ABOUT THE AUTHOR

Sonja Molin, MD

Dr. Sonja Molin is Associate Professor and Division Chair of Dermatology at Queen's University in Kingston, Ontario. She completed her training in Dermatology and Allergy at the Ludwig Maximilian University in Munich, Germany, where she worked for 11 years before she joined Queen's University in 2018. The main focus of her clinical expertise and research are inflammatory skin diseases, mainly hand eczema and contact allergy as well as psoriasis. Dr. Molin specializes as an occupational dermatologist and is a member of the executive board of the German Society for Occupational Dermatology since 2015. She is chair of the Research Planning and Development Committee of the American Contact Dermatitis Society and chairs the classification of hand eczema subgroup for the current renewal of the hand eczema guidelines of the European Contact Dermatitis Society.

HAND ECZEMA IN THE YEAR 2021

The ongoing COVID-19 pandemic has changed our hand hygiene awareness and practices. Frequent handwashing or use of hand disinfectant have become far more common in our daily life and, though necessary to curb the spread of the virus, add further stress on our skin and skin barrier function. As a consequence, more people have started suffering from dry skin or developing hand eczema.

Introduction

Hand eczema (HE) was already a common skin disease even pre-COVID-19, with a prevalence of about 10% in the general population.[1,2] It has an important socioeconomic impact due to its high indirect health care costs and association with prolonged sick leave.[3,4] Hand eczema is a clinically heterogeneous entity whose classification has historically been controversial.[1] Recent publications, though varying slightly in the details, share similarities in their approach to classifying HE. Approaches to classifying hand eczema into certain subtypes according to underlying pathogenesis are more common and often discriminate between irritant or allergic contact dermatitis, atopic hand eczema and protein contact dermatitis.[5-7] The clinical picture is used as an additional feature when etiological factors remain unclear. Recently, the question of whether hyperkeratotic hand eczema might have to be considered as an entirely different and separate disease entity from "hand eczema" in general has been postulated. Additional research has addressed the diagnostic challenges associated with hyperkeratotic hand eczema.[8,9] Dyshidrotic endogenous eczema has been described as a separate entity in a similar way[5,6,10] and poses challenges with regards to diagnosis and treatment. It has been observed in association with allergic contact dermatitis.[10]

A comprehensive understanding of the molecular pathogenesis of hand eczema is still lacking, though more details emerge.[11,12] Future classification systems will likely include molecular subtyping.

The pathogenesis of hand eczema is multifactorial.[13] Endogenous and exogenous factors contribute to its development, including atopic predisposition, skin irritation by repeated contact with water or irritants or wearing of occlusive gloves.[2-4] The strongest independent risk factor for the development of hand eczema is a history of atopic dermatitis in childhood.[14]

To date, there has been no peer-reviewed data demonstrating an association between the increased prevalence of hand eczema in adults with the onset of the COVID-19 pandemic. Two recent publications from Denmark have thoroughly investigated this topic in young children at daycare centres and in school-aged children. Both studies demonstrated that 28.6% of daycare and 40.9% of school children, with no previous history of hand eczema developed hand eczema upon their return to daycare or school after lockdown.[15,16]

Skin barrier function

The common denominator in the pathogenesis of different hand eczema sub-types is skin barrier dysfunction.[13] An intact skin barrier protects individuals from environmental stressors, from the loss of water or heat[2], and also prevents the penetration of irritating substances and microorganisms.[17-20] Epidermal barrier dysfunction enables increased penetration of allergens and development of contact allergy which affects approximately 20% of the adult population.[2,18,21,26,27] Both endogenous and exogenous factors can contribute to epidermal barrier dysfunction such as genetic predisposition and exposure to irritants or allergens.[2]

The epidermal barrier function is largely based on an intact stratum corneum (SC), which is formed by the corneocytes and lipids and often described as a "brick and mortar" model.[2] Its protein mass consists mostly of keratin intermediate filaments and filaggrin (FLG), but it also contains proline-rich-proteins, hornerin, involucrin, loricrin and antimicrobial peptides.[2]

In a recent study on the hand eczema proteome, our research group identified specific patterns of barrier protein expression in hand eczema using mass spectrometry. The results of our research indicate that FLG, filaggrin 2 and hornerin all were downregulated compared to healthy skin, whereas desquamation-related enzymes, such as cystatin E/M, and kallikrenin-related peptidase 5 and 7 all were upregulated along with the antimicrobial peptides S100A7 and S100A8/A9.[12] Genetic abnormalities in genes coding for epidermal barrier proteins and a dysfunctional immune response both play an important role in the dysfunction of the epidermal skin barrier.[2]

Several studies have described an increased risk for hand eczema among FLG mutation carriers[22] or patients with contact sensitization.[23] FLG is essential for the structural integrity of the epidermal barrier and its degradation products are largely involved in the process of moisturization and maintenance of the skin's acidic milieu. This is essential for lipid synthesis, desquamation and skin inflammation.[2] The concept of the "acid mantle of the skin" was established by Alfred Marchionini in 1928 and refers to the acidic nature of the stratum corneum, which is essential for the homeostasis of the barrier, proper functioning of the epidermal barrier and for the skin's antimicrobial defence mechanisms. Normal skin flora grows optimally at acidic pH levels, whereas pathogenic bacteria grow well in a neutral pH milieu.[24] Various factors like age, skin texture, anatomic site, sweat, skin care, cleansing products and irritants can influence the skin's pH.[24]

Environmental factors like skin contact to irritants or water can play an important role in developing an impaired epidermal skin barrier. Irritant contact dermatitis is the most frequent subtype of hand eczema.[6] Wet-work occupations are considered high-risk factors for the development of hand eczema. A recent study looked at transepidermal water loss (TEWL) after skin occlusion of the hands for either 72 consecutive hours or 8 hours per day for seven days. In healthy skin, occlusion did not affect the TEWL, whereas in skin that was irritated by sodium lauryl sulfate beforehand, it was increased ($P = 0.049$).[25] This study demonstrates that in already-irritated skin, occlusion should be avoided or reduced to a minimum.

How to care for your hands during COVID-19

During the COVID-19 pandemic, irritant exposure has substantially increased and, subsequently, the overall risk of developing irritant contact dermatitis and hand eczema has also increased. It is important to match good hand hygiene with diligent hand care to reduce the effect of damaging influences. Skin care recommendations can be found online from different dermatological societies, including the American Contact Dermatitis

Society.[28] Moisturizing is the most important element of good hand care. Preferably, products free of fragrances, preservatives and dyes should be used on a regular basis, ideally after every hand-washing. Moisturizers come in various galenic bases. Ointments are preferred for use on very dry skin.[28] Emollients are important components of moisturizing products. Emollients work by providing a seal and helping to restore the epidermal barrier function through hydration and retention of moisture.[2] Newer products focus on active ingredients that stimulate production of intercellular lipids and contribute to the restoration of lipid bilayers. Emollients containing ceramides improve the skin barrier function through skin hydration and reduce the transepidermal water loss.[2,29] Through occlusive substances like beeswax or petrolatum, a physical barrier function can be added to a moisturizer.[28] Barrier creams provide a protective layer on the skin and are often recommended for prophylaxis. However, it has still not been fully elucidated whether their effect is superior to that of a regular moisturizer.[2,30] Jordan et al. studied the effect of a combined regimen involving the use of hand protection cream, cleanser and a repair cream in 42 healthy male and female adult volunteers prone to occupational irritant contact dermatitis due to frequent wet work or contact with detergents and found this three-step approach to be successful in skin hydration and improvement of epidermal barrier function.[31]

Skin cleansing products can cause irritation and dryness of the skin. Adding moisturizing components can alleviate their negative influences on the skin barrier. Soaps wash away intercellular lipids and damage barrier proteins, though they are effective in removing dirt and inactivating viruses. Synthetic detergents have a pH of 5.5-7 which is thought to be beneficial for the skin's acid mantel and natural microflora. They have less than 10% soap content and are generally less irritating than soap.[28] Alcohol-based hand sanitizers have become an integral part of our daily lives and are omnipresent. To protect the hands as much as possible from their irritating potential it is recommended to choose products containing moisturizers and to apply a moisturizer immediately after use. Washing hands with soap and water directly before or after using a hand sanitizer should be avoided (see **Figure 1**).[28]

Wearing protective gloves poses the risk for development of irritant as well as allergic contact dermatitis to the glove itself. The culprit allergens are often rubber accelerators, and the sweating and the occlusive milieu under the gloves further promote skin barrier impairment and break down. Choosing accelerator-free gloves and applying a moisturizer beforehand will help to protect the skin.[28] Ideally, wearing cotton gloves underneath is recommended if protective gloves are required for a duration of more than 10 minutes.[1]

Perspective

Hand eczema is a common skin disease with a high socioeconomic impact. As a result of the COVID-19 pandemic, the prevalence of hand eczema is on the rise. The treatment landscape for hand eczema has suffered from a lack of innovation with no new novel therapeutic options having been made available in over a decade.

Fortunately, this situation may change in the near future as several new therapeutic approaches like topical delgocitinib or gusacitinib are currently under investigation and may alter our approach to the management of this disease profoundly.[32] With continued good skin care practices and an enhanced therapeutic armamentarium it may be possible to get hand eczema under control.

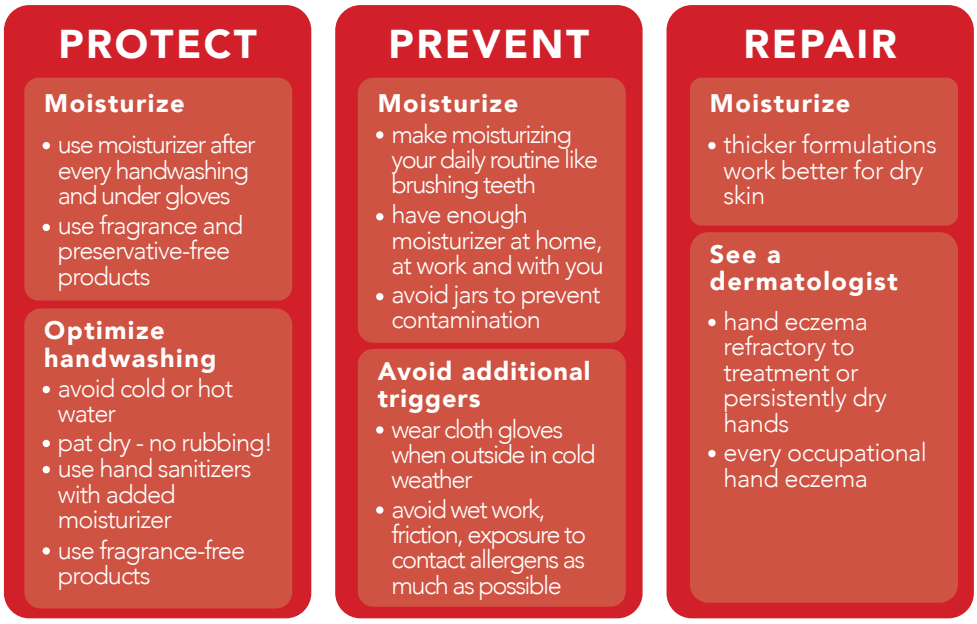

Figure 1. Hand skin care recommendations for patients courtesy of Sonja Molin, MD

References

1. Diepgen TL, Andersen KE, Chosidow O, et al. Guidelines for diagnosis, prevention and treatment of hand eczema. J Dtsch Dermatol Ges. 2015;13(1):e1-22.

2. Aviv H, Herzinger T, Molin S. Skin Barrier Dysfunction in Contact Dermatitis and Atopic Dermatitis-Treatment Implications. Current Treatment Options in Allergy. 2020;7(3):390-402.

3. Heede NG, Thuesen BH, Thyssen JP, et al. Hand eczema, atopic dermatitis and filaggrin mutations in adult Danes: a registry-based study assessing risk of disability pension. Contact Dermatitis. 2017;77(2):95-105.

4. Coenraads PJ. Hand eczema. The New England journal of medicine. 2012;367(19):1829-1837.

5. Diepgen TL, Andersen KE, Brandao FM, et al. Hand eczema classification: a cross-sectional, multicentre study of the aetiology and morphology of hand eczema. Br J Dermatol. 2009;160(2):353-358.

6. Agner T, Aalto-Korte K, Andersen KE, et al. Classification of hand eczema. J Eur Acad Dermatol Venereol. 2015;29(12):2417-2422.

7. Menne T, Johansen JD, Sommerlund M, Veien NK, Danish Contact Dermatitis G. Hand eczema guidelines based on the Danish guidelines for the diagnosis and treatment of hand eczema. Contact Dermatitis. 2011;65(1):3-12.

8. van der Heiden J, Agner T, Rustemeyer T, Clemmensen KKB. Hyperkeratotic hand eczema compared to other subgroups of hand eczema - a retrospective study with a follow-up questionnaire. Contact Dermatitis. 2018;78(3):216-222.

9. Politiek K, Loman L, Pas HH, et al. Hyperkeratotic hand eczema: Eczema or not? Contact Dermatitis. 2020.

10. Johansen JD, Hald M, Andersen BL, et al. Classification of hand eczema: clinical and aetiological types. Based on the guideline of the Danish Contact Dermatitis Group. Contact Dermatitis. 2011;65(1):13-21.

11. Tauber M, Bérard E, Lourari S, et al. Latent class analysis categorizes chronic hand eczema patients according to skin barrier impairment. J Eur Acad Dermatol Venereol. 2019.

12. Molin S, Merl J, Dietrich KA, et al. The hand eczema proteome: imbalance of epidermal barrier proteins. Br J Dermatol. 2015;172(4):994-1001.

13. Molin S. [Pathogenesis of hand eczema]. Hautarzt. 2019;70(10):755-759.

14. Gronhagen C, Liden C, Wahlgren CF, et al. Hand eczema and atopic dermatitis in adolescents: a prospective cohort study from the BAMSE project. The British journal of dermatology. 2015;173(5):1175-1182.

15. Simonsen AB, Ruge IF, Quaade AS, Johansen JD, Thyssen JP, Zachariae C. High incidence of hand eczema in Danish schoolchildren following intensive hand hygiene during the COVID-19 pandemic: a nationwide questionnaire study. Br J Dermatol. 2020;183(5):975-976.

16. Simonsen AB, Ruge IF, Quaade AS, Johansen JD, Thyssen JP, Zachariae C. Increased occurrence of hand eczema in young children following the Danish hand hygiene recommendations during the COVID-19 pandemic. Contact Dermatitis. 2020.

17. Candi E, Schmidt R, Melino G. The cornified envelope: a model of cell death in the skin. Nature reviews Molecular cell biology. 2005;6(4):328-340.

18. Gimenez-Arnau A. Standards for the Protection of Skin Barrier Function. Current problems in dermatology. 2016;49:123-134.

19. Egawa G, Kabashima K. Multifactorial skin barrier deficiency and atopic dermatitis: Essential topics to prevent the atopic march. The Journal of allergy and clinical immunology. 2016;138(2):350-358.e351.

20. Thyssen JP, McFadden JP, Kimber I. The multiple factors affecting the association between atopic dermatitis and contact sensitization. Allergy. 2014;69(1):28-36.

21. Smith HR, Basketter DA, McFadden JP. Irritant dermatitis, irritancy and its role in allergic contact dermatitis. Clin Exp Dermatol. 2002;27(2):138-146.

22. Heede NG, Thyssen JP, Thuesen BH, Linneberg A, Johansen JD. Predictive factors of self-reported hand eczema in adult Danes: a population-based cohort study with 5-year follow-up. Br J Dermatol. 2016;175(2):287-295.

23. Elhaji Y, Sasseville D, Pratt M, et al. Filaggrin gene loss-of-function mutations constitute a factor in patients with multiple contact allergies. Contact Dermatitis. 2019;80(6):354-358.

24. Ali SM, Yosipovitch G. Skin pH: from basic science to basic skin care. Acta Derm Venereol. 2013;93(3):261-267.

25. Jungersted JM, Hogh JK, Hellgren LI, Jemec GB, Agner T. Skin barrier response to occlusion of healthy and irritated skin: differences in trans-epidermal water loss, erythema and stratum corneum lipids. Contact dermatitis. 2010;63(6):313-319.

26. Thyssen JP, Linneberg A, Menne T, Johansen JD. The epidemiology of contact allergy in the general population--prevalence and main findings. Contact dermatitis. 2007;57(5):287-299.

27. Friedmann PS, Sanchez-Elsner T, Schnuch A. Genetic factors in susceptibility to contact sensitivity. Contact dermatitis. 2015;72(5):263-274.

28. Rundle CW, Presley CL, Militello M, et al. Hand hygiene during COVID-19: Recommendations from the American Contact Dermatitis Society. J Am Acad Dermatol. 2020;83(6):1730-1737.

29. Meckfessel MH, Brandt S. The structure, function, and importance of ceramides in skin and their use as therapeutic agents in skin-care products. Journal of the American Academy of Dermatology. 2014;71(1):177-184.

30. Mostosi C, Simonart T. Effectiveness of Barrier Creams against Irritant Contact Dermatitis. Dermatology (Basel, Switzerland). 2016;232(3):353-362.

31.Jordan L. Efficacy of a Hand Regimen in Skin Barrier Protection in Individuals With Occupational Irritant Contact Dermatitis. Journal of drugs in dermatology : JDD. 2016;15(11):s81-s85.

32. Dubin C, Del Duca E, Guttman-Yassky E. Drugs for the Treatment of Chronic Hand Eczema: Successes and Key Challenges. Ther Clin Risk Manag. 2020;16:1319-1332.