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Parental occupation is a risk factor for childhood wheeze and asthma

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Abstract

This birth-cohort study investigated whether childhood wheeze and asthma is associated with parental exposure to occupational sensitisers that cause asthma.

Parental occupation from the Avon Longitudinal Study of Parents and Children was related to wheeze, asthma, ventilatory function, airway responsiveness and atopic sensitisation in children aged 0-102 months.

Occupation was recorded for 11,193 mothers and 9,473 fathers ante-natally, and for 4,631 mothers and 5,315 fathers post-natally. Childhood respiratory outcomes were not associated with parental occupational exposure to diisocyanates, glues/resins, dyes, animal dust, solder, enzymes, and wood-dust. Maternal post-natal occupational exposure to latex and/or biocide/fungicides increased the likelihood of childhood wheeze and asthma. High levels of latex or biocide/fungicide exposure were associated with odds ratios of 1.26 [1.07-1.50] and 1.22 [1.02-2.05] respectively for wheezing up to 81 months. Combined maternal latex and biocide/fungicide exposures increased the likelihood of childhood wheeze (OR 1.22 [1.03-1.43]) and asthma. High paternal occupational flour dust exposure was associated with an increased likelihood of wheeze after 30 months (OR 2.31 [1.05-5.10]) and asthma by 91-months (OR 3.23 [1.34-7.79]).

Maternal occupational exposure to latex and/or biocides and paternal exposure to flour dust increases the risk of childhood asthma. Further studies in this area are justified.

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Introduction

Occupational exposures are an established risk factor for asthma, accounting for 5-25% of incident asthma in working adults [1-3]. Para-occupational asthma has also been described, e.g. cases of asthma caused by exposure to toluene diisocyanate in people not directly working with this chemical, but working in the vicinity of factories using toluene diisocyanate [4]. Para-occupational exposure of children via parent(s) to asbestos, pesticides and organic solvents with health sequelae has been described [5-8]. There is also evidence that occupational allergens can be transported home, presumably on contaminated clothing and skin with subsequent atopic sensitisation of other household residents [9-12]**.**

Based on these observations we hypothesized that parental exposure to common occupational sensitisers increases the child's risk of developing asthma and respiratory symptoms. We tested this hypothesis in the Avon Longitudinal Study of Parents and Children (ALSPAC) cohort that prospectively collected data on parental occupation and childhood respiratory symptoms/asthma. Certain maternal occupations during pregnancy have been reported to increase the risk of asthma and allergic disease in older children [6]. The ALSPAC cohort enabled us to investigate possible effects of maternal ante-natal and also post-natal occupation on the likelihood of childhood respiratory symptoms and asthma.

Methods

Subjects and outcomes

ALSPAC is an English geographically defined population-based, birth-cohort study of children born to 14,541 women recruited during pregnancy in 1991/2. The 13,971 children surviving to one year were followed up by postal questionnaires and clinical assessments. Parents reported the occurrence of 'wheezing with whistling on the chest' in their child at age

6, 18, 30, 42, 54, 69 and 81 months, and at 91 months, whether a doctor had ever diagnosed asthma in their child (defined as asthma). Only the first born child from multiple births were included in the study, as were the first born children of women who had a second pregnancy during the recruitment period.

At age 91 months, all children were invited to a research clinic where measurements included serum total IgE (carried out in 4963 children, 35.5% of the initial cohort and 61.0% of those with questionnaire data at 91 months) and allergen skin prick testing (carried out in 6754 children, 48.3% of the initial cohort and 83.0% of those responding at 91 months). Children were defined as atopic if they had a positive reaction (mean wheal diameter-negative control ≥3mm) to at least one allergen [13]. Ventilatory function and airway responsiveness to methacholine [14] expressed as the dose response slope; percent decline in FEV_1/μmol methacholine, were measured at the age of 102 months in 6710 (48.0% of the initial cohort and 78.8% of those with questionnaire data at 102 months) and in 4364 (31.2% of the initial cohort and 52.8% of those responding at 102 months) children respectively.

The primary outcomes of interest were maternal reports of childhood wheeze at 0-6, 6-18, 18-30, 30-42, 42-54, 54-69, 69-81 months and asthma at 91 months. The secondary outcomes were atopic sensitisation at 91-months, ventilatory function and airway responsiveness at age 102-months. Full details about the study participants and data collection have been published elsewhere [15].

Parental Occupation

Responses to the question "Your present job or last main job: actual job, occupation, trade or profession" were recorded for 11,193 mothers (76.9% of the initial cohort of women) and

9,473 fathers (65.1% of the initial cohort of women) at 18-weeks gestation and for 4,631 (31.8%) mothers and 5,315 (36.6%) fathers 21-months post-natally. These descriptions were coded into 4-digit Standard Occupational Classification (SOC2000) codes [16] with corresponding certainty scores (1-100%) using the Computer Assisted Structured Coding Tool (CASCOT) [17]. CASCOT derived occupational codes with a certainty score >50% were accepted, whereas those scored ≤50% were assessed and coded manually. An analysis of 24,431 occupation code derived both manually and by CASCOT showed that with an acceptable amount of manual recoding (maternal ante-natal 19.1%; paternal ante-natal 23.9%), this coding strategy resulted in 91% agreement with manually coded occupations. In total, 353 individual 4-digit SOC2000 codes were identified from the 15,824 maternal and 14,788 paternal job descriptions during and after pregnancy.

Potential ante-natal and post-natal exposure of children to parentally transported sources of recognised occupational sensitisers was estimated by construction of a job exposure matrix (JEM). For each of 353 SOC2000 codes, two experienced occupational hygienists with experience of retrospective exposure assessment [18] independently derived semi-quantitative ratings (high, medium, low, zero) for the intensity of workplace and 'take-home' exposure to eleven major occupational sensitisers (wood, diisocyanate, flour, glues/resins, animals, solder, enzymes, biocides/fungicides, foods, natural rubber latex, dyes). Assessment of the intensity of workplace exposure was based on typical UK working conditions during the early 1990s and took account of control measures, personal protective equipment and ventilation/extraction methods in common use within that sector. Assessment of 'take-home' intensity utilised a similar knowledge base about hygiene practices, particularly the washing and removal of contaminated clothing at the end of workshifts. There was initial concordance between the two assessors of 95%, the final 5% being agreed by consultation.

The primary exposures of interest were potential maternal and paternal exposures to occupational sensitisers at 18-weeks gestation and 21-months post-natally.

Statistical methods

All analyses used SPSS v16 (SPSS Inc., Chicago, USA). Univariable associations between wheeze, asthma, atopic sensitisation, ventilatory function and airway responsiveness and parental occupational exposure to sensitisers, demographic and socio-economic determinants, neonatal measurements, and early life exposure to smoking were explored.

Variables with $p<0.25$ in univariable analyses were included in multivariable analyses. For binary outcomes logistic regression analysis was used and linear regression analysis was used for continuous outcomes. General Estimating Equations (GEE) take into account that repeated measurements in the same individual are correlated and were used to assess the associations between parental occupational exposure to sensitisers and childhood wheezing symptoms during the first 81 months of life simultaneously [19]. The following variables were included in the multivariable models as potential confounders: gender, birth weight, gestational age at delivery, and maternal: asthma, age at delivery, parity, highest education qualification, smoking during pregnancy, and home ownership status.

Results

The numbers of children included in the analyses at each stage of follow-up together with the numbers of those with complete data on outcomes and parental occupational exposure during ante-natal and post-natal periods are presented in table 1. By 81 months 5,287 (59.3%) children were reported to have wheezed, and at 91 months physician-diagnosed asthma was

reported by mothers of 1,660 (20.4%) children. The prevalence of wheeze and asthma in the children of parents who had and had not provided occupational data differed, but these differences were small (table 2).

A total of 3,415 (30.5%) mothers and 3,865 (40.8%) fathers were exposed to at least one occupational sensitiser during the ante-natal period and 1,458 (31.5%) mothers and 1,875 (35.3%) fathers were exposed to at least one occupational sensitiser during the post-natal period. The most frequent sensitisers to which mothers were exposed ante-natally and post-natally were biocides/fungicides (24.0% and 26.9%) and latex (17.5% and 18.8%), whereas for fathers the most common exposures ante-natally and post-natally were glues/resins (27.8% and 23.4%) and biocides/fungicides (23.8% and 20.2%).

Multivariable analysis demonstrated no strong evidence that parental exposures to diisocyanates, glues/resins, dyes, solder, enzymes, animals, foods and wood dust were associated with any childhood respiratory or allergy outcomes.

Maternal occupational exposure to latex during pregnancy or 21-months post-natally was associated with childhood wheeze from 0-81 months and with asthma at 91-months (table 3). There was evidence for dose-response associations. Maternal occupational exposure to biocides/fungicides during pregnancy or 21-months post-natally was associated with childhood wheeze from 0-81 months but only post-natal biocide/fungicide exposure was associated with asthma at 91 months (table 3). There was evidence for dose-response associations. For the analysis of maternal biocide/fungicide exposure the medium and highest categories were combined because of the small numbers in the highest exposure category. There was no strong evidence of associations between maternal latex or biocide/fungicide

exposure and measurements of ventilatory function, airway responsiveness or atopy (table E1, online data supplement). There was no strong evidence that paternal latex or biocide/fungicide exposure was associated with childhood respiratory outcomes.

Most mothers exposed to latex and/or biocides/fungicides whilst pregnant were also exposed post-natally. However, small numbers of women were exposed exclusively during pregnancy or in the post-natal period. To explore differential associations of occupational exposure during the ante-natal and/or post-natal periods, maternal high latex exposure in the ante and/or post-natal periods was related to wheeze and asthma in children. Isolated maternal high latex exposure during pregnancy was not associated with an increase in childhood respiratory symptoms or asthma, but the children of mothers with isolated post-natal high latex exposure were twice as likely to wheeze and have asthma than children of non-exposed women (wheeze: OR 2.21 95% CI [1.44-3.39], asthma: OR 2.40 [1.24-4.67]) (table 3). Combined high maternal latex exposure ante and post-natally was associated with an increased likelihood of asthma (OR 1.36 [1.01-1.81]).

Analysis of moderate maternal biocide/fungicide exposure in the ante and/or post-natal periods suggested that combined maternal exposure to these agents during and after pregnancy was associated with asthma (OR 1.41 [1.04-1.91]) (table 3).

Combined maternal exposure to latex and biocides/fungicides after pregnancy was associated with an increased likelihood of childhood wheezing up to 81 months (OR 1.22 [1.03-1.43]) and asthma at 91 months (OR 1.47 [1.14-1.89]), (figure 1, table 3).

Inclusion of ante/post-natal exposure for latex and biocides/fungicides along with appropriate interaction terms in multivariable analyses confirmed these associations, with isolated high/medium post-natal latex exposure increasing the risk of wheeze by 81 months (OR 2.10 [1.42-3.09], p<0.001). These analyses suggested that the association between wheeze and post-natal latex exposure was modified by ante-natal exposure (for interaction OR 0.46 [0.26-0.80], p=0.006) and that combined latex and biocide/fungicide exposure in the post-natal period was associated with a tenfold increase in the likelihood of wheeze up to age 81 months (for interaction OR 10.2 [1.4-73.8]). The associations between maternal latex and biocide/fungicide appeared to be consistent throughout the follow up period (online supplement figures E1-E3). Wheezing phenotypes before and after the age of 5 years (never, transient, late onset, persistent) were not differentially associated with maternal latex and biocide/fungicide exposure, however the number of children who wheezed only after the age of 5 years was very small (<3%).

The majority of mothers exposed to high levels of latex during and after pregnancy were in health care occupations (94.0% ante-natally, 94.2% post-natally). Similarly, maternal medium biocide/fungicide exposure was most common for nurses, nursing auxiliaries and midwives (88.7% ante-natally, 92.3% post-natally) (tables E2-E5 online data supplement). Children of healthcare workers were more likely to have parentally reported wheeze, particularly if the mother was a healthcare worker (table 4). This appeared to be specific for wheeze as healthcare parents were not more likely to report non-respiratory symptoms in their children (figure E5 online data supplement).

Seventeen percent of non-healthcare working mothers post-natally were exposed to latex (e.g. beauticians, chefs, hairdressers) and/or biocides/fungicides (e.g. bar staff, cleaners, kitchen

assistants). The children of these non-healthcare latex and/or biocide/fungicide occupationally exposed mothers were more likely to wheeze between birth and 81 months (OR 1.08 [1.02-1.14], p=0.007). The children of non-healthcare working mothers post-natally in occupations likely to expose them to viral infections (e.g. childminders, nursery nurses, teachers) were not more likely to wheeze.

Some fathers worked in occupations exposing them to flour dust at 18-weeks gestation (2.3%) and 21-months post-natally (2.0%). Paternal occupational flour exposure during the ante-natal period was not associated with childhood wheeze or asthma. Although high intensity paternal occupational flour exposure in the post-natal period was not associated with childhood outcomes before the age of 30 months, it was associated with an increased likelihood of asthma at 91 months (OR 3.23 [1.34-7.79], p=0.009) and wheeze between the ages 30-81 months (OR 2.31 [1.05-5.10], p=0.038) (online supplement figures E4).

Discussion

We believe this is the first study to investigate whether childhood asthma is associated with parental occupational exposure to recognised asthmagenic sensitisers. We have demonstrated that childhood wheeze and asthma are not associated with parental exposure to most recognised occupational sensitisers. There was evidence, however, suggesting that maternal occupational exposure to latex and/or biocides/fungicides in the post-natal period was associated with an increased likelihood of childhood wheeze and asthma, particularly if exposures were combined. Although skin prick testing with biocides and flour was not conducted in the ALSPAC birth-cohort, 14 of 2066 children (0.7%) developed a weal after

latex skin prick testing at 81 months [20] and these data could be linked to maternal ante and post-natal occupational data for 1719 and 816 mother-child pairs respectively. Despite very small numbers there was a suggestion that latex sensitisation in children was more likely if the mother had high occupational latex exposure at 21 months postpartum: 2/132 (1.5%) of children with high maternal latex exposure vs. 1/646 (0.2%) of children with no maternal latex exposure p=0.076. The data also suggest that wheeze and asthma in later childhood were associated with high intensity paternal occupational exposure to flour dust. The association between paternal occupational flour exposure and later childhood wheeze (30-81 months) is analogous to the time course of occupational asthma in adults when a latent period of exposure before disease manifests is well recognised.

The study hypothesis that the children of workers at risk of occupational asthma are more likely to develop asthma is supported by several studies. Transport home by bakery workers of wheat allergen and α-amylase has been demonstrated, but not related to symptoms in family members [9]. Reports of atopic sensitization to laboratory animals in the children of occupationally exposed parents, suggests that occupational allergens can be transported home and induce atopic sensitization of children [11]. A case of "baker's asthma" in a two-year-old exposed at his grandfather's bakery demonstrates that children can become sensitised to occupational sensitisers and develop asthma [12]. A Danish birth-cohort study reported some maternal jobs during the ante-natal period to be associated with an increased risk of wheeze, asthma and allergic diseases in children aged 14-18 years [6]. Some of the highlighted occupations (bakers, pastry cooks, confectionary makers, dental assistants) entail exposure to latex/biocides and flour. The ALSPAC cohort enabled us to investigate possible differential effects of parental ante-natal and post-natal occupation, and although the early phases of analysis revealed associations between ante-natal occupational exposures and child outcomes,

we were able to demonstrate that these ante-natal associations were a consequence of post-natal exposure and the concordance between ante-natal and post-natal occupation. The Danish study did not have post-natal occupational data. In the absence of post-natal occupational data we would have reported similar associations to the Danish study. In the present study isolated maternal post-natal latex exposure was associated with increased childhood wheeze and asthma. Intriguingly ante-natal and combined ante/post-natal latex exposure did not increase the risk of childhood wheeze or asthma possibly indicating that ante-natal latex exposure induces immunological tolerance to post-natal latex exposure. A similar, but weaker pattern was observed for maternal biocide/fungicide exposure. Although maternal latex/biocide exposure was associated with childhood outcomes there were no associations with paternal latex/biocide exposure. This differential effect of maternal and paternal allergen exposure may reflect differences in the interactions with children between mothers and fathers; a situation analogous to reported differential associations of maternal and paternal smoking habits with respiratory and other health outcomes in their children [21].

The reported associations between maternal exposure and childhood wheezing symptoms were consistent across the 81 month follow up period. Generalised Estimating Equations were used to reduce the number of comparisons performed and the likelihood of chance findings. Even so, the reported associations should be cautiously interpreted, especially in the absence of associations with objective outcomes (ventilatory function, airway responsiveness) and should be the stimulus for further, more definitive studies. A limitation of this study is the potential for confounding because we were unable to quantify individual parental exposures but instead attributed identical occupational exposures to all parents within an occupation. The associations with maternal latex and biocide/fungicide exposure could possibly result from a number of occupation associated factors. Parents exposed to these agents are more

likely to be asthmatic and recognise asthmatic symptoms in their offspring. However, the asthma prevalence in mothers exposed and not exposed to latex/biocides/fungicides did not differ significantly (12.0% vs. 11.1% latex, 11.4% vs. 11.2% biocides/fungicides). Another potential bias was that maternal latex/biocide/fungicide exposures were predominantly among healthcare workers who could be more likely to report symptoms in their children because of their medical background. This seems unlikely because although healthcare workers were more likely than non-healthcare workers to report wheeze and asthma in there children, they were just as likely to report non-respiratory symptoms. Healthcare workers could potentially 'take home' more respiratory viral infections, however the children of non-healthcare mothers in occupations likely to expose them to such infections were not at increased risk of wheezing. We were also able to demonstrate that the children of the small number of mothers exposed to latex and/or biocides/fungicides in non-healthcare professions were more likely to wheeze up to the age of 81 months ($p=0.007$). Although numbers were relatively small, we have highlighted possible adverse associations between paternal occupational exposure to flour dust and childhood respiratory outcomes. Reporting bias associated with a healthcare background is unlikely for flour exposure, but we cannot exclude the possibility of increased domestic use of, and exposure to, flour in the homes of men exposed to flour at work. As expected from a cohort study followed up for 8½ years there was loss to follow up of both parental occupational data and childhood outcomes (90.4% response at 1 month vs 58.2% at 91 months). A number of factors appeared to contribute to the loss of occupational data. For mothers, 85% of those participating at 18 weeks gestation provided occupational data, however only 41% of women participating at 21 months postnatally provided occupational data suggesting a sizeable proportion had not returned to work. Participation by partners was less than for mothers at all stages of the study, however partner occupational data were more complete for those participating at 18 weeks gestation (95%) and 21 months postnatally

(75%). The combination of loss to follow up and incomplete occupational data resulted in reduction in availability of occupational data between ante-natal and postnatal periods (maternal 77% vs. 32% and paternal 65% vs. 37%) and complete data sets from child and mother ante/postnatally from 29% to 23% of those originally participating, and for partners from 34% to 28%. Comparing the children of mothers with occupational data available at 18 weeks gestation only with children of mothers with occupational data available at both 18 weeks gestation and 21 months post-natally revealed no significant differences at any stage of follow up in wheeze symptoms or reported asthma suggesting that the wheeze and asthma profiles of complete and datasets with missing occupational data did not differ. In addition the early life wheezing profiles of those children whose mothers responded to the question about wheeze at 81 months did not significantly differ from those whose mothers failed to respond at 81 months. It would appear that missing parental occupational and childhood symptom data are unlikely to have significantly impacted on the reported associations.

Retrospective exposure assessment is difficult with limited occupational information. Parents in this study provided a job title but no information on chemical exposure, control measures or the tasks performed at work. Our study coded the job titles and constructed a JEM to the main classes of known occupational asthmagens [22] using our experience in other population-based occupational/health studies [18]. As with all JEMs there will be misclassification of exposure because of variability in the intensity of exposure within jobs [23] and our classification methods are likely to be similarly limited. Another source of exposure misclassification results from parental occupation being recorded once during the antenatal and postnatal periods. Consequently for some parents the recorded occupation did not reflect occupational asthmagen exposure for the majority of pregnancy and/or postnatally, eg mothers will have stopped working after 18 weeks gestation. It is therefore almost certain

that some mothers classified as having latex/biocide exposure during pregnancy may not have been so exposed. However, misclassification of actual exposure is likely to be random with respect to childhood outcomes and it is likely that the observed associations with latex/biocides in this study are underestimated than overestimated.

The present study is insufficient to justify changes in work practice. Nevertheless, there is sufficient evidence of a potentially remediable problem to justify further studies. Definitive studies need to objectively assess take-home carriage of allergen in relation to childhood respiratory disease. If occupational allergen carriage home increases the risk of childhood asthma, the implications would be significant. Intervention would be best targeted at the workplace where changing of work clothes or better washing of exposed skin should reduce carriage home. This would confer a greater responsibility on employers to provide better facilities for workers although in many cases better work hygiene practice should be sufficient. In the UK, introduction in the late 1990s of non-powdered, latex free gloves in the NHS has reduced latex exposure significantly, as has the widespread introduction of enclosed sterilizing systems to eliminate glutaraldehyde exposure (the most important biocide in this study). This has been of benefit as reported new cases of both latex and glutaraldehyde induced occupational asthma to the SWORD reporting scheme [24] has fallen in both cases by over 80% in the last decade in the UK. Consequently, as the children in the ALSPAC cohort in the context of this study, were exposed in the mid-1990s before these interventions exerted an effect, further investigation of these routes may not help in elucidating this mechanism. However, SWORD reported flour-induced occupational asthma has remained constant throughout the last 20 years and exploration of carriage home of flour allergens is an area worth pursuing to determine level of home contamination.

This study demonstrates that whilst the respiratory health of children is not affected by parental exposure to most occupational sensitisers, it may be adversely affected by maternal occupational latex and/or biocide/fungicide exposure and paternal occupational flour exposure. Before any changes in occupational hygiene are advocated, these results need to be replicated, and confirmed by studies of domestic exposure to latex, biocides/fungicides and flour.

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Table 1: Subjects included in the analyses

Cohort at	Total n of children	Total number with available childhood outcome data and					
		maternal occupational data			paternal occupational data		
		ante-natally	post-natally	both ante-/ post-natally	ante-natally	post-natally	both ante-/post-natally
0-6 months	11398	9657	4442	3990	8303	5124	4750
6-18 months	11056	9389	4445	3987	8121	5176	4785
18-30 months	10234	8756	4253	3825	7601	4980	4611
30-42 months	9986	8587	4166	3751	7464	4917	4569
42-54 months	9475	8169	3987	3596	7111	4719	4388
54-69 months	8651	7533	3726	3371	6602	4478	4177
69-81 months	8371	7306	3626	3287	6411	4390	4094
91 months	8131	7088	3506	3172	6237	4236	3957

Table 2 Prevalence of childhood wheeze and asthma by age in all children and in children with available parental occupational data

Childhood outcome	Respondants at time point	n (%) *p-value* for significance of difference compared to all children				
		all	Maternal occupation available		Paternal occupation available	
			ante-natal	post-natal	ante-natal	post-natal
Wheeze 0-6 months	11398	2261 (19.8)	1866 (19.3) *0.001*	772 (17.4) *<0.001*	1559 (18.8) *<0.001*	864 (16.9) *<0.001*
Wheeze 6-18 months	11056	2400 (21.7)	1991 (21.2) *0.002*	974 (21.9) *0.669*	1690 (20.8) *<0.001*	1032 (19.9) *<0.001*
Wheezed 18-30 months	10234	1786 (17.5)	1522 (17.4) *0.653*	756 (17.8) *0.466*	1303 (17.1) *0.162*	790 (15.9) *<0.001*
Wheeze 30-42 months	9986	1343 (13.4)	1139 (13.3) *0.180*	568 (13.6) *0.646*	973 (13.0) *0.037*	602 (12.2) *0.001*
Wheeze 42-54 months	9475	1515 (16.0)	1275 (15.6) *0.011*	618 (15.5) *0.268*	1096 (15.4) *0.008*	695 (14.7) *0.001*
Wheeze 54-69 months	8651	1049 (12.1)	895 (11.9) *0.070*	471 (12.6) *0.229*	782 (11.8) *0.305*	526 (11.7) *0.312*
Wheeze 69-81 months	8371	827 (9.9)	700 (9.6) *0.017*	366 (10.1) *0.565*	639 (10.0) *0.626*	418 (9.5) *0.249*
Doctor diagnosed asthma 91 months	8131	1660 (20.4)	1424 (20.1) *0.058*	716 (20.4) *0.990*	1248 (20.0) *0.099*	801 (18.9) *<0.001*

Table 3 Association between intensity of maternal ante-natal and post-natal exposure to latex and biocides/fungicides and childhood wheeze and asthma.

Exposure	Exposure intensity	Wheeze 0-81 months			Doctor diagnosed asthma 91 months		
		N*	OR** (95.0% CI)	p	N$	OR** (95.0% CI)	p
Latex	None	35171	1		5462	1	
Maternal ante-natal	Low	2067	1.01 (0.84-1.23)	*0.001*+	298	1.03 (0.77-1.37)	*0.050*+
	Med	366	1.20 (0.81-1.78)	*(trend)*	68	1.03 (0.56-1.88)	*(trend)*
	High	4909	1.24 (1.09-1.42)		767	1.22 (1.01-1.48)	
Latex	None	17748	1		2639	1	
Maternal post-natal	Low	813	0.86 (0.62-1.20)	*0.008*+	115	1.29 (0.83-2.00)	*<0.001*+
	Med	117	1.59 (0.89-2.86)	*(trend)*	18	1.39 (0.48-4.03)	*(trend)*
	High	3180	1.26 (1.07-1.50)		475	1.46 (1.15-1.85)	
Biocide/fungicide	None	33141	1	*0.004*+	5191	1	*0.206*+
Maternal ante-natal	Low	4924	1.06. (0.93-1.20)	*(trend)*	727	0.96 (0.79-1.17)	*(trend)*
	Med/high	4448	1.23 (1.07-1.40)		672	1.20 (0.98-1.47)	
Biocide/fungicide	None	16206	1	*0.036*+	2421	1	*0.008*+
Maternal post-natal	Low	2788	1.04 (0.87-1.25)	*(trend)*	403	1.08 (0.82-1.40)	*(trend)*
	Med/high	2864	1.22 (1.02-2.05)		418	1.47 (1.14-1.88)	
Latex (high)	No ante, No post	15477	1		1927	1	
Maternal ante-natal	Yes ante, No post	433	1.11 (0.73-1.69)	*0.250*	54	1.04 (0.52-2.07)	*0.910*
and/or post-natal	No ante, Yes post	338	2.21 (1.44-3.39)	*<0.001*	40	2.40 (1.24-4.67)	*0.010*
	Yes ante, Yes post	2555	1.09 (0.90-1.33)	*0.360*	326	1.36 (1.01-1.81)	*0.040*
Biocide/fungicide	No ante, No post	14044	1		1771	1	
(medium)	Yes ante, No post	288	1.23 (0.79-1.93)	*0.360*	35	1.19 (0.53-2.69)	*0.670*
Maternal ante-natal	No ante, Yes post	295	1.56 (0.93-2.61)	*0.090*	38	1.65 (0.80-3.42)	*0.180*
and/or post-natal	Yes ante, Yes post	2233	1.11 (0.90-1.35)	*0.340*	283	1.41 (1.04-1.91)	*0.026*
Latex (any) and/or	No Latex, No Bio	15507	1		1957	1	
biocide/fungicide	Latex only	699	1.02 (0.73-1.43)	*0.910*	78	1.39 (0.81-2.36)	*0.230*
(any)	Bio/fungicide only	2241	1.01 (0.82-1.24)	*0.920*	248	1.09 (0.77-1.53)	*0.640*
Maternal post-natal	Latex & bio/fungicide	3411	1.22 (1.03-1.43)	*0.022*	432	1.47 (1.14-1.47)	*0.003*

* Number of data points of childhood wheezing status summated over the seven follow up ages, included in the GEE model for each level of maternal occupational exposure.

**Adjusted for child's: gender, birth weight, gestational age at delivery; maternal: asthma, age at delivery, parity, highest education qualification, smoking at pregnancy, and home ownership status

$ Number of data points of childhood asthma status at 91 months, included in the logistic regression model for each level of maternal occupational exposure.

+p values labelled (trend) are derived from tests of linear trend across increasing exposure categories, p values not so labelled are for the individual adjacent exposures listed.

Table 4**.** Likelihood of childhood illness/symptoms by maternal post-natal occupation: medically associated occupations* vs. non medical

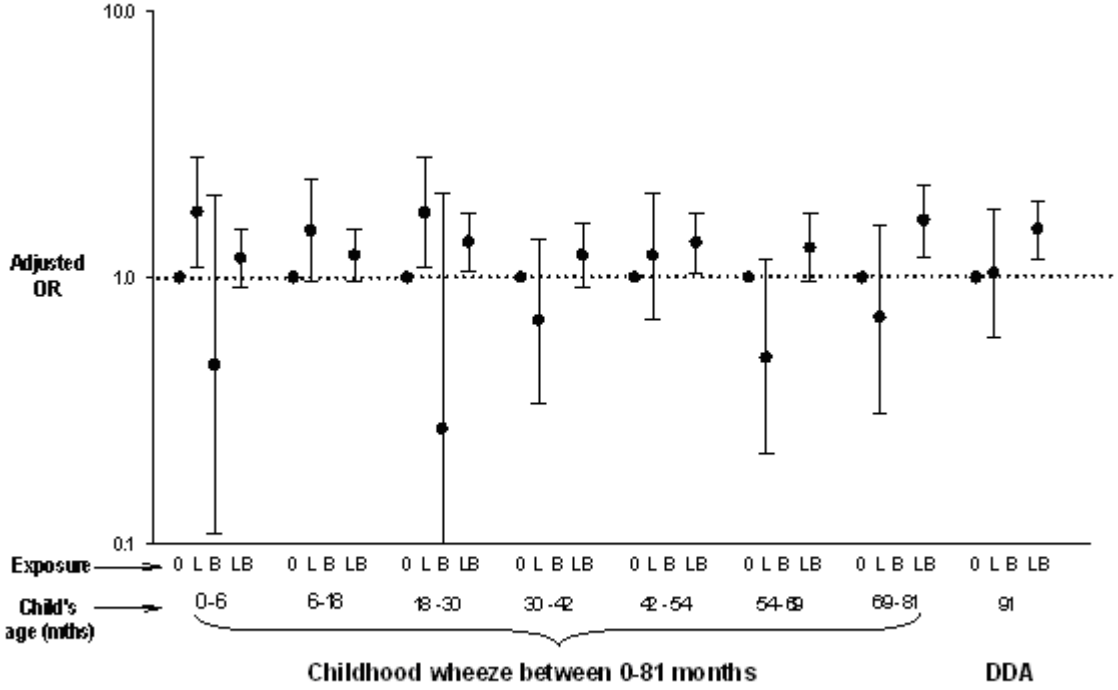
	Odds Ratio (95% CI)	*p*
Wheeze 0-81 months	1.26 (1.08-1.47)	*0.001*
Doctor diagnosed asthma 91 months	1.28 (1.02-1.61)	*0.033*
Ear ache past year at 81 months	1.04 (0.84-1.29)	*0.726*
Ear discharge past year at 81 months	0.99 (0.64-1.54)	*0.974*
Stomach ache past year at 81 months	0.86 (0.71-1.04)	*0.122*
Accident past year at 81 months	1.29 (0.97-1.71)	*0.077*
Hospitalised past year at 81 months	1.06 (0.70-1.61)	*0.781*

*Nurses, nurse auxiliaries and assistants, medical practitioners, and midwives

Figure legend

Figure 1. Association between childhood wheeze and asthma and maternal post-natal combined high-moderate latex and/or biocides/fungicides exposure. Adjusted for child's: gender, birth weight, gestational age at delivery; maternal: asthma, age at delivery, parity, highest education qualification, smoking at pregnancy, and home ownership status (0- neither latex nor biocides/fungicides exposure, L- only latex, B- only biocides/fungicides, LB- both latex and biocides/fungicides exposures, DDA- doctor diagnosed asthma)

For category B- only biocide/fungicide exposure, at age 6-18 months and from the age of 30 months numbers were too small to compute sensible odds ratios and confidence intervals and have been omitted


10.0
1.0
0.1
Adjusted OR
Exposure
0 L B LB
Child's age (mths)
0-6
6-18
18-30
30-42
42-54
54-69
69-81
91
Childhood wheeze between 0-81 months
DDA

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