two centres. Two groups of psoriasis patients were treated for 3 weeks with either 8 g 0.05% clobetasol-17-propionate ointment (Dermovate® ointment) daily, divided over two applications, or the same treatment on 3 days each week and the same amount of only the ointment base on the other 4 days. All patients with psoriasis distributed at least over the trunk and extremities and an intensity score of 4-6 for at least one area, were considered eligible for the trial. The treatment was carried out double-blind as follows. In a randomized way, each patient received either three sets of 7 active 8-g tubes each (continuous treatment) or three sets of 3 active and 4 placebo tubes each (intermittent treatment). Each set was labelled with the name of the patient and the day of the week the tube was intended for. Scaling and erythema/infiltration were scored separately for the scalp, arms, trunk, hands, and feet at the beginning of the treatment and after 1, 2, and 3 weeks, according to the following intensity scale (to facilitate scoring, a photograph of each of the indicated states was provided):

### *Desquamation*

8 very thick desquamation  
6 relatively thick desquamation  
4 moderate desquamation  
2 slight desquamation  
1 hardly any desquamation  
0 no desquamation

### *Erythema/infiltration*

8 strong infiltration  
6 moderate infiltration  
4 slight infiltration  
2 erythema only  
1 slight erythema  
0 normal skin colour or leukoderma

## RESULTS

At the end of the trial, 20 patients had been treated, 8 in one centre and 12 in the other, both groups divided equally between the two treatments. Because the differences between the results obtained in the two centres were relatively small, the data were pooled for the statistical analysis. Furthermore, since the number of patients was small and in some the psoriasis was not present on all five