

Aalborg Universitet

A global perspective on the treatment and maintenance of mature skin using gentle cleansers and moisturizers

Fluhr, Joachim W.; Alexis, Andrew F.; Andriessen, Anneke; Ferero Barrios, Olga L.; Bjerring, Peter; Foley, Peter; Gold, Michael H.; Kaderbhai, Hashim; Zhang, Chengfeng

Published in:

International Journal of Dermatology

DOI (link to publication from Publisher): 10.1111/ijd.17375

Creative Commons License CC BY-NC-ND 4.0

Publication date: 2024

Document Version Publisher's PDF, also known as Version of record

Link to publication from Aalborg University

Citation for published version (APA):

Fluhr, J. W., Alexis, A. F., Andriessen, A., Ferero Barrios, O. L., Bjerring, P., Foley, P., Gold, M. H., Kaderbhai, H., & Zhang, C. (2024). A global perspective on the treatment and maintenance of mature skin using gentle cleansers and moisturizers. International Journal of Dermatology, 63(12), 1676-1684. https://doi.org/10.1111/iid.17375

General rights

Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

- Users may download and print one copy of any publication from the public portal for the purpose of private study or research.
 You may not further distribute the material or use it for any profit-making activity or commercial gain
 You may freely distribute the URL identifying the publication in the public portal -

If you believe that this document breaches copyright please contact us at vbn@aub.aau.dk providing details, and we will remove access to the work immediately and investigate your claim.

Review Article

A global perspective on the treatment and maintenance of mature skin using gentle cleansers and moisturizers

Joachim W. Fluhr, ¹ Andrew F. Alexis, ² Anneke Andriessen, ³ Dolga L. Ferero Barrios, ⁴ Peter Bjerring, ⁵ Peter Foley, ⁶ Michael H. Gold, ⁷ Hashim Kaderbhai, ⁸ and Chengfeng Zhang ⁹

¹Institute of Allergology, Charité
Universitätsmedizin, Berlin, Germany,

²Weill Cornell Medical Medicine, New York,
New York, USA, ³Andriessen Consultants,
Malden, The Netherlands, ⁴Centro de
Dermatologia, Porto Alegre, Brazil,

⁵Department of Dermatology, Aalborg
University Hospital, Aalborg, Denmark,

⁶Skin Health Institute, Carlton, Vic.,
Australia, ⁷Gold Skin Care Center,
Vanderbilt University School of Nursing,
Nashville, TX, USA, ⁸Aga Khan University
Hospital, Nairobi, Kenya; and ⁹Department
of Dermatology, Huashan Hospital, Fudan
University, Shanghai, China

Keywords

xerosis; ceramide; moisturizers; mature skin; skincare.

Correspondence

Anneke Andriessen
Andriessen Consultants
Zwenkgras 25
6581RK
Malden
The Netherlands
E-mail: anneke.a@tiscali.nl

Conflict of interest: None.

Funding source: Joachim W. Fluhr, Andrew F. Alexis, Anneke Andriessen, Olga L. Ferero Barrios, Peter Bjerring, Michael H. Gold, Hashim Kaderbhai, and Chengfeng Zhang received support from CeraVe International for the research of this project and consultancy fees for attending the meeting.

doi: 10.1111/ijd.17375

Abstract

Xerosis is highly prevalent in the population aged over 50 years and substantially impacts quality of life due to the associated stigma, related pruritus, and potential sequelae. We propose that the term mature xerosis be used for subjects over 50 who suffer from age-related xerosis and replace senile xerosis to describe the phenomenon. The etiology of xerosis depends on genetic and environmental factors that affect stratum corneum hydration and skin barrier function. Skincare to restore barrier function is essential in xerosis treatment and is relevant for maintaining and preventing its progression. Many moisturizers and cleansers are available for xerosis; however, they are underutilized by patients with mature xerosis. A panel of eight global dermatologists reviewed the unique aspects of xerosis in mature skin and discussed the specific needs, relevance, and considerations for skincare selection to prevent, treat, and maintain skin with mature xerosis. The panel selected five statements based on evidence from a literature review and the panel's clinical experience to provide clinical considerations and recommendations for dermatologists and other healthcare providers treating patients with mature xerosis. Increased recognition of the burden of xerosis in mature skin is warranted. Gentle cleansers and barrier-restoring ceramide-containing moisturizers are essential to xerosis management, reducing signs and symptoms of xerosis, including associated pruritus.

Introduction

In the literature, the term senile xerosis has been used for aging populations that show symptoms of xerosis. However, the

etiology of xerosis and age of occurrence lack definition. The panel proposes the term mature xerosis be used for subjects over 50 who suffer from age-related xerosis and replace senile xerosis to describe the phenomenon.

Xerosis is characterized by reduced stratum corneum (SC) hydration and skin barrier dysfunction. 1-3 Xerosis is highly prevalent in the aging population and affects about half of people aged 65 and over. 1,2 Multiple factors, including an age-related decline in skin barrier function, cutaneous nerve fiber changes, polypharmacy, and medical comorbidities, contribute to the high prevalence of mature xerosis and pruritus. 1,3,4 Some evidence suggests that pruritus associated with mature xerosis is more prevalent in populations with richly pigmented skin. 4,5 Skin barrier differences between racial/ethnic populations likely contribute to the ethnic variations in the prevalence and severity of mature xerosis and the related pruritus. 6

Globally, awareness of mature skin changes and increased associated vulnerabilities remains low among healthcare providers. The complex factors influencing mature xerosis and related pruritus make diagnosis and management more challenging. Effective xerosis treatment includes gentle cleaners and moisturizers, but patients may also require prescription therapy when xerosis is associated with dermatitis (e.g., asteatotic or nummular eczema). Furthermore, mature xerosis patients may have complex personal needs, comorbidities, and cultural preferences, which require clinician awareness and consideration. 1.4

Methods

The project used a modified Delphi process comprising faceto-face discussions and online follow-up.^{7,8}

Literature review

Structured literature searches on August 1, 2022, on PubMed and Google Scholar (secondary source) of the English-language literature (January 2010-July 30, 2022) informed a previous publication on mature skin xerosis.9 On September 1, 2023, the information on mature skin xerosis (English-language literature September 1, 2022-August 31, 2023) was updated using the same criteria as for the first searches. A dermatologist and a physician/scientist reviewed the titles, the abstracts, and the full papers while prioritizing studies on mature skin xerosis, SC barrier function, and skincare benefits using cleansers and moisturizers. The search terms for mature skin included senile xerosis, xerosis in aging skin, and xerosis in over 50 years old subjects, explored present clinical guidelines, treatment options, and therapeutic approaches addressing mature skin xerosis using the following terms: Mature skin xerosis AND skin barrier physiology OR function OR dysfunction OR depletion of stratum corneum lipids OR atopic dermatitis; Mature skin xerosis AND skincare OR cleansers OR moisturizers OR emollients OR ceramides OR ceramide containing skincare OR efficacy OR safety OR tolerability.

The searches yielded 35 papers deemed clinically relevant to mature skin xerosis and skin care to restore a healthy skin

barrier and potential mitigation of xerosis using over-the-counter skincare and ceramide-containing cleansers and moisturizers.

Role of the panel

The panel of eight dermatologists from Australia, Brazil, China, Denmark, Germany, Kenya, and the US convened for a meeting (July 3, 2023) during the World Congress of Dermatology in Singapore to review unique aspects of xerosis in mature skin from a global perspective and to discuss nuances in the treatment and maintenance of mature skin xerosis using gentle cleansers and moisturizers. The 14 draft statements were evaluated and discussed during the meeting in a plenary session to adopt five evidence-based, clinically relevant statements.

Results

Statement 1

Aging beyond 50 causes several fundamental changes in the skin with significant and widespread dermatological implications, such as xerosis and related pruritus.

Growth in population size and the proportion of older people has been an ongoing trend in high-income countries, but now low and middle-income countries have the most significant increase in population aging. ^{10,11} Global population aging has substantial and widespread implications for health status and healthcare due to the advanced age-related disease burden, including mature skin disorders such as xerosis and pruritus.

Reduced skin barrier function and SC hydration are associated with age, potentially leading to xerosis, pruritus, and cutaneous inflammation exacerbations. The prevalence of mature xerosis and related pruritus in the population over 50 varies, with rates reported at approximately 30%–85% and 20%–60%, respectively. 4.5,10

Aging may be associated with cutaneous changes, contributing to damaged and diseased skin, including xerosis. One study measured SC composition, including water, lipid/protein ratio, cholesterol, and ceramides, in 40 healthy women in four age groups.

11 Measurements were done on the cheek, protected, and exposed arm sites. Transepidermal water loss (TEWL) decreased slightly with age, partially explained by the age-dependent increase in SC thickness.

12 The lipid/protein ratio and lipid compactness decreased significantly with age only for the arm sites.

Another study assessed the influence of aging on skin barrier function, including TEWL, SC hydration, sebum content, and pH value in 150 healthy women aged 18–80 divided into five age groups with 30 subjects each. Sebum production decreased significantly with age, with the lowest skin surface lipid levels measured in subjects older than 70. EWL and SC hydration showed only minor variations with aging.

Age-related skin changes in cytokines, chemokines, and biologic analytes correspond with the pro-inflammatory shift with

Statement 2

1678

The quality of life of patients with mature skin xerosis may be highly affected, and scratching can lead to secondary infections, ulcerations, and chronic wounds.

A cross-sectional explorative study showed that patients with xerosis reported a lower quality of life (QoL) (more dysmorphic concerns and anxiety) than individuals without xerosis.³ Xerosis frequently presents with recurrent and chronic pruritus, impacting sleep and reducing quality of life, as reported by several studies.^{12,14,16,17} A trial assessing the QoL impact of chronic pruritus in 73 patients found symptom severity and single marital status significantly reduced QoL, and factors such as symptom type, duration, and other demographic characteristics did not correlate with significant QoL reduction.¹⁸

Mature skin pruritus is characterized by intense itch sensations associated with an excessive scratching response that further perpetuates pruritus. ¹⁸ Often referred to as the itch-scratch cycle, the scratch behavior further diminishes skin barrier function and produces damaged epithelial cells, resulting in aggravation of inflammation and pruritus exacerbation. Various factors contribute to xerosis and pruritus by decreasing skin barrier function and inducing epidermal immune stress responses. ¹⁹ Without appropriate pruritus treatment, severe scratching can cause skin damage, including abrasions, erythema, hyperpigmentation, ulcers, and lichenification, leading to secondary infections. ²⁰ Using barrier-restoring skincare to improve skin condition and resilience may help avoid progressing to more severe forms of xerosis associated with pruritus and impact on QoL.

In addition to xerosis, chronologic aging is associated with many other skin changes, such as wrinkling, laxity, and pigmentation on the face and the body. 17 Skin is an important component of outward beauty, and perceived aging skin and xerosis can be associated with stigma and reduced QoL. 21,22 Xerosis can be associated with greater stigmatization in some populations; for example, the scale of xerotic skin can appear conspicuously gray in the context of darkly pigmented skin, and this, coupled with cultural perceptions of skin health, can contribute to the psychosocial impact of xerosis in populations with skin of color. 4-6

Statement 3

The etiology of xerosis may depend on several genetic, environmental, and pathophysiologic factors that affect the keratinization process and lipid content in the stratum corneum, including intrinsic age-related changes, medications, systemic conditions, and the effects of indoor heating or air conditioning.

A better understanding of cutaneous changes associated with aging and xerosis etiology may help improve best practices in mature skin xerosis treatments, improving patient QoL. Several studies have evaluated the effect of cutaneous aging on SC barrier function, which may alter SC barrier structure, barrier function, pH, hydration, lipid composition, epidermal calcium gradient, and microbiome. 19,21,23

One study evaluated epidermal aging by comparing skin barrier function in 21 healthy young adults (20–30 years) versus older (>80 years) adults.²⁴ Induced experimental stress perturbation of the skin barrier revealed underlying alterations in epidermal integrity and barrier recovery.²⁵ A decrease in lipid content leads to changes in lamellar bilayer morphology, which likely causes impaired skin barrier function. The functional changes found in the study may be attributed to a global deficiency in SC lipids, resulting in decreased lamellar bilayers in the SC interstices. Several studies investigated the relationship between skin surface pH and barrier function/aging, which showed a slight but significant increase in skin surface pH with age.^{22,23,25} Lower pH emulsions can help promote skin surface acidification, accelerate barrier recovery, improve the SC barrier function, and maintain barrier homeostasis in mature skin.^{26,27}

Xerosis etiology can also be influenced by a complex interplay of environmental factors, such as harmful components in skin care products, bathing habits, air pollution, UV exposure, and overuse of heaters or air conditioners.^{2,24,28}

An ex vivo skin and a clinical model used lipidomic analysis of UV-exposed skin. They showed shifts to the composition of the ceramide subclass NP and reduced very long-chain acyl moieties, which are essential in repairing the SC barrier. The investigators suggested that lipid alterations may be attributed to changes within the ceramide biosynthesis process and that topical application of ceramide-containing suncare products helps maintain a healthy skin barrier, SC-essential ceramides, and chain length during daily sun exposure.^{24,28}

One study investigated xerosis-associated factors and prevalence in 756 adults ≥65. It showed treatments that can potentially cause xerosis, itching during sweating, a history of xerosis, and a history of atopic dermatitis were factors associated with xerosis. The xerosis prevalence was 56% and significantly associated with age and female gender. Another study evaluated the dermatological disorders underlying xerosis and its prevalence in 48,630 adults. Xerosis prevalence was 29% and significantly associated with age but not gender. Disorders associated with xerosis were axillary dermatitis, atopic eczema, exsiccation eczema, psoriasis, plantar warts, seborrheic dermatitis, and atopic disposition. A higher risk of xerosis has been

1679

associated with filaggrin null gene mutations, which are also associated with AD and ichthyosis vulgaris.26

Successful xerosis management relies on mitigating the impact of cutaneous aging, the underlying genetic mechanisms, and limiting environmental factors.^{2,4} This includes altering the ambient humidity, changing bathing habits, restoring the damaged SC barrier, and maintaining the moisture content via skincare.2,4,22

Racial and ethnic variation in xerosis prevalence and reporting

Racial/ethnic variations in aging skin hydration suggest differences in xerosis prevalence and severity. One study measured skin dryness in 311 American women from four ethnic groups (African American, Caucasian, Chinese, and Mexican) and identified ethnic differences in skin hydration in individuals over 50 years of age.6

Data on racial/ethnic variations in xerosis are limited. (Table 1). Of the 31 references on mature skin xerosis cited herein, only 20% (6) reported racial/ethnic demographic data. and only 10% (3) included participants with skin of color (SOC).

While the presentation of mature xerosis is broadly similar across the board, there are observable differences in appearance in patients with richly pigmented skin. Erythema may be challenging to detect in patients of African descent as it appears violaceous with a gray hue. Xerosis and pruritus are also more diffuse and frequent in African American patients.8

According to the panels' experience and opinion, skin cleansing and moisturizing practices may differ; however, skincare studies are mainly conducted in the Western world on predominantly Caucasian patients.

Statement 4

Gentle cleansers and moisturizers, which can help promote a healthy skin barrier and reduce pruritus, are underused in mature skin xerosis and may be impacted by cultural factors.

The multiple factors contributing to the high xerosis prevalence in populations over 50 years, including a reduced skin barrier function, changes in cutaneous nerve fibers, polypharmacy, and medical comorbidities 1,4,16 make xerosis and related pruritus diagnosis and management more challenging. Effective treatment should include appropriate skin care, regardless of the cause or severity of mature skin xerosis. Proper skincare should be formulated with ingredients and technologies to improve SC hydration and restore SC barrier function adequately.^{2,4} Pruritus-related cutaneous inflammation or neural dysfunction management may require topical or systemic medications.4

The panel recommended preventive strategies such as more frequent body checks and xerosis assessments to help maintain mature patients' skin quality.2 More frequent examinations durroutine dermatology visits and through patient self-examinations will help assess and monitor xerosis severity

and progression, including scaling erythema, fissuring, and ichthyotic skin.² Frequent assessments could provide an inexpensive and valuable approach to improve patient care outcomes if implemented early and with appropriate skincare. The benefits of quality moisturizers are restoration of skin barrier function, reduction in xerosis, and related pruritus. 1,20,21,27,29,30 Although moisturizers are used in mature skin xerosis treatment, there is limited understanding of differences between products because robust comparative studies are lacking.^{21,30} Mature skin xerosis may be exacerbated by irritants, such as harsh surfactants, alkaline soap, hot showers, and saunas that reduce skin moisture and recovery of the skin barrier function.²² Thus, short showers with gentle cleansers containing mild surfactants and moisturizers containing lipids such as ceramides that promote a healthy SC barrier are recommended. Patients with skin of color may require nuanced approaches to xerosis treatment due to potential racial/ethnic variations in physiologic and cultural factors related to skin hydration and its impact. 1,6,8 Cultural norms related to moisturization and bathing practices differ across diverse populations, and consideration of this is important when offering skincare recommendations for xerosis and pruritus. 1 Balancing evidence-based xerosis and pruritus skincare recommendations with cultural norms and patient preferences is essential to improve outcomes.

Statement 5

The unmet need for skincare in mature skin xerosis can be addressed with ceramide-containing cleansers and moisturizers supported by clinical data.

A lack of clear skincare recommendations for mature skin xerosis contributes to the unmet need for skincare in the aging population. Several clinical studies have established the efficacy of moisturizer components such as ceramides and urea in mature skin xerosis treatment and have demonstrated that some skincare ingredients or practices can induce cutaneous inflammation or disrupt SC barrier function. 22,31

SC barrier dysfunction in mature skin xerosis may be associated with SC lipid deficiencies, such as ceramides. 21,31 Several studies have demonstrated that a ceramide-containing skincare regimen promotes a healthy skin barrier, reducing xerosis. 20,29,32,33,34

A study, which included 30 men and women over 70 with mature skin xerosis, applied a ceramide-containing cleanser and moisturizer at least once daily for 4 weeks.³⁵ The mean physician scores (5-point scale) at Week 4 decreased for roughness and desquamation from 3.1 to 0.6 (-82%), discomfort due to xerosis from 2.9 to 0.2 (-93%), and fissures from 2.3 to 0.1 (-97%).35 Patient scored QoL improved, with 77% no longer feeling embarrassed due to their condition and ≥90% not feeling that their condition affected their social or daily activities. 11

Another study evaluated the efficacy of a ceramide-containing moisturizer in 53 women with Fitzpatrick skin type I-VI with

Table 1 Skin xerosis and the use of cleansers and moisturizers

First author/year	Study population/N	Fitzpatrick skin type	What was studied?	Key findings
Alexis 2022	Expert panel recommendations	Racial/ethnic variations extensively discussed	AD and related xerosis clinical presentation, variations in SOC patients, and the role of skin care in improving outcomes	More frequent and pronounced AD and related xerosis variations in patients with SOC impact patient QoL
Angelova-Fischer 2018	20 adults	NR	Efficacy of water-in-oil emulsions with either pH 4 or pH 5.8	pH 4 emulsion improves the SC barrier function and maintenance of barrier homeostasis in aged skin
Augustin 2018	48,630 adults in Germany	Skin type classification	The xerosis prevalence in the German adult population	Xerosis is more frequent in the older population and needs special attention
Boireau-Adamezyk 2014	40 French women divided into four age groups	NR	Age-dependent changes in stratum corneum barrier function	Skin aging, body site, and environmenta exposure affect SC barrier function, structure, and lipid content
Choi 2019	Review	NR	Skin barrier aging	Topical restoration of the antioxidant barrier of the SC may be another therapeutic strategy for the aged skin barrier
Christensen 2009	Review	NR	The challenges in aging populations	Population aging is increasing globally
Chung 2020	Review	NR	Pruritus pathophysiology and treatment in aging adults	Pruritus is prevalent in older people as part of skin diseases, secondary, systemic, or psychotic diseases
Clerc 2017	Review	NR	Diagnosis and treatment of mature pruritus	Pruritus is prevalent in the older population, and QoL can be greatly reduced
Danby 2016	42 adults >60 years with healthy skin-to-severe xerosis	I–IV	Efficacy of an emollient containing 5% urea, CER NP, and lactate on the skin barrier properties in aging adults	CER-emollient improved xerotic-aged skin, supporting it as first-line therapy for mature skin xerosis
Danby 2022	34 adults with dry, eczema- prone skin	I-V	Effect of SC lipid structure on skin barrier function, pruritus, and xerosis	CER-containing moisturizer facilitated skin barrier restoration and improved pruritus and xerosis
Diridollou 2007	311 women from four ethnic groups	I-VI	Age-related stratum corneum hydration in four ethnic groups	Skin hydration varies according to ethnicity, and age effects are influenced by ethnicity
Draelos 2020	53 adult women with healthy skin-to-severe xerosis	I–IV	Efficacy of a CER-containing moisturizer on stratum corneum lipid levels in xerotic skin	CER moisturizer increased SC intercellular lipid levels and hydration and reduced visible signs of xerosis and subject perceived discomfort
Filippi 2023	Review	NR	CER-containing skincare effectiveness and improvement in QoL in elderly patients with xerosis	CER-based skincare improves xerosis and QoL elderly patients
Garibyan 2013	Review	NR	Addressing an unmet need in advanced aging skin and itch	Pruritus prevalence and impact on QoL
Ghadially 1995	21 Adults	NR	Age impact on epidermal barrier function	Lipid content reduction leads to alterations in lamellar bilayer morphology, contributing to impaired SC barrier function
Gold 2024	30 adults >70 with mature xerosis	NR	Promoting a healthy skin barrier using skin care in people with mature skin xerosis	CER-containing cleanser and moisturize improved skin barrier and QoL, reducing fissures and discomfort due to xerosis
Kaufman 2018	Review	Racial/ethnic variations extensively discussed	Variations in AD and related xerosis epidemiology, genetics, clinical presentation, and treatment	More frequent and pronounced AD and related xerosis variations in patients with SOC impact patient QoL

Table 1 Continued

First author/year	Study population/N	Fitzpatrick skin type	What was studied?	Key findings
Khavkin 2011	Review	NR	Histology, physiology, and pathology of aging skin	Knowledge of skin histology and physiology fosters a better understanding of cutaneous changes associated with aging
Kilic 2019	20 adults >55 years	II-III	Efficacy of water-in-oil emulsions with either pH 4 or pH 5.8	pH 4 emulsion improves the epidermal barrier and SC organization in aged skin
Kim 2021	52 adults with moderate-to- severe xerosis	NR	Efficacy of mild cleanser and moisturizer on xerosis	Gentle cleanser and moisturizer improved total clinical score, visual dryness score, and itch-related QoL
Kini 2011	73 adults with chronic pruritus	NR	Pruritus impact on quality of life	Chronic pruritus substantially impacts QoL, and the severity of symptoms and support network use determine the impact
Kinn 2015	23 adults divided into three age groups	NR	Age-related changes in skin properties, cytokines, chemokines, and biologic analytes from SC	TEWL, erythema, and 7 cytokines, chemokines, and biologic analytes decreased in an age-dependent manne
Lacarrubba 2021	20 adults >65 with moderate- to-severe xerosis	NR	Clinical evaluation of 10% urea cream in mature xerosis	Urea-based cream resulted in a significant, progressive clinical improvement of mature xerosis and related pruritus.
Luebberding 2013	150 women divided into five age groups	NR	Age-related changes in skin barrier function	Some parameters related to skin barrier function are influenced by aging, including sebum production and skin surface pH
Man 2019	Review	NR	SC hydration regulates key epidermal function and serves as an indicator and contributor to other conditions	SC hydration measurements could assess cutaneous conditions, and routine applications of emollients could improve skin health
Patsatsi 2023	1399 adults with mild-to- severe AD, psoriasis, severe xerosis other than AD, or mature skin xerosis	NR	Effect of a novel "emollient plus" formulation on mild-to-severe atopic dermatitis and other dry skin-related diseases	Significant reduction in symptoms of mild-to-severe xerosis after application of the "emollient plus" formulation over 2 months
Paul 2011	756 adults >65	NR	Xerosis prevalence and risk factors associated with age	Xerosis is highly prevalent in patients of age and with a history of atopy
Schikowski 2020	Review	NR	The impact of air pollution on skin aging	The association between traffic-related air pollution and skin aging has been well-established
Schreml 2012	97 women	NR	The impact of age and body site on skin surface pH in women	Skin surface pH on the forehead, the temple, and the volar forearm increases slightly with age
Steinhoff 2023	Review	NR	Pruritus origin, diagnostics, and management in older patients	Pruritic dermatoses occur more commonly in older people due to physiologic and molecular changes in aging skin
Ständer 2017	70 adults with xerosis-related pruritus	NR	Randomized, double-blind pilot study in xerosis-related pruritus treatment	Xerosis and pruritus treatment with a lotion containing a TRPM8 agonist ameliorates severe pruritus
Visse 2017	100 adults with xerosis- related pruritus	NR	Efficacy of body lotion containing n- palmitoylethanolamide in subjects with chronic pruritus due to xerosis	No significant improvement in pruritus and QoL between treatment with lotion with and without n-palmitoylethanolamide
Wang 2020	Review	Racial/ethnic variations in xerosis briefly discussed	Alterations and clinical significance in epidermal function associated with aging	Chronologically aged skin displays multiple alterations in epidermal functions, which contribute to the development of cutaneous disorders

and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons Licenso

Fluhr et al

First author/year	Study population/N	Fitzpatrick skin type	What was studied?	Key findings
White-Chu 2011	Review	NR	Xerosis in patients of age	Xerosis is prevalent in older adults, and multiple environmental and genetic factors contribute to the presence and severity
Ye 2019	63 adults ≥58	NR	Topical CER-containing emollient effect on circulating pro- inflammatory cytokine levels	CER-containing emollient reduced circulating pro-inflammatory cytokine levels in aging adults

AD, atopic dermatitis; CER, ceramide; NR, not relevant; QoL, quality of life; SC, stratum corneum; SOC, skin of color; TEWL, transepidermal water loss.

xerosis and pruritus.³¹ The moisturizer increased SC ceramides. cholesterol, free fatty acid levels, and skin hydration, demonstrating an immediate and sustained reduction of xerosis symptoms.31 Another study evaluated the efficacy of ceramide and Vitreoscilla filiformis lysate-containing emollient in 1399 adults with mild-tosevere mature skin xerosis, severe xerosis, psoriasis, or AD. 16 The ceramide and Vitreoscilla filiformis lysate-containing emollient significantly reduced xerosis severity and symptoms, including skin dryness, inflammatory lesions, pruritus, sleep quality, and discomfort in >90% of patients. Another study evaluated the effect of ceramide and urea-containing emollients on skin barrier properties in 21 adults >60 years of Fitzpatrick skin type I-IV with xerosis. 19 The ceramide and urea-containing emollient significantly improved SC hydration and skin barrier function in mature skin xerosis patients. However, this study's lack of placebo control limits the broader application of these results. Another study investigated the effect of improved epidermal function via a ceramide-containing emollient treatment on pro-inflammatory cytokine levels in 63 adults >58 years.33 The ceramidecontaining emollient significantly enhanced SC hydration and epidermal barrier function. Furthermore, circulating levels of two key, age-related plasma cytokines, IL-1β, and IL-6, normalized, whereas tumor necrosis factor-alpha (TNFα) levels declined substantially. These results demonstrate that ceramide-containing emollients improve SC lipid levels, SC hydration, and barrier function, reducing xerosis severity and symptoms. These results support the role of ceramide-containing emollients in first-line treatment for mature skin xerosis.

A double-blind, split-body study with 34 subjects ages 20-89 with eczema compared a ceramide-containing cream with a paraffin-based emollient to the forearms and lower legs for 4 weeks. Across the adult age groups, skin hydration and lipid levels increased, and lipid bilayer organization, SC barrier integrity, and protection from dryness and irritation improved more with the ceramide-containing cream versus the paraffin-based emollient.34

Urea is another widely used emollient component in xerosis treatment, and its efficacy has been established in several clinical studies.²⁹ Two studies evaluated the efficacy of urea-containing creams on skin barrier properties and in xerosis treatment^{32,34,} improved all patients' SC hydration, skin barrier function, xerosis, and related pruritus.34

Other moisturizer components have also been investigated in xerosis treatment with varying success. For example, hyaluronic acid-containing moisturizer improved xerosis severity and symptoms in ≥80% of xerosis patients.21 Whereas a lotion with the endogenous fatty acid N-palmitoyl ethanolamine, another common moisturizer component, did not significantly improve xerosis and related pruritus.30

Patients with mature skin xerosis-related chronic pruritus often use emollients containing the TRPM8 agonist, menthol. for a cooling effect to relieve pruritus, which may be irritating and further exasperate severe pruritus.36 One study evaluated the efficacy and safety of two TRPM8 agonists with more robust TRPM8 activation than menthol in alleviating pruritus in 70 adults with xerosis-related pruritus and significantly improved pruritus and related QoL compared to vehicle treatment.

Conclusions

Mature skin xerosis is highly prevalent and substantially reduces QoL due to associated pruritus, excoriation, and potential complications and sequelae. The panel recommended a proactive approach to xerosis in mature skin through more frequent self- and provider-driven assessments among adults in the sixth or later decades of life. Evidence-based skincare using gentle cleansers and moisturizers, such as those containing ceramides and other moisturizing ingredients, should be integral to xerosis and related pruritus treatment to help maintain the skin barrier and reduce disease severity and symptoms. Research and clinician education is needed to raise awareness of challenges and needs associated with mature xerosis while considering patient perspectives on skincare cultural norms and treatment priorities.

References

1 Paul C. Maumus-Robert S. Mazereeuw-Hautier J. Guven CN. Saudez X, Schmitt AM. Prevalence and risk factors for xerosis

1683

- in the elderly: a cross-sectional epidemiological study in primary care. Dermatology. 2011;223:260-5. https://doi.org/10. 1159/000334631
- 2 White-Chu EF, Reddy M. Dry skin in the elderly: complexities of a common problem. Clin Dermatol. 2011;29:37-42. https://doi. org/10.1016/j.clindermatol.2010.07.005
- 3 von Stülpnagel CC, Augustin M, da Silva N, Schmidt L, Nippel G, Sommer R. Exploring the burden of xerosis cutis and the impact of dermatological skin care from patient's perspective. J Dermatolog Treat. 2022;33:2482-7. https://doi.org/10. 1080/09546634.2021.1970704
- 4 Kaufman BP, Guttman-Yassky E, Alexis AF. Atopic dermatitis in diverse racial and ethnic groups-Variations in epidemiology, genetics, clinical presentation and treatment. Exp Dermatol. 2018;27:340-57. https://doi.org/10.1111/exd.13514
- 5 Alexis A, Woolery-Lloyd H, Andriessen A, Callender V, Gonzalez M, Heath C, et al. Insights in skin of color patients with atopic dermatitis and the role of skincare in improving outcomes. J Drugs Dermatol. 2022;21:462-70. https://doi. org/10.36849/JDD.6609
- 6 Diridollou S, de Rigal J, Querleux B, Leroy F, Holloway BV. Comparative study of the hydration of the stratum corneum between four ethnic groups: influence of age. Int J Dermatol. 2007;46:11-4. https://doi.org/10.1111/j.1365-4632.2007.03455.x
- 7 Trevelyan EG, Robinson N. Delphi methodology in health research: how to do it? Eur J Intear Med. 2015;7:423-8. https://doi.org/10.1016/j.eujim.2015.07.002
- 8 Brouwers MC, Kho ME, Browman GP, Burgers JS, Cluzeau F, Feder G, et al. AGREE II: advancing guideline development, reporting and evaluation in healthcare. CMAJ. 2010;182: E839-42.
- 9 Gold M, Andriessen A, Burgess C, Callender V, Goldberg D, Hougeir F, et al. Promoting a healthy skin barrier using skin care in people with mature skin xerosis. J Drugs Dermatol. 2024;23:1253-9. https://doi.org/10.36849/JDD.7560
- 10 Augustin M, Kirsten N, Körber A, Wilsmann-Theis D, Itschert G. Staubach-Renz P. et al. Prevalence, predictors and comorbidity of dry skin in the general population. J Eur Acad Dermatol Venereol. 2019;33:147-50. https://doi.org/10.1111/jdv.
- 11 Boireau-Adamezyk E, Baillet-Guffroy A, Stamatas GN. Agedependent changes in stratum corneum barrier function. Skin Res Technol. 2014;20:409-15. https://doi.org/10.1111/srt.12132
- 12 Kini SP, DeLong LK, Veledar E, McKenzie-Brown AM, Schaufele M, Chen SC. The impact of pruritus on quality of life: the skin equivalent of pain. Arch Dermatol. 2011;147:1153-6. https://doi.org/10.1001/archdermatol.2011.178
- 13 Luebberding S, Krueger N, Kerscher M. Age-related changes in skin barrier function—quantitative evaluation of 150 female subjects. Int J Cosmet Sci. 2013;35:183-90. https://doi.org/10. 1111/ics.12024
- 14 Kim S, Ly BK, Ha JH, Carson KA, Hawkins S, Kang S, et al. A consistent skincare regimen leads to objective and subjective improvements in dry human skin: investigator-blinded randomized clinical trial. J Dermatolog Treat. 2022;33:300-5. https://doi.org/10.1080/09546634.2020.1751037
- 15 Kinn PM, Holdren GO, Westermeyer BA, Abuissa M, Fischer CL, Fairley JA, et al. Age-dependent variation in cytokines, chemokines, and biologic analytes rinsed from the surface of healthy human skin. Sci Rep. 2015;5:10472.
- 16 Patsatsi A, Vakirlis E, Kanelleas A, Stefanaki I, Kemanetzi C, Loizidis C, et al. Effect of a novel "emollient plus" formulation on mild-to-severe atopic dermatitis and other dry skin-related

- diseases as monotherapy or adjunctive therapy: an observational study on efficacy, tolerance and quality of life in adult patients. Eur J Dermatol. 2023;33:137-46. https://doi. org/10.1684/ejd.2023.4449
- 17 Khavkin J, Ellis DA. Aging skin: histology, physiology, and pathology. Facial Plast Surg Clin North Am. 2011;19:229-34. https://doi.org/10.1016/j.fsc.2011.04.003
- 18 Steinhoff M, Al-Khawaga S, Buddenkotte J. Itch in elderly patients: Origin, diagnostics, management. J Allergy Clin Immunol. 2023;152:42-9. https://doi.org/10.1016/j.jaci.2023.05.
- 19 Ghadially R, Brown BE, Sequeira-Martin SM, Feingold KR, Elias PM. The aged epidermal permeability barrier. Structural, functional, and lipid biochemical abnormalities in humans and a senescent murine model. J Clin Invest. 1995;95:2281-90. https://doi.org/10.1172/JCI117919
- 20 Chung BY, Um JY, Kim JC, Kang SY, Park CW, Kim HO. Pathophysiology and treatment of pruritus in elderly. Int J Mol Sci. 2020:22:174.
- 21 Choi EH. Aging of the skin barrier. Clin Dermatol. 2019;37:336-45. https://doi.org/10.1016/j.clindermatol.2019.04.
- 22 Schreml S, Zeller V, Meier RJ, Korting HC, Behm B, Landthaler M, et al. Impact of age and body site on adult female skin surface pH. Dermatology. 2012;224:66-71. https://doi.org/10. 1159/000337029
- 23 Angelova-Fischer I, Fischer TW, Abels C, Zillikens D. Accelerated barrier recovery and enhancement of the barrier integrity and properties by topical application of a pH 4 vs. a pH 5.8 water-in-oil emulsion in aged skin. Br J Dermatol. 2018;179:471-7. https://doi.org/10.1111/bjd.16591
- 24 Schikowski T, Hüls A. Air pollution and skin aging. Curr Environ Health Rep. 2020;7:58-64. https://doi.org/10.1007/s40572-020-00262-9
- 25 Kilic A, Masur C, Reich H, Knie U, Dähnhardt D, Dähnhardt-Pfeiffer S, et al. Skin acidification with a water-in-oil emulsion (pH 4) restores disrupted epidermal barrier and improves structure of lipid lamellae in the elderly. J Dermatol. 2019;46:457-65. https://doi.org/10.1111/1346-8138.14891
- 26 Sergeant A, Campbell LE, Hull PR, Porter M, Palmer CN, Smith FJ, et al. Heterozygous null alleles in filaggrin contribute to clinical dry skin in young adults and the elderly. J Invest Dermatol. 2009;129:1042-5. https://doi.org/10.1038/jid.2008.324
- 27 Man MQ, Elias PM. Stratum corneum hydration regulates key epidermal function and serves as an indicator and contributor to other conditions. J Eur Acad Dermatol Venereol. 2019;33:15-6. https://doi.org/10.1111/idv.15374
- 28 Barresi R. Dumbuva H. Liao IC. Chen Y. Yan X. Wangari-Olivero J, et al. Alteration to the skin ceramide profile following broad-spectrum UV exposure. J Drugs Dermatol. 2022;21:77-85. https://doi.org/10.36849/JDD.6331
- Lacarrubba F, Verzì AE, Dinotta F, Micali G. 10% urea cream in senile xerosis: clinical and instrumental evaluation. J Cosmet Dermatol. 2021;20:5-8. https://doi.org/10.1111/jocd.14093
- 30 Visse K, Blome C, Phan NQ, Augustin M, Ständer S. Efficacy of body lotion containing N-palmitoylethanolamine in subjects with chronic pruritus due to dry skin: a dermatocosmetic study. Acta Derm Venereol. 2017;97:639-41. https://doi.org/10. 2340/00015555-2593
- 31 Draelos ZD, Baalbaki NH, Raab S, Colón G. The effect of a CER-containing product on stratum corneum lipid levels in dry legs. J Drugs Dermatol. 2020;19:372-6. https://doi.org/10. 36849/JDD.2020.4796

32 Danby SG, Brown K, Higgs-Bayliss T, Chittock J, Albenali L, Cork MJ. The effect of an emollient containing urea, CER NP, and lactate on skin barrier structure and function in older people with dry skin. Skin Pharmacol Physiol. 2016;29:135–47. https://doi.org/10.1159/000445955

1684

- 33 Ye L, Mauro TM, Dang E, Wang G, Hu LZ, Yu C, et al. Topical applications of an emollient reduce circulating pro-inflammatory cytokine levels in chronically aged humans: a pilot clinical study. J Eur Acad Dermatol Venereol. 2019;33:2197–201. https://doi.org/10.1111/jdv.15540
- 34 Danby SG, Andrew PV, Kay LJ, Pinnock A, Chittock J, Brown K, et al. Enhancement of stratum corneum lipid structure improves skin barrier function and protects against irritation in

- adults with dry, eczema-prone skin. *Br J Dermatol.* 2022;**186**:875–86. https://doi.org/10.1111/bjd.20955
- 35 Filippi F, Chessa MA, Bardazzi F, Pileri A, Patrizi A. An easy to use, ceramide containing skincare routine: effectiveness and improvement of quality of life in elderly patients with xerosis. *Ital J Dermatol Venerol*. 2023;**158**:429–36. https://doi.org/10.23736/S2784-8671.23.07533-3
- 36 Ständer S, Augustin M, Roggenkamp D, Blome C, Heitkemper T, Worthmann AC, et al. Novel TRPM8 agonist cooling compound against chronic itch: results from a randomized, double-blind, controlled, pilot study in dry skin. J Eur Acad Dermatol Venereol. 2017;31:1064–8. https://doi.org/10.1111/jdv. 14041