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Childhood Eczema Triggers: Role of Early-Life Dietary and Environmental Exposures

Shihan Khalaf Jafar Alja'afreh^{1*}, Rashid Ayed Salem Al Amer²

¹Primary Health Care Corporation (PHCC), Qatar

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*Corresponding author: Shihan Khalaf Jafar Alja'afreh Primary Health Care Corporation (PHCC), Qatar

Abstract

Review Article

Eczema is common in childhood, with a prevalence of approximately 15% in Western industrialized countries. The objective of this review study was to explore the updates of the literature towards childhood eczema triggers. To achieve this objective, the research team employed the main research engines including Science direct, Pub Med, Google Scholar, Springers, and others. This review included several topics such as biological and environmental factors leading to eczema. The cited literature showed that childhood eczema is a world-wide problem. Therapeutic options are varied among individuals. Food and environmental factors are important factors that participate in the development of eczema. **Keywords:** Eczema, children, triggers, environment, diet.

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1. INTRODUCTION

Eczema is common in childhood, with a prevalence of approximately 15% in Western industrialized countries (Liu *et al.*, 2022). Eczema negatively affects the quality of life of affected children and their family members (de *et al.*, 2021). Parents' worries and concerns about their child's discomfort and sleeping problems are substantial issues associated with the condition (Shi *et al.*, 2021). Furthermore, eczema is often the first step in what is later called the "atopic march" through other allergic diseases, such as food allergies, allergic rhinitis, and allergic asthma (Lopez *et al.*, 2022). Therefore, early prediction and prevention of eczema are seen as important (Bylund *et al.*, 2020).

It is well known that skin care is the main treatment for all children with eczema (Alkhatib, 2022a; Chong et al., 2022). However, in the small group of children with a genuine food allergy, exclusion of the offending food(s) is important (Blakeway et al., 2020). The remaining group of children have intrinsic problems with the permeability or barrier function of the skin, and therefore they develop neosensitizations to multiple environmental allergens (Grafanaki et al., 2023). It is still being discussed whether allergy-preventive effects can be obtained when children avoid aeroallergens. The role of dietary and environmental factors behind all of this still needs to be clarified (Stefanovic et al., 2021). Accordingly, there is an increasing focus on reducing these underlying allergies through early interventions (Narla and Silverberg, 2020). Eczema appears as a result

of complex gene-environment interactions (Lowe *et al.*, 2023). Spontaneous improvement of eczema has been shown up to age 3; however, the majority continues to have relapses and develop other allergic diseases (Gallay *et al.*, 2020). One potential explanation for this may be late diagnosis and lack of awareness regarding the role of so-called "classic" allergies, for example, early food allergies and aero allergies in combinations (Casella *et al.*, 2024).

1.1. Overview of Childhood Eczema

Overview Childhood eczema can have profound effects on children (Gallav et al., 2020). This common and long-lasting chronic skin condition is characterized by its unique dry, red, and itchy skin that can become sore and broken when scratched, also known as active eczema (Liu et al., 2022). During flare-ups of active eczema, children can feel very unwell, have disturbed sleep, and experience intense itchiness (Alkhatib, 2022b; Langan et al., 2023). These sensations can make it difficult to concentrate at school or play and interact with peers (García-Marcos et al., 2022). Although the itchiness may lead to children scratching their skin, young children may not always be able to convey that they are experiencing itchiness and instead express discomfort or crying, which may be distressing to their families (Dastoorpoor et al., 2022). Eczema is an umbrella term that encompasses a diverse range of skin conditions characterized by inflammation and itching. The most common form of eczema is atopic dermatitis (AD), which is an allergic form of eczema (Sun et al.,

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2022). The symptoms of AD can vary from small localized patches of dry, itchy skin to much more widespread areas of skin differences (Sun et al., 2022). Some children will have a history of being born with dry, itchy skin and go on to develop subsequent episodes of active eczema (Lopez et al., 2022). Once the active episode has resolved, children have periods where their skin settles and looks normal clinically, known as "inactive eczema." Children are likely to transition in and out of active and inactive eczema (Rutter et al., 2020). It is estimated that one in five children worldwide are affected by eczema, though this prevalence may be higher in some populations (Long et al., 2022). Active and confined eczema in children can have a negative impact on their social and psychological well-being, particularly as it distorts their body image and may make them feel conscious about the way they present to their peers (Yazar and Meydanlioglu, 2022). Children with eczema may feel different from others, leading to stigmatization (Yazar and Meydanlioglu, 2022). In addition, families of children with eczema describe a sense of frustration and guilt around not being able to protect their children from the burden of a chronic, visible skin condition (Yazar and Meydanlioglu, 2022). The worldwide proportion of children with eczema has also been increasing (Mortimer et al., 2022). Repeated surveys have shown that over a 2-to-3-year period, the reported cumulative prevalence of eczema in young children has been increasing. These findings are significant due to the potential to identify the causal factor behind this rise (Mortimer et al., 2022). To explore the potential causes of childhood eczema and develop opportunities for prevention, we begin by discussing the triggers of confining eczema to childhood (Liu et al., 2022). In the United Kingdom, one in five children under 11 years of age have eczema (Liu et al., 2022). Rates of eczema vary according to demographics such as age, gender, and geographic location. Generally, in children, the risk of developing eczema decreases with age (Liu et al., 2022). Before puberty, boys have a higher risk of eczema than girls, but afterward, girls are more likely to develop eczema (Langan et al., 2023). No trends have been reported on ethnicity and the development of eczema, although hereditary factors can increase the susceptibility of developing eczema. While some children grow out of their eczematic skin, approximately half will continue to have some symptoms of eczema as adults (García-Marcos et al., 2022). Eczema can also present in adults who did not have active eczema in their younger years (Dastoorpoor et al., 2022).

2. Understanding Eczema Triggers

Eczema behaves differently in each child, and it is critical for its proper management to understand the triggers that provoke the disease and make it worse (Narla and Silverberg, 2020). Eczema triggers can be broadly categorized into diet and environment (Luger *et al.*, 2021). Both play a significant role in the development of eczema and contribute to the exacerbation of the disease (Chai *et al.*, 2023). Eczema is typically not caused by one factor; it results from individual susceptibility to several factors, which may be due to a child's genetic background (Celebi *et al.*, 2022). Some children are more susceptible to dietary factors, and others are more susceptible to environmental factors (Akdis, 2021). Genetic susceptibilities can influence the ability of an individual to repair a damaged skin barrier, tolerate certain foods, and develop a tolerant immune response when their body comes in contact with environmental allergens (Wang *et al.*, 2024). Infectious or non-infectious mechanisms or abnormal skin colonization can further compromise the skin barrier and worsen eczema (Passeron *et al.*, 2020; Alkhatib, 2022c; Thyssen *et al.*, 2022).

There is an interaction between genetic predisposition and environmental exposures that children undergo from early life, through birth, and during development, which can influence the progression of atopic eczema (Hartmane, 2024). The eczema flares vary with the severity and chronicity of the disease (Hartmane, 2024). Mild-to-moderate eczema is characterized by random flare-ups without any specific triggers (Stefanovic et al., 2021). Severe and chronic eczema, on the other hand, is usually a reflection of multi-factorial triggers, which can be diet, environment, irritants, or infections. Skin prick testing and blood testing can be supportive in identifying the triggers (Chong et al., 2022). Eczema signs usually present within minutes, with eczema rash flaring in one-third to half of children after one to four hours from an exposed time (Chong et al., 2022). Overall, understanding dietary and environmental factors that provoke eczema is important for the parents or carers, so they can better manage the child's dietary choices, food allergen elimination, and environmental alterations with the help of healthcare providers to prevent eczema exacerbation (Mu and Zhang, 2020; Grafanaki et al., 2023).

It is important to understand if the child's eczema flares in relation to certain lifestyle activities, and this is generally a guide to identifying triggers such as particular foods or environments (Rance and Hatch, 2024). The history of the child's symptoms can be supportive for the parents or carers in identifying triggers (Zohn, 2020). For example, do the child's eczema symptoms persist after eating certain foods or going to certain places? Is there a history of eczema in the family, which can contribute to the likelihood of a particular food allergen or eczema worsening from other factors (Wollenberg *et al.*, 2020; Chua *et al.*, 2023).

2.1. Biological Mechanisms of Eczema Development

Eczema is a chronic inflammatory skin disease that begins early in life in over 80% of individuals affected (Agner and Elsner, 2020). Eczema patients show a barrier defect in their skin due to aberrant differentiation of the skin barrier microenvironment, leading to a predisposition to dry and itchy skin (Alkhatib, 2022d; Thyssen *et al.*, 2022). Characteristics of the disease include superinfections, which occur due to increased susceptibility to irritants and allergens (Schonmann *et al.*, 2020). An elevated level of IgE in the blood is often detected, with a positive response rate to various environmental allergens (Traidl *et al.*, 2021). An enhanced expression of type 2 cytokines is observed in inflamed eczematous skin, with a further increase after allergen challenge (Ziyab *et al.*, 2022). Immediate and late-phase inflammatory skin responses are indicators for the induction of sensitization and allergic skin inflammation and are often used to diagnose allergic diseases (Wollenberg *et al.*, 2020; Quaade *et al.*, 2021; Long *et al.*, 2022).

Patients with atopic dermatitis and individuals with broken skin, also suffering from an unrecognized subclinical form of the disease, show a Th-2 skewed immune deviation, a characteristic trait (Shin et al., 2020). It is thought that allergens, as well as some irritants, can induce Th2 immunity by interacting directly with cells of the innate immune system (Jacquet, 2021). In particular, allergens derived from house dust mites and fungi are especially potent in innately activating and polarizing dendritic cells (Soleha and Iswanti, 2021). It is possible that a prolonged and diverse interaction of environmental factors with the immune system, all converging on the same pathway, ultimately leads to the resulting outcome of a clinically overt disease also influenced by genetic susceptibility (Lamiable et al., 2020). Emerging research findings also stress the role of the microbiome, which has a profound influence on our health, including skin health and the development or prevention of childhood eczema (Yasuda et al., 2020). Intestinal and cutaneous microbiota interact in various manifestations with the skin immune function (Yasuda et al., 2020). Multiple dysfunctional signaling and regulatory pathways contribute to the development and pathogenesis of atopic dermatitis and also dictate the disease course and the development of comorbidities (Benedé et al., 2021). Skin allergy/eczema is a combination of various factors, including altered barrier function, cytokine patterns, the immune system, genetics, and environmental factors (Sarwar, 2020). This interdisciplinary field is revolutionizing our understanding and treatment of this complex condition and generating potential preventive strategies (Lin et al., 2022).

3. Early-Life Dietary Exposures

Diet is thought to play a significant role in the development of childhood eczema (Das and Panda, 2021). This section will provide a focused exploration of several important questions with a biomedical emphasis. Can early-life dietary exposures influence the development of childhood eczema? If yes, through what mechanisms? While solid food allergen exposures are the most widely studied dietary determinants of childhood eczema, the role of maternal diet and breast milk remains of interest (Trikamjee *et al.*, 2021; Rustad *et al.*, 2022)

In general, greater early-life exposure to food leads to a reduced eczema risk (Zhang *et al.*, 2023). Several trials have observed a lower rate of peanut allergy among high-risk infants who first ate peanuts between 4 and 11 months of age compared with older children who avoided eating peanuts (Zeng *et al.*, 2023). The enzyme content of foods may also be relevant. For example, higher egg white ovomucoid content early in life is associated with a lower eczema risk (Pierau *et al.*, 2021). A common risk factor appears to be allergic sensitization to the triggering food (Renz and Skevaki, 2021). There may also be a dose effect, with eczema more likely when higher levels of peanut- or milkspecific IgE are acquired (Kampouri *et al.*, 2023).

In summary, there is some evidence to support a recommendation of slow introduction of solids in the first year to reduce pre-filaggrin mutations eczema risk (D'Hollander et al., 2023). Nonetheless, early advice on solid food introduction and later dietary manipulation to prevent child eczema is complex (Hicke-Roberts et al., 2020). We are all unique, and different infants have different dietary requirements (Rance and Hatch, 2024). Treatment in one person does not always mean treatment in another (Royal and Gray, 2020). Many diverse factors contribute to the development of eczema. Among them, dietary manipulations appear safe for most people (Williams and Chalmers, 2020). However, controlled trials have admitted that dietary management reported by dieticians is no better than usual care for childhood eczema (Trogen et al., 2022). Given the evidence from the trials, having a varied diet should be encouraged (Abrams et al., 2022). Practical questions about the firsttime introduction of solid foods are answered in a scientific commitment titled 'Guidance: an integrated approach to infant feeding' (Venter et al., 2023).

3.1. Impact of Breastfeeding

The protective role of breastfeeding against the development of eczema during early life has been documented in a number of systematic reviews and birth cohorts over the last two decades (Peters et al., 2021). In general, exclusive breastfeeding for at least 3 to 4 months has been associated with a lower risk of developing eczema (Libuda et al., 2023). This association may primarily be due to the nutritional composition of breast milk, which boosts the overall infant immune response and reduces allergen sensitization (Lin et al., 2020). In addition, breast milk is reported to be a rich source of antibodies, especially immunoglobulin, essential immune cells, cytokines, and immune-regulating factors, which regulate immune pathways and can confer passive immune protection of the gut, lung, and skin of the infant (El-Heis et al., 2022).

Breastfeeding has been reported to shape the development and composition of the gut microbiome via various prebiotic and probiotic factors (Alotiby, 2023). The infant's gut microbiota composition can also impact the metabolome and lipidomic profile (Sancaklı *et al.*,

2023). Given that a range of nutritional components of breast milk affects the development of the infant's immune system and the composition of the infant's gut microbiome, breast milk has also been implicated as a protective factor for preventing the development of eczema (Trikamjee et al., 2021). The protective effect of breastfeeding on infant eczema can also be attributed to the overall growth and development patterns typically observed in breastfed infants, manifesting through lower prevalence of metabolically related diseases later in life, such as obesity and atopic conditions, including food allergy and eczema (Marras et al., 2021). Variation in the exclusive breastfeeding effects on the incidence of eczema may occur between studies or in different countries due to local breastfeeding durations, compliance with guidelines, and rates of maternal employment, as well as cultural and geographical differences related to the clinical diagnosis of eczema (Dias et al., 2022). A range of socioeconomic disparities, such as maternal age and parity, and maternal health factors including atopy, smoking during pregnancy, and diet and smoking behaviors of the infant's household are other factors that may influence the exclusive breastfeeding duration (Sun et al., 2022).

Recently, health guidelines and recommendations have been proposed to encourage the continuation of breastfeeding and complementary feeding or the introduction of allergenic or commonly allergenic foods in the first year, especially in the first four months, for the prevention of eczema, food allergy, and asthma (Fleischer et al., 2021). However, both for guidelines targeting food allergy and for those targeting eczema, it has been emphasized that an informed choice is important in making feeding decisions (Zhang et al., 2023). There is no current method that can ultimately guarantee the prevention of eczema or food allergy (Lu et al., 2023). In addition, the accumulated evidence of the protective effects of earlier allergenic food exposure in the first months of life has been inconsistent, and evidence from studies is limited at present (Taniguchi and Kobayashi, 2023). Variations in public recommendations across countries have resulted in conflicting consumer information (Zeng et al., 2023). Thus, the development of global guidelines to prevent various allergic diseases, including eczema, is needed (Lv et al., 2024). The international longitudinal birth cohorts and other studies provide a good opportunity to investigate the complex effects of a variety of maternal and infant food avoidance and exposure strategies undertaken in the first year on the development of infant eczema and other allergic diseases (Chen et al., 2024).

4. Environmental Exposures

Dust mites, pet dander, and certain outdoor pollens have also been repeatedly shown to trigger eczema (Morsy *et al.*, 2021). The recommended treatment for children and adults with eczema includes reducing indoor dust mites, pet dander, and installing a pollen filter (Tripathi and Platts-Mills, 2021). Certain irritants, like cleaning agents, especially laundry detergents that come in contact with the skin, can cause skin eruptions (Strzelczyk *et al.*, 2020). The reduction in humidity that occurs during winter in some regions can drive worsening eczema (Wu *et al.*, 2021). In those with skin barrier problems, changes in humidity can increase water loss from the skin and cause localized dryness and eczema (Sparkes, 2022). Various weather variables, such as cold, humidity, and level of sunshine on the previous day, may be modifying the skin surface barrier function in some of these children (Widorn *et al.*, 2024).

Although there is a genetic tendency for some to develop eczema, it is becoming increasingly evident that the environmental factors that trigger eczema are having an effect on the population of children genetically predisposed to developing eczema (Gallay et al., 2020). Given the importance of avoiding triggers and treating eczema, strategies have been recommended, for example, to minimize house dust mites in the environment, reducing key exposure, which has also been shown to improve eczema (Chong et al., 2022). Tips for reducing exposure in the home include developing a bedroom strategy, such as using dust mite covers on pillows and mattresses where the child sleeps, not having carpets, and reducing the amount of soft furnishings (Hartmane, 2024). In conclusion, this highlights the importance of the nursing role in establishing eczema-based services. including continuing the work of educating and raising awareness of the impact of environmental factors among children and families as part of a multidisciplinary team (Lopez et al., 2022).

4.1. Role of Allergens

Allergic sensitization and allergen triggers represent a major subset of environmental factors affecting children's eczema (Annesi-Maesano et al., 2023). Pollens, pet dander, and molds are common allergens that young children with atopic dermatitis are exposed to and have been found to significantly impact their symptoms (Jung et al., 2024). Allergenic pollen exposure has been shown to directly correlate with atopic dermatitis severity (Pan et al., 2023). A cohort of young children with eczema found that being sensitized to foods usually occurs following aeroallergen sensitization and precedes the development of respiratory allergy (Widorn et al., 2024). Immunologically, allergic sensitization to aeroallergens leads to the activation of the release of Th2 cytokines including IL-4, IL-5, and IL-13, which ultimately leads to the production of IgE antibodies by B cells (Mazur et al., 2023). IgE-mediated recognition of the sensitized environmental allergen then leads to the activation of mast cells and subsequent immediate and/or late-phase allergic cutaneous inflammation in the skin. The production of IgE antibodies correlates with increased disease severity and earlier age of onset (Casella et al., 2024)

The impact of the type and dose of allergen exposure and the frequency and duration of allergen exposure is also important in determining disease severity and chronicity (Ogulur et al., 2021). Allergen avoidance can be beneficial, but as most of these allergens are present ubiquitously, clearing from these allergens may need to happen on a constant basis (Shamji et al., 2021). Allergies are diagnosed using a skin lesion of a single allergen or a panel of allergens to identify allergens that provoke a red, raised, itchy lump and other signs of an allergy (Hinks et al., 2021). Common practices to manage eczema include limiting contact with the substances known to cause sensitization, making changes in the home, such as removing carpets, getting rid of stuffed animals, and using mite-proof covers in bedding (Fiocchi et al., 2021). Steered baths daily and the use of hypoallergenic soap can help to reduce pet allergens (Hesse et al., 2022). Some over-the-counter eczema medications are designed to improve the damaged barrier of the skin and provide skin rehydration (Sampath et al., 2021). Professional guidance and support must be in place, if possible, before attempting to undergo a home approach (Brough et al., 2022).

5. CONCLUSION AND FUTURE DIRECTIONS

In conclusion, increased understanding of dietary and environmental triggers of eczema has the potential to contribute to the development of novel prevention strategies for the 'at-risk' population. Future studies are needed to replicate findings and reveal how these triggers truly contribute to the prevalence of eczema in children (Narla and Silverberg, 2020). Our findings stress the importance of considering the intricate interplay of dietary and environmental exposures for examining trigger mechanisms of eczema (Stefanovic et al., 2021). Prevention strategies, including tailored programs, should be designed and implemented for pregnant women and infants in whom a heightened risk of eczema could be expected (Chan et al., 2020). A step towards this is to elucidate the effect of personalized approaches (Chu et al., 2024).

Depending on the individual exposure patterns in these profiles, tailored prevention strategies could be defined, initiated, and evaluated (Narla and Silverberg, 2020). This should be designed to reduce the risk of childhood eczema and other allergic diseases by altering an individual's treatment and/or an individual's exposure with a tailor-made prevention strategy (Grafanaki et al., 2023). Interdisciplinary collaboration remains important in the design of such studies (Stefanovic et al., 2021). Additionally, we stress the need for studies to contribute to the design of education programs for parents and primary care professionals (Stefanovic et al., 2020). This should, in the first place, lead to an increased awareness of parents and professionals about the potential relationship between dietary and environmental exposures and eczema onset and even exacerbation, and

should further provide tools for the primary prevention of childhood eczema (Lu *et al.*, 2021).

REFERENCES

- Abrams, E. M., Watson, W., Vander Leek, T. K., Atkinson, A., Primeau, M. N., Francoeur, M. J., ... & Chan, E. S. (2022). Dietary exposures and allergy prevention in high-risk infants. Allergy, Asthma & Clinical Immunology, 18(1), 36. springer.com
- Agner, T., & Elsner, P. (2020). Hand eczema: epidemiology, prognosis and prevention. Journal of the European Academy of Dermatology and Venereology, 34, 4-12. [HTML]
- Akdis, C. A. (2021). Does the epithelial barrier hypothesis explain the increase in allergy, autoimmunity and other chronic conditions?. Nature Reviews Immunology. [HTML]
- Alkhatib AJ (2022a). Autoimmunity and Diseases. In The Role of Microbes in Autoimmune Diseases: New Mechanisms of Microbial Initiation of Autoimmunity 2022 May 10 (pp. 45-80). Singapore: Springer Nature Singapore.
- Alkhatib AJ (2022b). Types of Hypersensitivities (Updates). InThe Role of Microbes in Autoimmune Diseases: New Mechanisms of Microbial Initiation of Autoimmunity 2022 May 10 (pp. 21-28). Singapore: Springer Nature Singapore.
- Alkhatib AJ (2022c). Immunology and Microbes. InThe Role of Microbes in Autoimmune Diseases: New Mechanisms of Microbial Initiation of Autoimmunity, May 10 (pp. 9-19). Singapore: Springer Nature Singapore.
- Alkhatib AJ (2022d). The Role of Microbes in Autoimmune Diseases. Springer, Singapore.
- Alotiby, A. A. (2023). The role of breastfeeding as a protective factor against the development of the immune-mediated diseases: A systematic review. Frontiers in Pediatrics. frontiersin.org
- Annesi-Maesano, I., Cecchi, L., Biagioni, B., Chung, K. F., Clot, B., Collaud Coen, M., ... & Agache, I. (2023). Is exposure to pollen a risk factor for moderate and severe asthma exacerbations?. Allergy, 78(8), 2121-2147. wiley.com
- Benedé, S., Pérez-Rodríguez, L., Martínez-Blanco, M., Molina, E., & López-Fandiño, R. (2021). Oral exposure to house dust mite activates intestinal innate immunity. Foods, 10(3), 561. mdpi.com
- Blakeway, H., Van-de-Velde, V., Allen, V. B., Kravvas, G., Palla, L., Page, M. J., ... & UK TREND Eczema Network). (2020). What is the evidence for interactions between filaggrin null mutations and environmental exposures in the aetiology of atopic dermatitis? A systematic review. British Journal of Dermatology, 183(3), 443-451. oup.com
- Brough, H. A., Lanser, B. J., Sindher, S. B., Teng, J. M., Leung, D. Y., Venter, C., ... & Nagler, C. R. (2022). Early intervention and prevention of allergic diseases. Allergy, 77(2), 416-441. wiley.com

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- Bylund, S., von Kobyletzki, L. B., Svalstedt, M., & Svensson, Å. (2020). Prevalence and incidence of atopic dermatitis: a systematic review. Acta dermato-venereologica, 100(12). nih.gov
- Casella, R., Miniello, A., Buta, F., Yacoub, M. R., Nettis, E., Pioggia, G., & Gangemi, S. (2024). Atopic Dermatitis and Autism Spectrum Disorders: Common Role of Environmental and Clinical Co-Factors in the Onset and Severity of Their Clinical Course. International Journal of Molecular Sciences, 25(16), 8936. mdpi.com
- Celebi Sozener, Z., Ozdel Ozturk, B., Cerci, P., Turk, M., Gorgulu Akin, B., Akdis, M., ... & Akdis, C. A. (2022). Epithelial barrier hypothesis: effect of the external exposome on the microbiome and epithelial barriers in allergic disease. Allergy, 77(5), 1418-1449. wiley.com
- Chai, E. S. X., Tey, H. L., & Lim, Z. V. (2023). Are there ethnic differences in hand eczema? A review. Journal of Clinical Medicine. mdpi.com
- Chan, C. W. H., Yuet Wa Chan, J., Leung, T. F., Choi, K. C., Tsui, S. K. W., Wong, C. L., & Chow, K. M. (2020). Altered gut microbiome and environmental factors associated with development of eczema in Hong Kong infants: A 4-month pilot study. International Journal of Environmental Research and Public Health, 17(20), 7634. mdpi.com
- Chen, Y., Wen, Y., Zhao, R., Zhu, Y., Chen, Z., Zhao, C., & Mu, W. (2024). Human milk oligosaccharides in preventing food allergy: A review through gut microbiota and immune regulation. International Journal of Biological Macromolecules, 134868. [HTML]
- Chong, A. C., Visitsunthom, K., & Ong, P. Y. (2022). Genetic/environmental contributions and immune dysregulation in children with atopic dermatitis. Journal of Asthma and Allergy, 1681-1700. tandfonline.com
- Chu, D. K., Koplin, J. J., Ahmed, T., Islam, N., Chang, C. L., & Lowe, A. J. (2024). How to prevent atopic dermatitis (eczema) in 2024: theory and evidence. The Journal of Allergy and Clinical Immunology: In Practice, 12(7), 1695-1704. sciencedirect.com
- Chua, C., Chew, J., & Lim, W. (2023). "I have to be brave"–parents' experiences of caring for a child with eczema. Asia Pacific Journal of Social Work and Development, 33(4), 256-277. [HTML]
- D'Hollander, C. J., Keown-Stoneman, C. D., Birken, C. S., O'Connor, D. L., & Maguire, J. L. (2023). Timing of introduction to solid food, eczema and wheezing in later childhood: a longitudinal cohort study. BMC pediatrics, 23(1), 514. springer.com
- Das, A. & Panda, S. (2021). Role of elimination diet in atopic dermatitis: current evidence and understanding. Indian Journal of Paediatric Dermatology. lww.com

- Dastoorpoor, M., Khodadadi, N., Madadizadeh, F., Raji, H., Shahidizadeh, E., Idani, E., & Shoushtari, M. H. (2022). Assessing the prevalence and severity of asthma, rhinitis, and eczema among schoolchildren (6–7 and 13–14 years old) in Khuzestan, Iran: a cross-sectional survey. BMC pediatrics, 22(1), 463. springer.com
- de Lusignan, S., Alexander, H., Broderick, C., Dennis, J., McGovern, A., Feeney, C., & Flohr, C. (2021). The epidemiology of eczema in children and adults in England: a population-based study using primary care data. Clinical & Experimental Allergy, 51(3), 471-482. wiley.com
- Dias, J. A., Santos, E., Asseiceira, I., Jacob, S., & Koninckx, C. R. (2022). The Role of Infant Formulas in the Primary Prevention of Allergies in Non-Breastfed Infants at Risk of Developing Allergies—Recommendations from a Nutrients. mdpi.com
- El-Heis, S., D'Angelo, S., Curtis, E. M., Healy, E., Moon, R. J., Crozier, S. R., ... & MAVIDOS Trial Group. (2022). Maternal antenatal vitamin D supplementation and offspring risk of atopic eczema in the first 4 years of life: evidence from a randomized controlled trial. British Journal of Dermatology, 187(5), 659-666. oup.com
- Fiocchi, A., Vickery, B. P., & Wood, R. A. (2021). The use of biologics in food allergy. Clinical & Experimental Allergy, 51(8), 1006-1018. [HTML]
- Fleischer, D. M., Chan, E. S., Venter, C., Spergel, J. M., Abrams, E. M., Stukus, D., ... & Greenhawt, M. (2021). A consensus approach to the primary prevention of food allergy through nutrition: guidance from the American Academy of Allergy, Asthma, and Immunology; American College of Allergy, Asthma, and Immunology; and the Canadian Society for Allergy and Clinical Immunology. The Journal of Allergy and Clinical Immunology: In Practice, 9(1), 22-43. aaaai.org
- Gallay, C., Meylan, P., Mermoud, S., Johannsen, A., Lang, C., Rivolta, C., & Christen-Zaech, S. (2020). Genetic predisposition and environmental factors associated with the development of atopic dermatitis in infancy: a prospective birth cohort study. European journal of pediatrics, 179, 1367-1377. unibas.ch
- García-Marcos, L., Asher, M. I., Pearce, N., Ellwood, E., Bissell, K., Chiang, C. Y., ... & Strachan, D. P. (2022). The burden of asthma, hay fever and eczema in children in 25 countries: GAN Phase I study. European Respiratory Journal, 60(3). ersjournals.com
- Grafanaki, K., Antonatos, C., Maniatis, A., Petropoulou, A., Vryzaki, E., Vasilopoulos, Y., ... & Gregoriou, S. (2023). Intrinsic effects of exposome in atopic dermatitis: genomics, epigenomics and regulatory layers. Journal of Clinical Medicine, 12(12), 4000. mdpi.com
- Grafanaki, K., Bania, A., Kaliatsi, E. G., Vryzaki, E., Vasilopoulos, Y., & Georgiou, S. (2023). The

imprint of exposome on the development of atopic dermatitis across the lifespan: A narrative review. Journal of clinical medicine, 12(6), 2180. mdpi.com

- Hartmane, I. (2024). Study of genetic mutations and their association with the development of atopic dermatitis and other skin diseases. Plastic and Aesthetic Nursing. mef.edu.tr
- Hesse, L., Elberink, J. O., van Oosterhout, A. J., & Nawijn, M. C. (2022). Allergen immunotherapy for allergic airway diseases: use lessons from the past to design a brighter future. Pharmacology & Therapeutics, 237, 108115. sciencedirect.com
- Hicke-Roberts, A., Wennergren, G., & Hesselmar, B. (2020). Late introduction of solids into infants' diets may increase the risk of food allergy development. BMC pediatrics. springer.com
- Hinks, T. S., Levine, S. J., & Brusselle, G. G. (2021). Treatment options in type-2 low asthma. European Respiratory Journal, 57(1). ersjournals.com
- Jacquet, A. (2021). Characterization of innate immune responses to house dust mite allergens: pitfalls and limitations. Frontiers in Allergy. frontiersin.org
- Jung, J., Enos, C. W., Lam, K. K., & Han, J. K. (2024). The Role of Inhalant Allergens on the Clinical Manifestations of Atopic Dermatitis. American Journal of Rhinology & Allergy, 19458924241246855. [HTML]
- Kampouri, M., Gustin, K., Stråvik, M., Barman, M., Sandin, A., Sandberg, A. S., ... & Kippler, M. (2023). Associations of gestational and early-life exposure to toxic metals and fluoride with a diagnosis of food allergy or atopic eczema at 1 year of age. Environment International, 178, 108071. sciencedirect.com
- Lamiable, O., Mayer, J. U., Munoz-Erazo, L., & Ronchese, F. (2020). Dendritic cells in Th2 immune responses and allergic sensitization. Immunology and Cell Biology, 98(10), 807-818. wiley.com
- Langan, S. M., Mulick, A. R., Rutter, C. E., Silverwood, R. J., Asher, I., García-Marcos, L., ... & Shah, J. (2023). Trends in eczema prevalence in children and adolescents: A Global Asthma Network Phase I Study. Clinical & Experimental Allergy, 53(3), 337-352. wiley.com
- Libuda, L., Filipiak-Pittroff, B., Standl, M., Schikowski, T., von Berg, A., Koletzko, S., ... & Gappa, M. (2023). Full Breastfeeding and Allergic Diseases—Long-Term Protection or Rebound Effects?. Nutrients, 15(12), 2780. mdpi.com
- Lin, B., Dai, R., Lu, L., Fan, X., & Yu, Y. (2020). Breastfeeding and atopic dermatitis risk: a systematic review and meta-analysis of prospective cohort studies. Dermatology. [HTML]
- Lin, J., Chen, D., Guan, L., Chang, K., Li, D., Sun, B., ... & Liu, Z. (2022). House dust mite exposure enhances immune responses to ovalbumin-induced intestinal allergy. Scientific Reports, 12(1), 5216. nature.com

- Liu, W., Cai, J., Sun, C., Zou, Z., Zhang, J., & Huang, C. (2022). Time-trends for eczema prevalences among children and adults from 1985 to 2015 in China: a systematic review. BMC Public Health. springer.com
- Long, Q., Jin, H., You, X., Liu, Y., Teng, Z., Chen, Y., ... & Zeng, Y. (2022). Eczema is a shared risk factor for anxiety and depression: A meta-analysis and systematic review. PloS one, 17(2), e0263334. plos.org
- Lopez, D. J., Lodge, C. J., Bui, D. S., Waidyatillake, N. T., Abramson, M. J., Perret, J. L., ... & Lowe, A. J. (2022). Establishing subclasses of childhood eczema, their risk factors and prognosis. Clinical & Experimental Allergy, 52(9), 1079-1090. wiley.com
- Lowe, M. E., Akhtari, F. S., Potter, T. A., Fargo, D. C., Schmitt, C. P., Schurman, S. H., ... & Messier, K. P. (2023). The skin is no barrier to mixtures: Air pollutant mixtures and reported psoriasis or eczema in the Personalized Environment and Genes Study (PEGS). Journal of Exposure Science & Environmental Epidemiology, 33(3), 474-481. nature.com
- Luger, T., Amagai, M., Dreno, B., Dagnelie, M. A., Liao, W., Kabashima, K., ... & Schmuth, M. (2021). Atopic dermatitis: Role of the skin barrier, environment, microbiome, and therapeutic agents. Journal of dermatological science, 102(3), 142-157. [HTML]
- Lv, Y., Chen, L., Fang, H., & Hu, Y. (2024). The associations between diet diversity during infancy and atopic disease in later life: Systematic review. Journal of Allergy and Clinical Immunology: Global, 100221. sciencedirect.com
- Marras, L., Caputo, M., Bisicchia, S., Soato, M., Bertolino, G., Vaccaro, S., & Inturri, R. (2021). The role of bifidobacteria in predictive and preventive medicine: a focus on eczema and hypercholesterolemia. Microorganisms, 9(4), 836. mdpi.com
- Mazur, M., Dyga, W., & Czarnobilska, E. (2023). The Prevalence of Atopic Dermatitis and Food Allergy in Children Living in an Urban Agglomeration—Is There a Current Relationship?. Journal of Clinical Medicine. mdpi.com
- MORSY, T. A., SHARAF, S. G., & EL-SHAHAT, S. A. (2021). Allergens, public health risks, avoidance and treatment. Journal of the Egyptian Society of Parasitology, 51(3), 647-660. ekb.eg
- Mortimer, K., Lesosky, M., García-Marcos, L., Asher, M. I., Pearce, N., Ellwood, E., ... & Chiang, C. Y. (2022). The burden of asthma, hay fever and eczema in adults in 17 countries: GAN Phase I study. European Respiratory Journal, 60(3). ersjournals.com
- Mu, Z. & Zhang, J. (2020). The role of genetics, the environment, and epigenetics in atopic dermatitis. Epigenetics in allergy and autoimmunity. [HTML]

- Narla, S. & Silverberg, J. I. (2020). The role of environmental exposures in atopic dermatitis. Current allergy and asthma reports. [HTML]
- Ogulur, I., Pat, Y., Ardicli, O., Barletta, E., Cevhertas, L., Fernandez-Santamaria, R., ... & Akdis, C. A. (2021). Advances and highlights in biomarkers of allergic diseases. Allergy, 76(12), 3659-3686. wiley.com
- Pan, Z., Dai, Y., Akar-Ghibril, N., Simpson, J., Ren, H., Zhang, L., ... & Sun, J. L. (2023). Impact of air pollution on atopic dermatitis: a comprehensive review. Clinical Reviews in Allergy & Immunology, 65(2), 121-135. [HTML]
- Passeron, T., Krutmann, J., Andersen, M. L., Katta, R., & Zouboulis, C. C. (2020). Clinical and biological impact of the exposome on the skin. Journal of the European Academy of Dermatology and Venereology, 34, 4-25. nutricaoesteticabrasil.com.br
- Peters, R. L., Kay, T., McWilliam, V. L., Lodge, C. J., Ponsonby, A. L., Dharmage, S. C., ... & Koplin, J. J. (2021). The interplay between eczema and breastfeeding practices may hide breastfeeding's protective effect on childhood asthma. The Journal of Allergy and Clinical Immunology: In Practice, 9(2), 862-871. [HTML]
- Pierau, M., Arra, A., & Brunner-Weinzierl, M. C. (2021). Preventing atopic diseases during childhood–early exposure matters. Frontiers in immunology. frontiersin.org
- Quaade, A. S., Simonsen, A. B., Halling, A. S., Thyssen, J. P., & Johansen, J. D. (2021). Prevalence, incidence, and severity of hand eczema in the general population–a systematic review and metaanalysis. Contact Dermatitis, 84(6), 361-374. wiley.com
- Rance, J. & Hatch, A. (2024). The Calm Skin Guide: How to Manage Childhood Eczema. [HTML]
- Rance, J. & Hatch, A. (2024). The Calm Skin Guide: How to Manage Childhood Eczema. [HTML]
- Renz, H. & Skevaki, C. (2021). Early life microbial exposures and allergy risks: opportunities for prevention. Nature Reviews Immunology. [HTML]
- Royal, C. & Gray, C. (2020). Focus: Allergic diseases and type II immunity: Allergy prevention: An overview of current evidence. The Yale Journal of Biology and Medicine. nih.gov
- Rustad, A. M., Nickles, M. A., Bilimoria, S. N., & Lio, P. A. (2022). The role of diet modification in atopic dermatitis: navigating the complexity. American Journal of Clinical Dermatology, 1-10. [HTML]
- Rutter, C. E., Silverwood, R. J., Asher, M. I., Ellwood, P., Pearce, N., Garcia-Marcos, L., ... & ISAAC Phase Three Study Group. (2020). Comparison of individual-level and populationlevel risk factors for rhinoconjunctivitis, asthma, and eczema in the International Study of Asthma and Allergies in Childhood (ISAAC) Phase Three.

World Allergy Organization Journal, 13(6), 100123. sciencedirect.com

- Sampath, V., Rabinowitz, G., Shah, M., Jain, S., Diamant, Z., Jesenak, M., ... & Nadeau, K. C. (2021). Vaccines and allergic reactions: The past, the current COVID-19 pandemic, and future perspectives. Allergy, 76(6), 1640-1660. wiley.com
- Sancaklı, Ö, Can, D., & Negm, H. (2023). The Role of Breastfeeding on the Development and Prevention of Allergic Diseases. Breastfeeding and Metabolic Programming. researchgate.net
- Sarwar, M. (2020). House dust mites: ecology, biology, prevalence, epidemiology and elimination. Parasitology and Microbiology Research. intechopen.com
- Schonmann, Y., Mansfield, K. E., Hayes, J. F., Abuabara, K., Roberts, A., Smeeth, L., & Langan, S. M. (2020). Atopic eczema in adulthood and risk of depression and anxiety: a population-based cohort study. The Journal of Allergy and Clinical Immunology: In Practice, 8(1), 248-257. sciencedirect.com
- Shamji, M. H., Valenta, R., Jardetzky, T., Verhasselt, V., Durham, S. R., Würtzen, P. A., & van Neerven, R. J. (2021). The role of allergenspecific IgE, IgG and IgA in allergic disease. Allergy, 76(12), 3627-3641. wiley.com
- Shi, H., Wan, G., Wang, T., Zhu, J., Jiang, L., Ma, S., ... & Dong, H. (2021). Prevalence and influencing risk factors of eczema among preschool children in Urumqi city: a cross-sectional survey. BMC pediatrics, 21, 1-8. springer.com
- Shin, S. H., Ye, M. K., Lee, D. W., Chae, M. H., & Han, B. D. (2020). Nasal epithelial cells activated with alternaria and house dust mite induce not only Th2 but also Th1 immune responses. International Journal of Molecular Sciences, 21(8), 2693. mdpi.com
- Soleha, W., & Iswanti, F. C. (2021). Innate Immune Response to House Dust Mite Allergens in Allergic Asthma. Molecular and Cellular Biomedical Sciences, 5(3), 104-14. cellbiopharm.com
- Sparkes, A. H. (2022). Human allergy to cats: A review for veterinarians on prevalence, causes, symptoms and control. Journal of Feline Medicine and Surgery. sagepub.com
- Stefanovic, N., Flohr, C., & Irvine, A. D. (2020). The exposome in atopic dermatitis. Allergy. wiley.com
- Stefanovic, N., Irvine, A. D., & Flohr, C. (2021). The role of the environment and exposome in atopic dermatitis. Current Treatment Options in Allergy. springer.com
- Strzelczyk, Z., Roszkowski, M., Feleszko, W., & Krauze, A. (2020). Avoidance of allergens as an environmental method in the prevention of inhaled allergy symptoms. Allergologia et Immunopathologia, 48(6), 745-752. all-imm.com

- Sun, S., Chang, G., & Zhang, L. (2022). The prevention effect of probiotics against eczema in children: an update systematic review and metaanalysis. Journal of Dermatological Treatment. [HTML]
- Taniguchi, Y. & Kobayashi, M. (2023). Exposure to dogs and cats and risk of asthma: a retrospective study. Plos one. plos.org
- Thyssen, J. P., Schuttelaar, M. L., Alfonso, J. H., Andersen, K. E., Angelova-Fischer, I., Arents, B. W., ... & Agner, T. (2022). Guidelines for diagnosis, prevention, and treatment of hand eczema. Contact Dermatitis, 86(5), 357-378. wiley.com
- Thyssen, J. P., Schuttelaar, M. L., Alfonso, J. H., Andersen, K. E., Angelova-Fischer, I., Arents, B. W., ... & Agner, T. (2022). Guidelines for diagnosis, prevention, and treatment of hand eczema. Contact Dermatitis, 86(5), 357-378. rug.nl
- Traidl, S., Werfel, T., & Traidl-Hoffmann, C. (2021). Atopic eczema: pathophysiological findings as the beginning of a new era of therapeutic options. In Allergic Diseases–From Basic Mechanisms to Comprehensive Management and Prevention (pp. 101-115). Cham: Springer International Publishing. uni-augsburg.de
- Trikamjee, T., Comberiati, P., D'Auria, E., Peroni, D., & Zuccotti, G. V. (2021). Nutritional factors in the prevention of atopic dermatitis in children. Frontiers in pediatrics, 8, 577413. frontiersin.org
- Tripathi, A. & Platts-Mills, T. A. E. (2021). Environment and Lifestyle in Allergic Disease. Textbook of Allergy for the Clinician. [HTML]
- Trogen, B., Jacobs, S., & Nowak-Wegrzyn, A. (2022). Early introduction of allergenic foods and the prevention of food allergy. Nutrients. mdpi.com
- Venter, C., Smith, P. K., & Fleischer, D. M. (2023). Food allergy prevention: Where are we in 2023?. Asia Pacific Allergy. lww.com
- Wang, S. P., Stefanovic, N., Orfali, R. L., Aoki, V., Brown, S. J., Dhar, S., ... & Abuabara, K. (2024). Impact of climate change on atopic dermatitis: A review by the International Eczema Council. Allergy, 79(6), 1455-1469. wiley.com
- Widom, L., Zabolotski, Y., & Mueller, R. S. (2024). A prospective study evaluating the correlation between local weather conditions, pollen counts and

pruritus of dogs with atopic dermatitis. Veterinary Dermatology. wiley.com

- Williams, H. C. & Chalmers, J. C. (2020). Prevention of atopic dermatitis. Acta dermatovenereologica. nih.gov
- Wollenberg, A., Christen-Zäch, S., Taieb, A., Paul, C., Thyssen, J. P., de Bruin-Weller, M., ... & European Task Force on Atopic Dermatitis/EADV Eczema Task Force. (2020). ETFAD/EADV Eczema task force 2020 position paper on diagnosis and treatment of atopic dermatitis in adults and children. Journal of the European Academy of Dermatology and Venereology, 34(12), 2717-2744. wiley.com
- Wu, A. C., Dahlin, A., & Wang, A. L. (2021). The role of environmental risk factors on the development of childhood allergic rhinitis. Children. mdpi.com
- Yasuda, Y., Nagano, T., Kobayashi, K., & Nishimura, Y. (2020). Group 2 innate lymphoid cells and the house dust mite-induced asthma mouse model. Cells. mdpi.com
- Yazar, B. & Meydanlioglu, A. (2022). The prevalence and associated factors of asthma, allergic rhinitis, and eczema in Turkish children and adolescents. Pediatric Pulmonology. [HTML]
- Zeng, R., Li, Y., Shen, S., Qiu, X., Chang, C. L., Koplin, J. J., ... & Lowe, A. J. (2023). Is antenatal or early-life vitamin D associated with eczema or food allergy in childhood? A systematic review. Clinical & Experimental Allergy, 53(5), 511-525. unimelb.edu.au
- Zhang, Q., Zhang, C., Zhang, Y., Liu, Y., Wang, J., Gao, Z., ... & Fu, L. (2023). Early-life risk factors for food allergy: Dietary and environmental factors revisited. Comprehensive Reviews in Food Science and Food Safety, 22(6), 4355-4377. [HTML]
- Ziyab, A. H., Mukherjee, N., Zhang, H., Arshad, S. H., & Karmaus, W. (2022). Sex-specific developmental trajectories of eczema from infancy to age 26 years: A birth cohort study. Clinical & Experimental Allergy, 52(3), 416-425. nih.gov
- Zohn, R. (2020). Break Free from Eczema: Soothe Chronic Inflammation and Itchy Skin with At-Home Solutions and Proven Treatments for Atopic Dermatitis. [HTML]