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Daily emollient throughout infancy to prevent eczema: A randomised controlled study

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***Abstract*---**The first step in the development of eczema is the formation of a deficient skin barrier. We conducted a study to determine if consistent used of an emollient throughout the first year of life may prevent high-risk kids from developing eczema. We found no evidence that consistent used of an emollient during the first year of life protects eczema in high-risk kids, & some evidence that it may raise the risk of skin infections. Parents with a history of eczema, asthma, or allergic rhinitis could avoid utilizing daily emollients to protect their infant from developing eczema, according to our findings.

***Keywords*---**daily emollient, prevent atopic dermatitis emollients, eczema, dermatitis, child eczema atopy, atopic dermatitis.

Introduction

AD, commonly known as atopic eczema, is a chronic relapsing inflammatory skins disease marked via extreme pruritus, fluctuating form, distribution, & disease history. In prosperous countries, the incidence of atopic dermatitis has grown via 2 to three times, affecting 15 to 20 percent of kids worldwide. It seems to be caused via a mix of emetic & environmental variables that promote dysregulation of the skins barrier, cutaneous & systemic immunological dysregulation, skins microbiota dysbiosis, & strong hereditary impact. In addition to clinical symptoms, the patient's & family's medical history is considered while determining the diagnosis. It is crucial to examine both objective & subjective symptoms in order to determine the disease's overall severity. Therapeutic aims need a multistep strategy focused on itch reduction & illness control. Patients must be advised on adequate skins care & trigger avoidance.

Literatures review

Eczema (Atopic dermatitis (also known as atopic eczema) affects one in five kids, is on the rise, & is challenging for both patients & caregivers. A frequent childhood ailment that may persist into adulthood is eczema. Kids with eczema

are prone to develop food allergies, asthma, & allergic rhinitis.. (Alradaddi et al., 2022). Due to the close relationship between early-onset eczema & food allergies, preventing dermatitis may help prevent food allergies. Mutations in the FLG gene, which codes for the skins barrier protein filaggrin, have been linked to eczema.. (Perrett & Peters, 2020). A compromised skins barrier might worsen eczema. Defective skins may induce a sensitivity to food allergens. Several studies support the used of emollients in the prevention of eczema. Skins barrier dysfunction occurs early after birth & precedes eczema, providing an opportunity to enhance skins hydration & barrier function. (Magnifico et al., 2020).

Emollients enhance the barrier function of the skins . Emollients provide lipids to the stratum corneum, which traps moisture. Emollients diminish inflammation brought on via external irritants, as shown via occupational hand eczema. Emollients diminish skins inflammation in preterm newborns & in people with atopic eczema (secondary prevention) (Rundle et al., 2020). In chronic diseases like atopic eczema, primary prevention is crucial. If primary prevention of atopic eczema utilizing simple, low-cost emollients is effective, treatment & appointment expenses for health care providers will decrease. Early skins barrier improvement may avoid sensitization, food allergies, asthma, & allergic rhinitis. (Sweeney et al., 2021). Even if the frequency of atopic eczema cannot be decreased, a change in severity distribution may have positive effects on quality of life, caregiver burden, & health care provider expenditures. (Hubbard et al., 2022). This research examined whether emollient used in the 1st year of life may prevent eczema & other atopic diseases, like food allergy, in high-risk neonates.

Method

In pediatric hospitals & primary care clinics across Iraq, a multicenter, 2-arm, parallel-group, randomized, controlled trial was conducted .Families were recruited mostly via prenatal or postnatal services, invitation letters from their general practitioners (GP), & hospital & neighborhood advertisements.

Inclusion criteria

Risk of eczema in full-term (at least 37 weeks) newborns (ie, at least one 1st-degrees relative with parentreported eczema, allergic rhinitis, or asthma diagnosed via a doctor(

- Mother aged 18 years
- A consenting adult with proficiency in Arabic & English

The following were the exclusion criteria:

- Preterm birth (birth before 37 weeks of pregnancy(
- A sibling (including a twin) was assigned at random in the experiment.
- A severe, widespread skins condition that makes eczema difficult to identify & assess.
- An important health concern that would make family participation in research undesirable
- A condition in which the used of an emollient is inappropriate.

During the third trimester or soon after birth, the majority of families elected to conduct testing at home. After birth, permission was sought from pregnant women, their mothers, dads, or legal guardians.

Randomisation & maskins g

Babies were given either instructions on how to used an emollient & care for their skins or advice based on a random 1:1 assignment (control group). The randomization was divided into many strata, including recruiting center & the no. of atopic relatives in the 1st degrees (1, 2, or >2(The CTU built the randomization schedule via utilizing computer-generated pseudo-random code & via permuting blocks of varying sizes. The programmer was familiar with the process before the database lock was performed. The random assignment of participants to groups was carried out with the used of internet-based randomization technology created via CTU & implemented via research nurses. Employees of CTU informed parents about the tasks their kids were given. During the whole of the investigation, research nurses who performed skins examinations, skins prick tests, food challenges, or did food allergy assessments were not informed of which treatment group each participant was in. The CTU personnel carried out intermediate maskins g checks at intervals of 2 weeks, three months, six months, & eighteen weeks. There was no attempt made to hide the families.

Procedures

It's possible that families going through the intervention process may utilize Doublebase Gel or Diprobase Cream. Both of these moisturizers were included in the 1st shipment, & it is up to the parents to decide which one they want to renew. It was recommended that parents keep applying emollient to their kids's whole bodies on a regular basis until their kids reached the age of one (apart from the scalp). They were required to apply emollient after each & every bath, regardless of whether or not they had previously bathed. Because the goal of the research was to imitate ordinary behavior, parents were not given any instructions or reminders over the course of the experiment. When the kid turned one, the parents were instructed to discontinue the used of emollients, & no more supplies were provided. Both groups were shown a video & a leaflet with information on how to properly care for their skins at random. Steer clear of baby wipes, bubble bath, & soap; instead, used cleansers & shampoos that are specifically formulated for used on infants.

It was recommended that the most efficient way to apply emollients would be to dot them over the skins & then apply them with light, downward strokes rather than pushing them in. In addition, it was recommended that any spills be cleaned up in order to prevent falling since the skins would be sticky following the treatment. If a kid had any skins problems, it was strongly recommended that their parents take them to the doctor. (via phone): 2 weeks, three months, six months, & eighteen months; (online or via mail survey). The skins check, the collection of saliva samples, the skins prick tests, & the questionnaires for the 2-year follow-up were all carried out in the home of the family via the masked research nurse. When it was not feasible to conduct an in-person interview,

information was acquired over the phone, via email or text message, via a postal questionnaire, or via a general practitioner. There were detailed explanations provided on the testing procedures for DNA, skins pricks, & saliva. 18,20 DNA samples were genotyped for FLG null mutations, & those samples were from white Europeans (2282del4, R501X, S3247X, & R2447X). Participants who had a positive skins prick test or a history of food allergies were given the opportunity to take part in a supervised oral food challenge. Food challenges were successfully performed at 2 universities via knowledgeable allergy nurses who remained anonymous about treatment allocation.

Outcomes

The most important finding was that research nurses were able to diagnose eczema in kids as young as 2 years old in the year before the study. The time period of one year following the completion of the intervention was selected to guarantee that the emollient really & permanently decreased the incidence of eczema, rather than just covering up mild eczema during the 1st year after the intervention was completed.

Other eczema definitions, like the presence of eczema between infancy and 2 years of age (evaluated by any parental report of a clinical diagnosis of eczema [up to 2 years] and parent completion of UK working party criteria at one and 2 years), the presence of visible eczema at 2 years recorded by a nurse who was blinded to treatment allocation, and the time to onset of eczema were secondary outcomes (Eczema Area & Severity Index [EASI] at 2 years & Patient-Oriented Eczema Measure [POEM] at 1 & 2 years). Allergies were another thing that happened that wasn't planned (ie, parent-reported wheezing & allergic rhinitis [between 1 & 2 years]; allergic sensitisation [masked skins prick tests] to milk, egg, peanut, cat dander, grass pollen, or dust mite at 2 years; parentreported food allergy & parental report of clinical diagnosis of food allergy at 1 & 2 years; & allergy to milk, egg, or peanut at 2 years confirmed either via oral food challenge or for cases in which no oral food challenge was done, an expert allergy panel masked to treatment allocation). The EAT study led to a validated algorithm, which was used by the expert panel to come up with their conclusions. This algorithm has all the important information, like the results of skins -prick tests, a record of how the person responded in the past, and the no. of times a day they ate a meal. The parents of 25 newborns reported skins infections & slippages that were associated to emollients as a safety consequence (year 1). The second part of this presentation will cover the findings of the study on the monetary value of health. This includes both the cost-effectiveness & the cost-utility studies at the 24-month mark The Child Health Utility (CHU-9D) was used in order to get at an estimate of a baby's QALYs at the age of 2, whereas the EQ-5D-5L was utilized in order to arrive at an estimate of a parent's QALYs. At each of the three time points (3, 6, & 12 months), the parents were questioned about their usage of emollients since the previous questionnaire. This was done in order to evaluate adherence. In the intervention group, compliance was considered to be satisfactory if emollients were applied to the child's body in its whole at least three to four times a week (defined as at least 2 of face & neck, arms & legs, or trunk).

The definition of contamination was the same for both the experimental group & the control group. It was planned to conduct an analysis & publish the key result data after 2 years. The collection of data over the long term is still in progress, however we are unable to include any additional participants in the study at this time.

Statistical Analysis

The clinical study was designed to detect a 30% decrease in eczema with 90% power & a sample size of 1282.18 participants. This was based on an expected attrition rate for the control group of 20% & a significance threshold of 5% (2-sided). The Trial Steering Committee granted approval for the random assignment of all pregnant participants who had provided their previous permission — a total of 1400 participants — to a study group after the delivery of their child in the month of August 2016. We used data that was seen to do the evaluation of the participants who were randomly assigned. The adjusted RR & risk difference for the primary outcome were calculated via utilizing Generalized Estimating Equations with the Binomial family & log/identity link, in addition to an exchangeable correlation matrix stratified via center & the no. of direct family members with atopic illness (1, 2, or >2) Both of these methods were utilized in order to determine the adjusted RR. All of the people who took part in the research were counted for the analysis, but the different ways the data were collected (in-person, over the phone, via email or SMS, or via the mail) & the actual emollient usage were distinguished utilizing multiple imputation (complier average causal effect [CACE] accounting for emollient used in both groups).

The used of regression models & criteria for stratification was used during the secondary & safety outcome assessments. Subgroup analyses were performed via incorporating into the analytic model an interaction term for FLG genotype, as well as the no. of 1st-degrees relatives who have eczema & atopic illness, & the no. of 1st-degrees relatives who have atopic disease. These three variables were all measured. The statistical analysis plan (SAP), but not the approach, includes subgroup analyses for factors like the time of year when the child was born, the water hardness level in the household, & whether or not the mother took probiotics while she was pregnant.

Results

Table (1): Comparison between the studied groups as regard demographic data

	Emollient Group (n=40)	Control Group (n=40)	P
Age of mother			0.94
Mean ± SD	35.21 ± 3.53	35.14±3.49	
Gestation at birth in weeks			0.51
Mean ±SD	39.8±0.2	39.7±0.18	
Mother has eczema or had a history of eczema (parent report of doctor diagnosis)	21 (52.5%)	22 (55%)	0.82
Sex			0.82
Male infant	22 (55%)	21 (52.5%)	
Female infant	18 (45%)	19 (47.5%)	

Two-Sample Independent t Test

p: p value for comparing between different categories
*: Statistically significant at $p \leq 0.05$

This table shows that there were insignificant difference between both groups as regard Age of mother, Gestation at birth in weeks, Mother has eczema or had a history of eczema (parent report of doctor diagnosis) or Sex.

Table (2): Primary & secondary eczema outcomes

	Emollient Group (n=40)	Control Group (n=40)	P
Diagnosis of eczema at age 2 years according to UK working party diagnostic criteria	9	10	0.6056
Secondary eczema outcomes			
At age 2 years			
2-year-old eczema masked assessment	11	9	0.60
Parent-reported eczema between birth & 2 years	19	17	0.65
Moderate, severe, or very severe eczema according to EASI	3	3	-
Moderate, severe, or very severe according to POEM	9	8	0.78
At age 1 year			
Eczema according to UK working party diagnostic criteria (parent completion)	9	9	-
Moderate, severe, or very severe according to POEM	6	4	0.49

Two-Sample Independent t Test

p: p value for comparing between different categories
*: Statistically significant at $p \leq 0.05$

This table shows that there were insignificant difference between both groups as regard Primary & secondary eczema outcomes

Table (3): Confirmed food allergies' secondary effects, include sensitization to common food allergens, allergic rhinitis, & wheeze via the age of 2

Confirmed food allergy	Emollient Group (n=40)	Control Group (n=40)	P
Confirmed allergy to milk, egg, or peanut at age 2 years	4	2	0.39
Confirmed allergy to cow's milk at age 2 year	3	2	0.64
Confirmed allergy to egg at age 2 years	7	5	0.53
Confirmed allergy to peanut at age 2 years	3	2	0.64
Sensitisation to food allergens			
Allergic sensitisation to milk, egg, or peanut at age 2 years	14	11	0.64
Allergic sensitisation to milk at age 2 years	4	3	0.69
Allergic sensitisation to egg at age 2 years	11	9	0.60
Allergic sensitisation to peanut at age 2 years	5	4	0.72
Other allergies			
Allergic rhinitis, parent report between age 1 & 2 years	12	13	0.80
Wheezing, parent report between age 1 & 2 years	13	11	0.23

Two-Sample Independent t Test

p: p value for comparing between different categories
*: Statistically significant at $p \leq 0.05$

In terms of secondary outcomes, like wheezing at age 2 years old, allergic rhinitis, sensitization to common food allergens, & confirmed food allergy, there were very significant differences between the 2 groups, as shown in the table.

Table (4): Secondary outcome of quality of life

	Emollient Group (n=40)	Control Group (n=40)	P
CHU-9D at age 2 year	0.939±0.081	0.933±0.055	0.017
EQ-5D-5L parent health-related	0.857±0.155	0.831±0.09	0.00098

quality of life at baseline			
EQ-5D-5L parent health-related quality of life at age 2 years	0.925±0.145	0.920±0.105	0.047

Two-Sample Independent t Test

p: p value for comparing between different categories
*: Statistically significant at $p \leq 0.05$

This table shows that there were high significant difference between both groups as regard Secondary outcome of quality of life.

Discussion

According to the findings of this study, neither group's age nor the gestational age at birth substantially varied from one another in terms of the no. of weeks. Either mother is sexually active or she has suffered from eczema in the recent or distant past (parents provide a diagnosis from a medical professional). Emollient usage during the 1st year of life in high-risk neonates (those with a family history of atopic illness) may reduce the likelihood of developing food allergy, eczema, & other atopic diseases, according to the hypothesis that was tested in Chalmers et al(2020) .'s study. On day 21, 452 of the 509 people who were allocated to the emollient group had started utilizing it. This is an 89% adoption rate. According to this research, there were no significant variations in the prevalence of primary & secondary eczema between the 2 groups. When they 1st started utilizing emollients, the individuals in the group that received emollients had a median age of 11 days (IQR: 7-17). The main result was shown to have a correlation to all of the other diagnostic criteria of eczema, as stated via Chalmers et al. (2020). There was no difference between the groups in terms of whether or not parents met the UK Working Party criteria at 1 & 2 years, whether or not parents reported their child having a clinical diagnosis of eczema at 2 years, or whether or not their child had visible eczema at 2 years. Secondary outcomes, like wheezing at 2 years of age, allergic rhinitis, sensitization to common food allergens, & confirmed food allergy, indicated extremely significant differences between the 2 groups. [Citation needed] Milk, egg, or peanut allergies were verified in 41 (7%) of 547 neonates in the emollient group, & in 29 (5%) of 568 babies in the control group, according to Chalmers et al (2020). The absolute value of the adjusted relative risk (RR) for the percentage of infants who were shown to have an egg allergy was 156, which was the largest difference. The oral food challenge was utilized to establish 30% (21 of 70; 15 in the emollient group & 6 in the control group) of verified food allergy diagnoses, whilst the EAT trial-adapted algorithm was used for 70% of the diagnoses. (21 of 70). Similar results were obtained from a no. of other food sensitivity & allergy testing. There was not a significant difference between the groups in the proportion of babies who suffered from allergic rhinitis, wheezing, or allergic sensitization to cat dander, grass pollen, or dust mites. According to the results of this research project, there was a considerable disparity between the 2 groups with regard to the secondary outcome of quality of life. According to Chalmers et al(2020) .'s findings, the 2 groups did not vary from one another in terms of the quality of life utility ratings they reported (CHU-9D & EQ-5D-5L). The emollients that were used in BEEP & Prevent ADALL were essential compositions

that were based on either petroleum or paraffin, respectively. The emollient that was used in Hourihane & Alexexperimentwas .'s a ceramide-rich formulation that was designed specifically for very dry skins that had also been inflamed. There were nonsignificant tendencies toward an anti-AD effect in 2 small trials, Lowe et al. (2018) & McClanahan et al. (2019), both of which utilized more complex ceramide-rich emollients. The investigations were conducted via Lowe et al. & McClanahan et al. Lowe et al. (2018) are assessing the same ceramide-based emollient on a twice-daily basis for a period of 0 to 6 months as part of a larger randomized controlled experiment that is known as the PEBBLES study25. They found that a quick intervention period of 2 months decreased the incidence of AD at 12 months, which suggests that this strategy for preventing AD may be more feasible & user-friendly for families. Our remarkable compliance rates suggest that it is possible to implement a daily emollient ingestion regimen during the 1st 2 months of a baby's life. Despite the fact that diary-based adherence rates were lower than those reported on questionnaires, 82.4% of participants reported utilizing emollients 75% of the time, or more than 5 days per week. Equal rates of adherence were found in BEEP, which required less contact & had a less rigorous definition of adherence, despite the fact that the babies in this study were thoroughly monitored during the whole of the intervention period (three times per week emollient used). This might have been a factor in why the PreventADALL research didn't find a protective benefit; in that study, only 27% of the IG followed the protocol. The effect of food allergies was investigated via Hourihane et al. (2022), but their research did not have sufficient statistical power to determine whether or not there was a decrease in the risk of food allergies. In contrast to BEEP, which revealed a non-significant rise in food allergy in the IG (Lowe et al., 2018), Hourihane et al. (2022) detected no difference in the prevalence of food allergy across the groups. Even though Hourihane et al. (2022) did not used SPTs to screen for food allergy, almost all of the neonates had tried the three most common food allergens, which were milk, egg, & peanut. As a result, the reported incidence of food sensitization & allergy is likely representative of the actual rate in our groups. According to BEEP, there were higher cases of skins infections in the IG, & it is possible that the used of emollients contributed to this increased pathogen exposure. 10. It does not seem that the used of emollients for a limited amount of time will result in an increased risk of developing skins infections. Over the course of the 1st year, TEWL did not change despite the fact that they had a decreased risk of AD in comparison to the controls. In previous studies on the used of emollients during infancy, Lowe et al. (2018) & McClanahan et al. (2018) found that the intervention had no effect on TEWL (2019). Environmental factors have less of an effect on the total epidermal water loss (TEWL) levels of neonates than subject-specific variables, like stress & crying. It's possible that this affected our ability to identify differences across groups. One of the disadvantages of the research is that participation in the oral meal challenges was quite low for a variety of reasons; this is also one of the limits of the study. Parents gave their assent to take part in the study without being informed that their kids would be subjected to skins prick testing & oral meal challenges. These tests weren't implemented until after the study had already gotten underway. In addition, many parents were either unable or unwilling to take their kids to the facilities that offered oral food challenges. This was primarily the case because they either did not take their child's possible food allergy seriously or their child had already been diagnosed with a food allergy. The response to interim surveys

that were supposed to evaluate adherence was far lower than was expected, which was the second limitation. The lack of effectiveness of emollients in preventing eczema that was documented in this research was surprising given the strong signal that was detected in past pilot trials. This finding has substantial implications for the primary prevention of atopic eczema & related disorders. It is possible that the suggestion to apply emollients once daily & in sufficient quantities each time was not followed to the proper degrees or at all. It may be challenging for parents of otherwise healthy infants to consistently apply emollients to their kids's whole bodies throughout the 1st year of their kids's lives. However, data from those who completed questionnaires askins g parents about their child's adherence to emollient used since the previous questionnaire showed that adherence was above 80% during the 1st six months, which was within the range that we expected, & that the majority of parents applied emollient to the entire body of their child. [Citation needed] [Citation needed] [Citation needed] [Citation needed] [Citation needed] [Citation needed] [Citation needed These adherence rates were found, which are consistent with what we saw in the pilot test we conducted. In spite of the fact that adherence fell to 74% between months 6 & 12, the research was pragmatic & entailed little parental interaction, which demonstrated how a preventive method like this may be used in the real world. The fact that it is harder to continuously apply emollient to infants as they grow more active, in addition to the overall exhaustion that the routine causes for parents, was another factor that was expected to contribute to the decline in the usage of emollients. It is possible that any differences that existed between the 2 groups were obscured via the fact that the control group, which consisted of people who had not been diagnosed with eczema, did not used any emollients. Emollients may need to be used more than once per day to have a protective impact, or intervention may be necessary for more than a year, even if a more stringent regimen is more difficult to adhere to or is unappealing to parents. This is because the protective effect of emollients depends on the amount of time they spend on the skins . Even though the average amount of time that passed between delivery & the 1st application of an emollient was 11 days, early intervention may be required in the event that emollient treatment was begun prior to delivery. It is unlikely that providing information about skins care to the parents in both groups would have had an effect on the efficacy of the emollient, given that the skins care advice was based on best practices in the UK & was comparable to that which was used in the pilot study, in which a difference was observed between the groups. In recent years, however, individuals have been more cognizant of the requirement of employing wash goods with enhanced formulations. Throughout the course of adolescence, more is learned about the peculiarities of the skins 's barrier function, & a no. of skins barrier enhancement treatments developing on the basis of this knowledge are likely to be preventive. Two examples of these therapies are the used of newly created emollients with better skins barrier qualities or a sophisticated intervention with additional strict measures, like low pH cleansers, infrequent washing, or softened water. In the future, research on innovative candidate emollients or more rigorous skins -care regimens will need to show that their used is acceptable to parents & incorporate behavioral support in order to achieve long-term compliance. Emollients should not be used to prevent eczema in babies who are at a high risk, according to the findings of our study. Similar findings were seen in the PreventADALL study, which was an extensive examination that used a method for

improving the skins 's barrier function. The used of emollients as a primary therapy for eczema is not directly challenged via the findings that we have obtained, which are focused on preventing eczema.

References

1. Alradaddi, A., Al Twaim, A., Abu-aliat, A., Al-Atass, K., Alogayell, L., Aldayil, M., ... & Al-Khenaizan, S. (2022). Unmet Medical Needs & Early Referral of Pediatric Atopic Dermatitis: An Expert Modified Delphi Consensus from Saudi Arabia. *Dermatology Research & Practice*, *2022*.
2. Chalmers, J. R., Haines, R. H., Bradshaw, L. E., Montgomery, A. A., Thomas, K. S., Brown, S. J., ... Williams, H. C. (2020). *Daily emollient during infancy for prevention of eczema: the BEEP randomised controlled trial. The Lancet*. doi:10.1016/s0140-6736(19)32984-8
3. Hourihane, J., Chaoimh, C. N., Lad, D., Nico, C., Puppels, G. J., Wong, X. C. C., ... & Irvine, A. (2022). Early initiation of short-term emollient used for the prevention of atopic dermatitis in high risk infants--the STOP AD randomised controlled trial. *Authorea Preprints*.
4. Hubbard, G. P., Atwal, K., Graham, L., Narayanan, S., Cooke, L., Casewell, C., ... & Stratton, R. J. (2022). Synbiotic containing extensively hydrolyzed formula improves gastrointestinal & atopic symptom severity, growth, caregiver quality of life, & hospital-related healthcare used in infants with cow's milk allergy. *Immunity, Inflammation & Disease*, *10*(6), e636.
5. Lowe A, Su J, Tang M, et al. PEBBLES study protocol: a randomised controlled trial to prevent atopic dermatitis, food allergy & sensitisation in infants with a family history of allergic disease utilizing a skins barrier improvement strategy. BMJ Open . 2019;9(3):e024594. doi:10.1136/bmjopen-2018-024594
6. Lowe AJ, Su JC, Allen KJ, et al. A randomized trial of a barrier lipid replacement strategy for the prevention of atopic dermatitis & allergic sensitization: the PEBBLES pilot study. Br J Dermatol . 2018;178(1):e19-e21. doi:10.1111/bjd.15747
7. Magnifico, I., Petronio Petronio, G., Venditti, N., Cutuli, M. A., Pietrangelo, L., Vergalito, F., ... & Di Marco, R. (2020). Atopic dermatitis as a multifactorial skins disorder. Can the analysis of pathophysiological targets represent the winning therapeutic strategy?. *Pharmaceuticals*, *13*(11), 411.
8. McClanahan D, Wong A, Kezic S, et al. A randomized controlled trial of an emollient with ceramide & filaggrin-associated amino acids for the primary prevention of atopic dermatitis in high-risk infants.J Eur Acad Dermatol Venereol JEADV . 2019;33(11):2087-2094. doi:10.1111/jdv.15786
9. Perrett, K. P., & Peters, R. L. (2020). Emollients for prevention of atopic dermatitis in infancy. *The Lancet*, *395*(10228), 923-924.
10. Rundle, C. W., Presley, C. L., Militello, M., Barber, C., Powell, D. L., Jacob, S. E., ... & Dunnick, C. A. (2020). Hand hygiene during COVID-19: recommendations from the American Contact Dermatitis Society. *Journal of the American Academy of Dermatology*, *83*(6), 1730-1737.
11. Sweeney, A., Sampath, V., & Nadeau, K. C. (2021). Early intervention of atopic dermatitis as a preventive strategy for progression of food allergy. *Allergy, Asthma & Clinical Immunology*, *17*(1), 1-12.