Beyond the Barrier: Understanding Chronic Hand Eczema as a Multifactorial, Heterogeneous Skin Disease

Infographic 1 of 2 in the 'CHE disease education' series

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What is Chronic Hand Eczema?

CHE is a long-term, heterogenous, multifactorial inflammatory skin disease on the hands and wrist. Characterised by key symptoms of itch and pain with potentially overlapping aetiological subtypes.[1-5]

Key signs include erythema, scaling, lichenification, hyperkeratosis, vesicles, oedema, and fissures with no reliable link between the visible signs of CHE and the underlying aetiological cause.[3-6]

Due to CHE, patients see increased risk of *S. aureus* infection. [7,8]

CHE pathogenesis is multifactorial with exogenous and endogenous factors, warranting a holistic treatment approach:[9]

Exogenous factors

Allergens | Pathogens | Irritants

Endogenous factors

Inflammation | Skin barrier defects

CHE and AD: Two Distinct Diseases

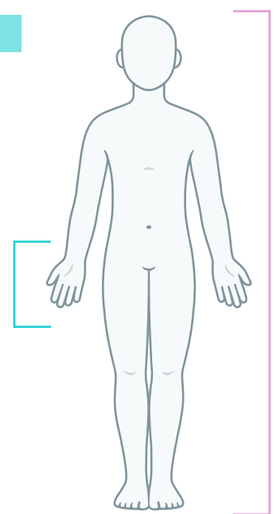
There is considerable overlap in the pathophysiology of CHE and AD;[9] however, both have distinct immune profiles that require individual targeted approaches.[10-14]

CHE

Symptoms **localised to hands and wrist**[1-5]

Different aetiological subtypes show different immune signatures including **Th1/Th17 and Th2/Th22**[10-12]

Broad, potentially mixed immune signature activation may require broad coverage MoA therapeutic interventions[11,12]



AD

Symptoms can **affect skin across the whole body**[10]

Several immune pathways are involved in pathogenesis, with the **Th2/Th22** immune signatures playing a pivotal role[11-14]

Narrow immune signature may require more selective treatment[11,12]

Impaired Skin Barrier Function and Dysregulated Immune Response in CHE

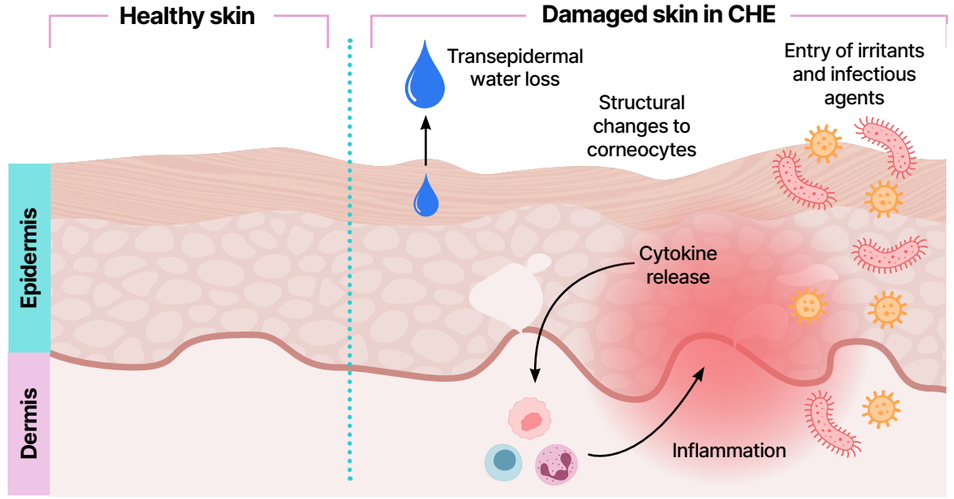
Skin barrier dysfunction is a defining feature of CHE, independent of aetiology.[5,15] In healthy skin, the barrier effectively protects against external stressors.[16] In CHE, barrier impairment facilitates the penetration of irritants and allergens, eliciting immune activation that drives a self-perpetuating cycle of disease across all subtypes.[15,16]

Patients with CHE have notably impaired skin barrier with:[15-19]

- Increased transepidermal water loss
- Higher degree of *Staphylococcus* colonisation
- Higher IL-8 level on the skin surface
- Higher frequency of filaggrin mutations

Immune dysregulation occurs in CHE when allergens, irritants, or pathogens breach the impaired skin barrier, inducing keratinocyte cytokine release.[15,16]

Cytokines activate immune cells which promote pruritus, epidermal hyperplasia, and further barrier dysfunction.[5,14]



JAK-STAT Signalling Drives CHE Across Subtypes[5,9,18,19]

Although CHE pathophysiology can vary by subtype,[8] all subtypes are driven by multiple cytokines through the JAK-STAT pathways.[5,18-21]

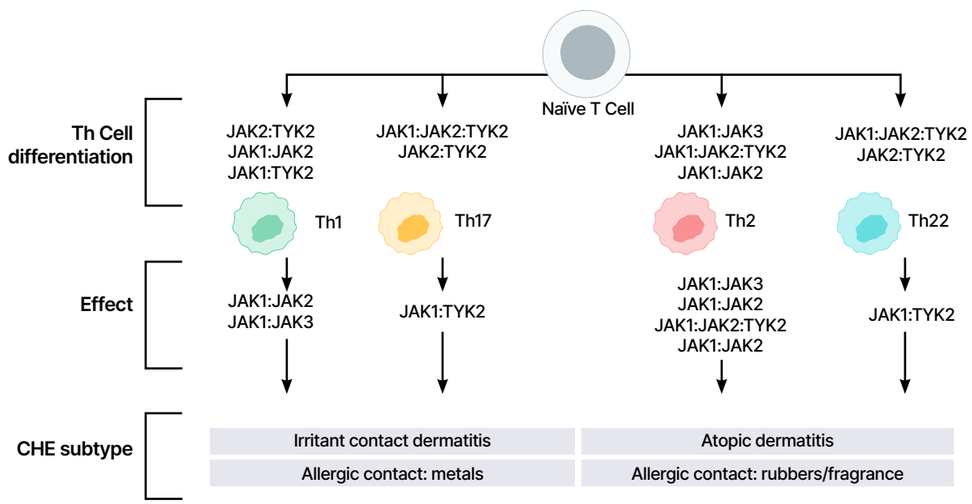


Figure adapted from Virtanen A et al.,[18] Pan Y et al.,[19] and Dubin C et al.[9]

The JAK-STAT pathway provides a broad target that may facilitate the holistic treatment approach required to address the complex nature of CHE.[9,11,18-22]

Key Learnings:

> CHE is a distinct inflammatory skin disease marked by **barrier dysfunction** and **immune dysregulation**.[1-9]

> CHE and AD have unique immune profiles that require their own individual targeted approaches.[9-14]

> Although CHE pathophysiology can vary by subtype, all subtypes are driven by cytokine activity through **JAK-STAT signalling pathways**.[5,18-21]

> The JAK-STAT pathway provides a broad target that may contribute to the **holistic treatment approach** warranted to address the complex nature of CHE.[9,11,18-22]

Abbreviations:

AD: Atopic dermatitis; CHE: chronic hand eczema; HR-QoL; health-related quality of life; IL: interleukin; JAK: Janus kinase; STAT: signal transducer and activator of transcription; *S. Aureus: Staphylococcus Aureus*; Th: T helper (cell); TYK: tyrosine kinase.

References:

1. Thyssen JP et al. Contact Dermatitis. 2022;86(5):357-78. 2. Molin S et al. Acta Derm Venereol. 2025;105:adv42596. 3. Lynde C et al. J Cutan Med Surg. 2010;14(6):267-84. Erratum in J Cutan Med Surg. 2011;15:360. 4. Menné T et al. Contact Dermatitis. 2011;65(1):3-12. 5. Lee GR et al. Dermatol Ther. 2019;32(3):e12840. 6. Haslund P et al. Br J Dermatol. 2009;161(4):772-7. 7. Mernelius S et al. Eur J Clin Microbiol Infect Dis. 2016;35(8):1355-61. 8. Dubin C et al. Ther Clin Risk Manag. 2020;16:1319-32. Erratum in: Ther Clin Risk Manag. 2021;17:233. 9. Rosenberg FM et al. Contact Dermatitis 2024;90(1):23-31. 10. Quaade AS et al. J Allergy Clin Immunol. 2025;155(4):1250-63. 11. Di Domizio C, Gillet C. Oral Presentation D1T09.1A. EADV Congress 2024. 25-28 September, 2024. 12. Napolitano M et al. Front Med (Lausanne) 2023;10:1165098. 13. Huang IH et al. Front Immunol. 2022;13:1068260. 14. Tauber M et al. J Eur Acad Dermatol Venereol. 2020;34(7):1529-35. 15. Smith AR et al. Curr Allergy Asthma Rep. 2017;17:6. 16. Gittler JK et al. J Allergy Clin Immunol. 2013;131:300-13. 17. Virtanen A et al. BioDrugs. 2019;33(1):15-32. 18. Pan Y et al. Front Immunol. 2022;13:911546. 19. Worm M et al. Br J Dermatol 2022;187(1):42-51. 20. Tancredi V et al. Int J Mol Sci. 2023;25(1):362. 21. Scheinman PL et al. Nat Rev Dis Primers. 2021;7:38.