

Traffic-related air pollution and development of allergic sensitization in children during the first 8 years of life

Olena Gruzieva, MD, MSc,^{a,b} Tom Bellander, PhD,^a Kristina Eneroth, PhD,^c Inger Kull, PhD,^{a,d} Erik Melén, MD, PhD,^{a,e} Emma Nordling, MSc,^a Marianne van Hage, MD, PhD,^f Magnus Wickman, MD, PhD,^{a,g} Vitaliy Moskalenko, MD, PhD,^b Olesya Hulchiy, MD, PhD,^h and Göran Pershagen, MD, PhD^a *Stockholm, Sweden, and Kiev, Ukraine*

Background: The role of exposure to air pollution in the development of allergic sensitization remains unclear.

Objective: We sought to assess the development of sensitization until school age related to longitudinal exposure to air pollution from road traffic.

Methods: More than 2500 children in the birth cohort BAMSE (Children, Allergy, Milieu, Stockholm, Epidemiological Survey) from Stockholm, Sweden, were followed with repeated questionnaires and blood sampling until 8 years of age. Outdoor concentrations of nitrogen oxides, as a marker of exhaust particles, and particles with an aerodynamic diameter of less than 10 μm (PM₁₀), mainly representing road dust, were assigned to residential, day care, and school addresses by using dispersion models. Time-weighted average exposures were linked to levels of IgE against common inhalant and food allergens at 4 and 8 years of age.

Results: Air pollution exposure during the first year of life was associated with an increased risk of pollen sensitization at 4 years of age (odds ratio, 1.83; 95% confidence interval, 1.02-3.28) for a 5th to 95th difference in exposure to nitrogen oxides. At 8 years, there was no general increase in the risk of sensitization; however, the risk of food sensitization was increased, particularly among children free of sensitization at 4 years of age (odds ratio, 2.30; 95% confidence interval, 1.10-4.82). Results were similar by using PM₁₀. No associations between air pollution exposure after the first year of life and sensitization were seen.

Conclusion: Traffic-related air pollution exposure does not seem to increase the overall risk of sensitization to common inhalant

and food allergens up to school age, but sensitization to certain allergens might be related to exposure during infancy. (J Allergy Clin Immunol 2011;■■■:■■■-■■■.)

Key words: Air pollution, children, cohort, IgE, long-term exposure, sensitization, traffic

Allergic diseases are of great public health concern and constitute one of the most prevalent childhood illnesses. During the last decades, the prevalence of IgE-associated allergic diseases has increased in most industrialized countries, although recent reports indicate that the occurrence in some regions has stabilized.¹⁻⁵ Several epidemiologic studies have reported increased risks of allergic sensitization in relation to ambient air pollution exposure measured as nitrogen dioxide,⁶⁻⁸ particulate matter,⁸⁻¹² or ozone,¹³ whereas others did not find any associations.¹⁴⁻¹⁹ Differences in study design, as well as in methods for assessment of exposures and outcomes, complicate the interpretation of the findings. For example, there are only a few prospective cohort studies on specific IgE sensitization in children from birth to school age with detailed longitudinal assessment of exposure to air pollution.

A role of traffic-related air pollution in the development of sensitization is supported by experimental evidence obtained in human volunteers, animals, and *in vitro* test systems suggesting that diesel exhaust particles can enhance immunologic responses to allergens and elicit inflammatory reactions in the airways at relatively low concentrations and short exposure durations.²⁰ In an earlier article based on the population-based birth cohort BAMSE (Children, Allergy, Milieu, Stockholm, Epidemiological Survey), exposure to moderate levels of locally emitted air pollution from traffic early in life appeared to influence the development of sensitization in 4-year-old children.¹⁰ Particularly strong associations were found in a genetically defined subgroup.²¹ The aim of this study was to assess the effect of exposure to traffic-related air pollutants on allergic sensitization in the same birth cohort over an 8-year period. Furthermore, the exposure assessment was enhanced by including not only residential addresses but also addresses of day care facilities and schools.

METHODS

Study population

A total of 4089 children born between 1994 and 1996 in Stockholm, Sweden, were included in a population-based birth cohort (BAMSE). The study design, enrollment, criteria for inclusion, and procedures for data collection have been described elsewhere.²² In brief, the study population comprised 75% of all eligible children born in predefined areas of 4 municipalities representing urban and suburban environments. Data on parental

From ^athe Institute of Environmental Medicine, Karolinska Institutet, Stockholm; ^bthe Department of Social Medicine and Health Care and ^cSocial Hygiene and Organization of Health Protection for Advance Training of Managers in the Health Industry, National O.O. Bohomolets Medical University, Kiev; ^dEnvironment and Health Administration, Stockholm; ^ethe Department of Clinical Science and Education, Karolinska Institutet, Södersjukhuset, Stockholm; ^fAstrid Lindgren Children's Hospital, Karolinska University Hospital, Stockholm; ^gthe Department of Medicine, Clinical Immunology and Allergy Unit, Karolinska Institutet and University Hospital, Stockholm; and ^hthe Department of Paediatrics, Sachs' Children's Hospital, Stockholm.

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Corresponding author: Olena Gruzieva, MD, MSc, Karolinska Institutet, Institute of Environmental Medicine, Nobels väg 13, Box 210, SE-17177, Stockholm, Sweden. E-mail: olena.gruzieva@ki.se.

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Abbreviations used

BAMSE: Children, Allergy, Milieu, Stockholm, Epidemiological Survey

NO_x: Nitrogen oxides

OR: Odds ratio

PM₁₀: Particles with an aerodynamic diameter of less than 10 μ m

age, conditions in the perinatal period, lifestyle, allergies within the family, and detailed housing characteristics were collected by using a postal questionnaire sent to the parents at recruitment (median child's age, 2 months). The socioeconomic status of the parents was determined by using questions on educational level and profession. When the children were approximately 1, 2, 4, and 8 years old, the parents received questionnaires with a main focus on the children's symptoms related to wheezing and allergic diseases, but information on various exposures was also obtained. The response rates were 96%, 94%, 91%, and 84%, respectively. Blood was drawn from 2614 (64%) and 2480 (61%) of the children at 4 and 8 years of age, respectively. In 2033 children blood samples were obtained at both 4 and 8 years of age. The study was approved by the Ethics Committee of Karolinska Institutet. The parents of all participating children provided informed consent.

Air pollution exposure assessment

The assessment of exposure to locally emitted air pollution was based on a methodology developed to estimate long-term source-specific exposure.^{10,23} It entails geocoding of a person's address information and using an emission inventory together with dispersion models to estimate outdoor levels of selected pollutants from different emission sources over time at relevant geographic locations. Information on residential, day care, and school addresses was retrieved from the postal questionnaires and transformed into geographic coordinates by using a property register developed and managed by the Swedish mapping, cadastral, and land registration authority. In case of incomplete data or inconsistencies in the address histories, supplemental information was obtained from the Swedish tax authority. The geographic location was successfully assessed for 97.8% of the 8503 unique addresses, either automatically (91.6%) or manually (6.2%). Only 2.2% of addresses could not be geocoded, either because of incompleteness (32 addresses) or being abroad (155 addresses).

Temporally and spatially resolved emission calculations were based on the emission inventory of the Stockholm and Uppsala Air Quality Management Association. Information in this database has been updated yearly by the municipalities in the region since 1993. It contains detailed information about emissions from various sources, such as road and ferry traffic, petrol stations, industrial areas, and households.²⁴ For the present study, only emissions from road traffic were included by using nitrogen oxides (NO_x) as a marker of exposure to exhaust particles and particles with an aerodynamic diameter of less than 10 μ m (PM₁₀) as a marker for road dust. The road-traffic emissions of NO_x are described by using emission factors for different vehicles and road types obtained from the EVA model of the Swedish National Road Administration.²⁵ Emission factors for PM₁₀ were obtained from simultaneous measurements of PM₁₀ and NO_x concentrations in a street canyon and an adjacent urban background by using NO_x as quantitative tracers.²⁶ During the period from 1990 to 2004, the NO_x emissions calculated by using the EVA model decreased by more than 20% because of stricter European vehicle regulations and rejuvenation of the vehicle fleet. On the other hand, PM₁₀ emissions do not show any prominent trend in Stockholm because local emissions of PM₁₀ are dominated by mechanically generated particles from the use of studded tires, which has been relatively stable during the period of the present study.²⁷

The annual mean concentrations of NO_x and PM₁₀ were calculated by using a Gaussian air quality dispersion model and a wind model, both of which are part of the Airviro Air Quality Management System (<http://airviro.smhi.se>). The calculations were performed on a 25-m resolution grid for 67% of the unique addresses in the more densely populated areas, such as urban areas. Outside these areas, the model was run with a 100-m grid (17%) or a 500-m calculation grid (7%). For 9% of the unique addresses, no concentration could

be assessed because they were located outside the counties of Stockholm and Uppsala. Adjustments were made based on the concentration gradient from roads with more than 10,000 vehicles per day to compensate for the coarse resolution of the dispersion calculations over rural areas.

The estimated air pollutant concentrations using the dispersion modeling are regularly validated against measurements at air quality-monitoring stations. When comparing time-series calculations with measured annual mean concentrations of NO_x for the urban background station in Stockholm during the period 1998 through 2005, the R^2 values ranged from 0.74 to 0.80 for the different years.²⁸ Another study found the R^2 values to be 0.71 for NO₂ concentrations and 0.61 for daily means of PM₁₀ and PM_{2.5} concentrations.²⁹ Emission databases for NO_x concentrations were available for the years 1990, 1995, 2000, 2002, 2003, and 2004. The model calculations were interpolated to obtain NO_x concentrations for all years during the period of interest. PM₁₀ model calculations were only performed for the year 2004, when the most complete database was available, and applied to all years during the observation period.

The model estimates air pollution concentrations 2 m above ground level and treats the buildings by using a roughness parameter, which implies that the concentrations are underestimated in street canyons with heavy traffic.³⁰ Therefore a street canyon contribution was calculated for addresses in the most polluted street segments in the Stockholm inner city with multistory houses on both sides ($n = 106$ unique addresses) by using the Airviro street canyon model (<http://airviro.smhi.se>). Calculated concentrations at half-height level in the street canyons (about 10 m above the ground level) were assigned to addresses situated up to 40 m from the polluted street segments.

Age- and municipality-specific information on the time children were at day care facilities and schools was used to estimate the number of hours spent at home, day care facilities, and schools each year. Time-weighted average exposure to NO_x and PM₁₀, respectively, was estimated for each child depending on the duration of time spent at the different addresses. In case parents provided 2 residential addresses for the same time period (eg, related to divorce), the child was assumed to have spent 50% of the time at each place. For the first year of life, only residential addresses were considered because children in Sweden rarely start day care before 12 months of age.

Definition of sensitization

Blood samples were analyzed with Phadiatop (a mix of common inhalant allergens: birch, timothy, mugwort, cat, dog, horse, mold [*Cladosporium herbarum*], house dust mite [*Dermatophagoides pteronyssinus*]) and fx5 (a mix of common food allergens: cow's milk, egg white, soy bean, peanut, cod fish and wheat; ImmunoCAP System; Phadia AB, Uppsala, Sweden). Sera that were scored positive for Phadiatop or fx5, which was defined as an IgE antibody level of 0.35 kU_A/L or greater, were further analyzed for allergen-specific IgE antibodies to the single airborne and food allergens.

Statistical analyses

The associations between air pollution and allergic sensitization were analyzed by using multiple logistic regression, and the results are presented as odds ratios (ORs) and 95% CIs. Air pollution concentrations were entered as continuous variables without transformation, and the results are presented for the 5th to 95th percentile difference in time-weighted average concentration among children of the cohort who provided blood samples. Imputations were performed for 131 study subjects, so that missing air pollution estimates were replaced with average exposure levels across the whole cohort for the corresponding age and address type (ie, home, day care, and/or school). The final models were adjusted for covariates identified in a previous study¹⁰ and included known or suspected risk factors for sensitization or allergy, as well as variables that had influence on the effect estimates (ie, municipality, socioeconomic status, heredity [mother and/or father with a doctor's diagnosis of asthma and asthma medication and/or doctor-diagnosed hay fever in combination with furred animals and/or pollen allergy]), mother's smoking during pregnancy and infancy (≥ 1 cigarette per day), year that the house was built, damp or mold in the home at birth, and child's sex. Parental socioeconomic status was classified in 6 categories according to the Nordic standard

TABLE I. Descriptive data for the BAMSE cohort and of those with data on sensitization at 4 and 8 years of age

Covariates*	Full cohort (n = 4089 [%])	Subjects with blood tests at 4 y (n = 2545)†	Subjects with blood tests at 8 y (n = 2174)‡
Girls	2024 (49.5)	1244 (48.9)	1058 (48.7)
Mother's smoking during pregnancy or at birth of child	563 (13.8)	333 (13.1)	263 (12.1)
Socioeconomic status of parents			
Unskilled blue-collar workers	260 (6.4)	148 (5.8)	116 (5.3)
Skilled blue-collar workers	435 (10.7)	256 (10.1)	193 (8.9)
Low-level white-collar workers	605 (14.9)	380 (14.9)	322 (14.8)
Intermediate-level white-collar workers	1179 (29.0)	783 (30.8)	664 (30.5)
High-level white-collar workers	1539 (37.4)	956 (37.6)	856 (39.4)
Others (students, unemployed)	54 (1.3)	22 (0.8)	23 (1.1)
Year that house was built			
Before 1940	1270 (31.1)	812 (31.9)	713 (32.8)
1940-1975	17.01 (41.6)	1046 (41.1)	882 (40.6)
After 1975	1115 (27.3)	687 (27.0)	579 (26.6)
Mold or dust in house of birth	1034 (25.4)	651 (25.6)	564 (25.9)
Heredity			
No parental allergy or asthma	2841 (70.5)	1762 (69.2)	1464 (67.3)
One parent with allergy or asthma	1066 (26.4)	705 (27.7)	638 (29.4)
Both parents with allergy or asthma	125 (3.1)	78 (3.1)	72 (3.3)
Exposure in the first year of life‡			
Traffic-related PM ₁₀ , mean/median (5th-95th percentile)	4.2/3.8 (0.9-8.1)	4.2/3.8 (0.9-8.1)	4.2/3.8 (0.9-7.9)
Traffic-related NO _x , mean/median (5th-95th percentile)	21.5/16.6 (3.4-50.1)	21.6/16.7 (3.4-50.5)	21.4/16.7 (3.4-49.4)
Exposure between 1-4 y of life‡			
Traffic-related PM ₁₀ , mean/median (5th-95th percentile)	3.7/3.4 (0.8-7.6)§	3.7/3.5 (0.9-7.6)	3.7/3.5 (0.9-7.5)
Traffic-related NO _x , mean/median (5th-95th percentile)	14.8/11.5 (2.6-37.5)§	14.8/11.7 (2.7-37.0)	14.7/11.5 (2.7-36.5)
Exposure between 4-8 y of life‡			
Traffic-related PM ₁₀ , mean/median (5th-95th percentile)	3.5/3.1 (0.7-7.5)¶	—	3.5/3.2 (0.8-7.4)
Traffic-related NO _x , mean/median (5th-95th percentile)	10.6/7.9 (1.7-27.7)¶	—	10.7/8.4 (1.8-27.5)

*Covariates relate to the first year of the child's life.

†Data include subjects with a full set of confounders.

‡Source-specific contribution to residential outdoor levels estimated from local sources with dispersion models.

§Data for 3529 children who attended clinical examinations and had complete exposure information for the 1- to 4-year life period.

¶Data for 3115 children who attended clinical examinations and had complete exposure information for the 4- to 8-year life period.

occupational Swedish socioeconomic classification.³¹ Complete confounder sets were available for 2545 children with blood samples at 4 years and 2174 children with blood samples at 8 years (Table I). Exposure time windows were defined as 0 to 1 years (from birth to the first-year birthday), 1 to 4 years (from first-year birthday until the date of clinical examination at 4 years), and 4 to 8 years (time between dates of clinical examinations at 4 and 8 years of age). NO_x and PM₁₀ concentrations were highly correlated; thus we only assessed 1 pollutant model. All statistical analyses were performed with STATA Release 11.1 (StataCorp, College Station, Tex).

RESULTS

The distribution of potential confounders and exposure to air pollutants for the relevant time periods are summarized in Table I. The distribution of the potential confounders between children in the whole cohort and those providing blood samples was very similar. The air pollutant concentrations appeared highest and had the widest numeric range during the first year of life. The mean local contribution above regional background to the children's outdoor air pollution exposure levels was 4.2, 3.7, and 3.5 μg/m³ for PM₁₀ and 21.5, 14.8, and 10.6 μg/m³ for NO_x from traffic during the first year of life, 1 to 4 life years, and 4 to 8 life years, correspondingly. Exposure levels were similar in children with blood samples and in those of the whole cohort. As expected, traffic-related PM₁₀ and traffic-related NO_x concentrations were highly correlated during the study period ($r = 0.96$, 0.95, and 0.95 at the first year of life, 1-4 life years, and 4-8 life

TABLE II. Prevalence of sensitization at 4 and 8 years of age in children of the BAMSE birth cohort

IgE sensitization*	Prevalence of sensitization (%)	
	4 y (n = 2545)	8 y (n = 2174)
No sensitization	1931 (75.9)	1409 (64.8)
Food or inhalant sensitization	614 (24.1)	765 (35.2)
Food sensitization	406 (16.0)	440 (20.2)
Milk	216 (8.4)	218 (10.0)
Egg	123 (4.8)	128 (5.9)
Soybean	76 (3.0)	110 (5.1)
Peanut	136 (5.3)	178 (8.2)
Fish	18 (0.7)	9 (0.4)
Wheat	96 (3.8)	131 (6.0)
Inhalant sensitization	389 (15.3)	570 (26.2)
Pollen	280 (11.1)	454 (21.0)
Birch	222 (8.7)	339 (15.6)
Timothy	147 (5.8)	316 (14.5)
Mugwort	38 (1.5)	157 (7.2)
Furred animals	189 (7.5)	349 (16.1)
Cat	150 (5.9)	281 (12.9)
Dog	115 (4.5)	257 (11.8)
Horse	79 (3.1)	152 (7.0)

*Sensitization is defined as an IgE antibody level of 0.35 kU_A/L or greater.

years, respectively). Also, strong correlations were observed between early and later exposure time windows ($r = 0.70$ -0.89) for both pollutants. Children with the highest exposure levels

TABLE III. Air pollution exposure during the first year of life and from 1 to 4 years in relation to allergic sensitization at 4 years of age (n = 2545)

IgE sensitization at 4 y	No.	Traffic-related NO _x		Traffic-related PM ₁₀	
		OR* (95% CI)		OR* (95% CI)	
		First year	1-4 y	First year	1-4 y
No sensitization†	1931	1.00		1.00	
Food or inhalant sensitization‡	614	1.29 (0.83-2.01)	0.97 (0.66-1.42)	1.40 (0.80-2.43)	0.88 (0.58-1.34)
Food sensitization	406	1.24 (0.73-2.11)	0.95 (0.60-1.50)	1.26 (0.65-2.43)	0.91 (0.55-1.50)
Inhalant sensitization	389	1.43 (0.84-2.44)	0.88 (0.54-1.42)	1.60 (0.82-3.11)	0.74 (0.44-1.23)
Pollen§	280	1.83 (1.02-3.28)	1.05 (0.61-1.81)	2.07 (0.98-4.39)	0.84 (0.46-1.52)
Furred animals¶	189	1.05 (0.48-2.34)	1.01 (0.52-1.94)	1.19 (0.46-3.07)	0.89 (0.44-1.82)

*ORs are calculated for a difference in the air pollution level from the 5th to 95th percentiles, corresponding to 7.2 and 6.7 $\mu\text{g}/\text{m}^3$ for PM₁₀ and 46.7 and 34.3 $\mu\text{g}/\text{m}^3$ for NO_x (during the first year of life and 1-4 years correspondingly), and adjusted for municipality, socioeconomic status, heredity, mother's smoking during pregnancy and infancy, year that the house was built, damp or mold in the home at birth, and sex of the child.

†Reference category.

‡Food allergens according to fx5 and inhalant allergens according to Phadiatop.

§Birch, timothy, or mugwort.

¶Cat, dog, or horse.

TABLE IV. Air pollution exposure during the first year of life, as well as from 1 to 4 and 4 to 8 years in relation to allergic sensitization at 8 years of age (n = 2174)

IgE sensitization at 8 y	No.	OR* (95% CI)		
		First year	1-4 y	4-8 y
NO _x				
No sensitization†	1409		1.00	
Food or inhalant sensitization‡	765	1.14 (0.73-1.78)	0.95 (0.65-1.38)	0.92 (0.65-1.29)
Food sensitization	440	1.50 (0.89-2.53)	1.31 (0.84-2.03)	1.27 (0.85-1.89)
Inhalant sensitization	570	1.10 (0.66-1.82)	0.88 (0.57-1.35)	0.80 (0.54-1.18)
Pollen§	454	1.30 (0.76-2.22)	0.80 (0.50-1.29)	0.72 (0.47-1.11)
Furred animals¶	349	1.15 (0.62-2.14)	0.98 (0.59-1.63)	0.75 (0.47-1.20)
PM ₁₀				
Food or inhalant sensitization‡	765	1.35 (0.79-2.31)	0.98 (0.65-1.48)	0.99 (0.69-1.40)
Food sensitization	440	1.77 (0.93-3.37)	1.37 (0.83-2.25)	1.32 (0.86-2.02)
Inhalant sensitization	570	1.35 (0.74-2.48)	0.91 (0.58-1.45)	0.90 (0.61-1.34)
Pollen§	454	1.53 (0.79-2.96)	0.76 (0.46-1.25)	0.79 (0.51-1.21)
Furred animals¶	349	1.43 (0.68-3.03)	0.89 (0.51-1.56)	0.78 (0.49-1.26)

*ORs are calculated for a difference in the air pollution level from the 5th to 95th percentiles, corresponding to 7.2, 6.7, and 6.6 $\mu\text{g}/\text{m}^3$ for PM₁₀ and 46.7, 34.3, and 25.7 $\mu\text{g}/\text{m}^3$ for NO_x (during the first year of life and 1-4 and 4-8 years correspondingly), and adjusted for municipality, socioeconomic status, heredity, mother's smoking during pregnancy and infancy, year that the house was built, damp or mold in the home at birth, and sex of the child.

†Reference category.

‡Food allergens according to fx5 and inhalant allergens according to Phadiatop.

§Birch, timothy, or mugwort.

¶Cat, dog, or horse.

tended to come from families of high socioeconomic status, largely because they more often lived in the inner city, where air pollution levels are higher (data not shown).

Prevalence rates of sensitization among the children are shown in Table II. A total of 614 (24%) children were sensitized to inhalant or food allergens at age 4 years, and 765 children (35%) were sensitized at age 8 years. A total of 11% and 21% of the children were sensitized to any pollen (9% and 16% to birch pollen), and 7.5% and 16% were sensitized to furred animals at 4 and 8 years, respectively. Sensitization to cow's milk dominated among the food allergens and occurred in 8% of 4-year-olds and 10% of 8-year-olds.

There was no overall risk of sensitization at 4 years of age associated with traffic-related air pollution exposure (Table III). However, exposure during the first year of life was associated with an increased risk of sensitization to pollen (OR, 1.83; 95%

CI, 1.02-3.28) for traffic-related NO_x and 2.07 (95% CI, 0.98-4.39) for traffic-related PM₁₀. On the other hand, there was no apparent effect of exposure to air pollution after the first year of life on the development of sensitization.

At 8 years of age, there was also no clear increase in the risk of overall sensitization associated with exposure to traffic-related air pollution (Table IV). However, a tendency to an increased risk of sensitization against food allergens was indicated, with an OR of 1.50 (95% CI, 0.89-2.53) for NO_x exposure during the first year of life and an OR of 1.77 (95% CI, 0.93-3.37) for PM₁₀ exposure during the first year of life. Associations for pollen appeared less consistent, particularly with regard to exposure after infancy.

Because sensitization at 8 years of age might be influenced by sensitization at 4 years, we wanted to explore the role of early exposure for the development of allergic sensitization later in life. In children who were free from sensitization at 4 years, we found

TABLE V. Air pollution exposure during the first year of life, as well as from 1 to 4 and 4 to 8 years in relation to allergic sensitization at 8 years of age in children not sensitized at 4 years (n = 1472)

		OR* (95% CI)		
IgE sensitization at 8 y	No.	First year	1-4 y	4-8 y
NO _x				
No sensitization†	1197		1.00	
Food or inhalant sensitization‡	275	1.37 (0.74-2.52)	1.11 (0.67-1.85)	1.04 (0.65-1.68)
Food sensitization	131	2.30 (1.10-4.82)	1.55 (0.81-2.97)	1.38 (0.74-2.57)
Inhalant sensitization	180	1.05 (0.49-2.24)	1.08 (0.59-1.99)	0.96 (0.54-1.70)
Pollen§	125	1.34 (0.59-3.05)	1.07 (0.53-2.15)	0.88 (0.45-1.71)
Furred animals¶	77	1.12 (0.37-3.38)	1.58 (0.71-3.51)	1.22 (0.54-2.72)
PM ₁₀				
Food or inhalant sensitization‡	275	1.50 (0.70-2.20)	1.13 (0.63-2.02)	1.13 (0.68-1.87)
Food sensitization	131	2.56 (0.96-6.86)	1.39 (0.63-3.06)	1.20 (0.60-2.39)
Inhalant sensitization	180	1.30 (0.52-3.24)	1.19 (0.60-2.38)	1.20 (0.65-2.19)
Pollen§	125	1.44 (0.51-4.09)	1.05 (0.47-2.34)	0.98 (0.49-1.98)
Furred animals¶	77	1.57 (0.42-5.95)	1.61 (0.59-4.39)	1.44 (0.59-3.52)

*ORs are calculated for a difference in the air pollution level from the 5th to 95th percentiles, corresponding to 7.2, 6.7, and 6.6 $\mu\text{g}/\text{m}^3$ for PM₁₀ and 46.7, 34.3, and 25.7 $\mu\text{g}/\text{m}^3$ for NO_x (during the first year of life and 1-4 and 4-8 years correspondingly), and adjusted for municipality, socioeconomic status, heredity, mother's smoking during pregnancy and infancy, year that the house was built, damp or mold in the home at birth, and sex of the child.

†Reference category.

‡Food allergens according to fx5 and inhalant allergens according to Phadiatop.

§Birch, timothy, or mugwort.

¶Cat, dog, or horse.

an excess risk of food sensitization at 8 years in relation to NO_x exposure in the first year of life (OR, 2.30; 95% CI, 1.10-4.82) and PM₁₀ exposure in the first year of life (OR, 2.56; 95% CI, 0.96-6.86; Table V). When investigating the food allergens separately, the risk increase was statistically significant only for peanut allergens (OR, 2.01; 95% CI, 1.00-4.05). The risks appeared less increased for the subsequent exposure periods. Pollen sensitization tended to be higher only in relation to air pollution exposure during infancy. Time-weighted average lifetime air pollution exposure at residential addresses was highly correlated with total exposure estimates also including day care and school addresses ($r = 0.98$). Thus when performing analyses with only residential addresses, the estimates did not deviate substantially from those considering all addresses (data not shown).

DISCUSSION

We found no clear associations between estimated ambient exposure to traffic-related air pollution and overall sensitization to common inhalant and food allergens in a Swedish birth cohort of 8-year-old children. However, the results suggest increased risks of sensitization both against food and pollen related to exposure during infancy but with slightly different patterns in relation to duration of follow-up. Our findings are in line with some earlier results, although to date, only few cohort studies have evaluated effects of exposure to air pollution on the development of sensitization in young children. A Dutch cohort study reported an increased risk for food allergy at 4 years of age.⁸ A positive association between air pollution and sensitization to pollen among 6-year-old children was found in a German study.¹¹ Some additional studies have reported increased risks of allergic sensitization related to air pollution exposure in children of young school age, but these were of cross-sectional design.^{6,7,12} A causal association is supported by experimental evidence indicating that exhaust particles can enhance immunologic responses to allergens and inflammatory reactions in the airways.²⁰ Cross-

reactions between pollen and certain food allergens might contribute to the observed associations between air pollution exposure and food allergy. Thus, looking at separate food items, we observed the clearest risk for peanut allergens, which are known to cross-react with pollen.³² In our cohort 74% of those sensitized to peanut allergens at 8 years were concomitantly sensitized to birch.³³

With regard to the effects of air pollution exposure after the first year of life, our results are consistent with those of several previous studies, in which no overall associations between traffic-related air pollutants and sensitization were found.¹⁴⁻¹⁹ In a Norwegian study with fairly similar levels of outdoor air pollution to those in Sweden, it was suggested that if an association between air pollution exposure and allergic sensitization exists, it might not be identified because of comparatively low exposure levels.¹⁶ A number of studies on various risk factors indicate that gestation and early childhood are important periods of immune development with regard to expression of atopy.^{10,34-38} The lack of focus on a potentially important time window for sensitization might have contributed to the diverging findings in previous studies on air pollution exposure and sensitization. In our study higher concentrations of combustion-related air pollutants during the infancy period than later in life might also have contributed to the higher risks associated with exposure during this period. The main explanation for the observed trends in traffic-related NO_x concentrations over the study period is that the recruitment of our cohort occurred shortly after the introduction of catalytic converters in private cars. This led to a reduction in the emissions for several air pollutants, which continued to decrease with the replacement of older vehicles.³⁹

The prospective design and large size, as well as high response rates and repeated measurement of sensitization status through blood testing, are strengths of the BAMSE birth cohort. Furthermore, the methodology for air pollution exposure assessment was validated and has been successfully applied in several

epidemiologic investigations.^{10,40,41} In the present analysis the individual exposure estimates for each cohort member were derived from a time- and space-resolved dispersion model with addition of street canyon contribution for addresses in the most polluted street segments. Model calculations of air pollution concentrations agree well with measurements.^{28,29} Measurements in Stockholm also show that ambient levels of NO₂ or NO_x are related to both soot levels⁴² and particle number concentrations,³⁰ indicating that NO_x might be a good indicator for combustion-related particles.

It is a disadvantage that calculations of air pollutant concentrations could only be performed for the years when emission databases were available (for NO_x: 1990, 1995, 2000, and 2002–2004). For PM₁₀, only the emissions data for 2004 were used. The constant percentage of studded tires in the Stockholm vehicle fleet, as well as the relatively stable traffic work in the inner city during the last decades, suggest that the emissions of PM₁₀ have not changed much during the period from 1994 to 2004.²⁷ Another weak point lies in the lack of meteorological adjustment for PM₁₀ concentrations. Contrary to NO_x (and exhaust particles), street moisture has a crucial influence on PM₁₀ concentrations.⁴³ Unfortunately, relevant data were not available to adjust for road moisture in estimating the yearly PM₁₀ concentrations.

To increase the precision in the exposure assessment, we took time-activity patterns into account, considering the time children spent at home, day care, and/or school, which has not been done in earlier birth cohort studies on the health effects of air pollution. It has been shown that the risk of allergic diseases, such as asthma related to exposure at school, was comparable with that of children whose exposure occurred primarily at home, even though the time spent at school only accounted for about one third of waking hours.⁴⁴ Our results indicate that home addresses well represent exposure to air pollution in young children of Stockholm. This is probably due to the fact that the children's kindergartens and schools are often located in the vicinity of their residential areas. Similar results were obtained in a French study in which topographic and traffic characteristics of residences and nurseries/schools were found to be similar.⁴⁵ Furthermore, air pollution levels at the home address are highly relevant as exposure estimates in infancy because in Sweden children usually do not start day care before 12 months of age.

In conclusion, our findings indicate that exposure to traffic-related air pollution during the first 8 years of life does not increase the overall risk of sensitization to common inhalant and food allergens. However, exposure during infancy might increase the risk of sensitization to certain types of allergens.

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Key messages

- Traffic-related air pollution exposure does not seem to increase the overall risk of sensitization to common inhalant and food allergens.
- However, sensitization to certain allergens might be related to exposure during infancy.

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