

Letter to the Editor

Traffic-related air pollution is associated with airway hyperresponsiveness

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Air pollution contributes to the increasing trend of asthma. Many epidemiologic studies have revealed an association between air pollution and asthma. Recently, birth cohort studies in which individual levels of exposure were measured have investigated the causal effects of air pollution on the development of asthma and found that air pollution increases the risk of asthma.¹⁻³ However, there are still conflicting results regarding the effects of air pollution on sensitization and airway hyperresponsiveness (AHR),^{4,5} both of which are important intermediate asthma phenotypes and may provide key insights into the underlying mechanisms of asthma. These inconsistent results suggest that the

effect of air pollution may be influenced by the age of great exposure and genetic background.⁶ In addition, AHR has not been fully investigated in epidemiologic studies of air pollution because of technical difficulties measuring AHR individually in large populations. Therefore, we examined the effects of air pollution on AHR in a nationwide prospective epidemiologic study.^{4,7}

The study population was derived from a prospective 2-year follow-up survey consisting of parental responses to the International Studies of Asthma Allergic diseases in Childhood (ISAAC) questionnaire and allergic evaluation, including methacholine challenge test, skin prick test, and pulmonary function test. Details about the study design and characteristics of the subjects are described elsewhere.⁴ We used the distance from road to home as a surrogate marker of exposure because motor vehicles are a

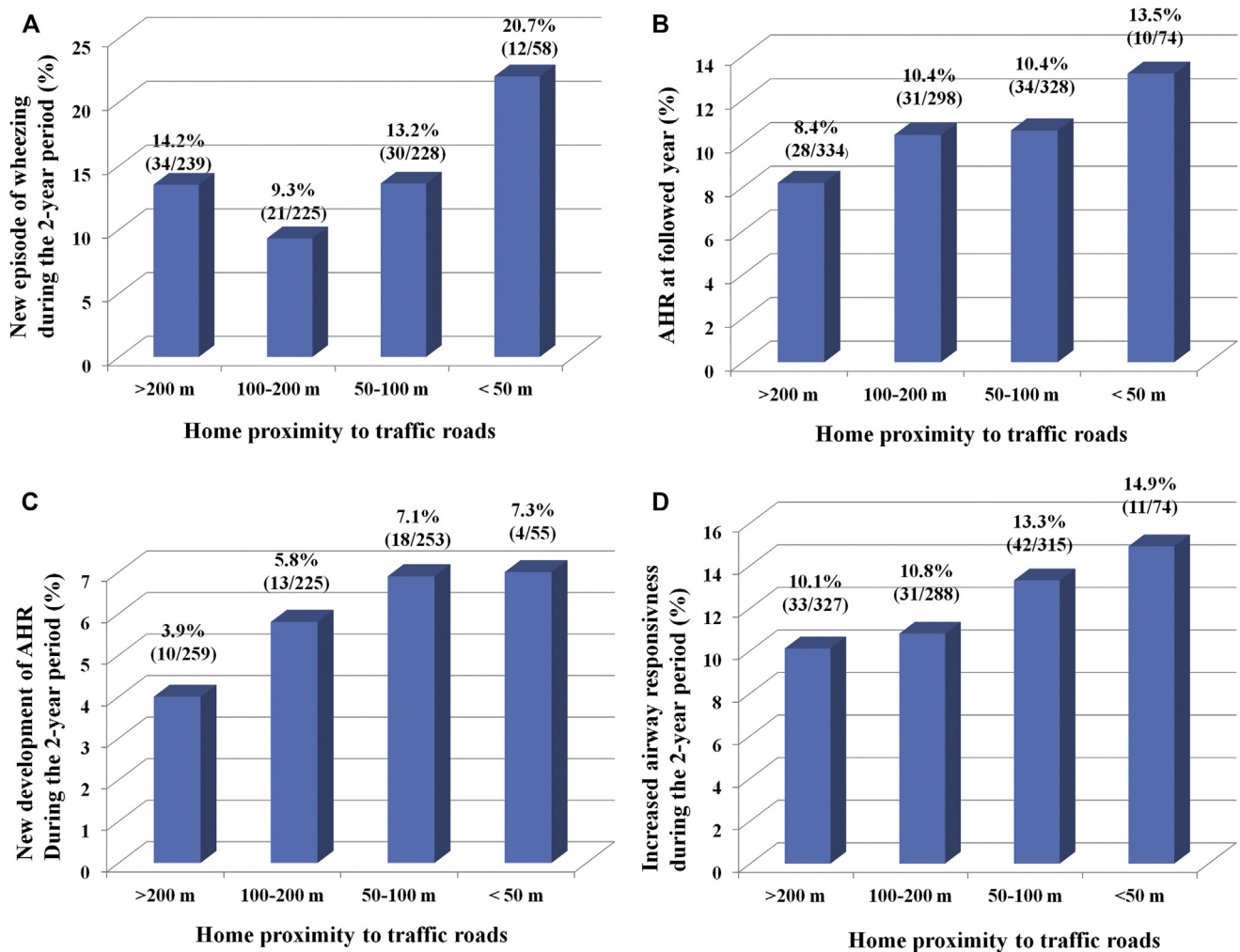


FIG 1. Associations between home proximity to traffic roads and AHR ($PC_{20} \leq 8$ mg/dL). **A**, Prevalence of new episode of wheezing during the 2-year study period according to home proximity to traffic roads. **B**, Rates of AHR ($PC_{20} \leq 8$ mg/dL) measured at 2 years after enrollment regardless of the initial AHR state. **C**, Rates of new development of AHR during the 2-year study period; hence, children need to have negative AHR ($PC_{20} > 8$ mg/dL) at enrollment. **D**, The rates of increased airway responsiveness. The PC_{20} value was decreased compared with the previous value regardless of crossing the threshold for AHR. Adjusted for age, sex, body mass index, paternal and maternal history of allergy, maternal education, family income, place of residence, environmental tobacco smoke (ETS) at home, and preterm birth.

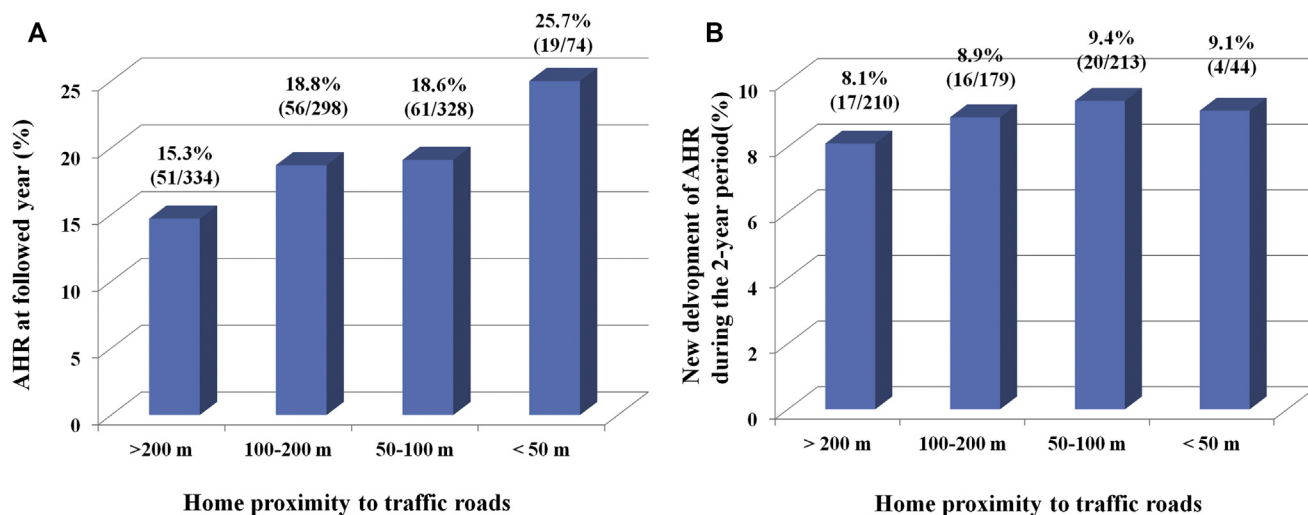


FIG 2. Associations between home proximity to traffic roads and AHR ($PC_{20} \leq 16$ mg/dL). **A**, Rates of AHR ($PC_{20} \leq 16$ mg/dL) measured at 2 years after enrollment regardless of the initial AHR state. **B**, Rates of new development of AHR during the 2-year study period; hence, the initial AHR had to be negative ($PC_{20} > 16$ mg/dL at enrollment).

significant source of urban air pollution. This traffic-related air pollution (TRAP) is mostly composed of nitrogen dioxide, particulate matter (PM), and carbon monoxide. Based on residential address at the time of enrollment, proximity of home to the nearest traffic road (≥ 4 lanes) was estimated using “near of proximity” of a geographic information system (Arc-Map, version 9.3; ESRI, Inc, Redlands, Wash). Subjects were categorized into 4 groups (≤ 50 m, 50–100 m, 100–200 m, and >200 m from the nearest traffic road). The association between home proximity to traffic roads and AHR ($PC_{20} \leq 8$ mg/dL) or prevalence of asthma was analyzed using multiple logistic regression models. Age, sex, body mass index, paternal and maternal history of allergy, maternal education, family income, place of residence, environmental tobacco smoke at home, and preterm birth were considered to be confounding factors and entered as covariates in all models.

A total of 1340 children (boys:girls = 514:48.6) with a mean age of 6.84 ± 0.51 years were included in the analysis on the basis of the availability of a completed ISAAC questionnaire and an allergy evaluation at both enrollment and follow-up (see Table E1 in this article’s Online Repository at www.jacionline.org). Of the 1340 children, 302 failed to give a complete residential address. The baseline prevalences of lifetime wheezing and AHR were 26.1% and 20.4%, respectively. Results of allergic evaluation were described previously.⁴ There was no significant relationship between lifetime wheezing or AHR and the distance to traffic roads at the start of the study period. However, new wheezing during the 2-year study period showed a trend toward greater prevalence in children who resided closer to traffic roads (OR [odds ratio] = 1.20; 95% CI = 0.91–1.55) (Fig 1, A). There was also an increasing trend in the prevalence of AHR at the follow-up year (OR = 1.25; 95% CI = 0.98–1.59) (Fig 1, B). The prevalence of new AHR (positive conversion from $PC_{20} > 8$ mg/dL at enrollment) was significantly associated with home proximity to traffic roads (OR = 1.61; 95% CI = 1.12–1.31) (Fig 1, C). The rate of increased airway responsiveness (any decreased PC_{20} value compared with the previous value) was also higher with decreasing distance to traffic roads (OR = 1.25; 95%

CI = 1.01–1.61) (Fig 1, D). When the cutoff value for AHR was set as 16 mg/dL, the rate of AHR was also increased even though new AHR rates were not significantly increased during a 2-year period (OR = 1.23, 95% CI = 1.02–1.49, and OR = 1.19, 95% CI = 0.87–1.63, respectively) (Fig 2). When AHR was analyzed as a continuous variable as log PC_{20} , children residing closer to the road tended to have a lower log PC_{20} (see Table E2 in this article’s Online Repository at www.jacionline.org).

This is the first study, to our knowledge, to find that TRAP increases AHR in children in a large prospective epidemiologic study. Children residing nearer to traffic roads tended to experience new wheezing and showed a greater increase in AHR. In contrast, Pujades-Rodriguez et al,⁵ who conducted a similar large epidemiologic study, found no association between home proximity to roads and AHR. However, their study population was a cohort of adults aged 18 to 70 years, and only cross-sectional association was analyzed. Therefore, it may be postulated that there is a critical period of development during which a person is vulnerable to air pollution. From this point of view, birth cohort studies using validated exposure models and allergy evaluation could reveal significant associations between exposure to TRAP and intermediate asthma phenotypes.^{1,2} However, these studies have not found significant associations between air pollution and AHR. These negative results could be largely due to misclassification of exposure level and health outcome. Previous birth cohort studies measured AHR only once in a subpopulation as part of asthma diagnosis. In the present study, we performed methacholine challenge twice, with a 2-year interval, in more than 1000 children from the general population. This enabled us to analyze the longitudinal effect of air pollution on change in AHR over time, yielding results that are reliable and can be generalized. In addition, we used home proximity to traffic roads as a marker for exposure to air pollution, which minimized exposure misclassification. The distance from road to home was correlated with individual exposure levels to air pollutants estimated by using the ordinary kriging method⁸ (Pearson’s

$r = -0.021$, -0.13 , and -0.14 for NO_2 , PM_{10} , and CO , respectively; $P < .01$ for all). The exposure data were previously reported.⁴

We previously reported a synergistic effect between TRAP and past episodes of bronchiolitis on the development of asthma.⁷ Thus, TRAP can interact with other genetic or environmental factors to modify the risk of asthma. The underlying mechanism may be related to air pollution-oxidative stress.⁹

In summary, we found, in a prospective epidemiologic study, that the rates of new AHR and increased airway responsiveness were higher in children residing closer to traffic roads. These findings support a causal effect of air pollution on AHR.

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TABLE E1. Characteristics of the subjects

Variable	Percent (n = 1340)	Included (n = 1038)	Excluded (n = 302)	P value
Sex (M:F)	51.4:48.6 (689:651)	51.5:48.5 (533:510)	50.7:49.3 (153:149)	NS
Age (y), mean $\pm$ SD	6.84 $\pm$ 0.51	6.83 $\pm$ 0.51	6.83 $\pm$ 0.48	NS
BMI	16.68 $\pm$ 2.34	16.72 $\pm$ 2.38	16.58 $\pm$ 2.20	NS
Paternal allergy	6.1	6.7	3.9	NS
Maternal allergy	9.1	9.2	9.1	NS
Address				
Metropolitan cities	46.3	48.0	40.4	.02
Industrial areas	53.7	52.0	59.6	
Prematurity, % (n)	5.3	5.0	6.3	NS
Breast-feeding > 3 mo, % (n)	38.7	40.1	32.9	.05
ETS at home, % (n)	29.0	44.7	42.7	NS
Home proximity to traffic roads (m)				
≤ 50		7.2		
50-100		31.7		
200-200		28.8		
>200		32.3		
AHR at enrollment				
Log PC ₂₀ (mg/dL)	1.34 $\pm$ 0.48	1.33 $\pm$ 0.49	1.38 $\pm$ 0.47	NS
PC ₂₀ $\leq$ 8 mg/dL	20.4	21.1	18.0	NS
PC ₂₀ $\leq$ 16 mg/dL	34.0	35.6	28.4	.02

AHR, Airway hyperresponsiveness; BMI, body mass index; ETS, environmental tobacco smoke; F, female; M, male; NS, not significant.

TABLE E2. Associations between home proximity to traffic roads and log PC₂₀

Log PC ₂₀	Home proximity to traffic roads (m)				<i>P</i> value
	>200	100-200	50-100	≤50	
At enrollment	1.35 ± 0.46	1.30 ± 0.51	1.35 ± 0.50	1.23 ± 0.54	>.05
At follow-up	1.55 ± 0.35	1.52 ± 0.37	1.52 ± 0.37	1.47 ± 0.40	>.05