Traffic-Related Air Pollution and Otitis Media

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BACKGROUND: Otitis media is one of the most common infections in young children. Although exposure to environmental tobacco smoke is a known risk factor associated with otitis media, little information is available regarding the potential association with air pollution.

OBJECTIVE: We set out to study the relationship between exposure to traffic-related air pollution and otitis media in two birth cohorts.

METHODS: Individual estimates of outdoor concentrations of traffic-related air pollutants—nitrogen dioxide, fine particles [particle matter with aerodynamic diameter ≤ 2.5 μm (PM2.5)], and elemental carbon—were calculated for home addresses of approximately 3,700 and 650 infants from birth cohort studies in the Netherlands and Germany, respectively. Air pollution exposure was analyzed in relation to physician diagnosis of otitis media in the first 2 years of life.

RESULTS: Odds ratios (adjusted for known major risk factors) for otitis media indicated positive associations with traffic-related air pollutants. An increase in 3 μg/m3 PM2.5, 0.5 μg/m3 elemental carbon, and 10 μg/m3 NO2 was associated with odds ratios of 1.13 (95% confidence interval, 1.00–1.27), 1.10 (1.00–1.22), and 1.14 (1.03–1.27) in the Netherlands and 1.24 (0.84–1.83), 1.10 (0.86–1.41), and 1.14 (0.87–1.49) in Germany, respectively.

CONCLUSIONS: These findings indicate an association between exposure to traffic-related air pollutants and the incidence of otitis media. Given the ubiquitous nature of air pollution exposure and the importance of otitis media to children’s health, these findings have significant public health implications.

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Materials and Methods

Study populations. The Prevention and Incidence of Asthma and Mite Allergy (PIAMA) study is a prospec- tive birth cohort study with an initial enrollment of 4,146 children (Brunkreft et al. 2002; Koopman et al. 2001; Wijga et al. 2001). The cohort was recruited in 1997–1998 during the second trimester of pregnancy from a series of communities varying from rural to large cities in the north, west, and center of the Netherlands. Mothers were classified as allergic or nonallergic on the basis of a validated screening questionnaire (Lakwijk et al. 1998). Nonallergic (based on a screening questionnaire) pregnant women were invited to participate in a “natural history” study arm (initial enrollment of 3,291). Pregnant women identified as allergic through a screening questionnaire were allocated primarily to an intervention arm (initial enrollment of 855), with a random subset allocated to the natural history arm. The intervention involved the use of mite-impermeable mattress and pillow covers. The study protocol was approved by the institutional review boards of each participating institute, and parents or guardians of all subjects gave written informed consent. All subjects with completed questionnaires at 2 years of age were included in the analyses.

The participants of the LISA-Munich (Influence of Lifestyle factors on the development of the Immune system and Allergies in East and West Germany) birth cohort study were recruited during pregnancy. From December 1997 to January 1999, newborns from six obstetrical clinics in Munich whose parents were born in Germany and had German nationality were defined as the target population for the study. A detailed description of selection, exclusion criteria, and characteristics of study population has been published previously (Gehring et al. 2002).

For this analyses, we selected all infants with birth addresses in Munich (without surrounding communities) for whom questionnaire data were available for the first year of life and who did not move away from Munich within the first year of life. A total of 673 subjects from the LISA cohort fulfilled these criteria. The study was approved by the ethics commission of the Landesaerztekammer Bavaria and was carried out in accordance with the institutional guidelines for the protection of human subjects. Parents or guardians of all subjects gave written informed consent.

Exposure assessment. Air pollution concentrations at the home address of each member of the cohort were calculated by combining air pollution measurements with a geographic information system (GIS; Brauer et al. 2003; Gehring et al. 2002). Briefly, air pollutants were measured at 40 individual sites in each country, designed to capture the maximum variability in pollution from traffic sources. Fine particles [particulate matter with aerodynamic diameter ≤ 2.5 µm (PM$_{2.5}$)] were collected with Harvard impactors (Air Diagnostics and Engineering, Harrison, ME, USA), nitrogen dioxide was collected by Palms tubes, and light-absorbing carbon was measured as the reflectance of the PM$_{2.5}$ filters, a method shown to be highly correlated with thermal elemental carbon measurement (Cyrys et al. 2003). At each location, measurements were conducted for four 2-week periods dispersed throughout 1 year and then adjusted for temporal trends, based on the difference between concentrations measured during each period to annual average measurements (Hoek et al. 2002), to calculate long-term average concentrations for the 40 locations.

Geographic data were also collected regarding traffic, road, and population density in the vicinity of each monitoring location. We developed regression models to relate the annual average concentrations at the 40 monitoring sites with the geographic variables. For example, in the Netherlands, the number of high-traffic roads within a 250-m radius of a location, the presence of a major road within a 50-m distance, the density of buildings (addresses) within a 300-m radius, and an indicator for the region of the country were used in the model to predict light-absorbing carbon concentrations. In Munich, the light-absorbing carbon model used traffic intensity within a 50-m distance, traffic intensity in a circular area between 50 and 250 m, and the population density within a 300-m radius and in a circular area between 300 and 5,000 m to predict concentrations. Models with similar variables describing traffic intensity were developed for PM$_{2.5}$ and NO$_2$. These models explained 73, 81, and 85% of the variability in the annual average concentrations for PM$_{2.5}$, light-absorbing carbon, and NO$_2$, respectively, in the Netherlands (Brauer et al. 2003) and 56, 67, and 62% of the variability in the annual average concentrations for PM$_{2.5}$, light-absorbing carbon, and NO$_2$, respectively, in Germany (Gehring et al. 2002).

We then applied these models to the same geographic variables measured at the home addresses of each individual in the cohort to obtain unique long-term ambient air pollution concentrations at the home address of each cohort member at the time of birth. Given our interest in early-life exposures, we estimated air pollutant concentrations only for the birth addresses of cohort members. However, in both locations only a small (9% in the Netherlands, 11% in Munich) percentage of the study population moved within the first year of life (Brauer et al. 2002; Gehring et al. 2002).

Questionnaire data. We assessed information on otitis media using a parent-completed questionnaire. Specifically, in the Netherlands the question “Did a doctor diagnose infection of the middle ear in your child in the last 12 months?” was asked when the child was 12 months and 24 months of age. In Munich, the question “Did a doctor diagnose otitis media in your child during the last 6 months?” was asked every 6 months. A series of potential confounding variables (listed in Table 1) were selected if exploratory data analysis suggested substantial variability within the cohort or if variables were suspected of being risk factors for otitis media. Confounder data were selected from the earliest questionnaire that was available, to coincide with the exposure data that were estimated for addresses at birth. ETS exposure was assessed by questionnaire (Table 1) and has been validated against home nicotine measurements for the Dutch cohort (Brunkreft et al. 2000).

Statistical analysis. We performed multiple logistic regression analyses to analyze the relationship between otitis media and estimated air pollution exposure for study subjects in each of the cohorts. Results are presented as crude and adjusted odds ratios (ORs) with 95% confidence intervals (CIs). We adjusted for potential confounding factors such as sex, parental atopy, maternal education, siblings, maternal smoking during pregnancy, ETS exposure at home, use of gas for cooking, indoor moulds and dampness, number of siblings, breast-feeding, and presence of pets in the home (Table 1). ORs are presented for standardized (between the two study locations) differences (approximating interquartile range differences in the two locations) in estimated exposures of 3 µg/m$^3$ for PM$_{2.5}$, 0.5 × 10$^{-9}$/m for particle light absorbance [corresponding to ~0.5 µg/m$^3$ elemental carbon, based on colocated sampling (Cyrys et al. 2003)], and 10 µg/m$^3$ for NO$_2$.

Results

In both cohorts, the prevalence of otitis media increased in the second year and was nearly identical at 2 years of age (Table 1). By that age, approximately 35% of each cohort had at least one occurrence of otitis media. The cohorts were similar with respect to maternal age and parental allergy/atopy. The rate of breast-feeding was much higher in the German cohort, whereas ETS exposure, the use of gas for cooking, and the presence of pets were much higher in the Dutch cohort. The German cohort had a somewhat higher level of education and a lower number of siblings.

Exposures to traffic-related air pollution are summarized in Table 2. Median and mean concentrations of light-absorbing carbon and NO$_2$ were similar between the Netherlands and Germany whereas PM$_{2.5}$ concentrations were higher in the Netherlands, probably due to higher regional background concentrations. Interquartile ranges were nearly twice as large in the Netherlands (3.2 µg/m$^3$, 0.54 10$^{-9}$/m, and 16.4 µg/m$^3$ for PM$_{2.5}$, light-absorbing...
carbon, and NO\(_2\) respectively) than in Munich (1.5 µg/m\(^3\), 0.34 10\(^{-5}\)/m, and 8.5 µg/m\(^3\)), reflecting the fact that the Dutch cohort included suburban and semirural areas that were not heavily affected by traffic-related air pollutants, whereas the German cohort was restricted to the Munich metropolitan area in which traffic emissions contribute to the urban background as well as to variability within the area.

Crude ORs indicated elevated risks for otitis media in association with all air pollutants, with associations reaching statistical significance in the larger Dutch cohort (Table 3). These ORs were similar for otitis media in the first year of life and for cumulative incidence over the first 2 years. ORs increased slightly but were largely unaffected by adjusting for covariates in both cohorts. Given the differences in prevalence of covariates between the two cohorts, this suggests sufficient control for potential confounding variables or that these covariates did not have a major impact in this analysis. Further, we specifically investigated the impact of ETS exposure in both cohorts but did not observe any association between ETS exposure or smoking during pregnancy and otitis media, and adjustment for these exposures did not change the associations between air pollution and otitis media.

Because attendance at a child care facility has been independently associated with respiratory tract infections in the Dutch cohort (Koopman et al. 2001) and is also a risk factor for otitis media occurrence (Bluestone and Klein 2001), we conducted a sensitivity analysis to evaluate its potential impact on the association with air pollution. Because child care attendance in Munich was very low—3% in the first year and < 15% at 2 years of age—and to retain similar analyses in both cohorts, we did not include child care attendance in the primary models. We therefore restricted the sensitivity analysis to the Dutch cohort that had higher levels of child care attendance. Of the 981 children (26%) who attended child care at 1 year of age, the median number of hours of child care attendance per week was 18, and 735 of these children attended child care > 10 hours per week. By 2 years of age, 1,256 children (34%) had reported attending child care. Adjusted ORs for otitis media with models incorporating child care attendance were somewhat reduced (e.g., for NO\(_2\) OR = 1.13 [95% CI, 0.99–1.28] at 1 year and OR = 1.10 [95% CI, 0.99–1.23] after 2 years of age) but still elevated. Additional stratified analyses indicate that the effect of air pollution on otitis media occurrence was not restricted to those children who attended child care.

**Discussion**

This analysis represents the first examination of the relationship between air pollution exposure and otitis media in a large cohort study. In two birth cohorts with a common exposure assessment approach, we have identified associations between individual estimates of traffic-related air pollution exposure and the incidence of otitis media. Given the widespread nature of air pollution exposure and the high prevalence of otitis media, these findings indicate an important and previously unrecognized societal impact of air pollution. Further, given the high direct and indirect costs associated with otitis media episodes, our results suggest a potentially important preventable risk factor for this common childhood disease.

In contrast to limited previous analyses that have been conducted with small study populations and have focused largely on cross-sectional comparisons between different geographic regions (Heinrich and Raghuyamshi 2004), we assessed exposure at the individual level with individual control for covariates. Perhaps the strongest prior evidence relating air pollution with otitis media comes from one of our earlier studies in which prevalence rates for otitis media among 7,000 school-age children in three East German areas (two polluted and one control area) were compared in repeated cross-sectional surveys (Heinrich et al. 2002). In addition, temporal changes of prevalence rates for otitis were studied in parallel with dramatic improvements in air quality [sulfur dioxide and total suspended particles (TSP)] after German reunification (Heinrich et al. 2000). Although adjusted lifetime prevalence
rates for otitis did not differ among children who grew up in areas with different levels of these air pollutants (Heinrich et al. 2002), there were significant increases in prevalence of other nonallergic respiratory illnesses (bronchitis, frequent colds, sinusitis, cough) and decreased lung function in children from the polluted areas (Frye et al. 2003; Heinrich 2003; Heinrich et al. 2002). In parallel with the decreases in SO2 and TSP in all three areas, prevalence rates for otitis decreased from 31% in 1992–1993 to 26% in 1995–1996 and 27% in 1998–1999 (Heinrich et al. 2002). The adjusted OR for a 50-µg/m3 change in TSP was 1.45 (95% CI, 0.89–2.37) and 1.42 (95% CI, 0.94–2.15) for a 100-µg/m3 change in SO2 concentration (Heinrich et al. 2002). However, these increased risk estimates of ambient air pollutants for otitis media were driven mainly by the temporal improvement of air quality and therefore may also parallel other unmeasured lifestyle changes, whereas the regional gradient of air pollution concentrations were not consistent with area-specific differences in prevalence rates. For several other nonallergic respiratory outcomes, temporal changes of prevalence rate (decreasing) were consistent with spatial differences (highest prevalence rate in the most polluted area).

In a somewhat similar design, ear infections were examined in two cross-sectional surveys of approximately 400 children 11–13 years of age from three districts of São Paulo, Brazil, conducted in 1986 and in 1998 (Ribeiro and Cardoso 2003). The three districts experienced different levels of SO2 in 1973–1983, and these differences were associated with crude prevalence rates (unadjusted for potential confounders) for current and frequent ear infection. Social indicators such as parental education and literacy also differed between the three districts. Further, temporal changes in ambient particulate matter concentrations were also associated with changes in frequent ear infection prevalence. Although this study has several limitations (small sample sizes, descriptive presentations of methods and main findings), the results are consistent with an association between prevalence of otitis media and ambient air pollution.

Other studies that have evaluated air pollution and otitis media typically lack exposure measurements or were conducted on small sample sizes (Caceres Udina et al. 2004; da Costa et al. 2004; Dostal et al. 2001; Holby et al. 1997) but also suggest associations. For example, a study of 1,156 children with OME in the United Kingdom did not measure exposures but used distances of the home of these children from known industrial emission points as an exposure proxy (Holby et al. 1997). A significantly greater portion of study entrants with OME lived within a 1,000-m buffer of an industrial point source, but no trend of decreasing prevalence rate of OME with increasing distance was observed.

Although our study has several major advantages over previous investigations (individual level exposure assessment and large study population), there are also inherent limitations to our approach. First, as is common with air pollution epidemiologic analyses, we estimated exposures instead of directly measuring them using personal monitoring. Additionally, for those children who moved or attended child care, estimating exposures at these locations may reduce exposure misclassification. Second, we assessed otitis media by questionnaire-based self-reporting of physician diagnosis and not by any objective measure. Third, we did not assess severity or address issues such as recurrent otitis media and interactions between air pollution and different treatment regimes. Such analyses, although important to understanding the public health significance of our findings, are probably best addressed in a longitudinal study design in which detailed information regarding otitis media occurrence and treatment is evaluated in relation to short-term changes in air pollution exposure. Finally, although we adjusted analyses for a large number of potential risk factors, the possibility for residual confounding remains, especially given that exposure estimates were based on spatial contrasts in air pollution that may also lead to spatial contrasts for other unmeasured otitis media risk factors. These limitations are, however, largely unavoidable for cohort studies of large populations.

These findings indicate an association between exposure to traffic-related air pollutants and the incidence of otitis media. This association is supported by a wealth of evidence linking exposure to high levels of air pollution indoors in developing countries with acute lower respiratory infections (Smith et al. 2000), more limited evidence of associations between levels outdoor air pollution in developed countries and upper respiratory tract infections (Chauhan and Johnston 2003; Lin et al. 2005; Romieu et al. 2002), and the fact that some upper respiratory tract infections may progress to otitis media (Rovers et al. 2004). The strong evidence linking otitis media with ETS exposure and the similarities between ETS and ambient air pollution add further support to our findings. The specific air pollutants that affect respiratory infections have not been clearly identified, although some evidence suggests that NO2 and coarse particles may be especially active in this regard (Chauhan and Johnston 2003; Lin et al. 2005). Additionally, the mechanism by which air pollution may lead to otitis media is not known. Air pollution exposure may result in a more severe or persistent infection—for example, by decreasing mucociliary clearance (Chauhan and Johnston 2003; Thomas and Zelikoff 1999)—making progression to otitis media more likely. For example, an interaction between respiratory syncytial virus infection and NO2 exposure before infection has been demonstrated to lead to increased severity of asthma exacerbations (Chauhan et al. 2003). Alternatively, air pollution may actively promote progression to otitis media. Addressing these or other possibilities will require further research. Although replication of our results in similar cohort studies is needed, the ubiquitous nature of air pollution exposure and the importance of otitis media to children’s health suggest that these findings have significant public health implications.

### Table 3. Association between long-term exposure to air pollution and otitis and respiratory infections in the two cohorts: crude and adjusted ORs and 95% CIs.

| Otitis media | The Netherlands | Munich, Germany |
|-------------|----------------|----------------|
|              | Unadjusted | Adjusted*  | Unadjusted | Adjusted*  |
| **At 1 year of age** |          |          |          |          |
| PM2.5        | 1.13 (1.00–1.29)* | 3,705 | 1.13 (0.98–1.32) | 2,984 | 1.09 (0.68–1.75) | 665 | 1.19 (0.73–1.92) | 620 |
| Light-absorbing carbon | 1.11 (1.00–1.23)* | 3,705 | 1.11 (0.98–1.26) | 2,984 | 1.07 (0.80–1.44) | 665 | 1.12 (0.83–1.51) | 620 |
| NO2          | 1.14 (1.02–1.27)* | 3,705 | 1.17 (1.03–1.34) | 2,984 | 1.03 (0.74–1.43) | 665 | 1.09 (0.78–1.54) | 620 |
| **At 2 years of age (cumulative)** |          |          |          |          |
| PM1.0        | 1.10 (0.99–1.22) | 3,642 | 1.13 (1.00–1.27)* | 2,970 | 1.18 (0.81–1.75) | 650 | 1.24 (0.84–1.83) | 605 |
| Light-absorbing carbon | 1.08 (0.99–1.18) | 3,642 | 1.10 (1.00–1.22)* | 2,970 | 1.08 (0.85–1.37) | 650 | 1.10 (0.86–1.41) | 605 |
| NO2          | 1.10 (1.01–1.21)* | 3,642 | 1.14 (1.03–1.27)* | 2,970 | 1.10 (0.85–1.42) | 650 | 1.14 (0.87–1.49) | 605 |

*ORs are calculated as described in "Materials and Methods."  
*Adjusted for mother's smoking during pregnancy, ETS exposure, mother's/father's education, sex, gas for cooking/heating, siblings, breast-feeding, molds, pets, parental allergy, mother’s age; in the Netherlands only, adjusted for ethnicity, study arm (intervention/natural history), and use of allergen-impermeable mattress cover. *Statistically significant elevated ORs (p < 0.05).
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