

DOI: 10.1111/all.13704

Cleanliness, hygienic habits, and aeroallergen sensitization: German Bitterfeld 3 study

To the Editor,

According to the modern re-formulations of the hygiene hypothesis, loss of symbiotic relationships with evolutionary relevant microorganisms prevents proper maturation of the immune system and is therefore proposed to be the underlying cause for the allergy epidemic in the Western world.¹ Biodiversity loss, diminished contact with environment, and altered lifestyles all lead to reduced microbiome diversity, which is related to allergic outcomes.¹ Large family size, presence of older siblings, pet ownership, and living on a farm have been demonstrated to reduce allergy risk, providing indirect support to the hygiene hypothesis.² However, almost no studies have investigated whether increased cleanliness and improved hygienic habits are related to allergic sensitization and manifestation. The results of our recent study in the German GINIplus and LISA cohorts have demonstrated that children who bathed or showered not more often than once per week were less likely to be sensitized to aeroallergens than their counterparts who bathed or showered every day.³ However, since the group of rare bathers/showerers constituted less than 3% of the analytic sample, this finding requires replication in an independent sample. Our current study aims to investigate whether less frequent bathing and showering, as well as frequency of hand washing, degree of cleanliness after playing outdoors, and nails cleanliness usually are associated with lower risk of aeroallergen sensitization in children.

We used cross-sectional data on 11- to 15-year-old children from the Bitterfeld 3 study residing in the towns of Hettstedt, Zerbst, and Bitterfeld in Sachsen-Anhalt, Germany, between September 1998 and July 1999.⁴ The Bitterfeld 3 study has been approved by the University of Rostock's Ethics Committee, and informed consent was obtained from the parents of all participating children. For the purpose of this study and in line with our previous analysis,³ we limited our main analysis to children without current allergies, that is, without current symptoms or treatment of asthma, eczema in the last 12 months, and symptoms of allergic rhinitis in the last 12 months. This was done to reduce the potential impact of reverse causality, as children with current allergic diseases may have different hygiene behavior. As a sensitivity analysis, we further excluded children who were ever doctor-diagnosed with asthma, eczema, or allergic rhinitis. We also present the results for allergic sensitization and current allergy for the entire study population. Allergic sensitization was defined as specific immunoglobulin E (IgE) ≥ 0.35 kU/L against birch pollen (t3), grass pollen (g6), mold (cladosporium, m2), house dust mites (*Dermatophagoides pteronyssinus*, d1), or cats (e1), as measured by the standardized radioallergosorbent test (RAST; Pharmacia,

TABLE 1 Description of the study population (n = 884)

Characteristic	n (%)
Area	
Zerbst	266 (30.1)
Bitterfeld	356 (40.3)
Hettstedt	262 (29.6)
Female sex	412 (46.6)
Age, years (median (minimum-maximum))	12 (11-15)
Parental school education ^a	
≤8 years	45 (5.1)
10 years	441 (49.9)
≥12 years	398 (45.0)
Parental atopy ^b	286 (32.4)
Frequency of bathing/showering	
Daily/3-6 times per week	635 (71.8)
1-2 times per week/more rarely	249 (28.2)
Frequency of hand washing after playing outdoors	
Mostly	718 (81.2)
Occasionally/seldom/never	161 (18.2)
Missing	5 (0.6)
Degree of cleanliness after playing outdoors	
Very clean/quite clean	306 (34.6)
Quite dirty/very dirty	572 (64.7)
Missing	6 (0.7)
Nails cleanliness usually	
Clean	744 (84.2)
Dirty	107 (12.1)
Missing	33 (3.7)
Any aeroallergen sensitization ^c	
Against birch pollen	124 (14.0)
Against grass pollen	197 (22.3)
Against mold	44 (5.0)
Against house dust mites	168 (19.0)
Against cats	81 (9.2)

^aDefinition based on highest parental level of education, classified according to the German education system.

^bDefined as self-report of asthma, allergic rhinitis, eczema, or other allergy by either of the parents.

^cDefined as specific immunoglobulin E (IgE) ≥ 0.35 kU/L against birch pollen (t3), grass pollen (g6), mold (cladosporium, m2), house dust mites (*Dermatophagoides pteronyssinus*, d1), or cats (e1), as measured by the standardized RAST method (Pharmacia, Freiburg, Germany).

Freiburg, Germany).⁵ Individual associations with each of the hygiene- and cleanliness-related exposures were analyzed by logistic regression models, adjusted for a priori selected covariates—area, sex, age, parental education, and parental atopy. To test whether associations differed across sexes, we stratified models by this factor. Associations were assumed present at α -level <0.05.

Of 884 children from the analytic sample (Figure S1), 47% were females and 35% were sensitized against at least one of the tested aeroallergens (Table 1). We observed that among 756 children without current allergy, those who bathed or showered at most 1-2 times per week had 31% lower odds of aeroallergen sensitization (Table 2) compared to those who bathed or showered more frequently. This association was more pronounced in males than females, but still only borderline significant. For the rest of the exposure variables, odds ratios tended to be below one but none reached formal statistical significance. In 685 children who never had allergies, odds ratios further decreased and association with bathing/showering in males became statistically significant (Table S1). In the entire study population, no associations were observed with aeroallergen sensitization. Degree of cleanliness after playing outdoors was related to lower odds of current allergy in all participants and in females (Table S2).

To our knowledge, this is the third epidemiological study to address the association between hygiene habits, cleanliness, and allergic sensitization. One previous study did not observe an association between cleanliness score (which included frequency of hand washing

and frequency of taking bath and shower) assessed at 8-11 years and atopic sensitization assessed at 5 years by skin prick test.⁶ We cannot directly compare our findings due to different age of children, as well as different exposure and outcome assessment. Nevertheless, the observation from our current study that less frequent bathing and showering is protective against aeroallergen sensitization is in line with the results of our previous cross-sectional analysis in 15-year-old children,³ which indicates that this is not a chance finding.

Recent advances in microbiome and immunologic studies have demonstrated that skin barrier epithelial cells play a role in important immune responses involving the activation of dendritic and T cells and in innate immunity to allergens.¹ Shampoos, soap, and shower gels typically contain antimicrobial agents, which have immune modulating properties. Several studies have reported that urine concentrations of those agents like triclosan and parabens were associated with allergic sensitization.⁷⁻⁹ Thus, thorough hygiene could lead to the development of atopy by reducing skin epithelial barrier integrity.² Reverse causality is a likely reason why the association of bathing/showering with aeroallergen sensitization or current allergy was not present in the entire population.

Our findings should be interpreted keeping in mind several limitations. Bitterfeld 3 study was not designed to answer the specific study question even though it collected hygiene-related data. Despite a relatively large sample size, we might have lacked statistical power to detect associations with some exposure variables. Nevertheless, we

TABLE 2 Association of hygienic variables with aeroallergen sensitization in children without current allergy (n = 756)^a, estimated by adjusted^b logistic regression

Exposure	All			Females			Males		
	n/N	OR (95% CI)	P-value	n/N	OR (95% CI)	P-value	n/N	OR (95% CI)	P-value
Frequency of bathing/showering									
Daily/3-6 times per week	543/756	1		231/352	1		312/404	1	0.059
1-2 times per week/more rarely	213/756	0.688 (0.475-0.999)	0.037	121/352	0.813 (0.470-1.406)	0.459	92/404	<i>0.608 (0.363 -1.018)</i>	
Frequency of hand washing after playing outdoors									
Mostly	612/753	1		276/350	1		336/391	1	0.829
Occasionally/seldom/never	141/753	0.977 (0.649-1.470)	0.910	74/350	0.885 (0.468-1.671)	0.705	54/391	1.062 (0.616-1.832)	
Degree of cleanliness after playing outdoors									
Very clean/quite clean	252/752	1		180/349	1		72/403	1	0.192
Quite dirty/very dirty	500/752	0.782 (0.541-1.132)	0.193	169/349	0.875 (0.523-1.464)	0.611	331/403	0.701 (0.412-1.194)	
Nails cleanliness usually									
Clean	637/731	1		320/340	1		317/391	1	0.560
Dirty	94/731	0.715 (0.435-1.175)	0.186	20/340	0.169 (0.022-1.298)	0.087	74/391	0.852 (0.498-1.459)	

CI, confidence interval; n, number of participants in each category; N, number of participants with available exposure data; OR, odds ratio. Significant associations ($P < 0.05$) are in boldface. Borderline significant associations ($P < 0.1$) are in cursive.

^aCurrent allergy defined as current symptoms or treatment of asthma, eczema last 12 months or symptoms of allergic rhinitis last 12 months, or absence of such information.

^bAll models adjusted for area, sex, age, parental education, and parental atopy.

dichotomized three exposure variables that originally had four categories to obtain balanced/sufficient numbers in each newly created category. Although current hygiene- and cleanliness-related habits may well reflect past behaviors, the cross-sectional design of our study precludes conclusions about the directionality of associations. Additionally, information on hygiene habits and cleanliness was collected by a questionnaire instead of examination; therefore, misclassification and recall bias are likely. Finally, it is difficult to directly compare current results to the results from our previous analysis³ or to generalize them to the entire German population. Due to more detailed categorization of possible responses, rare bathers/showerers in the Bitterfeld 3 study amounted to almost one-third of the analytic sample compared to 3% in GINIplus/LISA. Additionally, Bitterfeld 3 data were collected 16-12 years prior to the 15-year follow-up of GINIplus and LISA (1998-1999 vs. 2011-2014, respectively).

In summary, less frequent bathing and showering appears to be protective against aeroallergen sensitization in children without current allergy from this German study. More cleanliness was related to current allergy.

ACKNOWLEDGMENTS

The authors thank Hubert Schneller for data handling; Dr Doris Bodeseheim, Dr Irina Hörhold, Dr Ingo Keller, Brigitte Hollstein, Helga Machander, Runhild Müller, Doris Albrecht, and Christa Boettcher for gathering regional data and local assistance, and the local school authorities and healthcare centers for their support; and all parents and children for their participation.

FUNDING INFORMATION

This study was supported exclusively by a governmental funding source, the German Environment Agency (Umweltbundesamt – UBA) Grants No. 116 09 002, 116 002/02 and 298 61 724. The funding source had no involvement in the design of the study, collection, analysis and interpretation of data, writing of the report, and decision to submit the article for publication.

CONFLICT OF INTEREST

None.

Keywords

allergic sensitization, bath, epidemiology, hand washing, shower


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REFERENCES

- Lambrecht BN, Hammad H. The immunology of the allergy epidemic and the hygiene hypothesis. *Nat Immunol.* 2017;18:1076-1083.
- Platts-Mills TA. The allergy epidemics: 1870–2010. *J Allergy Clin Immunol.* 2015;136:3-13.
- Bowatte G, Markevych I, Standl M, et al. Hygienic behavior and allergic sensitization in German adolescents. *Allergy.* 2018;73:1915-1918.
- Heinrich J, Hoelscher B, Frye C, et al. Improved air quality in reunified Germany and decreases in respiratory symptoms. *Epidemiology.* 2002;13:394-401.
- Frye C, Heinrich J, Wjst M, Wichmann HE; Bitterfeld Study Group. Increasing prevalence of bronchial hyperresponsiveness in three selected areas in East Germany. Bitterfeld Study Group. *Eur Respir J.* 2001;18:451-458.
- Weber J, Illi S, Nowak D, et al. Asthma and the hygiene hypothesis. Does cleanliness matter?. *Am J Respir Crit Care Med.* 2015;191:522-529.
- Spanier AJ, Fausnight T, Camacho TF, Braun JM. The associations of triclosan and paraben exposure with allergen sensitization and wheeze in children. *Allergy Asthma Proc.* 2014;35:475-481.
- Savage JH, Matsui EC, Wood RA, Keet CA. Urinary levels of triclosan and parabens are associated with aeroallergen and food sensitization. *J Allergy Clin Immunol.* 2012;130:453-460.
- Bertelsen RJ, Longnecker MP, Lovik M, et al. Triclosan exposure and allergic sensitization in Norwegian children. *Allergy.* 2013;68:84-91.

SUPPORTING INFORMATION

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