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Emollients to Prevent Eczema in High-Risk Infants: An Integrative Review

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Abstract

The purpose of this integrative review was to assess the research on topical emollients to prevent atopic dermatitis (AD) also known as eczema, in infants at high risk for this condition. Atopic dermatitis is a common chronic inflammatory skin disorder. Skin barrier dysfunction plays a prominent role in its development. Topical emollients have been hypothesized to enhance the skin barrier and prevent AD.

Methods:

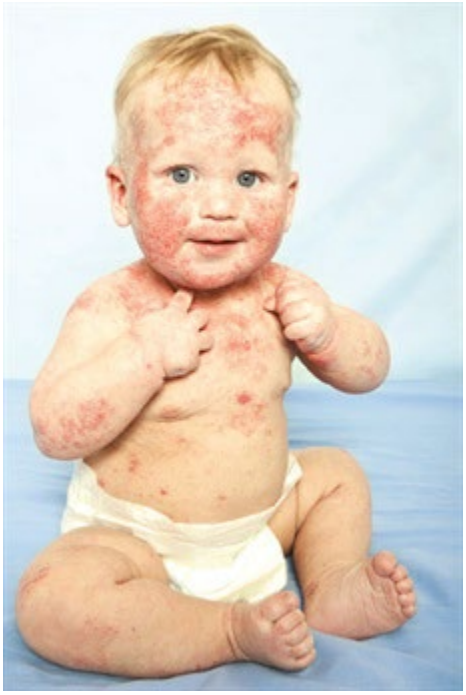
Searches were conducted in September 2021 in PubMed, CINAHL, Cochrane Library, and Web of Science using key word search terms *dermatitis, atopic, emollients, petrolatum*, and *infant, newborn*. Inclusion criteria were articles written in English published between 2010 and 2021 that tested emollients in high-risk infants and measured the development of AD.

Results:

Eight primary research articles were included. Six studies were limited by small sample sizes, short-term application of emollients, and short-term follow-up. These studies generated inconclusive results. Two large randomized controlled trials (RCTs) with a combined sample of 3,791 infants found no evidence that early, regular use of emollients prevents AD among high-risk infants.

Clinical Implications:

Findings from two high-quality RCTs indicate that clinicians should not recommend use of emollients to prevent AD. Clinicians may provide evidence-based recommendations for infant skin care, including bathe with water or a combination of water and liquid cleanser formulated for infants, and avoid soaps. Products applied to skin should be free of scent and contact allergens. Petroleum jelly or mineral oil is appropriate to moisturize infants' skin as needed.



Atopic dermatitis is heritable, and infants are considered at high risk for atopic dermatitis if they have a first-degree relative with a current, or historical, provider- diagnosed atopic dermatitis, asthma, or allergic rhinitis.

Atopic dermatitis (AD), also known as eczema, is a chronic, inflammatory skin disorder that usually begins in early childhood, typically at ages 3 to 6 months (Langan et al., 2020). Approximately 25% of children will be diagnosed with AD (American Academy of Dermatology Association, 2021). Eczema is the broader term and refers to chronic inflammatory skin conditions with eruptions of scaly papules and plaques. Atopic refers to a dermatitis caused by a hypersensitivity allergy reaction that occurs in a part of the body not in contact with the allergen. Many, but not all persons, with eczema have IgE-mediated allergic sensitization. Eczema and AD are commonly used synonymously in clinical practice and in publications (Langan et al.). Signs and symptoms of AD

include varying degrees of elevated IgE levels, skin lesions, dry skin, and pruritis. The skin changes of AD may present as erythematous papulovesicular plaque lesions, dry scaly hyperpigmented plaques, and areas of lichenification (Johnson et al., 2021). Some children will experience an early self-resolving condition, whereas others develop chronicity. Chronic AD may be a pattern of relapsing-remitting inflammation, chronic persistent dermatitis, or extended periods of remission followed by recurrence (Langan et al.). In estimates of prevalence of severity of AD, 67% of cases are mild, 26% are moderate, and 7% severe (Kent & Clark, 2018).

Atopic dermatitis can have detrimental effects on the lives of children and their families including social, academic, and occupational impacts and decreased quality of life (Drucker et al., 2017). Children affected by AD report a negative effect resulting from burdens of treatments, sleep deprivation from skin irritation, activity restrictions due to trigger avoidance, and psychologically distressing stigmatizing experiences due to visible rashes (Tollefson et al., 2014). Caregivers of children with AD report reduction in quality of life. In one study, 97% of caregivers reported decreased quality of life (Al Shobaili, 2010). Reduction in quality of life was significantly correlated to increasing severity of disease. Caregivers' and families' quality of life is affected by burdens of caregiving, lack of sleep, feelings of hopelessness and guilt, and financial burdens. In the United States, the annual estimated costs related to AD range from $364 million to $3.8 billion (Xu et al., 2017). For families, out-of-pocket costs average $274 per month excluding provider office visits (Filanovsky et al., 2016).

The specific cause of AD is unclear but is associated with genetic and immunologic factors that influence epidermal barrier function (Johnson et al., 2021). The strongest genetic link to AD is mutations in the gene encoding for filaggrin (FLG), which is a protein important to creating the skin barrier (Tollefson et al., 2014). Infants with a first-degree relative with a current, or historical, provider-diagnosed AD, asthma, or allergic rhinitis are considered at high risk for development of AD (Chalmers et al., 2017). It is hypothesized that a disrupted skin barrier allows allergens and irritants to penetrate the stratum corneum leading the keratinocytes and dendritic cells to initiate an inflammatory response with IgE formation and initiation of AD. Disruptions in the skin barrier can result from scratching, and skin dryness due to the environment, through applied skin products, or due to filaggrin mutation (Simpson et al., 2014). In infants, immaturity of the stratum corneum increases their risk for skin barrier dysfunction and risk for development of AD (Telofski et al., 2012).

During the first 12 to 24 months of life, infants' skin is thinner, dryer, and more alkaline than adult skin (Cooke et al., 2016; Horimukai et al., 2014; Telofski et al., 2012). Infants have low concentration of ceramides in their stratum corneum at birth. Ceramides are lipid molecules that help the skin retain moisture. As the concentration of ceramides increase in the weeks following birth, the barrier function of the skin improves (Lowe, Leung, et al., 2018). Infants' skin is slightly alkaline at birth (pH range 6.3 to 7.5), which increases the activity of protease enzyme that breaks down connective parts of the stratum corneum (Cooke et al.). Over the first weeks of life, sebum secretion, lactic acid in sweat, amino acids, and the generation of intracellular lipids cause the skin to transition to an acidic pH of 4.0 to 6.7, which is essential for epidermal barrier maturation and the repair process (Telofski et al.).

In the last decade, researchers have concentrated on the prominent role of skin barrier dysfunction in the development of AD, which has driven research toward strategies for primary prevention. One area of study has been topical emollients starting shortly after birth to enhance the barrier function of the stratum corneum to prevent AD (McClanahan et al., 2019). Emollients are lipid substances that moisten and soften skin (Lowe, Leung, et al., 2018). The lipids are transported through the cell membrane of the keratinocytes and metabolized within the cell to create a more functional protective epidermal barrier and increased capacity to trap water and improve hydration of the skin (Chalmers et al., 2017; Simpson et al., 2010; Telofski et al., 2012). The purpose of this integrative review was to assess the research on the regular application of emollients to the skin to prevent the development of AD in infants at high risk.

Search Strategy

Working with a medical librarian who established the search strategy, literature searches were conducted in the following electronic databases: PubMed, CINAHL (Cumulative Index to Nursing and Allied Health Literature), Cochrane Library, and Web of Science. The results were limited to English language only and published between 2010 through 2021. There was no limit on the type of publication. The search was conducted in September 2021. The search strategy was first established in PubMed using a combination of MeSH (medical subject headings; database-controlled vocabulary) and keywords. The MeSH headings were searched along with the keywords. Specific MeSH terminology included "Dermatitis, Atopic", emollients, petrolatum, and "Infant, Newborn." From there, the other database search strategies were developed, and searches were conducted. (See Table 1 supplemental digital content for list of search strategies at https://links.lww.com/MCN/A74.) With each database search, database-controlled vocabulary was searched in combination with keywords. The search is depicted in Figure 1. The initial search yielded 1,138 articles and 678 duplicates were removed. Two researchers worked together to scan 460 articles for inclusion criteria. Inclusion criteria included primary research studies that tested application of topical emollients early in life to prevent AD among infants at high risk for AD. High risk for AD was determined by positive family history of a first-degree relative with AD, allergic rhinitis, or asthma. The patient-oriented outcome of interest was prevention of the development of AD. Thirty-seven articles were reviewed. Of these, 1 was not retrieved and 28 did not meet inclusion criteria. Eight primary research articles were included in this integrative review.

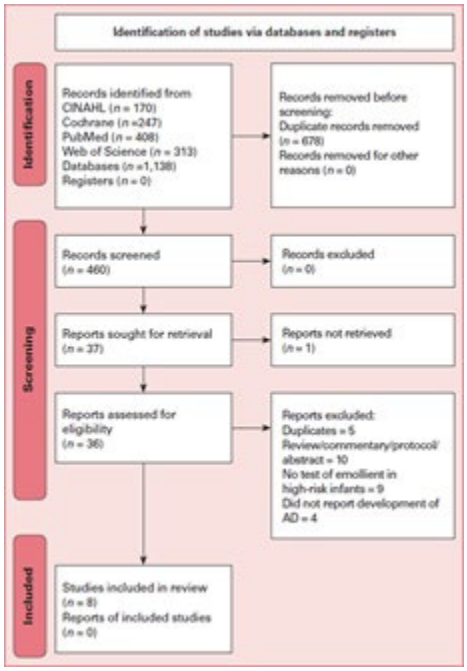


FIGURE 1.: PRISMA DIAGRAM

Evaluation of Evidence

The Strength of Recommendation Taxonomy (SORT) criteria were used to appraise the level of evidence of the individual studies included in this review and of the group of these studies together. Level of evidence is based on quality, quantity, and consistency of patient-oriented outcomes (Ebell et al., 2004).

Patient-oriented evidence measures outcomes that matter to patients such as morbidity, mortality, symptom improvement, cost reduction, or quality of life (Ebell et al., 2004). Level of evidence of individual studies was rated on a scale of 1 to 3 with 1 being the highest. Groups of studies are referred to as bodies of evidence. The strength of recommendation for the body evidence was rated A, B, or C based on quality of studies and

consistency of patient-oriented evidence across the group, with level A being a strong recommendation and level C a weak recommendation (Ebell et al.).

Literature Review

Four studies reported inconclusive results on emollient use and prevention of AD among infants at risk for AD (Lowe, Su, et al., 2018; McClanahan et al., 2019; Simpson et al., 2010; Thitthiwong & Koopitakkajorn, 2019). Two studies reported significant prevention of AD (Horimukai et al., 2014; Simpson et al., 2014) and three studies reported no evidence that daily emollient use prevented AD (Chalmers et al., 2020; Skjerven et al., 2020). There were no serious adverse effects reported in the studies included in this review. One randomized controlled trial (RCT) revealed small increases in skin infections among infants using daily topical emollients (intervention group; Chalmers et al.). Summary of included studies is in Table 2.

TABLE 2. - SUMMARY OF STUDIES (*N* = 8) TESTING USE OF EMOLLIENTS IN INFANTS TO PREVENT ATOPIC DERMATITIS

First Author, Year, Level of Evidence	**Location Design**	**Age, Sample Size**	**Intervention vs. Control**	**Limitations**	**Results**
Chalmers et al. (2020) Level 1	U.K. (United Kingdom) RCT	Newborn term infants *N* = 1,394	Daily application of petroleum-based emollient from 3 weeks of life to 12 months plus standard skin-care advice vs. standard skin-care advice only.	Small amount of emollient use in control group	At 2 years of life, daily emollient during the first year of life did not prevent AD in high-risk children.
Horimukai et al. (2014) Level 2	Japan RCT	Newborn term infants *N* = 118	Daily application of emulsion-type moisturizer from first week of life to 8 months vs. use of petroleum jelly 2 days per week.	Small sample size; follow-up ended at 8 months at end of study	Treatment led to 48% reduction in risk of development of AD (hazard ratio, 0.48; 95% CI, 0.27-0.86).
Lowe, Su, et al. (2018) Level 2	Australia Pilot RCT	Newborn term infants *N* = 74	Twice daily application of ceramide-dominant emollient from first 3 weeks of life to 6 months vs. usual care.	Small sample size; 39% of control group and 17% of intervention reported use of OTC emollients > 3 days per week	Intention to treat analysis showed no significant effect of routine barrier lipid replacement in early life on AD.
McClanahan et al. (2019) Level 2	Oregon, United States (U.S.) RCT	Newborn term infants *N* = 100	Daily application of ceramide and amino acid emollient from first 3 weeks of life to 24 months vs. usual care.	Study was under enrolled and did not reach target enrollment; adherence to daily emollient use dropped at each	Infants in intervention group had lower incidence of diagnosis of AD at 12 months and 2 years; however,

				assessment point; 45% of control group had regular use of OTC emollient.	the differences were not statistically significant.
Simpson et al. (2010) Level 2	U.S. Open-label prospective study	Newborn term infants *N* = 22	Daily application of petrolatum-based cream beginning in first week of life to follow-up 3-24 months.	Small sample size, no control group	15% of infants in study developed AD compared with expected risk of 30%-50% of developing AD among high-risk infants.
Simpson et al. (2014) Level 2	U.S. & U.K. Pilot RCT	Newborn term infants *N* = 124	Daily application of emollient from first 3 weeks of life to 6 months vs. no emollient.	Small sample size; follow-up ended at 6 months at end of intervention.	Relative risk reduction of 50% for development of AD in treatment group (relative risk, 0.50; 95% CI, 0.28-0.9; *p* = .017).
Skjerven et al. (2020) Level 1	Norway & Sweden RCT	Newborn term infants *N* = 2,397	Baths with emulsified oil and cream to face 4 days per week from 2 weeks of life to 8 months vs. usual care.	Low protocol adherence of 27% in the skin emollient group	Early skin emollients did not reduce development of AD at age 12 months.
Thitthiwong & Koopitakkajorn (2019) Level 2	Bangkok RCT	Newborn Infants *N* = 52	Daily application of petrolatum-based emollient vs. usual care from first 10 weeks of life to 9 months.	Small sample size; did not reach target enrollment; short-term use and follow-up	At 9 months, none of the infants in the treatment group developed AD compared with 4 (14.8%) in the control group (*p* = 0.045).

Note. RCT = randomized controlled trials; OTC = over-the-counter; AD = atopic dermatitis; CI = confidence interval.

Inconclusive Evidence for Emollients to Prevent Atopic Dermatitis

The primary pilot study on this topic (Simpson et al., 2010) began the investigation into the use of emollients to prevent AD. This open-label prospective study tested daily topical Cetaphil cream to prevent AD among 22 high-risk infants (Simpson et al., 2010). The intervention was started in the first 7 days of life. At 24 months follow-up, 15% (*N* = 3) of infants in this study had developed AD (Simpson et al., 2010). The researchers compared their results to the relative risk of 30% to 50% that high-risk infants have to develop AD. They reported that their results were inconclusive but promising that emollients might prevent AD in high-risk infants (Simpson et al., 2010).

Lowe, Su, et al. (2018) conducted a pilot RCT with 74 infants at high risk for AD. The treatment group used a specially formulated emollient twice daily from the first 3 weeks of life to 6 months. There were fewer infants diagnosed with AD at the 12-month follow-up (5% in treatment group vs. 15% in control group); however, an intention to treat analysis found that this was not a statically significant reduction (Lowe, Su, et al., 2018).

Most recently, an RCT by McClanahan et al. (2019) included 100 infants at high risk for AD. In this study, the intervention group used moisturizer daily to all body surfaces excluding the scalp and diaper area beginning within the first 3 weeks of life. Cumulative incidence of AD at 12 months was less, with 13% of the intervention group and 25% of the control group developing AD (McClanahan et al., 2019). However, this was an underpowered study that lacked statistical significance due to underenrollment and a higher-than-expected dropout rate (McClanahan et al.). There were no significant differences in incidence of AD between the intervention and control groups.

Thitthiwong and Koopitakkajorn (2019) conducted an RCT with 53 high-risk infants. They tested a hospital-formulated petroleum-based emollient compared with usual care. Beginning within the first 10 weeks of life, the emollient was applied all over the body once per day within 3 to 5 minutes after bathing and patting infant dry. At the 9-month follow-up, four infants in the control group developed AD compared with zero infants in the intervention group. This difference was significant at the $p = .045$; however, the authors recommended caution with interpreting these results due to the small sample size.

Evidence that Emollients Prevent Atopic Dermatitis

Horimukai et al. (2014) conducted an RCT that included 118 infants at high risk for AD. The treatment group used daily application of an emulsion-type emollient starting at the first week of life to 8 months versus use of petroleum jelly in the control group. Researchers reported a significant 32% reduction in diagnosis of AD after 32 weeks among the treatment group in comparison to the control group (hazard ratio, 0.48; 95% CI, 0.27-0.86).

A second study by Simpson et al. (2014) included 124 infants at high risk for AD. The treatment group received a daily body application of emollient at age 6 months beginning within the first 3 weeks of life (Simpson et al., 2014). Parents in the control group were asked to use no emollients. The treatment and control groups were given an information booklet on infant skin care that reflected current guidelines. Infants in the treatment group had a 50% relative risk reduction in AD at 6 months of age in comparison with the control group (relative risk, 0.50; 95% CI, 0.28-0.9; $p = .017$; Simpson et al., 2014).

Evidence that Emollients Do Not Prevent Atopic Dermatitis

Chalmers et al. (2020) performed a multicenter, pragmatic, parallel-group RCT that included 1,394 infants. The intervention group received a daily application of petroleum-based emollient beginning within the first 3 weeks of life until the child was 1 year of age. The intervention and control groups received a booklet and video containing instructions on general skin care. Follow-up occurred at 1 year post intervention when the children in the study were 2 years of age. There were no significant differences in incidence of AD at 2 years of age between the intervention and control groups.

Skjerven et al. (2020) conducted a primary prevention multicenter, RCT with 2,397 infants. This study included four groups, 1) the control group received usual care without specific skin care advice and recommendations to follow national guidelines for infant nutrition; 2) the skin intervention group received baths with added emollients followed by an application of face cream on at least 4 days per week; 3) the food intervention group received early complementary feedings of peanut, cow's milk, wheat, and egg; and 4) the combined skin and food group received the skin and food interventions. Interventions began at 2 weeks of life to 8 months of age.

Follow-up occurred at 12 months of life. The results of this study revealed no difference among the groups in the prevention of AD.

Discussion and Recommendation

Small studies reported promising results that routine application of emollients starting within the first month of life could prevent the development of AD in infants at high risk for this condition (Horimukai et al., 2014; Lowe, Su, et al., 2018; McClanahan et al., 2019; Simpson et al., 2010; Simpson et al., 2014; Thitthiwong & Koopitakkajorn, 2019). Results of these studies were limited by small sample sizes, short-term application of emollients, and short-term follow-up. These limitations made level of evidence for these individual studies level 2 and the strength of these group of studies was B. Still, results of these earlier studies supported the need for larger studies.

Two large studies with a combined sample size of 3,791 infants revealed no evidence that emollient use prevents AD among infants at high risk (Chalmers et al., 2020; Skjerven et al., 2020). These studies tested commonly used emollients and their protocols reflected practices that most families could accomplish without onerous burden. Use of common skin-care products within these studies and less stringent application of the emollients may have limited these results. Perhaps use of specially formulated emollient, applied beginning at birth, more than once per day, and for an extended period may prevent AD (Chalmers et al.). However, though potentially more effective, special emollients tend to be more expensive and not readily accessible, and most families can not follow a stringent skin-care protocol for an extended period. Consistent findings from two high-quality RCTs indicate that clinicians should not recommend use of emollients to prevent AD, the strength of this recommendation is A (Ebell et al., 2004).

Clinical Implications: Advice for Parents

The skin of infants, regardless of risk for AD, is vulnerable to impaired integrity due to immaturity during the first year of life. Although use of topical emollients will not prevent AD, they can still be recommended as part of infant skin care to prevent dry skin and keep the infant comfortable. Clinicians should educate caregivers on infant skin care and recommend suitable topical agents which do not adversely alter or affect the skin barrier including bathe infants two to three times per week (Johnson & Hunt, 2019), clean infants' skin with water alone or with a soap-free liquid cleanser formulated for infants, use soap-free cleansers, and apply emollients after bathing (Blume-Peytavi et al., 2016; Tollefson et al., 2014). Soap-free cleansers include synthetic detergents or syndets. Syndets are nonsoap surfactants that lower the surface tension in water to facilitate removal of dirt and oils. Syndets have a neutral or slightly acidic pH, are less drying to skin, and cause less irritation. The most widely used synthetic surfactants is sodium cocoyl isethionate, other syndets are sulfosuccinates, alpha oleficategoriess, alkyl glyceryl ether sulfonate, sodium cocoyl monoglyceride, and sulfate and betaines.

Use of soaps on infants' skin should be avoided (Blume-Peytavi et al., 2016). Soaps have high pH often within the range of 9 to 10, which is higher than the more alkaline pH of normal skin (Tarun et al., 2014). Soaps can increase the pH of the skin causing dehydration of skin, irritation, itching, and alteration of normal bacterial flora. Bar soaps and soap-based liquid cleansers can remove natural moisturizing factor and lipids from skin also causing irritation, erythema, and itching. In soaps, surfactants remove sweat, sebum, deposits, and oil from the skin, but they can also damage the stratum corneum leading to tightening of the skin, dryness, erythema, irritation, and itch (Blume-Peytavi et al.).

Emollients may be applied after bathing when the infant's skin is still moist from the bath. White petroleum jelly is an inexpensive emollient that does not contain contact allergens and is ideal for routine use of infants' skin (Johnson & Hunt, 2019). Pharmaceutical-grade oils such as mineral oil are generally regarded as safe and can be

applied in a thin layer to the skin or added to the bath water. Caregivers need to be careful when applying emollients and oils to ensure that they do not drop or cause the infant to fall because of the slipperiness.

Grocery oils, such as vegetable, olive, soybean, or mustard, are not recommended because they can leave film or cause irritation that damages the skin (Chalmers et al., 2017). These oils can be degraded in hot, humid environments or by cutaneous microbes present on the skin surface. Degraded oils become spoiled and support increased microbial growth within the oil itself and on the skin (Telofski et al., 2012). Sunflower and olive oils have been found to have an adverse effect by impeding the natural development of the intracellular lipids in the stratum corneum which is significantly associated with reducing the skin barrier thus increasing the risk of AD development (Cooke et al., 2016).

It is important for caregivers to read labels. Skin-care products may contain one or more common skin contact allergens such as fragrances, betaines, methylchloroisothiazolinone, and lanolin. These ingredients should be avoided as they may sensitize the infant and cause a Type IV hypersensitivity allergic contact dermatitis. Skin-care products that contain sodium lauryl (laureth) sulfate should be avoided as this surfactant impairs the integrity of the stratum corneum by making the lipids more water soluble, changing the molecular structure of keratin, and raising the pH of the skin (Blume-Peytavi et al., 2016).

Conclusion

Although at first promising, the most current research does not support the use of topical emollients as a means of preventing AD among infants. Clinicians may provide parents with evidence-based recommendations to care for infants' skin.

BULLET LIST OF CLINICAL IMPLICATIONS

- Recommend evidence-based skin care to prevent dry skin and increase infants' comfort.
- Bathe infants two to three times per week with water alone or with a soap-free liquid cleanser formulated for infants.
- Avoid use of soaps on infants.
- Apply emollients after bathing when skin is still moist.
- White petroleum jelly or mineral oil are safe and effective moisturizers.
- Avoid use of grocery oils, such as vegetable, olive, soybean, or mustard, on infants' skin.

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