

ORIGINAL ARTICLE

Perinatal exposure to solvents and wheezing, eczema and food allergies at age 2

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ABSTRACT

Objectives The time from the prenatal period through early childhood is an important window of vulnerability for the developing immune and respiratory systems, both sensitive to environmental chemicals such as solvents. This study sought to examine the effects of solvent exposure during the prenatal and postnatal periods on wheezing, eczema and food allergies in early childhood.

Methods This study, based on the PELAGIE cohort, included 1505 mother–child pairs with measurements of prenatal and postnatal solvent exposures and data on wheezing, eczema or food allergies. The maternal occupation reported at inclusion, in early pregnancy allowed us to define prenatal occupational solvent exposure (by three specific job-exposure matrices). Data on prenatal and postnatal domestic solvent exposure, that is exposure to products that contain solvents, were obtained from self-administered questionnaires, once at inclusion and again when the child was 2 years old. Outcome data was collected at the 2-year follow-up. Associations between exposures and outcomes were estimated by logistic regression models, after adjustment for potential confounders.

Results No association was observed between prenatal exposure to solvents and the outcomes studied. Postnatal exposure was associated with an increased risk of wheezing (OR=1.80 (95% CI 1.25 to 2.59)) which persisted after adjustment for prenatal exposure. No significant association was observed with eczema or food allergies.

Conclusions Postnatal exposure to solvent-containing products in the home may increase the risk of wheezing in early childhood. Follow-up studies are needed to determine if the health effects observed at age 2 persist at later ages.

INTRODUCTION

The prenatal and early childhood period is an important window of vulnerability for the developing immune and respiratory systems, both known to be very sensitive to environmental chemicals.^{1–2} Organic solvents, the immunotoxic properties of which have been shown in animal studies,^{3–5} are in widespread use in occupational and domestic settings. They belong to three main chemical families: oxygenated, petroleum and chlorinated solvents and are found in many products including paints, varnishes, glues, inks, grease removers, cosmetics and cleaning agents. Owing to the fact that solvents can cross the placental barrier, the fetus can be exposed.⁶ Young children are also exposed through dermal contact and inhalation. Solvents are an important component of volatile organic compounds (VOCs), which are major pollutants of

What this paper adds

- The developing immune and respiratory systems are vulnerable to environmental pollutants during the prenatal period and in early childhood.
- Epidemiological studies suggest that both prenatal and postnatal exposure to solvents are associated with an increased risk of respiratory and allergic symptoms during childhood, but few studies have taken these two periods of exposure into account simultaneously.
- Our cohort study shows that early prenatal exposure to solvents is not associated with wheezing, eczema or food allergies in early childhood, but that postnatal exposure may increase the risk of wheezing.

indoor air. Some studies have focused on the respiratory/allergic health effect of VOCs,^{7–8} or of exposure to renovation activities^{9–11} (shown to be a surrogate for VOCs exposure¹²) during perinatal life. They suggest an increased risk of wheezing^{9–10} or eczema¹¹ and allergy^{7–11} in children but, they did not assess the specific effects of solvents.

More specifically, one cohort study focused on prenatal occupational exposure to organic solvents and showed an association with allergic rhinitis but not with wheezing or eczema in childhood.¹³ Two other cohort studies have evaluated the effect of prenatal and postnatal exposure to products known to contain solvents (glues exposure in occupational setting¹⁴ and household use of cleaning products¹⁵). The first study did not find any association with wheezing or atopy¹⁴ while the second reported an increased risk of wheezing associated with both prenatal and postnatal solvent exposure.¹⁵ Several other surveys focused on exposure during the postnatal period only to products known to contain solvents (paints)^{16–17} or specific VOCs known to be used as solvents (such as toluene and benzene)^{18–22}; most of them found an increased risk of wheezing,¹⁶ asthma,^{18–19} eczema²⁰ and IgE sensitisation.²¹

To our knowledge, no published study has assessed the respiratory and immunological health effects of solvent exposure from both occupational and domestic settings during both the prenatal and postnatal periods. Our aim was to examine the effects of detailed perinatal solvent exposure on

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wheezing, eczema and food allergies in children during the first 2 years of life.

MATERIALS AND METHODS

Study population

The French PELAGIE cohort, fully described elsewhere,^{23 24} included 3421 pregnant women recruited before 19 weeks of gestation by gynaecologists or ultrasonographers in three districts of Brittany between 2002 and 2006. At inclusion, the women completed a self-administered questionnaire about their social and medical characteristics, lifestyle as well as occupation. At birth, medical information about pregnancy and birth outcomes was obtained from the medical staff. Around the time of the children's second birthday, we sent questionnaires to the 2996 eligible mother-child pairs (liveborn singletons, excluding those where mother or child had died (n=7) or the child was already older than 2.5 years (n=320)). These questionnaires were intended to collect socioeconomic and demographic characteristics and health and lifestyle information about the children and their parents. Of the 2996 eligible mothers, 770 could not be reached because of incorrect or no-longer-valid mailing addresses. Of the remaining 2226 mothers, 1505 (68%) mailed the completed questionnaire back to us with data available for at least one solvent exposure assessment and at least one outcome of interest. Participants provided informed consent for data collection, and the INSERM ethics committees approved the study procedures.

Solvent exposure assessment

Three types of child solvent exposures were defined according to the period (prenatal/postnatal) and the setting of exposure (occupational/domestic), classified as prenatal occupational exposure, prenatal domestic exposure and postnatal (domestic) exposure.

Prenatal occupational exposure was evaluated at the beginning of pregnancy, according to the job reported at inclusion, by three specific job-exposure matrices (JEMs) built by the occupational health department of the French Institute for Public Health Surveillance as part of the Matg  n   programmes.²⁵⁻²⁸ These JEMs assign a level of exposure to oxygenated, petroleum or chlorinated solvents by a combination of two codes: one occupation code²⁹ and one code of industrial activity.³⁰ Five categories of exposure were then defined according to the probability, the frequency and the intensity of exposure. Owing to the small number of women at the four higher levels of exposure, these five levels were finally combined into two categories (exposed or unexposed) for each of the three solvent families.

Prenatal domestic exposure corresponds to exposure, self-reported by mothers at inclusion, to chemical products considered to contain solvents (paint, glues, varnishes, wood treatment products, remover products or diluents) at home in the previous 3 months. Women exposed to at least one product classified the child as prenatally exposed.

Postnatal exposure was defined by the use, reported by mothers at the 2-year follow-up, of chemical products known to contain solvents (paints, glues, varnishes or solvents themselves) in the home since the child's birth. The use of at least one product classified the child as postnatally exposed.

Two composite variables were created from these variables. The first one combined children's prenatal and postnatal domestic exposure in four categories: not exposed either prenatally or postnatally, exposed prenatally but not postnatally, not exposed prenatally but exposed postnatally and exposed both prenatally and postnatally. The second variable combined prenatal

exposure regardless of the setting (occupational or domestic) and postnatal exposure with these same four categories.

Assessment of wheezing, eczema and food allergies

At the 2-year follow-up, the child's principal caregiver, usually the mother (98%), completed a questionnaire intended to evaluate the child's health since birth. Three outcomes were considered: wheezing, eczema and food allergies.

Wheezing was identified with five questions. Two were adapted from the International Study of Asthma and Allergies in Childhood (ISAAC) questionnaire³¹: (1) 'Has your child ever had wheezing or whistling in the chest at any time in the past?'; (2) 'Has your child ever had a medical diagnosis of asthma?' The three other questions sought to complete the wheeze assessment; (3) 'Did your child have an asthma attack before the age of 1 year?'; (4) 'Has your child had an asthma attack since he or she reached the age of 1 year?' and (5) 'Has your child ever had bronchiolitis or bronchitis?' Positive responses to at least one of the first four questions classified the child in the 'certain wheeze' category. The 'no wheeze' group included all children for whom all responses were negative. In France, wheeze before the age of two is often reported as bronchiolitis, while bronchitis does not involve wheeze symptoms. As the fifth question mixes these two diagnoses, it did not allow us to disentangle children with wheeze from those without wheeze. A positive response to this question only therefore led us to place the child in the 'probable wheeze' category.

Eczema was identified by a positive answer to both of the following questions (from the ISAAC questionnaire): 'Has your child ever had an itchy skin rash, which was coming and going?' and 'If yes, has this itchy rash affected any of the following places—the folds of the elbows, behind the knees, in front of the ankles, under the buttocks or around the neck, ears or eyes?' A positive answer to the single question 'Has your child ever had a medical diagnosis of eczema?' also identified the presence of eczema.

The presence of food allergies was identified by a positive answer to any one of the following three questions: 'Has your child ever had a medical diagnosis of cow's milk allergy?' 'Has your child ever had a medical diagnosis of any food allergies?' 'Has your child ever had an allergic reaction after eating food (swollen lips or face, gastrointestinal response)?' For the last question, time to the allergic reaction and the type of food involved were verified.

Statistical analysis

The associations between solvent exposures and outcomes were estimated by polytomous logistic regression for wheezing and binary logistic regression for eczema and food allergies, with the no-symptom group as the reference. Each category of exposure (prenatal occupational exposure, prenatal domestic exposure and postnatal exposure) was analysed separately, then integrated into a single model and finally with composite variables.

Each model was adjusted for a set of covariates. Variables known to be associated with each outcome were systematically included as potential confounders: mother's age (continuous), child's sex, child's age at follow-up (continuous) and family history of asthma or allergy (yes, no) for all three outcomes, prenatal (0, 1–5 cigarettes/day, ≥ 5 cigarettes/day) and postnatal (0, 1–20 cigarettes/day, ≥ 20 cigarettes/day) tobacco exposure, and preterm birth (<37 weeks of gestation) for wheezing and small-for-gestational age (<10th centile of the French birth weight distribution for gestational age and sex) for eczema. Additional variables were considered: maternal educational level

(≤ 12 , >12 years), maternal body mass index before pregnancy (<18.5 , 18.5 to <25 , 25 to <30 , ≥ 30 kg/m²), maternal prenatal alcohol consumption (never, occasionally or more), maternal fish ($<$ once a month, $1-4$ times a month, ≥ 4 times a month) and shellfish ($<$ once a month, $\geq$ once a month) consumption before pregnancy, caesarean section (yes, no), number of siblings at birth (0, 1, ≥ 2), feeding during the first 3 months of life (exclusive formula feeding, mixed, exclusive breast feeding), attendance at group daycare (yes, no), contact with farm animals (yes, no), presence of pets at home (yes, no), dampness and mould at home (yes, no) and proximity to a road with heavy traffic <200 m (yes, no). Variables related with outcomes with a p value <0.20 in the univariate analysis were then included in the multivariate model. Interactions with family history of allergy and with prenatal or postnatal tobacco consumption were tested. To handle missing data among covariates, a missing modality was coded. Results are reported as ORs and 95% CIs. Statistical analyses were performed with SAS software V.9.3 (SAS institute).

RESULTS

Compared with participants at the 2-years follow-up, the women lost to follow-up ($n=1491$) were younger at birth of the PELAGIE child, less educated and more likely to smoke during pregnancy. They also reported less occupational exposure to chlorinated ($p=0.056$) and oxygenated solvents ($p=0.054$) and less domestic exposure during pregnancy ($p=0.050$), but did not differ in terms of petroleum solvent exposure ($p=0.980$).

Mothers' mean age at delivery was 31 (± 4.2) years. Most had a high educational level; 13.7% reported smoking 1–5 cigarettes/day and 11.9% more than 5 cigarettes/day at the beginning of pregnancy, 15.3% reported consuming alcohol during pregnancy. Most of their children were born at term, by vaginal delivery, with a normal birth weight for gestational age (table 1).

Among the 1505 women in the study population, 1366 reported working at the beginning of pregnancy. Table 2 and web-only file 1 describe occupational exposures during pregnancy: 23.1% were classified as exposed to oxygenated solvents ($n=312$, mainly nurses (31.4%), cleaners and helpers (21.1%), nurses' aides (18.3%) and physicians (11.5%)), 10.7% to petroleum solvents ($n=145$, mainly cleaners and helpers (45.5%) and chemists and biologists (25.5%)) and 3.6% to chlorinated solvents ($n=49$, mainly chemists and biologists (83.7%)). Only 1.6% of the women were considered exposed to all three solvent families ($n=22$). Overall, the women worked until an average of 26.6 (± 7.1) weeks of gestation; half stopped working during the period between 22.6 and 32.1 weeks of gestation (median=28 weeks).

Prenatal domestic exposure concerned 16.3% of children ($n=235$), while 69.7% were postnatally exposed ($n=1009$; table 2). A positive association between these domestic exposures was observed ($p<0.001$): 80.5% of children exposed during the prenatal period were postnatally exposed, while 32.3% of those not exposed during the prenatal period were also not exposed postnatally. Whatever the setting of exposure (occupational or domestic), 10.8% ($n=138$) children were exposed only during the prenatal period and 39.3% ($n=501$) only during the postnatal period.

Table 3 presents results about outcome variables. The three outcomes were positively associated: wheezing and eczema ($p=0.003$), wheezing and food allergies ($p=0.04$) and eczema and food allergies ($p<0.001$).

Tables 4 and 5 describe the associations between solvent exposures and outcomes. When exposure variables were introduced separately into the statistical model, no association was observed between prenatal solvent exposure—occupational or domestic—

Table 1 Description of study population at the 2-year follow-up ($n=1505$, PELAGIE cohort, France, 2002–2006)

	Number (%)
<i>Maternal characteristics</i>	
Maternal age at birth (years)	31.0 (4.2)*
Educational level	
Primary or secondary education	220 (14.7)
Baccalaureate	278 (18.5)
Higher education	1003 (66.8)
BMI before pregnancy	
<18.5	97 (6.5)
$18.5-25$	1139 (75.9)
$25-30$	193 (12.9)
≥ 30	71 (4.7)
Family history of allergy (yes)†	374 (29.6)
<i>Child's characteristics</i>	
Child's age at follow-up (months)	26.7 (2.2)*
Sex (male)	777 (51.7)
Caesarean delivery (yes)	258 (17.5)
Preterm birth (<37 weeks)	49 (3.3)
Small-for-gestational-age (<10 th centile)	78 (5.2)
Number of siblings (≥ 2)	851 (56.9)
<i>Environmental characteristics</i>	
Tobacco exposure	
Tobacco smoke at the beginning of pregnancy	
No	1114 (74.4)
Yes	384 (25.6)
Number of cigarettes/day at home after birth	
0	884 (61.3)
1–20	467 (32.4)
>20	90 (6.3)
Feeding during the first 3 months	
Formula only	508 (34.5)
Mixed feeding	437 (29.7)
Breast feeding only	528 (35.8)
Daycare attendance (group)††	154 (11.0)
Contact with farm animals (yes)	464 (31.0)
Pets at home (yes)	768 (52.1)
Alcohol consumption during pregnancy (occasionally or more)	228 (15.3)
Maternal fish consumption	
<1 time a month	252 (16.8)
$1-4$ times a month	815 (54.3)
≥ 4 times a month	433 (28.9)
Maternal shellfish consumption	
<1 time a month	1006 (67.0)
≥ 1 time a month	496 (33.0)
Mould and/or dampness at home (yes)	46 (3.2)
Proximity <200 m to a road with heavy traffic (yes)	308 (20.7)

*Mean (SD).

Missing values: † $n=240$, †† $n=106$, $n<70$ for other variables.

BMI, body mass index.

and outcomes (table 4). Postnatal exposure was associated with an increased risk of 'certain wheezing' after adjustment for potential confounders. No association was observed between postnatal exposure and either eczema or food allergies. When all three types of exposure were included in the same model, results were similar (ORs did not differ by more than 15%; table 5). Analyses performed with composite exposure variables show that prenatal-only solvent exposure was not associated with any of the outcomes while postnatal-only and combined prenatal and

Environment

Table 2 Solvent exposures description (PELAGIE cohort, France, 2002–2006)

	Number (%)
Prenatal occupational exposure* (in women who reported working at the beginning of pregnancy; n=1366)	
Oxygenated solvent (yes)	312 (23.1)
Petroleum solvent (yes)	143 (10.7)
Chlorinated solvent (yes)	49 (3.6)
Domestic exposure†	
Prenatal (yes)	235 (16.3)
Postnatal (yes)	1009 (69.7)
Combined prenatal and postnatal domestic exposures	
Not exposed either prenatally or postnatally	374 (27.0)
Exposed prenatally, not exposed postnatally	45 (3.2)
Not exposed prenatally, exposed postnatally	784 (56.4)
Exposed both prenatally and postnatally	186 (13.4)
Combined prenatal domestic and occupational exposures and postnatal domestic exposure	
Not exposed either prenatally or postnatally	251 (19.7)
Exposed prenatally, not exposed postnatally	138 (10.8)
Not exposed prenatally, exposed postnatally	501 (39.3)
Exposed both prenatally and postnatally	384 (30.1)

*Oxygenated, petroleum and chlorinated solvent exposure available, respectively, for n=1357, 1334 and 1335 children.

†Prenatal and postnatal domestic exposure available, respectively, for n=1442 and 1447 children.

postnatal solvent exposure were both associated with an increased risk of ‘certain wheezing’ (table 4).

DISCUSSION

This study suggests that postnatal exposure to products known to contain solvents is associated with a higher risk of wheezing during the first 2 years of life. No association was observed with eczema and food allergies. Prenatal exposure was not associated with any of the outcomes studied.

Our results for prenatal exposure are consistent with two previous cohort studies that did not show any association between prenatal occupational exposure (domestic exposure not evaluated) to products known to contain solvents evaluated in early pregnancy (18 weeks of gestation)¹⁴ or as long as the women continue to work¹³ and the risk of wheezing^{13 14} or eczema¹³ in early childhood. To our knowledge, only one cohort study, that evaluated only respiratory symptoms, has shown an association between wheezing and prenatal household exposure (occupational exposure not evaluated), during the third trimester of pregnancy, to products known to contain solvents (cleaning products) and wheezing.¹⁵ The latter study also observed an increased risk of wheezing when exposure occurred during the first year of life. This observation is consistent with our results and one other study that has reported a positive association

between postnatal painting exposure and wheezing in early childhood.¹⁶ In addition, postnatal exposure to VOCs known to be used as solvents (toluene, benzene) appears to increase the risk of wheezing.^{18 19} However, contrary to suggestions in two epidemiological studies,^{20 21} we found no association between postnatal exposure and eczema and food allergies.

The exposure period (prenatal and postnatal) explored in this study is well known for its vulnerability (from the first weeks of pregnancy) to environmental factors that interfere with immune maturation.¹ Previous work suggests that solvents may modify immune system development through T-cell polarisation toward the Th2 phenotype; this modification appears to promote type 1 hypersensitivity and thereby the occurrence of allergic disorders.^{21 32} We therefore expected positive associations between exposure to solvents and eczema and food allergies, which usually involve these mechanisms. However, the study limitations described below may explain our non-significant results.

At age two, wheezing is not necessarily of allergic origin, and solvents may also interact via non-immunological pathways, for respiratory system development begins in utero and continues until adolescence.^{2 33} Many toxicants are known to affect airway development during this period of maturation.^{1 33 34} The consequences on the structure and the function of the respiratory system may be particularly strong during the third trimester of pregnancy and during the early postnatal period because of the development of pulmonary alveoli, the units of gas exchanges.^{2 33} This window of vulnerability for respiratory system development may explain the non-significant association we observed between prenatal solvent exposure and wheeze. Prenatal occupational solvent exposure was evaluated at inclusion and, pregnant women rarely changed job or tasks during pregnancy, then, occupational solvent exposure was stable as long as the women worked.³⁵ However, both our descriptive results about the duration of occupational activities during pregnancy and the legal length of maternity leave in France (starting at the end of the 35th week of gestation for the first and second pregnancies and at the end of the 33rd week for subsequent pregnancies), indicate that few women are occupationally exposed during the critical window. For prenatal domestic exposure, the assessment, which covered only a 3-month period in early pregnancy, did not allow us to estimate exposure in the second and third trimester of pregnancy, especially once the women stopped working and were at home all day. The specific time of prenatal solvent exposure evaluation chosen in the various studies—before 19 weeks in ours, 18 weeks of gestation in Tagiyeva *et al*, until the women stop working in Magnusson *et al* and the third trimester for Casas *et al*—may explain why only Casas *et al* observed a positive association.

Exposure assessment presents other limitations: only few women reported high level of occupational solvent exposure, leading us to combine the five levels of exposure into two categories (exposed or unexposed); solvents were not measured directly, and we cannot rule out the possibility that the association with postnatal exposure reported in this study might be due to exposure to other toxicants present in the environment with solvents.

Another limitation of the study is the attrition at follow-up. The questionnaire was self-administered, sent by the postal service, and quite long to fill out (about 2 h). Each of these factors may have discouraged participation. Non-respondents at follow-up reported lower prenatal domestic exposure and lower occupational exposure to oxygenated and chlorinated solvents and shared the characteristics of families with a higher prevalence of child respiratory or allergic problems; their absence is thus likely to have induced bias in the estimation of the

Table 3 Wheezing, eczema and food allergies description (n=1505, PELAGIE cohort, France, 2002–2006)

	Number	Per cent
Wheezing (n=1496)		
Certain wheeze	301	20.1
Probable wheeze	657	43.9
Eczema (yes) (n=1492)	477	32.0
Food allergies (yes) (n=1492)	136	9.1

Table 4 Association between solvent exposures and wheezing, eczema and food allergies (PELAGIE cohort, France, 2002–2006)

	Respiratory symptoms*			
	Probable wheeze OR (95% CI)	Certain wheeze OR (95% CI)	Eczemat† OR (95% CI)	Food allergies‡ OR (95% CI)
<i>Occupational exposure</i>				
Oxygenated solvent	n=1257		n=1314	n=1336
No	Ref.	Ref.	Ref.	Ref.
Yes	1.08 (0.79 to 1.47)	1.34 (0.91 to 1.95)	0.89 (0.67 to 1.18)	1.16 (0.74 to 1.82)
Petroleum solvent	n=1240		n=1292	n=1316
No	Ref.	Ref.	Ref.	Ref.
Yes	1.01 (0.66 to 1.53)	0.98 (0.58 to 1.68)	0.84 (0.57 to 1.25)	1.09 (0.55 to 2.13)
Chlorinated solvent	n=1241		n=1293	n=1317
No	Ref.	Ref.	Ref.	Ref.
Yes	0.71 (0.36 to 1.42)	0.99 (0.43 to 2.25)	0.85 (0.44 to 1.63)	0.95 (0.33 to 2.72)
<i>Prenatal domestic exposure</i>				
No	n=1333		n=1397	n=1421
Yes	Ref.	Ref.	Ref.	Ref.
Yes	1.03 (0.73 to 1.45)	1.34 (0.89 to 2.03)	1.13 (0.83 to 1.55)	1.11 (0.69 to 1.80)
<i>Postnatal domestic exposure</i>				
No	n=1341		n=1403	n=1426
Yes	Ref.	Ref.	Ref.	Ref.
Yes	1.22 (0.93 to 1.60)	1.80 (1.25 to 2.59)	1.10 (0.86 to 1.42)	1.32 (0.86 to 2.03)
<i>Combined prenatal and postnatal domestic exposures</i>				
Not exposed either prenatally or postnatally	n=1287		n=1346	n=1368
Exposed prenatally, not exposed postnatally	Ref.	Ref.	Ref.	Ref.
Exposed prenatally, not exposed postnatally	0.53 (0.26 to 1.09)	0.89 (0.34 to 2.31)	0.72 (0.35 to 1.50)	1.25 (0.41 to 3.80)
Not exposed prenatally, exposed postnatally	0.99 (0.74 to 1.32)	1.66 (1.11 to 2.47)	1.03 (0.79 to 1.36)	1.28 (0.80 to 2.03)
Exposed both prenatally and postnatally	1.28 (0.83 to 1.98)	2.50 (1.45 to 4.33)	1.23 (0.84 to 1.82)	1.32 (0.71 to 2.46)
<i>Combined prenatal domestic and occupational exposures and postnatal domestic exposure</i>				
Not exposed either prenatally or postnatally	n=1187		n=1235	n=1257
Exposed prenatally, not exposed postnatally	Ref.	Ref.	Ref.	Ref.
Exposed prenatally, not exposed postnatally	0.84 (0.52 to 1.38)	1.61 (0.83 to 3.14)	0.85 (0.53 to 1.35)	0.74 (0.32 to 1.74)
Not exposed prenatally, exposed postnatally	1.04 (0.73 to 1.48)	1.84 (1.11 to 3.06)	0.93 (0.67 to 1.29)	1.05 (0.61 to 1.82)
Exposed both prenatally and postnatally	1.23 (0.84 to 1.79)	2.60 (1.53 to 4.39)	0.95 (0.67 to 1.35)	1.31 (0.75 to 2.28)

*Adjusted for maternal age at birth, child's age, child's sex, family history of allergy, prenatal and postnatal tobacco exposure, preterm birth, number of siblings at birth, type of delivery, daycare attendance, and fish consumption.

†Adjusted for maternal age at birth, child's age, child's sex, family history of allergy, SGA (small-for-gestational-age), type of feeding during the first 3 months and daycare attendance.

‡Adjusted for maternal age at birth, child's age, child's sex, family history of allergy, educational level, daycare attendance, fish and shellfish consumption.

association between prenatal exposure to solvents and wheezing, eczema or food allergies and may explain our non-significant results. Moreover, measures of wheeze and eczema

were adapted from the ISAAC questionnaire. Although this method has only been validated for children aged 7 years and up,³¹ it is widely accepted in epidemiological studies among

Table 5 Association between postnatal solvent exposure and wheezing, eczema and food allergies adjusted for prenatal solvent exposures (PELAGIE cohort, France, 2002–2006)

	Respiratory symptoms*		Eczema† OR (95% CI)	Food allergies‡ OR (95% CI)
	Probable wheeze OR (95% CI)	Certain wheeze OR (95% CI)		
Postnatal exposure§	n=1166		n=1218	n=1237
No	Ref.	Ref.	Ref.	Ref.
Yes	1.17 (0.88 to 1.56)	1.81 (1.22 to 2.68)	1.00 (0.77 to 1.31)	1.25 (0.79 to 1.98)
Postnatal exposure¶	n=1151		n=1199	n=1220
No	Ref.	Ref.	Ref.	Ref.
Yes	1.18 (0.88 to 1.57)	1.76 (1.18 to 2.61)	0.95 (0.73 to 1.24)	1.24 (0.78 to 1.96)
Postnatal exposure**	n=1152		n=1200	n=1221
No	Ref.	Ref.	Ref.	Ref.
Yes	1.18 (0.88 to 1.58)	1.77 (1.19 to 2.63)	0.95 (0.72 to 1.24)	1.24 (0.78 to 1.96)

*Adjusted for maternal age at birth, child's age, child's sex, family history of allergy, prenatal and postnatal tobacco exposure, preterm birth, number of siblings at birth, type of delivery, daycare attendance, fish consumption.

†Adjusted for maternal age at birth, child's age, child's sex, family history of allergy, SGA (small-for-gestational-age), type of feeding during the first 3 months, daycare attendance.

‡Adjusted for maternal age at birth, child's age, child's sex, family history of allergy, educational level, daycare attendance, fish and shellfish consumption.

§Model adjusted for prenatal occupational (oxygenated solvents) and prenatal domestic exposure.

¶Model adjusted for prenatal occupational (petroleum solvents) and prenatal domestic exposure.

**Model adjusted for prenatal occupational (chlorinated solvents) and prenatal domestic exposure.

younger children.^{36–39} There was no confirmation of reports of outcomes by clinical examination or biological markers for atopy. These unsupervised methods may induce non-differential misclassification.

To our knowledge, our study is the first to investigate both occupational and domestic exposure during the prenatal and postnatal periods of vulnerability for the developing immune and respiratory systems, related to wheezing, eczema and food allergies. Since we, like most studies on this topic, used a cross-sectional assessment of the impact of postnatal exposures, the temporal relation between postnatal exposure and outcomes could not be established. However, unlike these studies, we took prenatal exposures into account. Moreover, the JEMs, considering current occupations and specific to the French population, enabled us to distinguish the three most common families of organic solvents.

CONCLUSION

In line with previous studies, our results suggest that postnatal exposure to products that contain solvents in the home is associated with an increased risk of wheezing in early childhood. Toxic exposure during the critical period of lung development in early childhood may be involved. Further studies that measure solvent exposure more objectively at different periods during pregnancy and after birth, using a prospective design are warranted. The question of the long-term consequences of early childhood exposure to solvents, in particular on the onset of asthma, should also be considered. The public health significance of these results may be substantial in view of the high prevalence of solvent exposure in dwellings.

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Contributors EB conducted the statistical analyses and wrote the first draft of the manuscript. CM and FR were responsible for the field study including questionnaires and medical data. RG and SC reviewed and revised the manuscript. SC designed the cohort and supervised the overall PELAGIE project. FP supervised this study, reviewed and revised the manuscript. All authors saw and approved the final manuscript.

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REFERENCES

- Dietert RR, Etzel RA, Chen D, *et al.* Workshop to identify critical windows of exposure for children's health: immune and respiratory systems work group summary. *Environ Health Perspect* 2000;108:483–90.
- Kajekar R. Environmental factors and developmental outcomes in the lung. *Pharmacol Ther* 2007;114:129–45.
- Seo M, Yamagawa T, Kobayashi R, *et al.* Augmentation of antigen-stimulated allergic responses by a small amount of trichloroethylene ingestion from drinking water. *Regul Toxicol Pharmacol* 2008;52:140–6.
- Satou N, Ishihara K, Hiratsuka M, *et al.* Induction of thymic stromal lymphopoietin production by xylene and exacerbation of picryl chloride-induced allergic inflammation in mice. *Int Arch Allergy Immunol* 2012;157:194–201.
- Fujimaki H, Win-Shwe T-T, Yoshida Y, *et al.* Dysregulation of immune responses in an allergic mouse model following low-level toluene exposure. *Toxicology* 2011;286:28–35.
- Rinaldo M. Barrière placentaire: état des connaissances sur l'exposition du fœtus aux xénobiotiques. In: *Grossesse et travail Quels sont les risques pour l'enfant à naître?* EDP Sciences, France: 2010:66–72.
- Lehmann I, Thøelke A, Rehagen M, *et al.* The influence of maternal exposure to volatile organic compounds on the cytokine secretion profile of neonatal T cells. *Environ Toxicol* 2002;17:203–10.
- Venn A, Cooper M, Antoniak M, *et al.* Effects of volatile organic compounds, damp, and other environmental exposures in the home on wheezing illness in children. *Thorax* 2003;58:955–60.
- Diez U, Rehagen M, Rolle-Kampczyk U, *et al.* Redecoration of apartments promotes obstructive bronchitis in atopy risk infants—results of the LARS Study. *Int J Hyg Environ Health* 2003;206:173–9.
- Jaakkola JJK, Parise H, Kisilitsin V, *et al.* Asthma, wheezing, and allergies in Russian schoolchildren in relation to new surface materials in the home. *Am J Public Health* 2004;94:560–2.
- Herbarth O, Fritz GJ, Rehagen M, *et al.* Association between indoor renovation activities and eczema in early childhood. *Int J Hyg Environ Health* 2006;209:241–7.
- Heinrich J. Influence of indoor factors in dwellings on the development of childhood asthma. *Int J Hyg Environ Health* 2011;214:1–25.
- Magnusson LL. Wheezing, asthma, hay fever, and atopic eczema in relation to maternal occupations in pregnancy. *Occup Environ Med* 2006;63:640–6.
- Tagiyeva N, Devereux G, Semple S, *et al.* Parental occupation is a risk factor for childhood wheeze and asthma. *Eur Respir J* 2009;35:987–93.
- Casas L, Zock JP, Carsin AE, *et al.* The use of household cleaning products during pregnancy and lower respiratory tract infections and wheezing during early life. *Int J Public Health* 2013;58:757–64.
- Emenius G, Svartengren M, Korsgaard J, *et al.* Indoor exposures and recurrent wheezing in infants: a study in the BAMSE cohort. *Acta Paediatr* 2004;93:899–905.
- Trevillian LF, Ponsonby A-L, Dwyer T, *et al.* Infant sleeping environment and asthma at 7 years: a prospective cohort study. *Am J Public Health* 2005;95:2238–45.
- Rumchev K. Association of domestic exposure to volatile organic compounds with asthma in young children. *Thorax* 2004;59:746–51.
- Hulin M, Caillaud D, Annesi-Maesano I. Indoor air pollution and childhood asthma: variations between urban and rural areas. *Indoor Air* 2010;20:502–14.
- Choi H, Schmidbauer N, Sundell J, *et al.* Common household chemicals and the allergy risks in pre-school age children. *PLoS ONE* 2010;5:e13423.
- Lehmann I, Rehagen M, Diez U, *et al.* Enhanced in vivo IgE production and T cell polarization toward the type 2 phenotype in association with indoor exposure to VOC: results of the LARS study. *Int J Hyg Environ Health* 2001;204:211–21.
- Diez U, Kroessner T, Rehagen M, *et al.* Effects of indoor painting and smoking on airway symptoms in atopy risk children in the first year of life results of the LARS-study. Leipzig Allergy High-Risk Children Study. *Int J Hyg Environ Health* 2000;203:23–8.
- Guldner L, Monfort C, Rouget F, *et al.* Maternal fish and shellfish intake and pregnancy outcomes: a prospective cohort study in Brittany, France. *Environ Health Glob Access Sci Source* 2007;6:33.
- Garlantézec R, Monfort C, Rouget F, *et al.* Maternal occupational exposure to solvents and congenital malformations: a prospective study in the general population. *Occup Environ Med* 2009;66:456–63.
- Groupe de travail Matgéné. Institut de Veille Sanitaire. Matrice emploi-exposition à au moins un solvant chloré. 2009. <http://exppro.invs.sante.fr>
- Groupe de travail Matgéné. Institut de Veille Sanitaire. Matrice emploi-exposition à au moins un solvant pétrolier. 2009. <http://exppro.invs.sante.fr>
- Groupe de travail Matgéné. Institut de Veille Sanitaire. Matrice emploi-exposition à au moins un solvant oxygéné. 2013. <http://exppro.invs.sante.fr>
- Félotte J, Dananché B, Delabre L, *et al.* Matgéné: a program to develop job-exposure matrices in the general population in France. *Ann Occup Hyg* 2011;55:865–78.
- International Labour Organization. *International standard classification of occupations*. 1968. <http://laborsta.ilo.org/applv8/data/isco68e.html> accessed Jul 2014.
- Insee. *Nomenclature des activités françaises, NAF*. NAF-CPF, Journal Officiel, fascicule n° 1402, édition novembre, Paris, 1999. <http://www.insee.fr/fr/methodes/default.asp?>
- ISAAC. The International Study of Asthma and Allergies in Childhood: Phase one manual. <http://isaac.auckland.ac.nz/phases/phaseone/phaseonemannual.pdf>
- Crinnion WJ. Do environmental toxicants contribute to allergy and asthma? *Altern Med Rev J Clin Ther* 2012;17:6–18.
- Harding R, Maritz G. Maternal and fetal origins of lung disease in adulthood. *Semin Fetal Neonatal Med* 2012;17:67–72.
- Plopper CG, Smiley-Jewell SM, Miller LA, *et al.* Asthma/allergic airways disease: does postnatal exposure to environmental toxicants promote airway pathobiology? *Toxicol Pathol* 2007;35:97–110.
- Pelé F, Muckle G, Costet N, *et al.* Occupational solvent exposure during pregnancy and child behaviour at age 2. *Occup Environ Med* 2013;70:114–19.
- Leermakers ETM, Sonnenschein-van der Voort AMM, Heppe DHM, *et al.* Maternal fish consumption during pregnancy and risks of wheezing and eczema in childhood: the Generation R Study. *Eur J Clin Nutr* 2013;67:353–9.
- Caudri D, Wijga A, Gehring U, *et al.* Respiratory symptoms in the first 7 years of life and birth weight at term: the PIAMA Birth Cohort. *Am J Respir Crit Care Med* 2007;175:1078–85.
- Willers SM, Devereux G, Craig LCA, *et al.* Maternal food consumption during pregnancy and asthma, respiratory and atopic symptoms in 5-year-old children. *Thorax* 2007;62:773–9.
- Pelé F, Bajoux E, Gendron H, *et al.* Maternal fish and shellfish consumption and wheeze, eczema and food allergy at age two: a prospective cohort study in Brittany, France. *Environ Health Glob Access Sci Source* 2013;12:102.



Perinatal exposure to solvents and wheezing, eczema and food allergies at age 2

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Supplementary materials.

Occupational activities and solvent exposure (n=1366)

	n (%)	JEM-assessed exposure		
		Oxygenated (Yes) n (%)	Petroleum (Yes) n (%)	Chlorinated (Yes) n (%)
Professional, technical, and related workers				
Medical, dental, veterinarians, pharmacists	95 (7.0)	36 (37.9)	0 (0.0)	0 (0.0)
Nurses, midwives, medical x-ray technicians	110 (8.1)	98 (89.1)	0 (0.0)	0 (0.0)
Architects, engineers, and related technicians	38 (2.8)	4 (10.5)	3 (7.9)	0 (0.0)
Statisticians, mathematicians, system analysts	33 (2.4)	0 (0.0)	0 (0.0)	0 (0.0)
Teachers	161 (11.9)	0 (0.0)	0 (0.0)	0 (0.0)
Social workers	26 (1.9)	0 (0.0)	0 (0.0)	0 (0.0)
Chemists, biologists, and related workers	48 (3.5)	15 (31.2)	37 (77.1)	41 (85.4)
Lawyers, journalists, and related workers	71 (5.2)	0 (0.0)	0 (0.0)	0 (0.0)
Other professional and technical workers	20 (1.5)	1 (5.0)	4 (21.0)	0 (0.0)
Managerial workers	19 (1.4)	0 (0.0)	0 (0.0)	0 (0.0)
Clerical and related workers				
Stenographers, typists	122 (9.0)	0 (0.0)	0 (0.0)	0 (0.0)
Bookkeepers, cashiers	80 (5.9)	0 (0.0)	0 (0.0)	0 (0.0)
Other clerical and related workers	77 (5.7)	0 (0.0)	0 (0.0)	0 (0.0)
Sales workers				
Technical saleswomen, commercial travelers	36 (2.6)	0 (0.0)	0 (0.0)	0 (0.0)
Saleswomen, shop assistants	79 (5.8)	0 (0.0)	0 (0.0)	0 (0.0)
Other sales workers	52 (3.8)	0 (0.0)	0 (0.0)	0 (0.0)
Services workers				
Cleaners and helpers	89 (6.5)	66 (72.5)	66 (74.2)	0 (0.0)
Nurses' aides	57 (4.2)	57 (100.0)	0 (0.0)	0 (0.0)
Hairdressers, beauticians	18 (1.3)	18 (100.0)	0 (0.0)	0 (0.0)
Other service workers	24 (1.8)	4 (16.7)	4 (16.7)	4 (16.7)
Agricultural workers	19 (1.4)	0 (0.0)	11 (57.9)	0 (0.0)
Production workers				
Textile workers	7 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
Food and beverage processors	17 (1.2)	1 (5.9)	1 (5.9)	1 (5.9)
Electronic or metal processors	21 (1.6)	5 (23.8)	10 (47.6)	3 (15.0)
Material handlers and related equipment operators	17 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)
Other production workers	22 (1.6)	7 (31.8)	9 (42.9)	0 (0.0)
Other or unknown occupations	8			
Total	1366	312	145	49