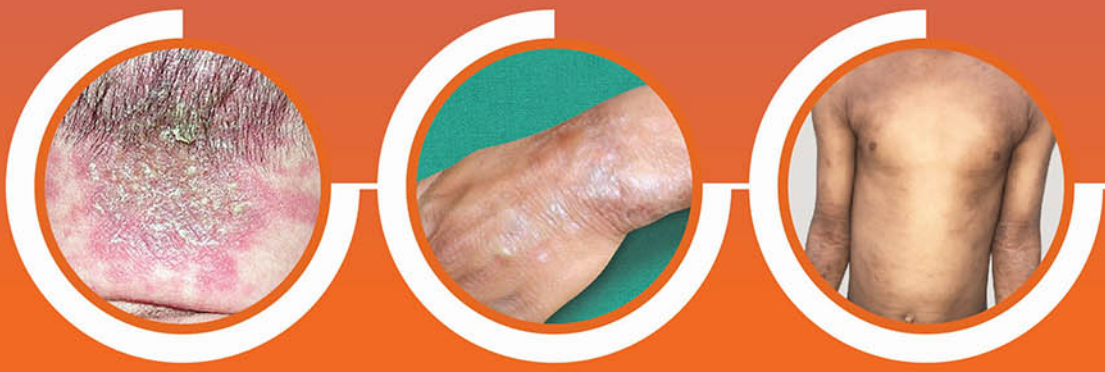
Handbook of ATOPIC DERMATITIS



Editor
Rashmi Sarkar

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CHAPTER

Moisturizers in Atopic Dermatitis

Jaspriya Sandhu, Rashmi Sarkar, Kittu Malhi

ABSTRACT

Atopic dermatitis (AD) is a chronic inflammatory dermatoses characterized by dry skin and the "atopic itch." Moisturizers primarily fall into three broad categories—(i) emollients, (ii) humectants, and (iii) occlusive. Natural moisturizing factors include amino acid such as pyrrolidone carboxylic acid, urocanic acid, inorganic salts, sugars, urea, and lactic acid. The most essential aspect of treating a patient of AD is diligent explanation of general measures. Moisturizers are the backbone of every prescription for AD and a thorough knowledge of formulations is crucial to effective management; after gentle pat drying of the skin, an emollient should be applied within 3 minutes on slightly wet skin.

INTRODUCTION

Atopic dermatitis (AD) is a chronic eczema characterized by a relapsing and remitting course. The primary defect lies in the faulty barrier function of the skin which leads to increased susceptibility to environmental allergens and thus a state of chronic inflammation in the skin. The genetic basis of the disease is the *FLG* gene coding filaggrin protein whose loss of function mutation leads to aberrant barrier function of the skin.[1] Additionally, ceramides and proteins constituting the cornified cell envelope appear to be deficient in AD secondary to genetic defects and immune response. So vital is the barrier function of the skin that it has been called the "raison d'être" of the epidermis.[2]

The most essential aspect of treating a patient of AD is diligent explanation of general measures. Moisturizers are the backbone of every prescription for AD and a thorough knowledge of formulations is crucial to effective management.

MOISTURIZERS

Dry skin results from a loss of intercellular lipids, i.e., the ceramides, cholesterol, and fatty acids that form the bilayers, which causes impairment of water barrier function. When there is breach in stratum corneum and moisture content is <10%, it results in dry skin.[3]

Moisturizers primarily fall into three broad categories:
1. Emollients
2. Humectants
3. Occlusives

Emollients

Emollients are derived from the Latin word *ēmollīre*, which means "to soften." Emollients are characterized as topical treatments that primarily consist of vehicle type substances and lack active ingredients.[4] They are saturated and unsaturated hydrocarbons which hydrate and smoothen the skin. Emollients include stearic, linoleic, oleic, and lauric acid and fatty alcohols naturally found in palm oil, coconut oil, and other vegetable oils **(Box 1)**. Emollients affect the skin barrier by influencing eicosanoid production and reducing skin permeability thereby potentiating the barrier function.[4]

Emollients are further subdivided into dry, fatty, astringent, and protective based on the inherent characteristics of the substances.[4]

Humectants

Humectants are hygroscopic compounds, i.e., they absorb water from the surrounding both from the dermis into epidermis as well as from the environment.[5] This increases the water content of the epidermis. Humectants are low molecular weight compounds like urea and lactic acid among others **(Box 2)**. Humectants may paradoxically augment the transepidermal water

BOX 1 Emollients.[4]

- *Dry emollients*: Isostearyl alcohol, isopropyl palmitate
- *Fatty emollients*: Propylene glycol, octyl stearate, glyceryl stearate, jojoba oil, castor oil
- *Astringent emollients*: Dimethicone, cyclomethicone, octyl octanoate, isopropyl myristate
- *Protective emollients*: Isopropyl isostearate, diisopropyl dilinoleate

BOX 2 Humectants.

- Alpha hydroxy acids
- Hyaluronic acid
- Glycerin
- Panthenol
- Gelatine
- Sorbitol
- Honey
- Ammonium lactate
- Propylene glycol
- Butylene glycol

BOX 3 Occlusives.

- Petrolatum
- Liquid paraffin
- Squalene
- Lanolin
- Stearic acid
- Cetyl alcohol
- Cholesterol
- Beeswax
- Mineral oil

loss by facilitating the uptake of water from the dermis into the epidermis.[6] Combination of humectants with occlusive agents circumvents the loss and acts synergistically to enhance skin hydration.[6]

Occlusives

Occlusives are inert compounds often derived from petroleum byproducts that act as effective moisturizers especially in inflamed, oozy skin **(Box 3)**. Occlusives demonstrate their greatest effectiveness when applied to skin that is slightly damp.[6] They create a hydrophobic barrier on the skin's surface and stabilize the intercorneocyte matrix.[6]

Natural Moisturizing Factors

Ceramides are a family of waxy lipid molecules composed of sphingosine and fatty acids. Ceramide-containing moisturizers have been advocated in AD due to replacement of natural ceramides lost due to barrier dysfunction.[7] However, a double-blind randomized controlled trial (RCT) comparing ceramide-based moisturizers with paraffin-based ones in mild-to-moderate AD failed to show any difference between the two with respect to the changes in objective disease activity scores and the quality of life.[8] Ceramide-based moisturizers tend to be more expensive per unit volume as compared to paraffin-based moisturizers.[8] Selection of one over the other should take into account cost-effectiveness as moisturizer therapy may be required for a long time in AD.

The term natural moisturizing factors (NMFs) was coined in the 1950s by Jacobi et al.[9] These are naturally occurring hygroscopic substances within the corneocytes. NMFs include amino acid such as pyrrolidone carboxylic acid, urocanic acid, inorganic salts, sugars, urea, and lactic acid **(Box 4)**.

BOX 4 Natural moisturizing factors.[7]

- Free amino acids
- Lactates
- Sugars, inorganic acids, peptides, other unidentified materials
- *Ammonia*: Uric acid, glucosamines, creatinine
- Urea
- Phosphate
- Magnesium
- Potassium
- Sodium

Probiotic-based Moisturizers

Skin colonization with *Staphylococcus (S.) aureus* appears to be common in AD complicating its course. *S. aureus* compromises the already defective skin barrier in AD by releasing toxins and proteases.[10] Activation of the innate and adaptive immune response by *S. aureus* also contributes to barrier dysfunction.[10] A vicious loop with bacterial dysbiosis as the main culprit thus comes into play in AD. Based on this concept, probiotic containing moisturizers are being tested in clinical trials for AD. The application of coagulase-negative staphylococci (CoNS) to the skin affected by AD appeared to decrease *S. aureus* colonization.[11] Similarly, topical application of a gram-negative bacillus Roseomonas mucosa decreased clinical severity by decreasing itch and flare-up.[11] However, further studies with probiotic-based moisturizers are required to assess long-term impact and effectiveness in AD.

Emollients with Nonmedicated Active Ingredients: Emollient "Plus"

Numerous nonmedicated topical products for treating atopic eczema (AE) are commercially accessible. These products include active ingredients but do not meet the criteria for requiring a license as topical drugs. They may contain components such as saponins, flavonoids, and riboflavins extracted from protein-free oat plantlets, or bacterial lysates derived from *Aquaphilus dolomiae* or *Vitreoscilla filiformis*.[12] Clinical efficacy of such emollient "plus" preparations vis-à-vis conventional emollient therapy needs to be determined.

PATHOLOGY IN ATOPIC DERMATITIS

Filaggrin (37 kDa) is a protein found in the corneocytes derived from the precursor molecule profilaggrin located in the keratohyalin granules of the stratum granulosum. Filaggrin plays an important role in the formation of the cell envelope of the corneocytes, as it catalyzes the formation of disulfide bond. Filaggrin in turn continues to be degraded in the stratum corneum to form NMF. The NMF-bound water is essential for hydration of the skin. A study by Mclean et al., showed that the filaggrin mutation is carried by 10% of the European population.[13] A loss of function of mutation of the *filaggrin* gene results in AE resulting in characteristic dry skin and impaired barrier function of the skin.[14]

BATHING AND MOISTURIZING FOR ATOPIC DERMATITIS

Hebra first proposed frequent bathing 3–4 times a day as supportive measure for eczema in the 19th century. It was in the mid-20th century that Scholtz first proposed that bathing causes dryness of the skin and advocated bathing avoidance and application of emollient.[15] Thus, the oft-repeated paradox "bathing dries the skin."

General measures need to be explained in detail to ensure compliance. Soaking of skin is recommended for short periods no longer than 10–15 minutes, with a nondrying soap or nonsoap cleanser. Most soaps are alkaline in pH, whereas the skin's normal pH is 4–5.5, syndet-based soaps may be preferred as they match the pH of the skin. Hot water baths, bath oil, scented oils, and scrubs are best avoided. Water if left to dry on its own results in greater transepidermal water loss. Thus, after gentle pat drying of the skin, an emollient should be applied within 3 minutes on slightly wet skin. Application of emollient on acutely inflamed skin is not recommended as it is poorly tolerated. Wet wrapping may be done during acute flares of the disease.

In a study it was found that in AD subjects, emollient alone yielded a significantly ($p < 0.05$) greater mean hydration over 90 minutes than bathing with immediate emollient, bathing and delayed emollient, and bathing alone.[16]

Contact Sensitization to Moisturizers

Propylene glycol can be irritating to children under 2 years old and should be avoided due to potential toxicity. There is also concern that using emollients containing intact proteins, like peanut allergens, or colloidal oatmeal, may raise the risk of skin sensitization and allergies.[17] To reduce this risk, it is advisable to use emollients without proteinaceous allergens or known contact allergens, like lanolin, especially in children under two. Emollients containing tannin and ammonium bituminosulfonate (ichthammol) can complement standard treatment, especially in mild cases or when topical corticosteroid treatment is not feasible due to patient concerns like steroid phobia.

Which moisturizer should be used?

- *For routine care*: Emollients are easy to use, nongreasy preparations that may be used for routine care immediately after bath.
- *During flare*: Occlusives may be used as they do not contain any preservative and thus do not irritate the inflamed skin.
- *For excessively dry skin*: Lotion formulations may be avoided as they lead to loss of water due to evaporation.
- Emollient preparations free of possible allergens such as lanolin and methylisothiazolinone should be selected.

How much moisturizer is to be applied?

Patients as well as their caregivers need to be educated about the appropriate amount of moisturizer to be applied where the fingertip unit chart may be given to the patient.[18] Application of moisturizer up to twice or thrice daily amounting to 150–200 g/week in children and 500 g in adults is recommended.[19] Patients should be educated about their medications and treatment objectives using the SMART method, i.e., specific, measurable, attainable, relevant, and time-based goals that is used for patient education in chronic disease **(Box 5)**.[20]

BOX 5 SMART goals for patients with atopic dermatitis.

- *What*? The patient should know the name of two formulations and why he/she is using them
- *Why*? To increase knowledge regarding the disease leading to better adherence to therapy
- *When*? At the end of 2 weeks, patient should be able to verbalize the names of the medication and why he/she is using it

CONCLUSION

Atopic dermatitis is a chronic disease whose treatment should be patient centric rather than physician centric. Patient education about the correct usage of moisturizers goes a long way in aiding successful management of disease. Patient acceptability, disease activity, as well as cost should be used as a guide while prescribing appropriate therapy.

A clear and succinct knowledge of various formulations and their optimum use is thus a useful resource in the dermatologist's armamentarium.

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Handbook of
ATOPIC DERMATITIS

Atopic dermatitis, also known as atopic eczema, is a very common skin condition that is characterized by severe itching, dry, scaling, or crusting skin, and red spots. It often appears in infants during the first year of life and can worsen, which has a significant effect on the quality of life associated with health. This extensive book covers the most recent advancements in the knowledge of and treatment for atopic dermatitis. For those working in allergy and general medicine, such as pediatricians, allergists, and primary care physicians, as well as dermatologists, this book will be a great resource for diagnosis and treatment.

Rashmi Sarkar MD(PGI) FAMS IFAAD is Director Professor of Dermatology at Lady Hardinge Medical College and Associated KSCH and SSK Hospital, New Delhi, India. She has done her MD (Dermatology) from PGIMER, Chandigarh, India. She was the Editor-in-Chief of the Pigment International Journal and World Clinics: Dermatology and co-editor of Asian Journal of Pediatric Dermatology. She was the Founder Editor of Asian Pigment Bulletin (APB). She has worked as Associate Editor for the Journal of Cutaneous and Aesthetic Surgery (2011–2014); is Associate Editor of International Journal of Dermatology, Journal of Cosmetic Dermatology, and International Journal of Women's Dermatology; and Editorial Board, Indian Journal of Dermatology, Venereology, and Leprology, Indian Journal of Dermatology, and Journal of Clinical and Aesthetic Dermatology, besides being a reviewer for 20 journals. She has 240 publications in peer-reviewed international and national journals and 80 chapters in textbooks of dermatology and pediatrics. She has edited 20 textbooks in dermatology. She was the President of Indian Association of Dermatologists, Venereologists, and Leprologists (IADVL) in 2022. She is the Regional Director of South Asia, Africa, and Middle East in International League of Dermatological Societies (ILDS); Chief Founder and President of Pigmentary Disorders Society; and Founding President of the Indian Women's Dermatologic Association. She is also a recipient of several prestigious awards and honors, including Maria Duran Medal from the International Society of Dermatology (ISD), Member Making a Difference Award from the American Academy of Dermatology (AAD), and International Pioneer Award and Career and Community Development Award from Women's Dermatologic Society (WDS). She has also received the prestigious ICMR Lala Ram Chand Kandhari Award (2020), Dr BM Ambady Oration from IADVL (2019), Dr Madhusudan Das Oration (2019), Dr BV Sathyanarayanan Oration (2015) from IADVL AP, and the prestigious "Inspiring Dermatologist" award from Economic Times in 2019. She has been an invited speaker in many international and national conferences, including the prestigious Annual AAD Meetings since 2006. She is on Board of Directors of ISD; President ASPCR (2020–2022); International Representative, Board of Directors in WDS (2011–2014; 2017–2018); former Board of Directors in Skin of Color Society (SOCS); Chair of International Mentorship Committee of ISD; and Member of International Affairs Committee of AAD.

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