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## Skin care interventions and early complementary food introduction for the prevention of atopic dermatitis in infants

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**Abstract:** atopic dermatitis and food allergy are common diseases that usually begin in early childhood and can occur together in the same individuals. The aim of this study was to assess the significance of interventions such as skin care products for the skin barrier improvement, breastfeeding and early complementary foods introduction for the primary prevention of atopic dermatitis and food allergy in infants by building logistic regression models. We performed a survey of 97 parents of children. The survey was conducted with the help of Google forms and distributed on the Internet. Method of building and analysing logistic regression models was used to analyse the association of the risk of atopic dermatitis in children with the factor characteristics. Characteristics were as follows: “Skin care 1: application moisturizers to the infant’s skin”, “Skin care 2: bathing infants with water containing moisturizing substances or moisturizing oils”, “Skin care 3: usage of less soap, bathing the child less often”, “paternal history of atopy”, “duration of breastfeeding less than 1 year”, “early introduction of supplementary food (up to the 6th month of life)”. We obtained the following results: 42.2% of respondents reported about the application of moisturizing cream, parents of 16.5% of children were using moisturizing oil for bathing the child, 12.4% of parents used less soap and bathed the child less often, 28.9% reported that they were not using any interventions. It was established that when applying care method 1, namely applying moisturizing agents to the infant’s skin, the risk of developing atopic dermatitis increases,  $OR=12.8$  (95% CI 3.89 - 42.3) ( $p<0.0001$ ). When constructing a three-factor logistic regression model for predicting the risk of food allergy, no dependence was found between the development of food allergy and the presence of allergic diseases in parents, the period of introduction of complementary foods, and the duration of breastfeeding. Thus, this study did not reveal the protective role of skin care products, breastfeeding, and early introduction of complementary foods for the development of atopic dermatitis and food allergies in children. Multivariate analysis showed that atopic dermatitis is associated with emollients application to the infant’s skin. The use of moisturizing creams for the treatment of already existing atopic dermatitis or the path of percutaneous sensitization to allergens could have influenced the data.

**Key words:** [atopic dermatitis](#), [breastfeeding](#), [children](#), [emollients](#), [food allergy](#).

### Introduction

Atopic dermatitis (AD) and food allergy are common diseases that usually begin in early childhood and can occur together in the same in-

dividuals (О.П. Волосовець та ін., 2021). These conditions may be associated with a violation of the skin barrier in early childhood. Whether trying to prevent or correct skin barrier disruption

early in life is effective in preventing AD or food allergy remains to be elucidated. In general, emollients are considered safe agents with few side effects. However, applying enough emollients every day can sometimes have a negative impact on the child and family due to burning sensation, especially on skin with existing eczema (Oakley R & Lawton S, 2016). There is a concern that emollients can actively sensitize to individual components, leading to skin reactions (Danby et al., 2011, Kunkiel et al., 2022) and even systemic allergic reactions (Voskamp et al., 2014).

Skin barrier protection can also be achieved by limiting water loss through the skin or by limiting skin contact with potentially harmful substances or irritants. Activities and substances that can damage the skin barrier, especially in people with existing eczema, include excessive bathing, detergents, and hard water. Thus, addressing any of these factors in the first months of life could potentially improve skin hydration and barrier function, thereby reducing further AD deterioration.

The close relationship between AD and food allergy suggests that reducing clinical manifestations of AD may potentially reduce the risk of food allergy, even if it is simply delaying the onset of AD in early childhood period (Martin et al., 2015). A small pilot study of the effectiveness of a ceramide-based emollient reported a reduction in allergic sensitization to food products (Lowe et al., 2018).

A Cochrane review of studies examining the value of infant skin care interventions for the development of AD and food allergy included 33 studies involving 25,827 infants (Kelleher et al., 2021). Skin care was compared with no skin care or usual care (standard care). A study on the development of AD, which included data from 3075 participants in seven randomized controlled trials, found that skin care interventions were unlikely to affect the development of AD between one and two years of age in healthy full-term infants compared with standard care. This Cochrane review also found that the skin care interventions were unlikely to change the time of eczema onset compared with the standard care (based on 3,349 participants in nine studies). This is thought to be important for the interaction between eczema and food allergy, as increased duration of eczema is

associated with an increased likelihood of food sensitization (Tsilochristou et al., 2019).

### **Aim**

The aim of this study was to assess the significance of interventions such as skin care products for the skin barrier improvement, breastfeeding and early complementary foods introduction for the primary prevention of atopic dermatitis and food allergy in infants by building logistic regression models.

### **Materials and methods**

We performed a survey of 97 parents of children in the period from May till June 2022. The survey was conducted with the help of Google forms and distributed on the Internet.

We included in the questionnaire all skin care interventions that could potentially enhance skin barrier function, reduce dryness, or reduce inflammation. They include:

- applying moisturizing agents to the child's skin;
- bathing infants with water containing moisturizing substances or moisturizing oils;
- use less soap, bathe the child less often.

During the survey, it was possible to indicate one, several or all options. The presence of undesirable effects from the use of the means was determined, in particular, the presence of irritation, burning, redness. The survey included questions about the presence of AD, defined as rash\dryness\flaking\crusting\itching of the skin lasting more than 4 weeks. The age of onset of the disease was also determined. The presence of a food allergy was defined as a reaction to food products that occurs within 2 hours after consuming the product; the questionnaire also included questions about the parent's allergic history, the duration of breastfeeding, and the age at which complementary foods were introduced. Children with parental allergy history were defined as a risk group.

Statistical processing of the obtained data was carried out using the statistical package IBM SPSS Statistics Base (version 22), EZR version 1.32 (graphical interface of the R environment (version 2.13.0)). The research database was systematized in the Microsoft Excel editor.

ROC-analysis with construction of a characteristic curve (ROC-curve, receiver operator

characteristic curve) was used. When constructing it, the sensitivity values for each value of the characteristic (the frequency of true positive results) are placed on the vertical axis, and 1 minus the specificity (the frequency of false positive results) is placed on the horizontal axis. The diagonal line shows the value of a completely uninformative random test result. Curves with greater significance are located closer to the upper left corner of the graph. The value of the area under the characteristic curve shows the ratio of sensitivity and specificity. The quality of the scale was assessed using the area under the curve (AUC): in the interval 0.9–1.0 – excellent, 0.8–0.9 – very good, 0.7–0.8 – good, 0.6–0.7 is mediocre, 0.5–0.6 is unsatisfactory. The larger the area under the ROC curve was, the higher was the predictive value of the predictor.

The prognostic significance of factors regarding the formation of AD was assessed by the odds ratio (OR) with a confidence interval (CI) of 95%. To determine independent predictors of the occurrence of adverse allergic events, stepwise multivariate regression analysis of Cox proportional hazards was used. The determination of standardized regression coefficients ( $\beta$ ) and determination of their exponents reflected the increase in the risk of occurrence of the expected event when the value of the factor changes by one unit. Factors that remained significant in multivariate analysis were interpreted as independent predictors. For all types of analysis, differences were considered probable at  $p < 0.05$ .

### Results

Parents of 97 children were involved in our survey between May 2022 and June 2022. The average age of the children was  $6.5 \pm 3.92$  years. 33.0% of the respondents reported that their children had an atopic parental history. According to the survey data, 42.2% of children received a moisturizing cream, parents of 16.5% of children reported using moisturizing oil for bathing the child, 12.4% of parents used less soap and bathed the child less often, 28.9% reported that they did not use none of these methods and means of care. 7.2% of respondents reported that skin irritation, redness, burning was noted when using the products, 92.8% did not encounter any unwanted effects or adverse reactions.

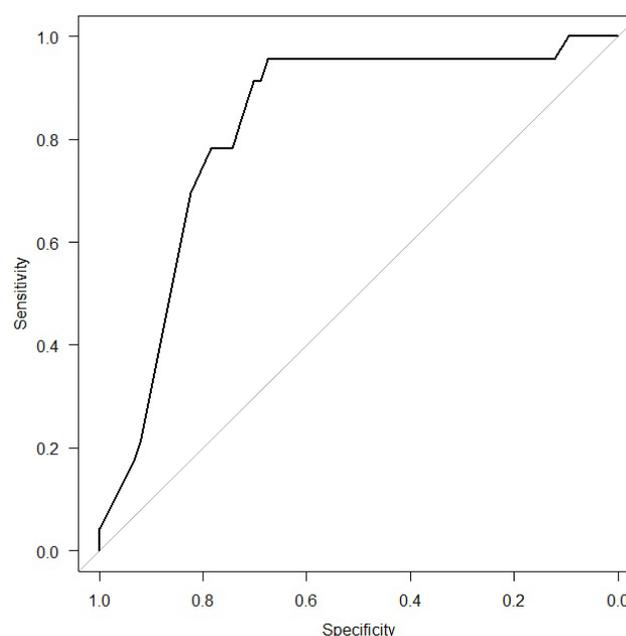
AD occurred in 23.7% children of interviewed. 18.6% of respondents reported that the child has reactions to food that occur within 2 hours after eating it.

Method of building and analyzing logistic regression models was used to analyse the association of the risk of AD in children (Y) with the factor characteristics. The characteristics were as follows: “Skin care 1: application moisturizers to the infant’s skin” (X1), “Skin care 2: bathing infants with water containing moisturizing substances or moisturizing oils” (X2), “Skin care 3: usage of less soap, bathing the child less often “ (X3), “paternal history of atopy “ (X5), “duration of breastfeeding less than 1 year “ (X6), “early introduction of supplementary food (up to the 6th month of life)” (X7). The analysis was conducted on the results of the examination of 97 children.

Based on the calculations in the EZR package, the ROC curve of the six-factor logistic regression model of AD risk prediction was obtained (see Fig. 1).

When building a six-factor model, the dependence of AD risk on factor characteristics was revealed, the area under the ROC curve  $AUC = 0.83$  (95% CI 0.73 – 0.92), statistically significance ( $p < 0.05$ ) exceeded 0.5, which was the evi-

**Fig. 1.** ROC curve of the six-factor logistic regression model of AD risk prediction.



**Table 1.** Coefficients of the 6-factor logistic regression model for predicting the risk of AD

Potential risk factors	The value of the coefficient of the model, $b \pm m$	The level of significance of the difference of the coefficient of the model from 0, p	OR (95% CI)
X1 Care (1) application moisturizers to the infant's skin	3,19±1,09	0,003*	24,2 (2,8–204)
X2 Care (2) bathing infants with water containing moisturizing substances or moisturizing oils;	1,39±1,3	0,29	4,0 (0,3–51,7)
X3 Usage of less soap, bathing the child less often	0,64±1,47	0,67	1,9 (0,1–33,8)
X5 Paternal history of atopy	0,52±0,6	0,39	1,7 (0,5–5,5)
X6 Duration of breastfeeding less than 1 year	-1,2±0,76	0,11	0,3 (0,1–1,3)
X7 Early introduction of supplementary food (up to the 6th month of life)	0,27±0,74	0,71	1,3 (0,3–5,6)
Constant	-3,21±1,06	0,002 *	

Note: \* –  $p < 0.05$ .

dence of the adequacy of the built model according to the quality scale “good”.

Table 1 shows the results of estimating model coefficients.

To select the minimum set of factor characteristics associated with the original variable, the method of stepwise rejection/inclusion of variables (“Stepwise”) was used. A single factor sign associated with the risk of AD was highlighted: “Skin care 1: applying moisturizers to the child's skin”. When comparing the prognostic characteristics of the one-factor logistic forecasting model (the area under the ROC curve  $AUC=0.78$  (95% CI 0.68–0.87), statistically significance ( $p < 0.05$ ) exceeds 0.5. Quality of the model built on all six variables did not reveal their deterioration. Table 2 shows the results of estimating model coefficients.

The obtained mathematical model of AD risk prediction can be expressed by the formula:

$$\ln(Y/1-Y) = -2.6 + 2.55X1$$

Thus, it was established that AD is associated with “Care (1) application of moisturizing agents to the infant's skin” ( $p < 0.05$ ). It was established that when applying care method 1, namely applying moisturizing agents to the infant's skin, the risk of developing AD increases, OR=12.8 (95% CI 3.89 - 42.3) ( $p < 0.0001$ ) (Table 2).

When constructing a three-factor logistic regression model for predicting the risk of food allergy, no dependence was found between the development of food allergy and the presence of allergic diseases in parents, the period of introduction of complementary foods, and the duration of breastfeeding.

**Table 1.** Coefficients of the one-factor logistic regression model of AD risk prediction

Potential risk factors (factor sign)	The value of the coefficient of the model, $b \pm m$	The level of significance of the difference of the coefficient of the model from 0, p	OR (95% CI)
X1 Care (1) application moisturizers to the infant's skin	2,55±0,61	<0,0001 *	12.8 ( 3.89 - 42.3)
Constant	-2,60±0,52	<0,0001*	

Note: \* –  $p < 0.05$ .

## Discussion

In this study the dependence of AD risk on factor characteristics was revealed by building a six-factor model. The role of such factors as skin care interventions (application moisturizers to the infant's skin, bathing babies with water containing moisturizing substances or moisturizing oils and usage of less soap), paternal history of atopy, duration of breastfeeding and early introduction of supplementary food was studied. The area under the ROC curve  $AUC = 0.83$  (95% CI 0.73 – 0.92) was statistically significant ( $p < 0.05$ ), so the adequacy of the built model according to the quality scale was "good". Multivariate analysis showed that AD is associated with emollients application to the infant's skin (OR=12.8 (95% CI 3.89 - 42.3) ( $p < 0.0001$ ). Although the questionnaire determined the use of emollients from birth, i.e. for the prevention of AD, there is a possibility that the use of moisturizing creams for the treatment of already existing AD could have influenced the data. In the opposite case, the path of percutaneous sensitization cannot be excluded, when microparticles of food or other allergens can get into the cream during the application of the emollient to the skin (Ryczaj et al., 2022).

Although studies on the effects of skin care and feeding interventions on the development of allergies are described in the literature, these practices vary greatly between countries and depend on traditional, cultural, socio-economic and other factors.

The BEEP trial of 1,394 infants, the first large randomized controlled trial to examine whether emollients could prevent eczema, found no evidence to support the hypothesis that the use of emollients daily could prevent AD (primary outcome), food allergy, sensitization, allergic rhinitis or asthma (secondary effects) (Chalmers et al., 2020). In addition, there was a slight increase in food allergy in the emollient group compared to the control group. The lack of benefit of emollients for the prevention of AD found in that study, same as in ours, was unexpected, especially given the reports in previously published pilot studies, and has serious implications for the primary prevention of AD and other diseases (Horimukai et al., 2014, Simpson et al., 2014). The increased risk of food allergy is likely due

to the increased transfer and absorption of food antigens through the skin when emollients are applied, leading to the epicutaneous sensitization (Brough et al., 2020).

Understanding of the properties of skin barrier function at an early age has improved, and it is possible that other approaches to strengthening the skin barrier, based on new knowledge, may have a preventive effect. These approaches may include the use of newly developed emollients with improved skin barrier properties or a comprehensive intervention that includes additional measures such as low-pH detergents, infrequent washing, or softened water.

## Conclusions

In this study we didn't find out the protective role of skin care products, breastfeeding, and early introduction of complementary foods for the development of atopic dermatitis and food allergies in children. Multivariate analysis showed that atopic dermatitis is associated with emollients application to the infant's skin. The use of moisturizing creams for the treatment of already existing atopic dermatitis or the path of percutaneous sensitization to allergens could have influenced the data.

## Financing

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## Conflict of interest

The authors declare no conflicts of interest.

## Consent for publication

Authors have obtained consent for publication of this work from all patients relevant to this manuscript.

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A – Research concept and design, B – Collection and/or assembly of data, C – Data analysis and interpretation, D – Writing the article, E – Critical revision of the article, F – Final approval of article

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## Догляд за шкірою та раннє введення прикорму для профілактики atopічного дерматиту у немовлят

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**Анотація:** atopічний дерматит і харчова алергія є поширеними захворюваннями, які зазвичай починаються в ранньому дитинстві і можуть виникати разом в одних і тих самих людей. Метою цього дослідження було оцінити значення втручань, таких як засоби по догляду за шкірою для покращення шкірного бар'єру, грудне вигодовування та раннє введення прикорму для первинної профілактики atopічного дерматиту та харчової алергії у немовлят шляхом побудови логістичних регресійних моделей. Ми провели опитування 97 батьків дітей. Опитування було проведено за допомогою гугл-форм і розповсюджено в Інтернеті. Метод побудови та аналізу моделей логістичної регресії використано для аналізу зв'язку ризику розвитку atopічного дерматиту у дітей із факторними характеристиками. Характеристики були такими: «Догляд за шкірою 1: нанесення зволожуючих засобів на шкіру немовляти», «Догляд за шкірою 2: купання немовлят водою, що містить зволожуючі речовини або зволожуючі масла», «Догляд за шкірою 3: використання меншої кількості мила, купання дитини рідше», «атопія в анамнезі батьків», «тривалість грудного вигодовування менше 1 року», «раннє введення прикорму (до 6-го місяця життя)». Згідно з даними опитування, 42,2% дітей отримували зволожуючий крем, батьки 16,5% дітей повідомили, що використовували для купання дитини зволожуючу олію, 12,4% батьків використовували менше мила і рідше купали дитину, 28,9% повідомили, що не використовувати жодного з цих методів і засобів по догляду. Встановлено, що при застосуванні методу догляду 1, а саме нанесення зволожуючих засобів на шкіру немовляти, підвищується ризик розвитку atopічного дерматиту,  $ВШ=12,8$  (95% ДІ 3,89 - 42,3) ( $p<0,0001$ ). При побудові трифакторної логістичної регресійної моделі прогнозування ризику харчової алергії не виявило залежності між розвитком харчової алергії та наявністю алергічних захворювань у батьків, періодом введення прикорму та тривалістю грудного вигодовування. Таким чином, дане дослідження не виявило захисної ролі засобів по догляду за шкірою, грудного вигодовування та раннього введення прикорму для розвитку atopічного дерматиту та харчової алергії у дітей. Багатофакторний аналіз показав, що atopічний дерматит пов'язаний із застосуванням пом'якшувальних засобів для шкіри немовляти. Використання зволожуючих кремів для лікування вже наявного atopічного дерматиту або шлях черезшкірної сенсibiliзації до алергенів могло вплинути на дані.

**Ключові слова:** atopічний дерматит, грудне вигодовування, діти, прикорм, емолієнти, харчова алергія.



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