The Relationship between Air Pollution from Heavy Traffic and Allergic Sensitization, Bronchial Hyperresponsiveness, and Respiratory Symptoms in Dutch Schoolchildren

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Studies have suggested that children living close to busy roads may have impaired respiratory health. This study was designed to test the hypothesis that exposure to exhaust from heavy traffic in particular is related to childhood respiratory health. Children attending 24 schools located within 400 m from busy motorways were investigated. The motorways carried between 5,190 and 22,326 trucks per weekday and between 30,399 and 155,656 cars per day. Locations were chosen so that the correlation between truck and car traffic counts was low. Air pollution measurements were performed at the schools for 1 year. Respiratory symptoms were collected by parent-completed questionnaire. Sensitization to common allergens was measured by serum immunoglobulin E and skin prick tests. Bronchial hyperresponsiveness (BHR) was measured with a hypertonic saline challenge. Respiratory symptoms were increased near motorways with high truck but not high car traffic counts. They were also related to air pollutants that increased near motorways with high truck traffic counts. Lung function and BHR were not related to pollution. Sensitization to pollen increased in relation to truck but not car traffic counts. The relation between symptoms and measures of exposure to (truck) traffic–related air pollution were almost entirely restricted to children with BHR and/or sensitization to common allergens, indicating that these are a sensitive subgroup among all children for these effects. ***Key words:*** **air pollution, allergy, bronchial hyperresponsiveness, children, diesel, lung function, respiratory symptoms.** ***Environ Health Perspect*** **111:1512–1518 (2003). doi:10.1289/ehp.6243 available via *http://dx.doi.org/* [Online 10 June 2003]**

Exposure to traffic-related air pollution has been implicated in impairment of respiratory health in children in several recent studies, although the literature is not entirely unequivocal (Brauer et al. 2002; Brunekreef et al. 1997; Ciccone et al. 1998; Duhme et al. 1996; Edwards et al. 1994; Gehring et al. 2002; Hirsch et al. 1999; Kramer et al. 2000; Livingstone et al. 1996; Oosterlee et al. 1996; Pershagen et al. 1995; van Vliet et al. 1997; Weiland et al. 1994; Wjst et al. 1993). Some of these studies were questionnaire based, relating self-reported exposures to self-reported health outcomes (Ciccone et al. 1998; Duhme et al. 1996; Weiland et al. 1994). Others have used objective measures of exposure such as distance to busy roads, traffic counts, and modeled or measured air pollution concentrations (Brunekreef et al. 1997; Oosterlee et al. 1996; Pershagen et al. 1995; Roorda-Knape et al. 1998; van Vliet et al. 1997; Wjst et al. 1993), and objective measures of respiratory function such as spirometry (Brunekreef et al. 1997; Wjst et al. 1993) and allergic sensitization by skin prick test (SPT) or serum immunoglobulin E (IgE) determination (Kramer et al. 2000). Some studies have also employed health care use data to assess the health impact of exposure to traffic-related air pollution (Edwards et al. 1994; Livingstone et al. 1996; Pershagen et al. 1995). Collectively, these studies suggest that living in situations with high exposure to traffic-related air pollution increases the prevalence of chronic respiratory symptoms; however, a relationship with lung function or allergic sensitization has been studied insufficiently to draw firm conclusions. Most studies have not been able to single out specific components of traffic-related air pollution, although some of the questionnaire studies have focused on self-reported exposure to truck traffic (Ciccone et al. 1998; Duhme et al. 1996; Weiland et al. 1994). One study conducted by us used automated traffic counts, which enables us to separate heavy from light traffic (Brunekreef et al. 1997; van Vliet et al. 1997). This study clearly suggested that the lung function was decreased, and chronic respiratory symptoms increased, in association with heavy traffic rather than light traffic. In this article, we describe a large study conducted among children attending 24 different schools that were all located close to motorways with varying densities and compositions of traffic.

Methods

Study design. We studied respiratory health of children from 24 schools situated within 400 m of a motorway, using the International Study of Asthma and Allergies in Childhood, phase II (ISAAC II) protocols for measurements of serum IgE, skin test reactivity, bronchial hyperresponsiveness (BHR), and questions on asthmatic and allergic symptoms. We assessed exposure to traffic-related air pollution using specific traffic-related characteristics (traffic counts for cars and trucks separately and distance of the homes and schools to the highway) as well as estimated annual average concentrations of particulate matter with an aerodynamic diameter ≤ 2.5 µm ($PM_{2.5}$), soot, and nitrogen dioxide (NO_2) outside all 24 schools (Janssen et al. 2001).

Study locations. First, we identified all city districts in the central southwestern part of the Netherlands that had a school and a large number of homes located within 400 m of a highway. Of the 36 city districts that were identified, 20 were selected. We selected sites to achieve a maximum variation in traffic densities (covering the full range of identified traffic densities) and a minimal correlation between car and truck traffic. If city districts were situated along motorways with similar traffic densities, one city district was chosen on the basis of the distance of the homes and school(s) to the motorway, the size of the city districts, and the number of children attending the school(s). In each city district, we collaborated with the municipal health service to approach one school. If a given school did not agree to participate, another school in the same city district or a school in a city district along a motorway with similar traffic densities was approached. In total, we approached 30 schools to obtain 20 participating schools. Reasons for nonparticipation were mostly nonspecific (reorganizations, recently been involved in other studies, etc.). In addition, four schools (of four approached) that were also involved in a study on respiratory health of children living near Schiphol airport participated, producing a total of 24 participating schools. The 24 schools were situated along 22 different motorway stretches. Three of the schools near Schiphol

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airport were situated along the same motorway stretch (two on the northeast side and one on the southwest side of the road).

Population. All children in classes 4–8 (7–12 years old) were invited to participate in the study. Parents of all children were asked to complete a questionnaire, and all children were invited to participate in lung function testing. In addition, children in the four highest classes (classes 5–8, 8–12 years old) were invited to participate in tests of BHR and of sensitization to common allergens (both blood sampling and SPT). Parents were asked to give written informed consent for all parts of the study separately. Measurements were conducted at the schools, in the period from April 1997 through July 1998. The study protocol was approved by the medical ethical committee of Wageningen University (where the principal authors were employed when the study was being prepared and conducted).

Exposure Variables

Traffic characteristics. Traffic counts were obtained from the Ministry of Public Works, which routinely collects counts for all motorway stretches in the Netherlands using induction loops. This method distinguishes vehicles shorter than and longer than 5.1 m, which we classified as cars and trucks, respectively. Weekday counts for 1997 were used. Distances of the schools to the motorways were measured using maps at 1:1,000 or 1:1,500 scale. Distances from the children's homes to the motorway were assessed using the geographic information system (GIS) Arc-Info (Environmental Systems Research Institute, Redlands, CA, USA).

Air pollution measurements. Outside each school, weekly averaged measurements were made of $PM_{2.5}$, NO_2, and benzene. Reflectance of $PM_{2.5}$ filters was measured as a proxy for elemental carbon (EC), a major part of diesel soot. The relationship between this proxy and actual measurements of EC was studied in a subsample, and a high correlation was established (Janssen et al. 2001). We made 5–10 measurements for each school, from April 1997 through May 1998. Annual average concentrations were calculated, after standardizing for differences in the background concentrations during the measurements. Details about the air pollution measurements and the calculation of the annual average air pollution concentrations are given elsewhere (Janssen et al. 2001). Outdoor benzene concentrations were strongly influenced by local sources (e.g., presence of a gasoline station) and were therefore not included in the data analysis for this report. Classroom measurements were also conducted, but because these measurements were conducted only during school hours (±28 hr/week, weekdays only), classroom concentrations were also not considered as exposure variables in this report.

Questionnaire. We used the ISAAC questionnaire to measure symptoms of asthma and allergic disease in the children (Asher et al. 1995). We used the questions on wheeze in the past year, nasal symptoms together with itchy or watery eyes in the past year, itchy rash in the past year, bronchitis in the past year, phlegm without a cold in the past year, asthma ever, hay fever ever, and eczema ever as end points. In addition, the questionnaires included questions on potential confounders such as age, sex, and various exposure variables (among others, housing characteristics, possession of pets, and passive smoking).

Sensitization to common allergens. Children were tested with SPTs as well as serum IgE determinations. SPTs were performed according to the standardized ISAAC II protocol (ISAAC 1998). The ISAAC panel of six aeroallergens was used: *Dermatophagoides farinae*, *Dermatophagoides pteronyssinus*, cat, *Alternaria tenuis*, mixed tree pollen (*Betula verrucosa*, *Alnus glutinosa*, *Corylus avellana*), and mixed grass pollen (*Dactylis glomerata, Lolium perennae, Festuca pratensis, Poa pratensis, Phleum pratense, Avena eliator*). In addition, dog allergen was added. Standardized allergen extracts (all but *Alternaria*) and controls (negative control and histamine 10 mg/mL as the positive control) were provided by the ALK Company (Horsholm, Denmark). The test was performed on the volar side of the left forearm using ALK lancets. After 15 min, the outside contour of the wheal was measured, and the mean of the longest diameter and the length of the perpendicular line through its middle was calculated. Values for children with a reaction (> 0 mm) to the negative control or no reaction to histamine were recorded as missing. A mean wheal diameter ≥ 3 mm is regarded as a positive reaction according to the position paper on skin tests from the European Academy of Allergy and Clinical Immunology (EAACI 1989).

Serum total and specific IgE were assessed by the CAP assay, and all analyses were performed at the same laboratory (Pharmacia CAP systems; Pharmacia & Upjohn Diagnostics, Woerden, The Netherlands). The PHADIATOP (Pharmacia & Upjohn Diagnostics) test for common inhalant allergens was used as a screening instrument (Duc et al. 1988), with further testing of all sera that were positive in the PHADIATOP for common allergens *Dermatophagoides pteronyssinus*, cat, molds (*Alternaria tenuis*, *Penicillinum notatum*, *Cladosporium herbarum*), mixed trees (*Betula verrucosa*, *Corylus avellana*, *Alnus incana*, *Quercus alba*, *Salix caprea*), mixed grasses (*Phleum pratense*, *Lolium perennae*, *Anthoxanthum odoratum*, *Secale cereale*, *Holcus lanatus*), and dog. A positive test result on total IgE and specific IgE was defined as a titer of 100 and 0.35 kU/L, respectively.

In total, 1,141 SPTs and 881 blood samples were successfully collected and analyzed. Results of the two tests, when dichotomized into a positive reaction to ≥ 1 specific allergen (yes or no), showed a good concordance (756 of 828 = 91.3% identical results). Because a considerably higher number of SPTs than blood samples was collected, only the results of the SPTs were used to define sensitization to common allergens. In addition to SPT reactivity for any (≥ 1) allergen, SPT reactivity for indoor or outdoor allergens specifically was defined. The outdoor allergens consisted of grasses and trees allergens, and the indoor allergens consist of cat, dog, and house dust mite allergens.

Lung function and bronchial challenge. Lung function was determined using a pneumotachometer (Jaeger, Würzburg, Germany). Three reproducible and technically acceptable measurements of forced expiratory volume in 1 sec (FEV_1) and forced vital capacity (FVC) were made according to the guidelines of the European Respiratory Society (ERS 1993; Gibson 1993). The highest values for FEV_1 and FVC were selected and values for maximum expiratory flow between 25 and 75% of expiration ($MEF_{25–75}$) were selected from the curve with the highest FVC. Low FVC and low FEV_1 were defined as a FVC and FEV_1 < 85% of predicted. Predicted values were calculated using the formulas from Zapletal et al. (1969), which are based on sex and height.

Bronchial challenge tests were performed with 4.5% sodium chloride according to the ISAAC protocol (Riedler et al. 1994a, 1994b). Children with a FEV_1 < 75% predicted were excluded. Parents were asked to stop their children's use of salbutamol 6 hr before the test and use of antihistaminics 48 hr before the test. Briefly, the protocol comprised inhalation of hypertonic saline aerosol in five inhalation steps of 0.5, 1, 2, 4, and 8 min, respectively, and two reproducible measurements of FEV_1 were collected 1 min after each inhalation step. The highest FEV_1 was selected. The test stopped after completion of all inhalation steps, or if there was a fall in FEV_1 of 15% or more compared with the reference value (highest prechallenge FEV_1). A positive test (BHR) was defined as a fall in FEV_1 ≥ 15% after inhalation of maximal 23 mL hypertonic saline.

Data Analysis

Statistical analysis was performed using the multilevel software package MlwiN (Rasbash et al. 2001). We used a random intercept model to account for the hierarchical structure of the data (children are clustered within schools). We used restricted iterative generalized least squares and second-order penalized quasi-likelihood. Only children who lived within 1,000 m of the motorway were included in the analysis.

Odds ratios (ORs) for traffic density and air pollution concentrations were expressed as the difference between the maximum and the minimum of the exposure indicator. ORs for distance to motorway, for both the school and the home address, were expressed as the difference between 100 and 400 m. The logarithm of distance was used because from general dispersion models an exponential decay in the contribution from the road with distance can be expected.

Results were adjusted for known potential confounders age, sex, non-Dutch nationality, cooking on gas, current parental smoking, current pet possession, parental education level (as a proxy for socioeconomic status), number of persons in the household, presence of an unvented water heater in the kitchen, questionnaire not filled out by the mother, and presence of mold stains in the kitchen, living room, or bedroom. Parental respiratory symptoms were not included as confounders in the main analysis because these symptoms could also be related to exposure to traffic-related air pollution. Instead, additional adjustment for parental asthma and hay fever was made in a sensitivity analysis. Additional sensitivity analysis included restricting the population to children living within 500 m of the motorway and restricting the population to children who had lived at their current address and had been attending the present school for > 1 year, and additional adjustment for bronchitis and for severe cold or flu in the 3 weeks preceding the study.

To evaluate the possibility of a stronger effect of traffic-related air pollution among susceptible children, we also conducted analyses separately for children with a positive SPT and for children with a positive BHR test. Effect estimates for these two subgroups were compared with those found for children with a negative result for both tests.

Results

Traffic characteristics and annual average air pollution levels at the participating schools are given in Table 1. There was a 4–5-fold range in the traffic densities of the various motorways. For soot, there was a 2.5-fold difference between the school with the highest and lowest annual average concentration. For $PM_{2.5}$ and NO_2, the range was smaller (1.4–1.7). Associations among traffic characteristics and air pollution concentrations are described elsewhere (Janssen et al. 2001). By design, car and truck traffic densities were weakly correlated ($R = 0.31$). Distance from the school to the motorway was moderately correlated with truck traffic ($R = 0.52$) but not with car traffic. Distance from the homes to the motorway was not correlated with any of the other traffic characteristics. Concentrations of $PM_{2.5}$ and soot significantly increased with increasing truck traffic density and significantly decreased with increasing distance of the school to the highway. Outdoor NO_2 concentrations significantly increased with increasing total traffic density.

Response rates were 65% for the questionnaire, 62% for the lung function test, 58% for the bronchial challenge, 49% for the SPT, and 43% for the blood sampling. Of 2,509 children for which a completed questionnaire was obtained, 2,083 (83%) lived within 1,000 m of the motorway. Percentages of children living within 1,000 m for the other parts of the study were similar (82–85%).

Table 2 shows the prevalence of selected allergic and respiratory symptoms, elevated total IgE, SPT reactivity, low lung function, and BHR. Of the 318 children with a positive SPT, 170 (14.9% of the total population, 53.5% of the SPT-positive children) children responded to outdoor allergens, and 250 children (21.9% of the total population, 78.6% of the SPT-positive children) responded to indoor allergens; 64 (20.1%) children responded to outdoor allergens alone, and 144 (45.3%) children responded to indoor allergens alone. About 63% of the children studied had a negative SPT and a negative bronchial challenge test. Prevalences of respiratory symptoms for children who participated in the bronchial challenge, SPT, and/or blood sampling did not differ significantly ($p < 0.05$) from the prevalences for children who did not participate in these tests (results not shown).

Table 3 shows the associations between the different exposure variables and selected respiratory symptoms. ORs for truck traffic and air pollution concentrations were consistently above unity, with (borderline) significantly elevated ORs found for current wheeze (truck traffic and NO_2), current conjunctivitis (truck traffic, $PM_{2.5}$, soot, and NO_2), hay fever ever ($PM_{2.5}$ and NO_2), and current itchy rash (truck traffic and $PM_{2.5}$). ORs for car traffic, however, were all below unity and not significant. When the variable for car traffic was excluded from the model, ORs for truck traffic all slightly decreased, but the association with current conjunctivitis (OR = 2.32) and current itchy rash (OR = 2.05) remained statistically significant. The association between truck traffic and current bronchitis (OR = 2.22) became of borderline ($p < 0.10$) significance. When truck traffic was excluded from the model, ORs for car traffic all increased slightly to values closer to unity (ranging from 0.62 for current phlegm to 1.14 for current bronchitis). No clear associations between respiratory symptoms and distance of the school or home to the highway were observed.

When the population was restricted to children living within 500 m to the highway ($n = 1,421$) or children who had lived at their current address and had been attending the current school for more than 1 year ($n = 1,694$), ORs generally increased and several ORs that were not significantly elevated in the total population reached statistical significance. For example, ORs for the association between current wheeze and truck traffic, $PM_{2.5}$, or NO_2 all became significant at the $p < 0.05$ level. Additional adjustment for parental

Table 2. Prevalence of respiratory or allergic symptoms and results of the SPT and BHR test.

Symptoms (total *n*)	No. (%)
Current[a] wheeze (2,071)	194 (9.4)
Asthma ever (2,053)	165 (8.0)
Current conjunctivitis (2,053)	150 (7.3)
Hay fever ever (2,040)	146 (7.2)
Current itchy rash (2,060)	305 (14.8)
Eczema ever (2,040)	611 (30.0)
Current phlegm, no cold (2,045)	198 (9.7)
Current bronchitis (2,037)	156 (7.7)
Elevated total IgE (881)	351 (39.8)
Positive SPT, any allergen (1,141)	318 (27.9)
Positive SPT, indoor allergens (1,141)	250 (21.9)
Positive SPT, outdoor allergens (1,141)	170 (14.9)
FVC < 85% of predicted (1,726)	237 (13.7)
FEV_1 < 85% of predicted (1,724)	136 (7.9)
BHR (949)	192 (20.2)
Negative SPT and negative BHR (765)	481 (62.9)

[a]Current = in the past 12 months.

Table 1. Distribution of traffic characteristics and annual average outdoor concentrations (μg/m^3) at the schools.

Characteristics	No.	Mean ± SD	Minimum	25th percentile	Median	75th percentile	Maximum
Traffic characteristics							
Truck traffic density (vehicles/weekday)	24	13,146 ± 4,880	5,190	9,571	11,814	16,817	22,326
Car traffic density (vehicles/weekday)	24	89,544 ± 35,843	30,399	61,013	87,843	114,780	155,656
Distance school—motorway (m)	24	220 ± 111	57	118	210	330	389
Distance homes—motorway (m)	2,083	407 ± 230	1	228	365	556	999
Outdoor air pollution							
$PM_{2.5}$ (μg/m^3)	24	20.5 ± 2.2	17.3	18.6	20.4	22.1	24.4
Soot (μg/m^3)	24	10.3 ± 2.1	6.2	9.0	10.5	11.2	15.5
NO_2 (μg/m^3)	24	34.8 ± 5.2	26.8	31.1	34.0	39.1	44.4

asthma or hay fever or for bronchitis, severe cold, or flu in the 3 weeks preceding the study did not substantially change the results.

Table 4 shows the associations between the different exposure variables and elevated total IgE, SPT reactivity, low lung function, and BHR. Elevated total IgE was significantly associated with soot and NO_2. SPT reactivities to any allergen and to indoor allergens were both significantly associated with NO_2, whereas SPT reactivity to outdoor allergens was significantly associated with truck traffic and $PM_{2.5}$. Lung function and BHR showed little association with any of the exposure variables. Analysis of the lung function parameters as continuous variables also did not show an association with any of the exposure variables (data not shown).

The association between truck traffic and SPT reactivity for outdoor allergens remained significant when car traffic was excluded from the model (OR = 2.17). Restriction to children living within 500 m of the highway, restriction to children who had lived at their current address and had been attending the current school for more than 1 year, or additional adjustment for parental asthma or hay fever did not substantially change the results.

Prevalences of current wheeze, asthma ever, current conjunctivitis, and hay fever ever were four to eight times higher among children with a positive SPT and/or BHR compared with children who had a negative result for both tests. Current phlegm and bronchitis prevalences among the children with a positive test were about three times higher, whereas for itchy rash and eczema ever the difference was about 2-fold.

Figure 1 shows the adjusted ORs between truck traffic and air pollution concentrations on the one hand, and respiratory symptoms on the other hand for children with a positive SPT, children with a positive BHR, and children with a negative result for both tests separately. Car traffic and distance of the school or home to the highway were not associated with respiratory or allergic symptoms in any of the subgroups (results not shown). For most of the symptoms that were analyzed (except current phlegm), ORs for children with a positive SPT or BHR were considerably higher than those for children with a negative result for both tests. Effects appear to be strongest for children with a positive BHR, especially for current wheeze and current bronchitis. The group of children with a positive BHR, however, also includes children with a positive SPT, and vice versa. For the 765 children for whom both tests were obtained, 76 of 152 (50%) children who were positive in the BHR test also responded to the SPT, and 76 of 208 (37%) children with a positive SPT also responded to the bronchial challenge. The groups of 76 children who were positive in the BHR test and not in the SPT and of 132 children who responded to the SPT alone but not BHR were considered too small to analyze separately.

Separate analyses for children with SPT reactivity for indoor or outdoor allergens specifically did not show clear differences between the two groups (results not shown). For current wheeze and current bronchitis, the associations with soot and NO_2 for children with a positive SPT to outdoor allergens were stronger than those for children with a positive SPT to indoor allergens, with ORs ranging from 3.88 to 5.31 (compared with

Table 3. Adjusted ORs[a] and 95% confidence limits (95% CI) of the association between respiratory and allergic symptoms, traffic characteristics, and annual average air pollution concentrations.

	Current wheeze OR (95% CI)	Asthma ever OR (95% CI)	Current conjunctivitis OR (95% CI)	Hay fever ever OR (95% CI)	Current itchy rash OR (95% CI)	Eczema ever OR (95% CI)	Current phlegm OR (95% CI)	Current bronchitis OR (95% CI)
Traffic characteristics[b]								
Truck traffic	1.96[#] (0.88–4.38)	1.02 (0.43–2.44)	2.57* (1.00–6.58)	2.40 (0.77–7.49)	2.65* (1.20–5.85)	1.27 (0.73–2.19)	2.14 (0.73–6.30)	2.41 (0.82–7.13)
Car traffic	0.56 (0.27–1.15)	0.92 (0.43–1.95)	0.80 (0.35–1.83)	0.70 (0.26–1.89)	0.58 (0.28–1.17)	0.69 (0.43–1.11)	0.48 (0.19–1.22)	0.84 (0.33–2.14)
Distance school–highway	1.19 (0.71–1.97)	0.93 (0.54–1.61)	1.55 (0.87–2.74)	1.04 (0.51–2.14)	1.17 (0.71–1.92)	0.95 (0.67–1.34)	1.52 (0.80–2.91)	1.18 (0.60–2.31)
Distance home–highway	1.20 (0.89–1.62)	1.04 (0.74–1.45)	0.61* (0.41–0.91)	0.92 (0.62–1.36)	0.90 (0.68–1.20)	1.00 (0.81–1.22)	0.88 (0.62–1.23)	1.21 (0.87–1.68)
Outdoor air pollution[c]								
$PM_{2.5}$	1.51 (0.90–2.53)	1.03 (0.59–1.82)	2.08* (1.17–3.71)	2.28* (1.13–4.57)	1.63[#] (0.91–2.89)	1.31 (0.94–1.83)	1.53 (0.74–3.19)	1.71 (0.84–3.50)
Soot	1.43 (0.66–3.07)	1.36 (0.62–2.98)	2.54* (1.15–5.60)	1.29 (0.40–4.14)	1.54 (0.68–3.49)	1.17 (0.71–1.92)	2.41[#] (0.96–6.04)	1.32 (0.44–3.94)
NO_2	1.74[#] (0.99–3.05)	1.39 (0.75–2.56)	2.60** (1.38–4.90)	1.98[#] (0.90–4.33)	1.25 (0.66–2.39)	1.27 (0.88–1.84)	1.72 (0.82–3.62)	1.37 (0.60–3.12)

[a]Adjusted for sex, age, current parental smoking, current pet possession, parental education level, non-Dutch nationality, cooking on gas, number of persons in the household, presence of an unvented water heater in the kitchen, questionnaire not filled out by the mother, and presence of mold stains in the kitchen, living room, or bedroom. ORs for traffic densities and air pollution are expressed for the difference between the maximum and the minimum of the exposure variable; ORs for distance to the highway are expressed for the difference between 100 and 400 m. [b]All four traffic characteristics together in the same model. [c]All three air pollution components separately in three different models; also adjusted for distance of the home to the motorway. [#]$p < 0.10$; *$p < 0.05$; **$p < 0.01$.

Table 4. Adjusted ORs[a] for elevated total IgE, SPT reactivity, lung function, and BHR in relation to traffic-related characteristics and annual average outdoor air pollution concentrations.

	Elevated total IgE (n = 881) OR (95% CI)	SPT reactivity: Any allergen (n = 1,141) OR (95% CI)	SPT reactivity: Indoor allergens (n = 1,141) OR (95% CI)	SPT reactivity: Outdoor allergens (n = 1,141) OR (95% CI)	FVC < 85% predicted (n = 1,726)[b] OR (95% CI)	FEV_1 < 85% predicted (n = 1,724)[b] OR (95% CI)	BHR (n = 949) OR (95% CI)
Traffic characteristics[c]							
Truck traffic	1.32 (0.51–3.39)	1.38 (0.67–2.85)	1.13 (0.51–2.51)	2.83* (1.18–6.82)	0.96 (0.36–2.59)	1.19 (0.34–4.23)	0.90 (0.38–2.14)
Car traffic	1.39 (0.61–3.19)	1.09 (0.57–2.07)	1.29 (0.64–2.59)	0.59 (0.26–1.30)	1.40 (0.61–3.22)	1.13 (0.40–3.16)	1.34 (0.63–2.87)
Distance school–highway	1.33 (0.73–2.41)	1.14 (0.72–1.82)	1.09 (0.65–1.83)	1.39 (0.79–2.42)	1.13 (0.59–2.15)	0.85 (0.38–1.93)	1.09 (0.64–1.86)
Distance home–highway	0.99 (0.73–1.35)	1.00 (0.75–1.33)	0.99 (0.73–1.35)	1.12 (0.80–1.59)	0.85 (0.61–1.18)	0.88 (0.58–1.33)	1.11 (0.79–1.57)
Outdoor air pollution[d]							
$PM_{2.5}$	1.45 (0.74–2.84)	1.33 (0.83–2.11)	1.17 (0.70–1.94)	1.90* (1.06–3.40)	0.54* (0.29–1.00)	0.88 (0.37–2.09)	0.93 (0.51–1.68)
Soot	2.67* (1.16–6.12)	1.24 (0.64–2.41)	1.39 (0.69–2.81)	1.41 (0.63–3.17)	1.12 (0.41–3.09)	1.45 (0.43–4.85)	1.44 (0.66–3.14)
NO_2	3.12** (1.81–5.38)	1.70* (1.03–2.81)	1.94* (1.13–3.33)	1.69[#] (0.91–3.14)	0.78 (0.38–1.61)	1.55 (0.69–3.49)	1.22 (0.66–2.27)

[a]Adjusted for sex, age, current parental smoking, current pet possession, parental education level, non-Dutch nationality, cooking on gas, number of persons in the household, presence of an unvented water heater in the kitchen, questionnaire not filled out by the mother, and presence of mold stains in the kitchen, living room, or bedroom. ORs for traffic densities and air pollution are expressed for the difference between the maximum and the minimum of the exposure variable; ORs for distance to the highway are expressed for the difference between 100 and 400 m. [b]Additional adjustment for cough or cold at the time of the lung function measurement, and bronchitis, severe cold or flu in the 3 weeks preceding the measurement and season. [c]All four traffic characteristics together in the same model. [d]All three air pollution components separately in three different models; also adjusted for distance of the home to the motorway. [#]$p < 0.10$; *$p < 0.05$; **$p < 0.01$.

0.63–1.17 for children sensitized to indoor allergens), but only the association between current wheeze and NO_2 was statistically significant (OR = 5.31; p = 0.04). For current itchy rash, ORs for children sensitized for outdoor allergens were higher and significant at the $p < 0.05$ level for all four exposure variables (trucks, $PM_{2.5}$, soot, and NO_2), with ORs ranging from 7.64 for $PM_{2.5}$ to 18.38 for soot. Again, the group of children sensitized to outdoor allergens also included children sensitized to indoor allergens and vice versa, but the numbers of children sensitized to indoor allergens alone (n = 144) or to outdoor allergens alone (n = 64) were too small to analyze separately.

Discussion

This study showed that truck traffic and air pollutants associated with truck traffic were associated with chronic respiratory symptoms in schoolchildren living close to motorways. There was no association with car traffic. There was also no association with BHR and sensitization to indoor allergens. Sensitization to outdoor allergens was increased in children exposed to high truck traffic counts and associated air pollution concentrations from the motorways. The associations between traffic-related air pollution and symptoms were much stronger in children with BHR and sensitization to common allergens than among children without these traits.

Could these results have been produced by bias? Although the parents who completed the questionnaires knew the study was about air pollution and must have known that they were living in the vicinity of a motorway, it was not disclosed to them that the study was specifically about traffic density and composition on the motorway. The traffic counts and the measured air pollution concentrations that form the basis for exposure assessment in this study were most certainly not known to the parents who completed the symptom questionnaires. Also, most children had never been tested for skin reactivity or bronchial reactivity before, and the results of these tests were not known to the parents when the symptom questionnaires were completed. We think it is unlikely that the parental responses to the questionnaire could have produced spurious associations between traffic-related air pollution and symptoms for the reasons mentioned.

Could there have been confounding that was overlooked? We adjusted for a comprehensive set of known risk factors for impaired respiratory health and found strong associations between (truck) traffic-related air pollution and respiratory health regardless. Of course, it is never possible to completely exclude that confounding may have occurred through the action of some unknown determinant of impaired respiratory health that was overlooked.

The results of this more comprehensive study in several ways confirm the results of our earlier work (Brunekreef et al. 1997; Roorda-Knape et al. 1998; van Vliet et al. 1997): Truck traffic and air pollutants associated with it were again specifically associated with impaired respiratory health, whereas car traffic was not. The main difference with the results of the earlier study was that, in the more comprehensive study reported here, there was no

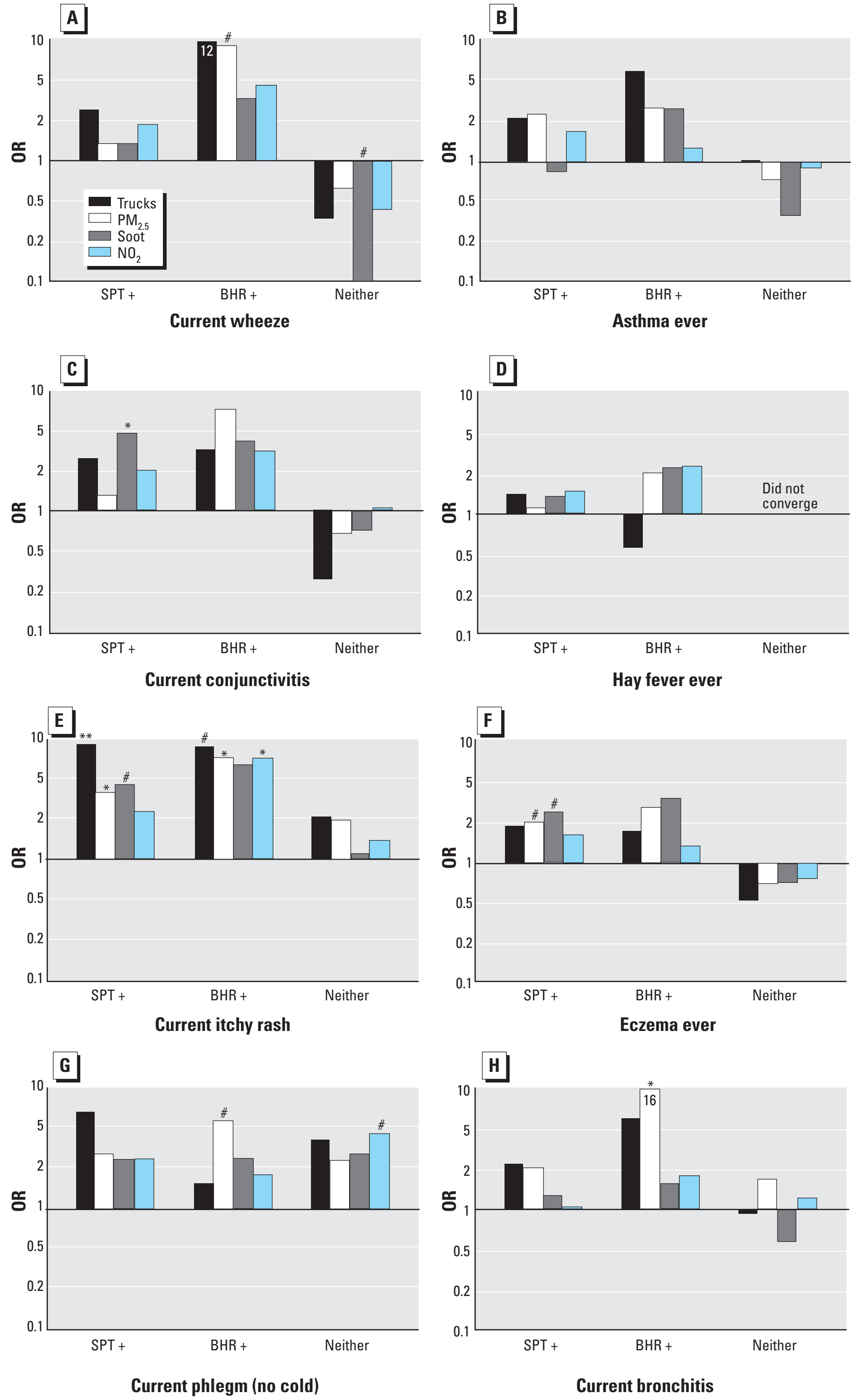

Figure 1. Adjusted ORs for the relationships between respiratory symptoms and truck traffic counts, $PM_{2.5}$, soot, and NO_2, for children with and without a positive SPT (SPT+) and positive BHR (BHR+) test separately. Neither = negative on both tests. In (*A*) and (*H*), 12 and 16, respectively, are the exact values. #$p < 0.10$; *$p < 0.05$; **$p < 0.01$.

association between truck traffic and lung function, as there was in the previous study. There is no ready explanation for this; graphs presented by Brunekreef et al. (1997) show that the association between truck traffic and lung function in the six areas that were studied in the past was not driven by just one or two of the areas. The range in truck traffic counts was larger in this study than in the previous one, so that it was also not a matter of lack of contrast. In the previous study, lung function measurements took place in a relatively short period in the early summer of 1995, using rolling-seal dry spirometers. In the present study, measurements were conducted over a period of > 1 year using heated pneumotachographs. Instruments were carefully volume-calibrated at frequent intervals in both studies, but we cannot completely exclude that some drift over the long study period may have occurred within the calibration limits that may have obscured exposure-related differences in lung function, because it was logistically impossible to study the schoolchildren in random order.

Our assessment of respiratory health was more comprehensive than in the previous study, including tests of BHR and allergic sensitization. Interestingly, BHR was not at all associated with any of the air pollution exposure variables, although wheeze, an important symptom of asthma, was. Also, there was little association between the air pollution exposure variables and allergic sensitization, although sensitization to outdoor pollen did show some association with the air pollution exposure variables. A study among adults living in Basel, Switzerland, found that sensitization to pollen was associated with the total traffic count on the street of residence, without finding a relationship with upper airway allergic symptoms and traffic counts (Wyler et al. 2000). A study from Germany found that in a small group of children living inside an urban area, hay fever, symptoms of allergic rhinitis, wheezing, and sensitization against pollen, house dust mites or cats, and milk or eggs were associated with outdoor NO_2 measured at the home address as an indicator of traffic related air pollution (Kramer et al. 2000). However, this relationship was largely lost when children living in rural areas with lower NO_2 exposures were included.

Few studies have included measurements of BHR in relation to traffic-related pollution. A recent study from Germany (Nicolai et al. 2003) found no relation between various measures of exposure to traffic-related air pollution and BHR, which was measured using the same technique as in our study. There was no relationship with lung function level, either.

A striking finding was the strong effect modification by BHR as well as sensitization. In this population, about 37% of the children had either a positive SPT or BHR test, or both, and it was in this group of children that the associations between air pollution exposure variables and chronic respiratory symptoms were almost exclusively found. Such effect modification has not often been investigated. The German study (Nicolai et al. 2003) reported that associations between exposure to traffic-related air pollution were significant only in the atopic children, as in our study, but commented that the percentage of symptomatic children in the nonatopic subgroup was low, so statistical significance was hard to reach. No comparison of effect estimates was given.

Experimental evidence obtained in studies on human volunteers, animals, and *in vitro* test systems suggests that diesel exhaust particles have the capability to enhance immunologic responses to allergens and to elicit inflammatory reactions in the airways at relatively low concentrations and short exposure durations (Diaz-Sanchez 1997; Diaz-Sanchez et al. 2000; Miyabara et al. 1998; Muranaka et al. 1986; Nordenhall et al. 2001; Rudell et al. 1996, 1999; van Zijverden and Granum 2000). Against this background, it seems reasonable to interpret our findings as showing increased airway inflammation, in particular, in subjects who already are sensitized to common allergens or have BHR. At the same time, there was little evidence that the prevalence of these conditions was increased by exposure to (heavy) traffic-related air pollution. In an earlier study on acute effects of air pollution, we also observed that children with BHR and high serum IgE responded more strongly to various measures of ambient air pollution, including black smoke, which may act as surrogate for diesel exhaust (Boezen et al. 1999).

The use of GIS to obtain more accurate measures of exposure to traffic-related air pollution has increased. The power of such systems was nicely illustrated by two subsequent analyses from Nottingham, the first one finding no relationship between traffic activity and wheeze in schoolchildren when analyzing traffic activity in the living area in tertiles (Venn et al. 2000). When the same material was analyzed for children living within short distances of major roads, a clear relationship with wheeze was observed (Venn et al. 2001). Similarly, the use of data on location of home with respect to roads and of data on traffic density on those roads resulted in observations of significant relationships with specific respiratory hospital admission rates in Toronto (Buckeridge et al. 2002), with childhood asthma hospitalization rates in Erie County, New York (Lin et al. 2002), and with childhood asthma medical care visits in San Diego County, California (English et al. 1999). These and other studies suggest that improvement of accuracy and precision of exposure classification helps to detect associations between adverse respiratory outcomes in children and (in a few studies) adults.

Conclusion

Our study showed that children attending schools close to motorways with high truck traffic counts in the Netherlands experienced more respiratory symptoms than did children attending schools near motorways with low truck traffic counts. These associations were observed primarily in children with BHR, positive SPTs to common allergens, or both.

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