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Hygienic behavior and allergic sensitization in German adolescents

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To the Editor:

According to the "hygiene hypothesis", frequent baths/showers and antimicrobial components in personal care products can alter skin microflora (1), leading to immune system impairment and allergic sensitization (2). The human skin provides a vital protection against the external environment. While frequent washing of hands, frequent baths/showers and use of soap and detergents aggravate the degradation of skin epithelium barrier (3), excess moisturizing of the skin makes it more sensitive to breakdown and increases permeability to foreign agents. Furthermore, almost all personal care products contain antimicrobial agents such as triclosan and/or parabens, which have been reported to have immune modulating properties in skin tissues and have the potential to induce or augment allergic disease (4). A degraded skin barrier through frequent baths/showers may result in a higher absorption of these chemicals into the body. To our knowledge, to date, no study has investigated the association between personal hygiene habits, such as frequent baths/showers and use of skin creams, and allergic sensitization.

For the current analysis, we used data collected mainly at the 15-year follow-up of the German GINIplus and LISA cohorts. Ethical approval for both cohorts was granted by the local ethics committees and informed consent was obtained from all families. Study methods are described in Online Supplement S1 and a flow chart of study participants is provided in Figure S1. We investigated cross-sectional associations of 1) having frequent baths/showers and 2) use of facial or 3) body cream on allergic sensitization to aero- and food-allergens while adjusting for potential confounders. Allergic sensitization was defined as a specific IgE value above 0.35 kU/L against a battery of 14 allergens. Our main analysis included subjects without "current allergies", defined as parent report of doctor diagnosis of asthma, eczema or allergic rhinitis during the last 12 months at the age of 15 years. The reason behind exclusion of participants with "current allergy" was to reduce impact of reverse causation. It is likely that people who already had "current allergies" may have

changed their bathing habits and use of cream. For example, someone already has eczema may use excessive amount of body creams compared to a person without eczema. Additionally, we repeated the analyses for subjects who did not report ever allergy and for the complete population. We also checked whether the associations were modified by sex.

The majority of participants (52.0%) were living in the Munich area. Three percent reported having less frequent (once per week or more rarely) baths/showers, 26% - never using facial cream, and 35.2% - never using body cream. The prevalence of current aero- and food-allergen sensitization was 45.7% and 10.9%, respectively (Table 1). Of the 15-year participants 13.9% reported current allergy.

In our main analysis concerning adolescents without current allergies we observed a protective effect for having baths/showers less than or equal to once per week and aeroallergen sensitization, compared to having baths/showers every day (aOR 0.51 95%CI 0.27, 0.98) (Table 2). However, these associations were no longer significant after participants with ever allergy were excluded. Results for the complete cohort is given in Table S2. There was no evidence of an association between use of facial or body cream and allergic sensitization (Table 2). Further, we did not observe an association between having frequent baths/showers and food allergen sensitization (Table 1). Even though females were more likely to have frequent baths/showers and use facial/body creams, we observed no evidence for a modifying effect by sex for the effects of having frequent baths/showers or use of creams on allergic sensitization (Table S 3, 4 & 5).

We observed a significant protective effect of having less frequent baths/showers and aero allergen sensitization in adolescents who did not report current allergies. This may be explained by less damage to the skin barrier and maintenance of healthy population of commensal microbiome on the skin in adolescents having less frequent showers/baths. Hygiene habits, including use of soap and detergents in baths/showers, accelerate epidermal barrier breakdown and results in an elevated pH level in the *stratum corneum*. A sustained increase of skin pH can cause damage to skin proteins and lipids. This may cause tightness, dryness, barrier damage, irritation and itching, allowing entry of foreign agents such as environmental allergens into the skin, which can then increase skin immune responses (5). Animal studies that used mechanical disruption of skin and allergen exposure have shown elevated antigen-specific IgE and IgG1 responses in skin (6); similar mechanisms can be expected in damaged human skin. Frequent baths/showers can influence microbiome diversity on skin epithelial cells, which leads to an altered immune response. These effects have been seen in some infant studies, but there is limited evidence for the immunoregulation and skin microbiome association in adults (2).

To our knowledge, there is no evidence in the published literature of the association between frequent baths/showers, as well as use of creams, and allergic sensitization. Nevertheless, some studies have investigated urine levels of parabens and triclosan in relation to allergic sensitization. Two US studies found that higher triclosan concentrations were associated with increased odds of food sensitization in children; one found the association only in children with eczema (7) and other only in males (8). A Norwegian study reported that urinal triclosan was associated with allergic sensitization against aeroallergens, but not against food allergen (9). Although some studies reported a link between triclosan and food allergen sensitization we did not find any associations between frequent baths or use of creams, and food allergen sensitization.

The strengths of our analysis include the large population size, prospectively collected data on allergic outcomes and the availability of detailed information on potential confounders. Although the GINIplus and LISA cohorts are both prospective birth cohort studies, we do not have prospectively

collected data on personal hygiene habits and use of creams. Given this limitation and even though we excluded participants with current allergy, we cannot completely rule out reverse causation as a driver of the observed associations. Similarly, the effects we observed cannot be ascribed to the frequency of baths/showers alone, since we do not have information on the use of personal care products such as soap, shampoo, etc. Also, there is a possibility of chance findings of significant associations.

Our study is the first to shed light onto the associations between having frequent baths/showers and use of creams, and allergic sensitization. In the general population, adolescents without allergies who have less frequent baths/showers had a protective effect against aeroallergen sensitization. Use of facial or body creams was not associated with allergic sensitization. Further, sex was not an effect modifier of these associations.

Table 1: Study characteristics of the subjects from GINIplus and LISA cohorts used for this statistical modeling (n = 2,755)

Characteristics of the study sample		**Frequency**	**%**
Study area	Munich	1,433	52.01
	Leipzig	272	9.87
	Bad Honnef	113	4.10
	Wesel	937	34.01
Study	GINI plus observation	897	32.56
	GINI plus intervention	891	32.34
	LISA	967	35.10
Sex	male	1,385	50.27
	female	1,370	49.73
Current allergy at 15 years[†]	no	2,256	86.11
	yes	364	13.89
Ever reported allergy[§]	no	1,483	53.83
	yes	1,272	46.17
Socio-economic status*	low	166	6.03
	medium	869	31.54
	high	1,720	62.43
Parent atopy[$]	no	1,099	39.89
	yes	1,656	60.11
Having baths/ showers	never/ less than once per week/ once per week	68	2.47
	2-6 times per week	1,537	55.79
	every day	1,150	41.74
Use of facial cream	never	704	26.00
	often	1,206	44.00
	every day	825	30.16
Use of body cream	never	975	35.60
	often	1,489	54.36
	every day	275	10.04
Aeroallergen sensitization[‡]	no	1,497	54.34
	yes	1,258	45.66
Food allergen sensitization[‖]	no	2,455	89.11
	yes	300	10.89

Aero or food allergen sensitization [#]	no	1,457	52.89
	yes	1,298	47.11

* defined as the highest number of years of school education of either parent: <10 years vs =10 years vs >10 years, according to the German educational system

[$] defined as parent's eczema, allergic rhinitis or asthma before birth of child

[§] defined as parent report of doctor diagnosis of asthma, eczema or allergic rhinitis ever during 3-15 years of age

[†] defined as parent-report of doctor diagnosis of asthma, eczema or allergic rhinitis during the last 12 months at 15 years of age

[‡] defined as specific IgE value above 0.35 kU/L against SX1 allergens: house dust mites, cats, dogs, mold, birch, rye, mugwort and timothy grass

[‖] defined as specific IgE value above 0.35 kU/L against FX5 allergens: milk, peanut, eggs, soya, cod, wheat flour

[#] defined as specific IgE value above 0.35 kU/L against SX1 or FX5 allergens

Table 2: Association between having baths/showers and use of creams, and allergic sensitization in adolescents without current allergies[§] (allergic sensitization N = 2,255; facial cream N = 2,241; body cream N = 2,244)

	Aero/food allergen sensitization		Aeroallergen sensitization		Food allergen sensitization		n
Baths/showers frequency	OR*	95% CI	OR*	95% CI	OR*	95% CI	
Every day	*Reference category*		*Reference category*		*Reference category*		912
2-6 times per week	1.12	0.94, 1.34	1.11	0.93, 1.32	1.07	0.78, 1.47	1,290
Never/ less than once per week/ once per week	0.54	0.28, 1.02	**0.51**	**0.27, 0.98**	1.27	0.49, 3.31	53
Facial cream Never	*Reference category*		*Reference category*		*Reference category*		573
Often	1.03	0.82, 1.27	1.02	0.82, 1.26	1.11	0.76, 1.62	988
Every day	1.00	0.77, 1.29	0.96	0.74, 1.25	0.98	0.62, 1.56	680
Body cream Never	*Reference category*		*Reference category*		*Reference category*		800
Often	0.98	0.79, 1.21	1.03	0.83, 1.27	0.82	0.57, 1.19	1,227
Every day	0.88	0.62, 1.25	0.85	0.59, 1.21	1.00	0.55, 1.83	217

[§] defined as parent report of doctor diagnosis of asthma, eczema or allergic rhinitis during the last 12 months at 15 years of age

*Adjusted for study center, cohort, sex, socio-economic status and parental history of allergy

OR: Odds Ratio, CI: Confidence Intervals, n = number of participants in each category

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Author contributions

GB conducted the analyses, interpreted the data, drafted the initial manuscript, and revised the manuscript. IM preprocessed the data. IM, MS, SD and JH contributed to the design of the analysis and interpretation of the data. MS, SK, IL, CPB, TS, AvB and DB contributed to the data collection and reviewed the manuscript. JH initiated and supervised the analysis. All authors approved the final manuscript as submitted and agree to be accountable for this work.

Conflict of interests

None.