# A Double-Blind Clinical Trial Comparing the Efficacy and Safety of Pure Lanolin Versus Ammonium Lactate 12% Cream for the Treatment of Moderate to Severe Foot Xerosis

Maureen B. Jennings, DPM; Donna M. Alfieri, DPM; Eunice Ramsey Parker, DPM; Lorraine Jackman, DPM; Susan Goodwin, PhD; Christine Lesczczynski

*Xerotic skin is a pattern of reaction to a variety of disorders (eg, winter xerosis, hereditary ichthyosis) with abnormalities of desquamation in common. The trial described in this article was a double-blind randomized-comparison clinical trial investigating the effect of pure lanolin versus ammonium lactate 12% cream in treating moderate to severe foot xerosis. Xerosis was clinically assessed at baseline visit, and designated sites were reevaluated after 1, 2, and 4 weeks of therapy. Ninety-two patients were enrolled; 41 of these were excluded from analysis (25 were lost to follow-up, 8 were noncompliant, 1 was discharged from study because of an adverse event after visit 1, and 7 were noncompliant after visit 2). Although there was significant improvement in xerosis scores for both treatment groups after 2 and 4 weeks of treatment, no differences were statistically significant. Used twice daily for 4 weeks, pure lanolin and ammonium lactate cream were both effective in treating moderate to severe xerosis.*

Accepted for publication July 29, 2002.
Drs. Jennings, Alfieri, Parker, and Jackman and Ms. Lesczczynski are from New York College of Podiatric Medicine, New York, New York. Dr. Goodwin is from New York Medical College, New York, New York.
This study was supported in part by Lansinoh Laboratories, Alexandria, Virginia.
Reprints: Maureen B. Jennings, DPM, New York College of Podiatric Medicine, 1800 Park Ave, New York, NY 10035 (e-mail: mjennin@nycpm.edu).

In normal skin, the stratum corneum serves as a protective barrier against excessive water loss (through evaporation) and environmental insults.[1] The health of the stratum corneum depends on its water content and environmental temperature.[1]

Xerosis is defined as dehydrated skin showing redness, dry scaling, and fine crackling. Xerotic skin may resemble crackled porcelain.[2] The hallmarks of xerosis are scaliness and loss of elasticity.[3] These changes are most frequently seen on the extremities, especially the legs and feet.[2]

In xerosis, the desquamation process is impaired, and desmosomes accumulate in the outer layers of the stratum corneum, leading to an increase in surface corneocytes.[4] In skin damaged by winter xerosis or UV radiation, there is a significant increase in desmoglein 1 in the superficial layers—an increase not found in the normal stratum corneum.[4] Desmoglein 1 is thought to be a major component of the intercorneocyte cohesion in the stratum corneum.[4]

Treatment of xerosis involves 3 aspects: replacing water content and maintaining hydration, alleviating symptomatology, and controlling keratinization to reduce scaling.[5] Therapy has been limited to topical applications of hydrating emollients designed to soften the stratum corneum and alleviate the dry scaliness.[6] Emollients (eg, lanolin, glycerin) are hydrophilic and form an occlusive barrier that decreases evaporation.[1,2] Certain skin protectants contain hygroscopic substances also known as humectants, which increase skin moisture and reduce water loss.[5]

**Xerosis Severity Scale***

| Severity | Rating | Description |
|---|---|---|
| Mild | 0 | Normal skin |
| | 1 | Dusty appearance, few minute skin flakes |
| | 2 | Generalized dusty appearance, many minute skin flakes |
| Moderate | 3 | Defined scaling with flat borders |
| | 4 | Well-defined heavy scaling with raised borders, shallow fissures |
| Severe | 5 | Large scale plates, fissures |
| | 6 | Large scale plates, deep erythematous fissures |

*Adapted from Rogers et al.[10]

Lanolin (from the Latin *lana* for wool and *oleum* for oil) is secreted by the sebaceous glands of sheep to soften fleece and protect it against the elements.[7] Traditionally, unmodified lanolin is considered an absorptive ointment that maintains internal moisture.[8] Rawlings et al[4] hypothesized that lanolin, like glycerol, aids in the enzymatically medicated digestion of superficial desmosomes, thereby improving the desquamatory process in xerosis. Lactic acid 12% cream is designed to produce humectant effects, which thereby reduce the xerotic disease state.[9]

The purpose of this study was to evaluate the safety and efficacy of pure lanolin versus ammonium lactate 12% cream in the treatment of moderate to severe xerosis.

## Methods

This trial was a double-blind randomized-comparison trial investigating the effect of pure lanolin versus ammonium lactate cream in the treatment of moderate to severe xerosis. Patients with bilateral moderate to severe xerosis, as designated by the Xerosis Severity Scale (XSS) created by Rogers et al[10] (Table), were included. Pregnant women and patients with peripheral vascular disease, preexisting immunosuppressive disease, known hypersensitivity to ammonium lactic acid or lanolin, or known dermatologic disease (eg, psoriasis, eczema, Darier disease) were excluded.

Treatment order was randomly predetermined. Each patient served as his or her own control, as all patients had bilateral xerosis. They each applied one test medication to one foot and the other test medication to the other foot.

Patients were enrolled after the inclusion and exclusion criteria were met, and informed consent was obtained. If possible, a dermatophyte test medium culture was taken to rule out fungal infection. In the event of a positive culture, the patient would be discharged from the study. After appropriate patients were selected and initial evaluation of each patient's xerosis site(s) was completed, treatment was begun. The chosen sites were reevaluated 1, 2, and 4 weeks after the start of treatment. All patients were at least 18 years of age and had a score of 3, 4, 5, or 6 on the XSS.

Medication was administered in the following manner. To avoid cross-treatment contamination, each patient used the right hand to apply medication to the left foot and the left hand to apply medication to the right foot. Pure lanolin and ammonium lactate 12% cream were supplied in identical tubes. A bright orange label was affixed to the right-foot tube; this label listed the patient number and the directions for applying medication with the left hand. A bright blue label was affixed to the left-foot tube; this label listed the patient number and the directions for applying medication with the right hand. Patients were advised to massage the affected site(s) until the medication was properly absorbed. Investigators used the XSS to evaluate the severity of xerosis for each patient. At each visit, tenderness was assessed by the patient and the investigator. They rated level of discomfort experienced by the patient with palpation of the feet on a 4-point scale with points labeled 0 (no discomfort), 1 (mild discomfort on deep palpation), 2 (moderate discomfort on moderate pal-

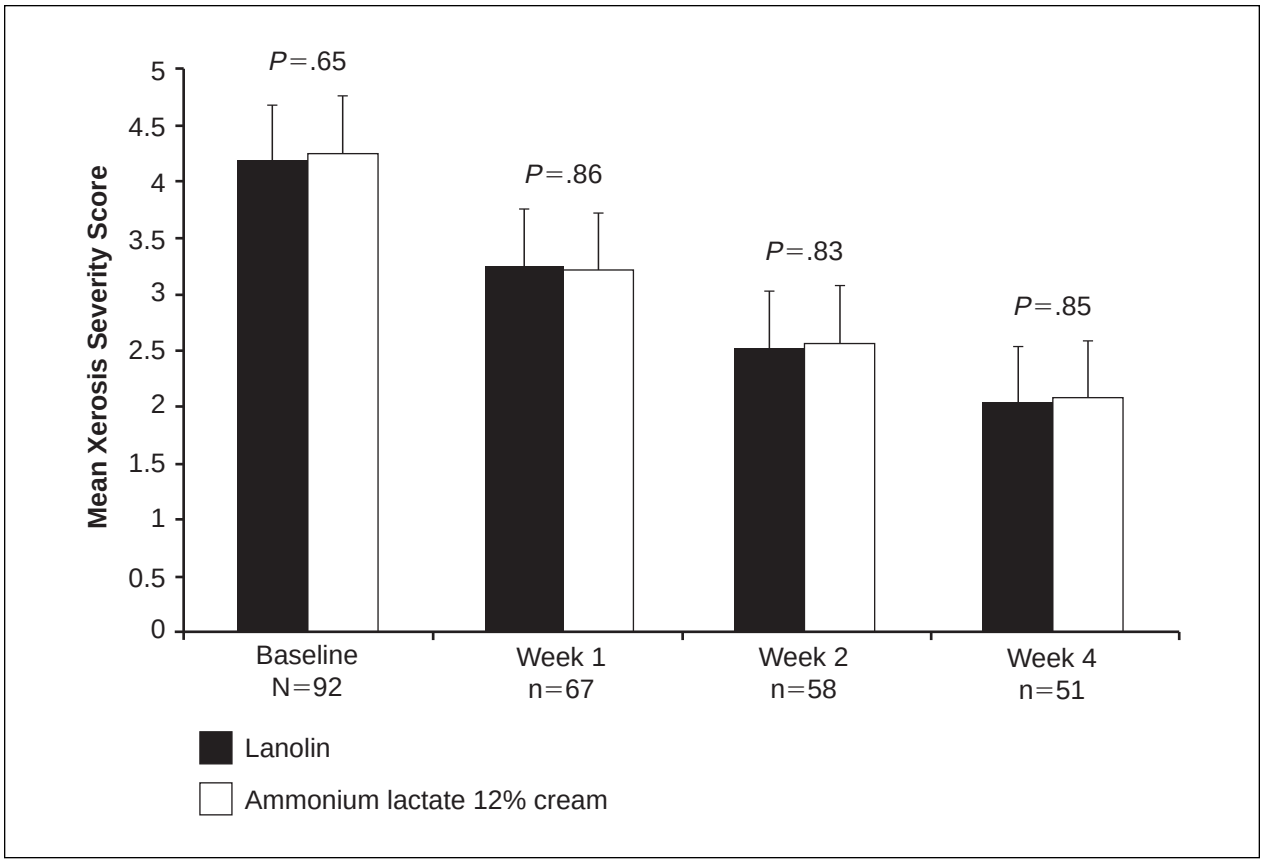


**Figure 1.** Mean xerosis severity score.

pation), and 3 (severe discomfort on slight palpation). At each visit, the patient was questioned regarding pruritus and was asked to assess its degree on a 4-point scale with points labeled 0 (none), 1 (mild or slight), 2 (moderate or somewhat), and 3 (severe or very).

After week 4 of treatment, the patient and clinician independently rated overall results on a 6-point scale: 0 (clear), 1 (good improvement), 2 (moderate improvement), 3 (slight improvement), 4 (no improvement), and 5 (worse).

To ensure patient compliance, both tubes of medication were weighed at all 4 visits (at initial screening, after 1 week of therapy, after 2 weeks of therapy, and after 4 weeks of therapy). Adverse events occurring during the trial were documented at each evaluation visit.

## Statistical Analysis

Demographic data, including age, ethnicity, and sex, were tabulated, and statistical analyses were performed for all tabulated efficacy variables. Mean XSS scores and mean overall treatment evaluation scores were analyzed using the Wilcoxon signed rank test. Mean differences in medication use were analyzed using the paired *t* test.

## Results

Analysis of results was based on evaluation of severity of skin dryness during treatment. Ninety-two patients were enrolled in the study and had baseline measurements taken. By week 1 (visit 1), 25 patients were lost to follow-up, leaving 67 patients with at least 2 measurements. After 2 weeks of therapy (visit 2), 9 patients were discharged and their data excluded—8 patients because of noncompliance and 1 patient because of an adverse event. Seven patients were excluded from the data analysis at week 4 (visit 3) because of noncompliance. No patients were discharged because of positive fungus culture.

Demographic characteristics for the 67 patients with at least one follow-up were compared with those of the original 25 patients lost to follow-up. Patients lost to follow-up after baseline did not differ significantly with respect to race or sex; this is a predominantly African American population with equal proportions of males and females. The

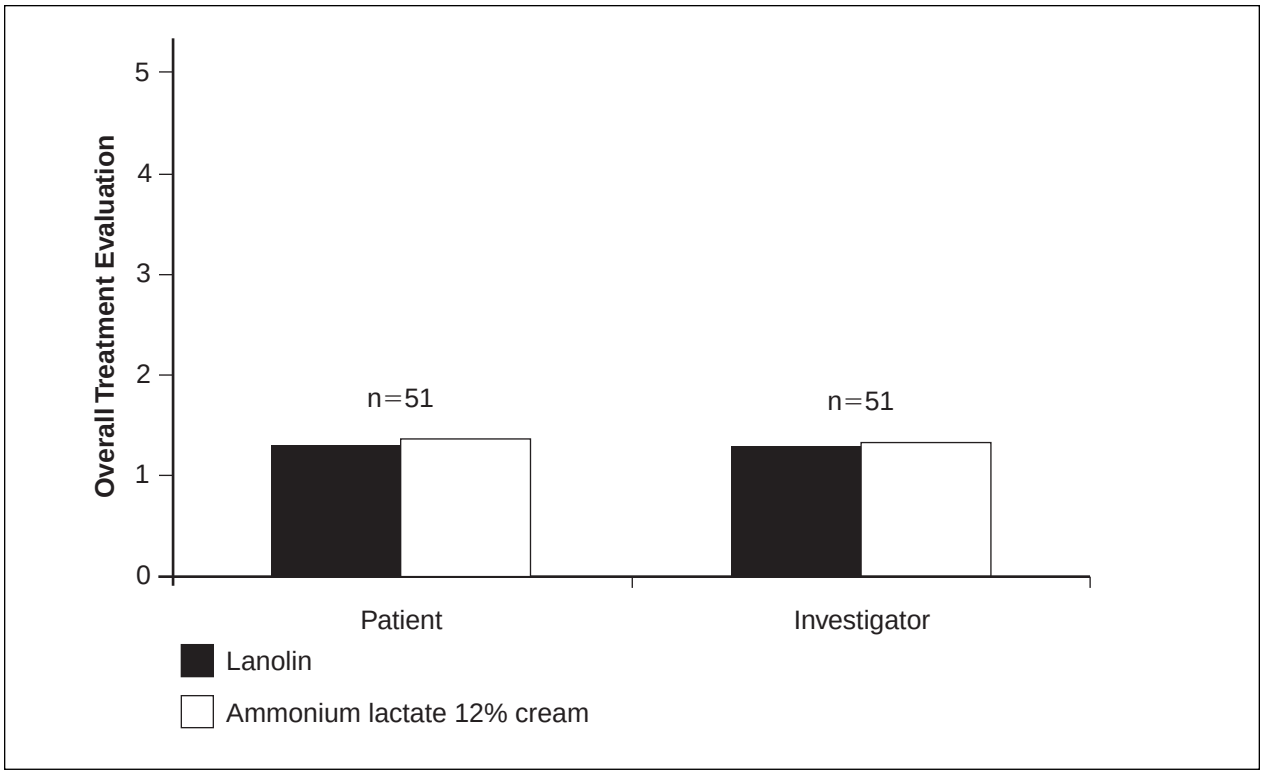


**Figure 2.** Mean comparison of the overall treatment evaluation by the patient and investigator after 4 weeks of treatment using a 6-point scale: 0 (clear), 1 (good improvement), 2 (moderate improvement), 3 (slight improvement), 4 (no improvement), and 5 (worse).

proportion of patients lost to follow-up was similar to the other 67 patients in the younger-than-45-years category but differed in the 45- to 65-year-old and older-than-65-years categories. The majority of patients lost to follow-up (60%) were in the 45- to 65-year-old category, and only 8% of patients lost to follow-up were in the older-than-65 category—as opposed to 44.8% and 22.4%, respectively, of the patients who stayed in the study.

At baseline, there was no statistically significant difference between mean XSS scores before treatment with pure lanolin and treatment with ammonium lactate cream ($P$=.65). Although there was improvement in XSS scores after 1, 2, and 4 weeks of treatment, no statistically significant difference was observed between treatment groups at either 1 week ($P$=.86), 2 weeks ($P$=.83), or 4 weeks ($P$=.85)(Figure 1). There was no statistically significant difference between patients' and investigators' mean overall treatment evaluation scores for pure lanolin versus ammonium lactate after 4 weeks of treatment (Figure 2).

Twenty-one patients reported adverse events, including pruritus, burning, and redness. Of these patients, 1 was discharged because of bilateral moderate burning. The other 20 adverse events were mild, did not require discontinuation of medicine, and were comparable between the 2 study groups.

Thirty-three of 51 patients who expressed a medication preference chose ammonium lactate because they felt it was easier to apply and better absorbed. The other 18 patients with a preference chose pure lanolin because of its thicker consistency and because they felt that this consistency contributed to the efficacy of the product.

There was a statistically significant difference between use of pure lanolin and use of ammonium lactate throughout the study. Patients on average used significantly more ammonium lactate than pure lanolin during each follow-up period.

## Discussion

Xerosis, a condition involving dehydration of the skin, is an entity commonly assessed and treated by both dermatologists and podiatrists. In this study, analysis of variance of effects over time indicated a significant improvement in severity of dryness with both pure lanolin and ammonium lactate 12% cream. Pure lanolin and ammonium lactate 12% cream are both effective in treating xerosis when used twice daily for 4 weeks.

Ammonium lactate 12% cream is a keratolytic topical formulation with the potential to cause adverse reactions such as tingling, burning, and erythema. In this study, however, incidence of such events was very low for both ammonium lactate cream and lanolin. The most commonly reported adverse event was pruritus, which either resolved or improved in all cases and may have been due to xerosis and not the study medications. All adverse events resolved.

Many people with diabetes have autonomic neuropathy, which predisposes them to excessive dryness of the skin with scaling, fissures, and potential ulcerations. Use of efficacious moisturizers such as pure lanolin and ammonium lactate 12% cream is especially important in this population. For patients with diabetes, however, promoting use of any keratolytic product is prudent only under the supervision of a healthcare professional.

*Acknowledgment*—We thank Charles Ross, DPM, for his assistance.

## REFERENCES

1. Bagatell FK, Smoot W. Observations on a lactate-containing emollient cream. *Cutis*. 1976;18:591-593, 600-602.
2. Arnold HL, Odom RB, James WD, eds. *Andrews' Disease of the Skin*. 8th ed. Philadelphia, Pa: WB Saunders; 1980:81.
3. Engelke M, Jensen J-M, Ekanayake-Mudiyanselage S, et al. Effects of xerosis and aging on epidermal proliferation and differentiation. *Br J Dermatol*. 1997;137:219-225.
4. Rawlings A, Harding C, Watkinson A, et al. The effect of glycerol and humidity on desmosome degradation in stratum corneum. *Arch Dermatol Res*. 1995;287:457-464.
5. Wehr R, Krochmal L, Bagatell F, et al. A controlled two-center study of lactate 12 percent lotion and a petrolatum-based creme in patients with xerosis. *Cutis*. 1986;37:205-207, 209.
6. Van Scott EJ, Yu RJ. Control of keratinization with alpha-hydroxy acids and related compounds. *Arch Dermatol*. 1974;110:586-590.
7. Harris I, Hoppe U. Lanolins. In: Harris I, Hoppe U, eds. *Dry Skin and Moisturizers: Chemistry and Function*. Boca Raton, Fla: CRC Press; 2000:259-267.
8. *Drug Information for the Health Care Professional*. 15th ed. Rockville, Md: US Pharmacopoeial Convention, Inc; 1995.
9. Buxman M, Hickman J, Ragsdale W, et al. Therapeutic activity of lactate 12% lotion in the treatment of ichthyosis. *J Am Acad Dermatol*. 1986;15:1253-1258.
10. Rogers RS, Callen J, Wehr R, et al. Comparative efficacy of 12% ammonium lactate lotion and 5% lactic acid lotion in the treatment of moderate to severe xerosis. *J Am Acad Dermatol*. 1989;21:714-716.