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LETTERS TO THE EDITOR

House dust mites: Does a clean mattress mean *Der p* 1-free breastmilk?

To the Editor,

House dust mites are a worldwide major source of allergens, with *Dermatophagoidespteronyssinus* (*Der p*) being the most allergenic and frequently implicated in respiratory allergy.[3] Determining the sources of exposure to *Der p* in infants may be particularly important in view of the accumulating evidence of an early life window of susceptibility for long-term risk of disease.[4] Our data gathered in various regions of the world revealed that breastmilk is a source of oral exposure to mite allergens.[1,5,6] This observation may be explained by evidence showing that most of the inhaled large particles and proteins, including *Der p* 1, are ingested.[3,7] While early oral exposure to an allergen may be expected to lead to protection, as shown for food allergy by early introduction of peanut in the diet,[8] allergy risk was increased upon oral exposure to *Der p*1 through breastmilk in mouse models[2,6] and birth cohorts.[1,2] There was a positive association between the levels of *Der p* 1 in maternal milk and the risk of allergic sensitization and respiratory allergy in children.[1] Some preliminary evidence in birth cohorts also suggests a role for *Der p* in breastmilk in food allergy risk.[2] In a mouse model, exposure to *Der p 1* through breastmilk disrupted the neonatal gut barrier and triggered critical immunologic events for the development of both respiratory and food allergy.[2,6] The priming effect of oral exposure to *Der p* was found to rely on the strong intrinsic adjuvant property of *Der p* allergens, that is their protease activity, which is absent from peanut's allergens.[2] These data suggest that controlling the levels of *Der p* in breastmilk may be required to promote allergy prevention through breastmilk. The first option clinicians and mothers will most probably consider in order to eliminate *Der p* from breastmilk will be to avoid *Der p* in maternal close environment. Therefore, there is a critical need to elucidate whether the level of *Der p* in the maternal environment is influencing the allergen load of breastmilk. To address this question, we investigated the relationship between *Der p* 1 content in maternal mattress dust and breastmilk within samples from the Prevention and Incidence of Asthma and Mite Allergy (PIAMA) birth cohort.

A total of 254 mothers from PIAMA cohort[9] were included in this study. Breastmilk and dust samples from the maternal mattress were collected according to standardized protocols[9] when their children were aged between 2 and 35 weeks. Written informed consent was obtained from all participants. Characteristics of full PIAMA population and study group are summarized in Table 1. *Der p* 1 levels in dust and breastmilk were quantified using enzyme immunoassay (Indoor Biotechnologies) as previously described.[6] Statistical significance was defined by a two-sided alpha-level of 5% (SAS 9.2).

Der p 1 was detected in more than one third of the 218 available breastmilk samples with concentrations ranging from <LOD to 1238 pg/mL (Table 2 and Figure 1A). The median concentration among *Der p* 1-positive samples was 174 pg/mL (IQR = 76-302 pg/mL, Table 2 and Figure 1A). Interestingly, the levels of *Der p* 1 in breastmilk and the percentage of positive sample in this cohort from the Netherlands are similar to those reported for other countries, that is, Brazil, France, Australia.[5,6] The allergic status of the lactating mother had null relation with *Der p* 1 allergen levels in breastmilk (Mann-Whitney *U* test, *P* = .16; Table 2). The concentration of *Der p* 1 in mattress dust was also similar between allergic and non-allergic mothers (Mann-Whitney *U* test, *P* = .11; Table 2). We also compared *Der p* 1 levels in breastmilk collected during winter (n = 17) and non-winter (n = 233). No significant difference was observed between both groups (Mann-Whitney *U* test, *P* = .66), and the ratio of geometric mean (95% CI) of the *Der p*1 levels of samples collected in winter to the samples collected in other seasons was 1.00 (0.68-1.46). This contrasts with previous observations from the EDEN French cohort where *Der p* 1 level was higher in mothers with a history of asthma or allergies and in breastmilk collected in winter.[1] To date, we do not have explanation for discrepancy of results. To get further insight into the factors controlling the presence of *Der p* 1 in breastmilk, we analyzed the association between *Der p* 1 load in mattress dust and in breastmilk. We detected *Der p* 1 in 64% of the dust samples, with a median concentration of 1130 ng/g of dust among samples with levels above the limit of detection (IQR = 540-3.895 ng/g, Table 2 and Figure 1B). No significant correlation was found between the amounts of *Der p* 1 in breastmilk and the allergen concentration in maternal mattress dust (Figure 1C, *r* = .05). We also compared the levels of *Der p* 1 in breastmilk from mothers with detectable versus non-detectable levels of *Der p* 1 in their mattress dust and found no differences (Figure 1D). There was a variation of 9 ± 18 days (mean ± standard deviation) between breastmilk sample and dust collection, which may explain this lack of correlation. We then analyzed the correlation of *Der p* 1 in dust and breastmilk in a subgroup of samples where dust and milk were collected within 5 days (n = 126). Similarly to the whole cohort, we found no

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TABLE 1 Characteristics of the participants (n = 254)

	Full cohort	Study participants	Allergic mothers	Non-allergic mothers
Infant male sex	2054/3963 (52%)	128/254(50%)	79/158 (50%)	49/96 (51%)
Maternal asthma, n/N (%)	314/3956 (8%)	41/254(16%)	41/158 (26%)	0/96 (0%)
Maternal allergy to house dust (mites), n/N (%)	618/3919 (16%)	97/249 (39%)	97/153 (63%)	0/96 (0%)
Season of breastmilk collection, n/N (%)				
Winter	—	17/250 (7%)	14/154 (9%)	3/96 (3%)
Spring	—	111/250 (44%)	68/154 (44%)	43/96 (45%)
Summer	—	69/250 (28%)	38/154 (25%)	31/96 (32%)
Autumn	—	53/250 (21%)	34/154 (22%)	19/96 (20%)
Maternal age at birth, mean (SD)	30.3 (3.9), n = 3871	31.0 (3.8), n = 248	31.1 (3.7), n = 154	30.9 (4.0), n = 94
Gestational age at birth, mean (SD)	39.8 (1.7), n = 3930	40.1 (1.4), n = 254	40.2 (1.3), n = 158	40.0 (1.5), n = 96
Caesarian section, n/N (%)	332/3895 (9)	20/253 (8%)	16/158 (10%)	4/96 (4%)
Infant age at breastmilk collection (days), mean (SD)	—	108 (29), n = 250	106 (28), n = 154	112 (31), n = 96
Pets at home during 1st year, n/N (%)	1877/3786 (50%)	104/248 (42%)	60/153 (39%)	44/95 (46%)

Note: Maternal history of allergies and/or asthma was defined from a validated self-reported questionnaire[9]

TABLE 2 Distribution of *Der p* 1 levels in breastmilk and dust samples collected from the maternal mattress

	Breastmilk (pg/mL)	Dust from maternal mattress (ng/g)
Total population		
Number of samples	218	218
Concentration range	<LOD-1238	52-101 562
Median [25%-75%]	<LOD [<LOD-84]	462 [155-1817]
Samples with detectable *Der p* 1 (%)	79 (36)	139 (64)
Median [25%-75%] for samples with detectable *Der p* 1	174 [76-302]	1130 [540-3895]
Allergic mothers		
Number of samples	130	130
Concentration range	<LOD-555	<LOD-101 562
Median [25%-75%]	<LOD [<LOD-67]	398 [<LOD-1042]
Samples with detectable *Der p* 1 (%)	42 (32)	81 (62)
Median [25%-75%] for samples with detectable *Der p* 1	151 [68-290]	849 [536-1818]
Non-allergic mothers		
Number of samples	88	88
Concentration range	<LOD-1238	<LOD-66 202
Median [25%-75%]	<LOD [<LOD-100]	639 [<LOD-4499]
Samples with detectable *Der p* 1 (%)	37 (42)	58 (66)
Median [25%-75%] for samples with detectable *Der p* 1	131 [77-312]	2312 [655-6742]

Note: Statistical analysis was performed for 218 participants where information on breastmilk and mattress dust *Der p* 1 levels was available. Comparison of *Der p* 1 levels in breastmilk and dust between allergic and non-allergic mothers (Mann-Whitney U test, two-sided, $P = .16$ and $P = .11$, respectively).The lower limit of detection (LOD) was 60 pg/mL for 2 times diluted breastmilk samples and 8ng/mL for 5-fold diluted dust samples. Breastmilk and dust samples with non-detectable amounts of allergen were assigned a value of two-thirds of the detection limit.

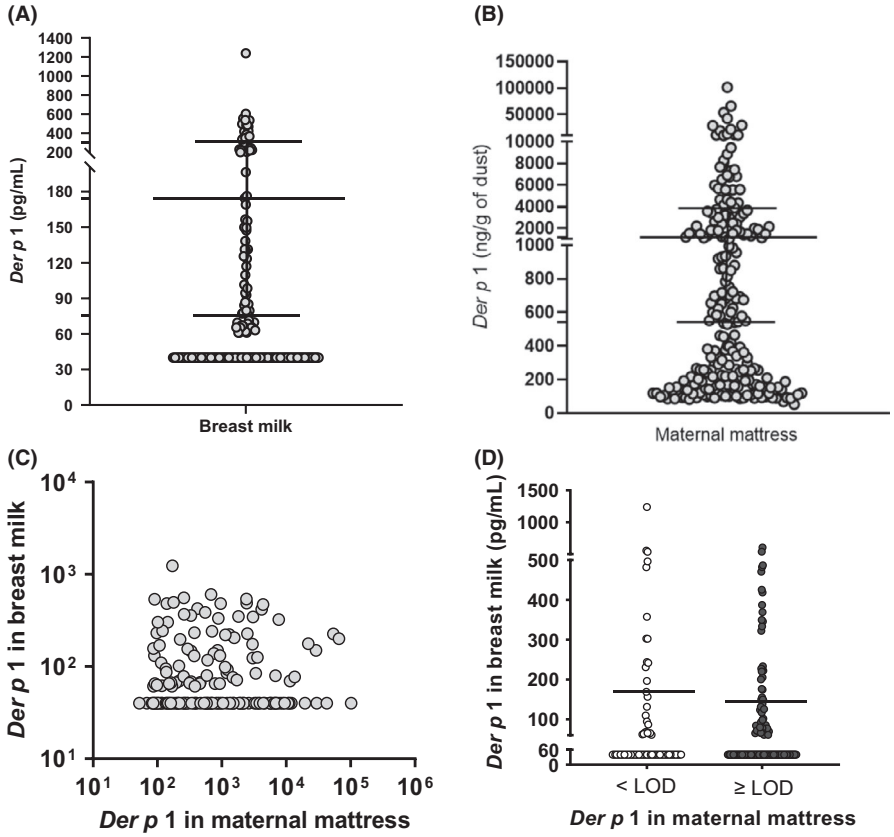

FIGURE 1 Association between *Der p* 1 levels in breastmilk and *Der p* 1 levels in maternal mattress dust. Distribution of *Der p* 1 levels in breastmilk (A) and dust from maternal mattresses (B). Dots represent individual values and horizontal bars represent medians, 25% and 75% percentiles among samples with levels ≥ LOD. (C) Correlation between *Der p*1 levels in breastmilk and dust samples collected on the maternal mattress. Spearman correlation was $r = .05$ ($P = .21$, n of pairs = 218). (D) Distribution of *Der p*1 levels in breastmilk for mothers with undetectable (n = 79) and detectable (n = 139) levels of *Der p* 1 in mattress dust. Horizontal plain lines represent the median values of *Der p* 1 among breastmilk with detectable *Der p* 1. Mann-Whitney U test was used to compare *Der p* 1 levels in both groups ($P = .49$). Logarithmic scales were used for all axes

correlation between *Der p* 1 levels on breastmilk and dust (spearman test $r = -.07$). The lack of correlation between *Der p* 1 levels in breastmilk and maternal mattress dust echoes with our previous observation from the French EDEN cohort.[1] In that cohort, *Der p* 1 was not associated with determinants of *Der p* exposure such as the presence of a carpet at home, high occupancy load in the residence, and lifestyle characteristics such as the habit of personally performing the house cleaning.[1]

Altogether, these data show that *Der p* 1 in breastmilk is not related to its concentration in maternal mattress dust. This aligns with the poor relation between the presence of dietary allergen in breastmilk and maternal food allergen consumption.[10]

Although the mattress is considered as the source with the highest levels of house dust mite allergen in homes, mothers may also have been exposed to other sources of exposure. In an elegant study, Tovey et al[11] monitored the individual exposure to mite aeroallergen using a portable air pump attached to the shoulder during the day and on the bed overnight. The authors demonstrated that aeroallergen exposure is closely related to personal lifestyle activities. In the present study, we did not have access to data on lifestyle activities that could indicate multiple sources of maternal aeroallergen exposure. It would also be informative to investigate whether *Der p* 1 is detected in breastmilk samples from mothers living at high altitude and lower indoor humidity regions where house dust mites cannot survive.[12]

Here, we demonstrated that *Der p* 1 concentration in breastmilk is not related to *Der p* 1 levels in maternal mattress dust and reveals that breastmilk is an independent source of *Der p*1 exposure. This pinpoints that actions to reduce *Der p* content in maternal indoor environment may be meaningless to avoid *Der p* 1 allergen in breastmilk. Future research is needed to clarify which factors govern *Der p* 1 in breastmilk. Maternal diet and gut microbiota represent attractive candidates as they are modifiable factors that may influence *Der p* 1 absorption through the gut.

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CONFLICT OF INTEREST

Dr Macchiaverni, Dr Gehring, Dr Rekima, Dr Wijga, and Prof. Verhasselt have nothing to disclose.

AUTHOR CONTRIBUTIONS

Patricia Macchiaverni: Conceptualization (equal); Formal analysis (equal); Investigation (equal); Methodology (equal); Visualization (equal); Writing–original draft (equal); Writing–review & editing (equal). **Ulrike Gehring:** Data curation (equal); Formal analysis (equal); Methodology (equal); Writing–review & editing (equal). **Akila Rekima:** Investigation (equal); Methodology (equal); Validation (equal); Writing–review & editing (supporting). **Alet H. Wijga:** Funding acquisition (equal); Project administration (equal); Resources (equal); Writing–review & editing (equal). **Valerie Verhasselt:** Conceptualization (equal); Funding acquisition (equal); Project administration (equal); Resources (equal); Supervision (equal); Writing–original draft (equal); Writing–review & editing (equal).

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