ENVIRONMENTAL EXPOSURE

Traffic related air pollution as a determinant of asthma among Taiwanese school children

B-F Hwang, Y-L Lee, Y-C Lin, J J K Jaakkola, Y L Guo

Thorax 2005;**60**:467–473. doi: 10.1136/thx.2004.033977

See end of article for authors' affiliations

Correspondence to: Dr Y L Guo, Department of Environmental and Occupational Health, National Cheng Kung University, Tainan, Taiwan; leonguo@mail.ncku.edu.tw

Received 27 August 2004
Accepted 3 February 2005

Background: There is evidence that long term exposure to ambient air pollution increases the risk of childhood asthma, but the role of different sources and components needs further elaboration. To assess the effect of air pollutants on the risk of asthma among school children, a nationwide cross sectional study of 32 672 Taiwanese school children was conducted in 2001.

Methods: Routine air pollution monitoring data for sulphur dioxide (SO_2), nitrogen oxides (NOx), ozone (O_3), carbon monoxide (CO), and particles with an aerodynamic diameter of 10 μm or less (PM_{10}) were used. Information on individual characteristics and indoor environments was from a parent administered questionnaire (response rate 93%). The exposure parameters were calculated using the mean of the 2000 monthly averages. The effect estimates were presented as odds ratios (ORs) per 10 ppb changes for SO_2, NOx, and O_3, 100 ppb changes for CO, and 10 μg/m^3 changes for PM_{10}.

Results: In a two stage hierarchical model adjusting for confounding, the risk of childhood asthma was positively associated with O_3 (adjusted OR 1.138, 95% confidence interval (CI) 1.001 to 1.293), CO (adjusted OR 1.045, 95% CI 1.017 to 1.074), and NOx (adjusted OR 1.005, 95% CI 0.954 to 1.117). Against our prior hypothesis, the risk of childhood asthma was weakly or not related to SO_2 (adjusted OR 0.874, 95% CI 0.729 to 1.054) and PM_{10} (adjusted OR 0.934, 95% CI 0.909 to 0.960).

Conclusions: The results are consistent with the hypothesis that long term exposure to traffic related outdoor air pollutants such as NOx, CO, and O_3 increases the risk of asthma in children.

There is a large worldwide variation in the prevalence of asthma in children and there is also evidence that the prevalence has been increasing.[1] Both genetic and environmental factors play important roles in the aetiology of childhood asthma, and there is probably also genetic susceptibility to the effects of air pollution.[2] Short term changes in the occurrence of asthma are more likely to be influenced by changes in the environment, diet, and lifestyle than by changes in the genetic pool. From a preventive perspective, information on environmental, dietary, and behavioural factors is crucial.[3] Identification of indicators of genetic susceptibility to environmental exposures could be useful from the preventive point of view. There is evidence that long term exposure to ambient air pollution increases the risk of childhood asthma, but the role of different sources and components needs further elaboration.[4–12]

In a nationwide cross sectional study in Taiwan, Guo *et al* found an association between traffic related air pollution concentrations and the risk of asthma in school children.[13] This study did not adjust for parental atopy or indoor exposures which are potential sources of confounding and effect modification. In 2001 we conducted a new nationwide cross sectional study in which we also collected information on these important potential determinants of allergic disease in children.

In the present study we have elaborated the relation between exposure to urban air pollution and the risk of asthma in school children, focusing on predominantly traffic related pollutants such as nitrogen oxides (NOx), ozone (O_3), and carbon monoxide (CO). We also assessed the role of air pollutants, mainly from other fossil fuel combustion sources such as sulphur dioxide (SO_2), and particles with an aerodynamic diameter of 10 μm or less (PM_{10}). Furthermore, we studied the joint effects of parental atopy and outdoor air pollution on the risk of asthma. Parental asthma, allergic rhinitis, and allergic atopic eczema were used as surrogates of the genes that are responsible for susceptibility to the effects of air pollutants on asthma. We applied a two stage hierarchical model to adjust for confounding and to elaborate effect modification at the individual level and to assess the effects of air pollution at the municipal level.[14 15]

METHODS

Data collection and study population

A nationwide cross sectional study was conducted in Taiwan in 2001 where a modified Chinese version of the International Study of Asthma and Allergies in Childhood (ISAAC-C) questionnaire was used to collect information on children's health, environmental exposures, and other relevant factors.[16] The study population was recruited from elementary and middle schools in 22 municipalities within 1 km from Taiwan Environmental Protection Agency (EPA) air monitoring stations. The questionnaire was taken home by students and answered by parents. A total of 35 036 children aged 6–15 years were approached. The response rate was 93.2%. 2364 children were excluded because of an incomplete questionnaire, leaving a final study population of 32 672 schoolchildren.

The study protocol was approved by the Respiratory Health Screening Steering Committee of the Taiwan Department of Health and the Institutional Review Board of National Cheng Kung University Hospital, and it complied with the principles outlined in the Helsinki Declaration.[17]

Health outcome

The outcome of interest was childhood asthma, which was defined on the basis of the answer to the question: ''Has a physician ever diagnosed your child as having asthma?''.

Abbreviations: CO, carbon monoxide; NOx, nitrogen oxides; O_3, ozone; PM_{10}, particles with aerodynamic diameter 10 μm or less; SO_2, sulphur dioxide

Exposure assessment

Complete monitoring data for the air pollutants including sulphur dioxide (SO_2), nitrogen oxides (NOx), ozone (O_3), carbon monoxide (CO), and particles with an aerodynamic diameter of 10 μm or less (PM_{10}), as well as daily temperature and relative humidity, are available from 1994 for 22 EPA monitoring stations on Taiwan's main island (fig 1). Concentrations of each pollutant are measured continuously and reported hourly—CO by non-dispersive infrared absorption, NOx by chemiluminescence, O_3 by ultraviolet absorption, SO_2 by ultraviolet fluorescence, and PM_{10} by beta-gauge. Exposure parameters in the present study were annual average concentrations, calculated from the monthly averages of the year 2000. Forty four schools in Taiwan's 22 municipalities were investigated. Stratified sampling by grade was applied in each school.[18]

Covariates

Information on potential confounders was obtained from the parent administered questionnaire. The covariates in the present analyses included age, sex, parental atopy, parental education, maternal smoking history during pregnancy, environmental tobacco smoke (ETS), and visible mould (table 1). Parental atopy was a measure of genetic predisposition to asthma and it was defined as the father or mother of the index child ever having been diagnosed as having asthma, allergic rhinitis, or atopic eczema.

Statistical methods

The odds ratio (OR) was used as a measure of the relation between exposure to air pollution and the risk of childhood asthma. Adjusted ORs were estimated in a two stage hierarchical model using logistic and linear regression analyses. The models assume two sources of variation—the variation among subjects in the first stage, part of which could be explained by the individual characteristics, and the variation among municipalities in the second stage, part of which could be explained by variables measured at the municipal level. In the analyses we assumed that (1) the outcome variable follows Bernoulli distribution; (2) intercept terms are random at the municipal level; and (3) all the explanatory variables are fixed effects. A logistic regression model was fitted in the first stage for the risk of childhood asthma as a function of site-specific intercepts j, where $\alpha j = 1, ..., 22$, and personal covariates. The adjusted site-specific intercepts and prevalence rates are related by $Pj = e^{\alpha j}/(1+e^{\alpha j})$. In the second stage these intercept terms representing the logit of the site-specific prevalence rates (Pj; $j = 1, ..., 22$), adjusted for personal covariates, were regressed on each site specific ambient pollutant level by using a linear "ecologic" regression—that is, logit $\alpha j = \alpha + Uj + \beta Zj$ where Uj denotes the random departure from the general prevalence αj on the logit scale for site j and Zj denotes the ambient pollution level for site j. Thus, β can be interpreted as the log OR (per unit change) for each pollutant, adjusted for personal characteristics. The results from the models are presented as ORs, along with their 95% confidence intervals (CIs).

The goodness of fit was assessed with likelihood ratio tests (LR) to determine whether a variable contributed significantly to the model. Firstly, we fitted a full model with a complete set of covariates. To study further the sources of confounding we fitted models with different combinations of covariates and compared the effect from models with and without the covariate of interest. If the adjusted OR differed from the crude OR by more than 10%, that covariate was be included in the final model. We first fitted one pollutant models and then considered two-pollutant models by fitting one traffic related and one stationary fossil fuel combustion related pollutant. Finally, we fitted two-pollutant models with O_3 and another pollutant. The two-pollutant models provide estimates of the independent effects of CO, NOx, SO_2, PM_{10}, and O_3 on childhood asthma, controlling for the second pollutant in the model. We also considered three-pollutant models with one traffic related, one stationary fossil fuel combustion related pollutant, and O_3. The effect of each pollutant on the risk of childhood asthma was presented as ORs per 10 ppb changes for SO_2, NOx, and O_3, 100 ppb changes for CO, and 10 $\mu g/m^3$ changes for PM_{10}, along with their 95% CIs. We assessed potential effect modification by parental atopy by comparing crude and adjusted effect estimates for children with and without atopic parents. The two-stage hierarchical model was used not only to derive more precise estimates of site specific parameters and site level effects, but also to adjust for multiple comparisons.[19]

Figure 1 The 22 municipalities with selected air pollution monitoring stations in this study in Taiwan 2001. Circles indicate 1 km catchment area.

RESULTS

Study population and occurrence of childhood asthma

The characteristics of the study population and the prevalence of childhood asthma according to the covariates are shown in table 1. The prevalence of asthma was 6.86% (95% CI 6.59 to 7.13). The prevalence of childhood asthma was related to young age, high level of parental education, male sex, parental atopy, maternal smoking during pregnancy and the presence of cockroaches and visible mould in the home. The prevalence of asthma was lower in children exposed to environmental tobacco smoke (ETS) than in those not exposed.

Air pollution

The distributions of the annual mean air pollutant concentrations, temperature, and relative humidity in the 22 monitoring stations in the year 2000 are presented in table 2 and the correlations between different pollutants are shown in table 3. The correlation between NOx and CO concentrations was high (0.88), which reflects the common source of motor vehicles. The concentrations of PM_{10} and SO_2 were

Table 1 Number of asthma cases, prevalence of asthma, and odds ratios (ORs) of asthma with 95% confidence interval (95% CI) by age, parental education, parental atopy, environmental tobacco smoke, maternal smoking during pregnancy, cockroaches, water damage, and visible mould in Taiwan 2001

Determinant	No of children	No with physician diagnosed asthma	Prevalence (%)	OR (95% CI)
Total	32672	2241	6.86	
Age (years)				
⩽7	4692	349	7.44	1.34 (1.09 to 1.64)
8	3559	251	7.05	1.26 (1.02 to 1.57)
9	3582	268	7.48	1.35 (1.09 to 1.67)
10	3760	290	7.71	1.39 (1.13 to 1.72)
11	3539	238	6.73	1.20 (0.97 to 1.49)
12	3809	273	7.17	1.29 (1.04 to 1.59)
13	3730	240	6.43	1.15 (0.92 to 1.42)
14	3634	198	5.45	0.96 (0.77 to 1.20)
15	2367	134	5.66	1.00
Sex				
Male	16540	1340	8.10	1.49 (1.37 to 1.63)
Female	16132	901	5.59	1.00
Parental education (years)				
<6	1831	74	4.04	1.00
6–8	5725	269	4.70	1.17 (0.90 to 1.52)
9–11	14749	937	6.35	1.61 (1.26 to 2.05)
⩾12	10367	961	9.27	2.43 (1.90 to 3.09)
Parental atopy*				
No	22761	1083	4.76	1.00
Yes	9208	1103	11.98	2.72 (2.50 to 2.97)
Environmental tobacco smoke*				
No	13212	990	7.49	1.00
Yes	19229	1232	6.41	0.85 (0.78 to 0.92)
Maternal smoking during pregnancy*				
No	31791	2168	6.82	1.00
Yes	706	56	7.93	1.18 (0.89 to 1.56)
Cockroaches noted monthly*				
No	6663	410	6.15	1.00
Yes	25507	1796	7.04	1.15 (1.03 to 1.29)
Water damage*				
No	29845	2055	6.89	1.00
Yes	2667	176	6.60	0.96 (0.81 to 1.12)
Visible mould*				
No	24308	1581	6.50	1.00
Yes	7573	616	8.13	1.27 (1.16 to 1.40)

*Numbers of subjects do not add up to total N because of missing data.

also highly correlated (0.58), indicating a common source of stationary fuel combustion, although SO_2 concentrations were also correlated with both traffic related pollutants. The concentration of O_3 was negatively correlated with the mainly traffic related pollutants but positively correlated with PM_{10} and SO_2, and it was only weakly correlated with that of traffic related and stationary fossil fuel combustion related air pollutants.

Air pollution and childhood asthma

In the one-pollutant model, the risk of asthma was not related to NOx levels (adjusted OR 1.005 per 10 ppb change (95% CI 0.945 to 1.060)). Addition of either SO_2 (adjusted OR 1.048 (95% CI 0.983 to 1.117)) or PM_{10} (adjusted OR 1.065 (95% CI 1.009 to 1.123)) increased the effect estimate for NOx substantially, and addition of O_3 (adjusted OR 1.029 (95% CI 0.973 to 1.089)) slightly (table 4). In the three-pollutant model the estimates for NOx were 1.113 (95% CI 1.038 to 1.194) and 1.152 (95% CI 1.082 to 1.227), respectively, when (SO_2 and O_3) or (PM_{10} and O_3) were added and showed statistical significances (table 5). The adjusted OR for 100 ppb change in CO was 1.045 (95% CI 1.017 to 1.074) and the estimates changed little when a second or third pollutant was added. The adjusted OR for a

Table 2 Mean and distribution of 2000 annual air pollution and meteorology data from 22 monitoring stations in Taiwan

	Mean (SD)	Minimum	25th percentile	Median	75th percentile	Interquartile range*	Maximum
CO (ppb)	664 (153)	416	540	647	752	212	964
NOx (ppb)	27.64 (8.38)	10.88	21.47	33.07	29.58	11.60	43.98
O_3 (ppb)	23.14 (3.25)	18.65	20.34	25.20	22.69	4.86	31.17
PM_{10} ($\mu g/m^3$)	55.58 (16.57)	29.36	42.96	53.81	70.37	27.41	99.58
SO_2 (ppb)	3.53 (2.00)	0.35	1.96	3.34	4.84	2.88	10.12
Temperature (℃)	23.65 (0.75)	22.36	23.20	23.50	24.17	1.17	25.27
Relative humidity (%)	74.0 (3.0)	69.0	72.2	74.1	76.5	4.3	80.0

*Range from 25th to 75th percentile of site specific concentrations.

Table 3 Correlations of air pollutants across 22 municipalities

	CO	NOx	O_3	PM_{10}	SO_2
CO	1.00	0.88*	− 0.37	0.27	0.40
NOx		1.00	− 0.39	0.34	0.50*
O_3			1.00	0.28	0.19
PM_{10}				1.00	0.58*
SO_2					1.00

*Correlation is significant at the 0.05 level.

10 ppb change in SO_2 alone was 0.874 (95% CI 0.729 to 1.054), but inclusion of either of the traffic related pollutants reduced the effect estimate substantially whereas addition of O_3 had little influence. The risk of childhood asthma was not related to PM_{10} concentrations in any combination of air pollutants. The risk of asthma was significantly related to O_3 in the one-pollutant model (OR 1.138 (95% CI 1.001 to 1.293)) and the addition of other pollutants increased the risk estimates further.

In summary, positive statistically significant associations were found for O_3 and traffic related pollutants (CO and NOx). In contrast, negative or weak associations were found for SO_2 and PM_{10}.

In order to elaborate the potential effect modification, we systematically conducted stratified analyses in categories of parental atopy. The stratified analyses did not indicate any major effect modification (table 6).

DISCUSSION

The risk of childhood asthma increased according to increased annual levels of the two traffic related pollutants NOx and CO, as well as O_3. The risk of asthma was not related to the levels of PM_{10} and SO_2 and, in multi-pollutant models, the risk of asthma was negatively associated with the levels of SO_2. The results did not provide evidence that hereditary atopy representing a genetic predisposition modifies the effects of exposure to outdoor air pollutants.

Validity of results

Routine air pollution monitoring data were used as the basis for exposure assessment. These data represented reasonably well exposures both in the school and in the home for two reasons. The schools were chosen to be in the vicinity of the monitoring stations. Almost all the children attended schools within 1 km of their homes because the density of elementary and middle schools in Taiwan is very high. Finally, the two-stage hierarchical modelling took into account the fact that municipal level exposure information was used. Although we did not collect information about the vicinity of the busy road, the present study and previous studies from German[20] and Mexican cities[21] provide consistent evidence that the outdoor NO_2 level is a better predictor of traffic exposure than exposure to NO_2 at the personal level.

From previous literature we know that a high proportion of traffic related outdoor air pollutants (NOx, CO) penetrate indoors, but the penetration proportion for particles is lower when mechanical filtration or an air conditioner is used.[22–24] Most of the Taiwanese school children spend at least 8 hours/day in school. Air conditioning is rare in Taiwanese classrooms. Mechanical filtration is practically the only type of filtration in Taiwanese homes during the summer, even if the home is air conditioned. Any known or unknown factors such as air change, penetration, deposition, as well as emission strengths for indoor pollutants could be responsible for the observed association between personal exposure and municipal level exposure. This was a common problem in all the previous studies assessing the effects of air pollution on the risk of asthma in school children.

In cross sectional studies, selection bias is a potential threat to validity. A plausible mechanism of selection is that parents of children with asthma move to residential areas with lower levels of air pollution which will lead to underestimation of the relation between exposure and outcome. Any random migration is likely to result in underestimation of the air pollution effects but would not introduce a positive bias in the associations. Information on residential history in a cross sectional study could be used to reduce the possibility of selection bias, whereas a longitudinal study would provide a stronger design for minimising this problem. We did not have sufficient information on children's residential history to formally assess the lifetime exposure to air pollution, so current exposure was used as the proxy of previous exposure. Most of the studies to date on the relationship between exposure to air pollutants and risk of asthma in children have been cross sectional.[7 9–12]

In our statistical analyses we controlled for a number of potential individual level confounders such as parental education and indoor environmental exposures. In stratified analyses on different levels of covariates, we studied the possibility of residual confounding. Parental education had a positive association with concentrations of traffic related pollutants. The prevalence of childhood asthma was also positively associated with the level of parental education, which could be explained by both the influence of air pollution and better access to health care.

Assessment of the independent effects of different pollutants is difficult because urban air pollution constitutes a complex mixture of several compounds. Although all the measured pollutants have several sources, NOx and CO are predominantly from vehicle emissions while SO_2 and PM_{10} are mainly from stationary fossil combustion processes.[25 26] In the present study, NOx and CO concentrations were highly correlated, indicating the common source of motor vehicle traffic emissions. SO_2 and PM_{10} concentrations were also correlated, their common sources being stationary fossil fuel combustion. In the modelling, we were able to control for one stationary fossil fuel pollutant at a time as a potential confounder when assessing the effect of one of the traffic related pollutants and vice versa. Due to collinearity problems, it was not possible to separate the impact of traffic related pollutants (NOx and CO) from each other.

Synthesis with previous knowledge

The results of the present study are in line with several previous studies from Seattle,[4] Illinois,[5] Los Angeles,[6] Austria,[7] the Netherlands,[8] Czech Republic and Poland,[9] Germany,[10] Japan,[11] and China[12] indicating that exposure to outdoor air pollutants increases the risk of asthma. All available studies suggest an increased risk for traffic related air pollutants (CO and NOx)[4 6–8 11 12] and O_3,[5 6] but the findings are inconsistent for stationary fossil fuel combustion related air pollutants (SO_2 and PM_{10}).[9 10 12]

A panel study conducted in Seattle showed no association between exposure to CO and the occurrence of asthma related symptoms.[4] In a cross sectional study carried out in Illinois, increased morning and evening asthma symptom

Table 4 Adjusted odds ratios (ORs) and 95% confidence interval (CIs) of physician diagnosed asthma in single and two-pollutant models

	Single-pollutant model	Two-pollutant model 1 (NO_x+SO_2)	Two-pollutant model 2 (NO_x+PM_{10})	Two-pollutant model 3 (NO_x+O_3)	Two- pollutant model 4 (CO+SO_2)	Two-pollutant model 5 (CO+PM_{10})	Two-pollutant model 6 (CO+O_3)	Two-pollutant model 7 (SO_2+O_3)	Two-pollutant model 8 (PM_{10}+O_3)
NO_x (10 ppb)	1.005 (0.954 to 1.060)	1.048 (0.983 to 1.117)	1.065 (1.009 to 1.123)	1.029 (0.973 to 1.089)					
CO (100 ppb)	1.045 (1.017 to 1.074)				1.066 (1.034 to 1.099)	1.079 (1.047 to 1.112)	1.063 (1.100 to 1.474)		
SO_2 (10 ppb)	0.874 (0.729 to 1.054)	0.724 (0.545 to 0.963)			0.689 (0.542 to 0.875)			0.826 (0.674 to 1.014)	
PM_{10} (10 μg/m^3)	0.934 (0.909 to 0.960)		0.920 (0.893 to 0.948)			0.912 (0.886 to 0.939)			0.925 (0.899 to 0.952)
O_3 (10 ppb)	1.138 (1.001 to 1.293)			1.208 (1.037 to 1.408)			1.274 (1.100 to 1.474)	1.166 (1.022 to 1.331)	1.253 (1.089 to 1.442)

*Two-stage hierarchical analysis adjusting for age, sex, parental education, parental atopy, environmental tobacco smoke (ETS), and visible mould.

scores were associated with the levels of O_3.[5] A population based cross sectional study in Los Angeles found positive associations between asthma symptoms and all the US criteria air pollutants (O_3, NO_2, SO_2, PM_{10}). The risk of more severe asthma symptoms was associated with 8 hour exposure to NO_2 levels above 1.4 ppb (OR 1.27, 95% CI 1.05 to 1.54).[6] Four recent studies from Austria, the Netherlands, Japan, and China examined the relationship between exposure to NO_2 and the risk of childhood asthma.[7 8 11 12] In the Austrian study, the risk of childhood asthma was associated with NO_2 levels (highest *v* lowest category, prevalence odds ratio (POR) 5.81, 95% CI 1.27 to 26.5).[7] In a cohort study conducted in the Netherlands, the risk of physician diagnosed asthma was associated with traffic related air pollution measured as NO_2 concentrations.[8] A survey in Japan found that a 10 ppb increase in the outdoor NO_2 concentration was associated with an increased risk of asthma with an adjusted OR of 2.10 (95% CI 1.10 to 4.75).[11] A study conducted in four Chinese cities suggested a positive association between the risk of childhood asthma and the levels of PM_{10} (OR 1.33, 95% CI 0.80 to 2.19), but weak or negative associations were found for SO_2 (OR 1.03, 95% CI 0.75 to 1.41) and NOx (OR 0.95, 95% CI 0.63 to 1.43).[12] In the Czech and Polish study the lifetime prevalence of physician diagnosed asthma in schoolchildren was associated with SO_2 (OR 1.39 per 50 μg/m^3 increase in SO_2, 95% CI 1.10 to 1.92).[9] In contrast, a study in Germany indicated that high levels of SO_2 in East Germany were associated with a lower prevalence of asthma compared with West Germany.[10]

Nitrogen dioxide has been shown to be an acute respiratory irritant in controlled exposure studies.[27] There are no plausible mechanisms through which CO exposure would influence the airways and increase the risk of childhood asthma. Both NOx and CO represent the complex mixture of traffic exhaust, and NO_2 is known to be the best indicator of motor vehicle traffic emissions. In the present study it was not possible to determine to what extent NOx would have direct effects on children's airways. CO is unlikely to have any direct effects on the airways.

A positive association between the risk of childhood asthma and exposure to O_3 was identified, compatible with toxicological studies.[28 29] The prevalence of childhood asthma was associated with O_3 levels. The effect was increased when adjusting for either a traffic related pollutant, stationary fossil fuel pollutant, or both. Ozone is a secondary pollutant in the atmosphere produced from traffic exhausts, but scavenged by direct motor vehicle emissions. It is a known respiratory irritant[30] and could be causally related to childhood asthma.

Our finding of a lack of association between the risk of childhood asthma and PM_{10} levels is consistent with the results from the Harvard 24 Cities Study in North America.[31] Although the risk of childhood asthma was not related to the levels of PM_{10}, it is likely that there is an association with fine particulate matter ($PM_{2.5}$) and ultrafine particles typically present in motor vehicle exhausts and, in particular, in diesel exhausts. Further studies should assess these relations. No association between childhood asthma and SO_2 was found in the present study, possibly because the average level of combustion related air pollutants such as SO_2 in Taiwan is substantially lower than levels reported in studies in the Czech Republic and Poland[9] and in East Germany.[10]

Conclusion

The present study provides additional evidence that exposure to outdoor air pollutants increases the risk of childhood asthma in school children. The observed relations between the risk of childhood asthma and NOx and CO levels suggests that emissions from motor vehicles play an important role. In

Table 5 Adjusted odds ratios (ORs) and 95% confidence interval (CIs) of physician-diagnosed asthma in three-pollutant models

	Three-pollutant model 1 ($NOx+SO_2+O_3$)	Three-pollutant model 2 ($NOx+PM_{10}+O_3$)	Three-pollutant model 3 ($CO+SO_2+O_3$)	Three-pollutant model 4 ($CO+PM_{10}+O_3$)
NOx (10 ppb)	1.113 (1.038 to 1.194)	1.152 (1.082 to 1.227)		
CO (100 ppb)			1.111 (1.074 to 1.150)	1.119 (1.084 to 1.155)
SO_2 (10 ppb)	0.585 (0.433 to 0.791)		0.528 (0.405 to 0.688)	
PM_{10} (10 μg/m^3)		0.888 (0.858 to 0.918)		0.886 (0.859 to 0.914)
O_3 (10 ppb)	1.360 (1.152 to 1.604)	1.501 (1.274 to 1.768)	1.500 (1.273 to 1.767)	1.587 (1.351 to 1.865)

*Two-stage hierarchical analysis adjusting for age, sex, parental education, parental atopy, environmental tobacco smoke (ETS), and visible mould.

Table 6 Crude and adjusted odds ratios (ORs) with 95% confidence interval (CIs) of physician diagnosed asthma stratified by parental atopy in the relation between childhood asthma and air pollutants

	Parental atopy	Crude OR (95% CI)	Adjusted OR (95% CI)*
NOx (10 ppb)	Yes	1.00 (0.93 to 1.08)	0.99 (0.92 to 1.07)
	No	1.04 (0.97 to 1.13)	1.02 (0.95 to 1.10)
CO (100 ppb)	Yes	1.05 (1.01 to 1.09)	1.04 (1.00 to 1.08)
	No	1.08 (1.04 to 1.12)	1.06 (1.02 to 1.10)
SO_2 (10 ppb)	Yes	0.76 (0.55 to 1.06)	0.86 (0.62 to 1.21)
	No	0.70 (0.51 to 0.95)	0.77 (0.56 to 1.07)
PM_{10} (10 μg/m^3)	Yes	0.93 (0.89 to 0.96)	0.94 (0.90 to 0.98)
	No	0.90 (0.87 to 0.94)	0.92 (0.89 to 0.96)
O_3 (10 ppb)	Yes	1.09 (0.89 to 1.33)	1.15 (0.93 to 1.42)
	No	1.08 (0.90 to 1.30)	1.20 (1.00 to 1.47)

*Two-stage hierarchical analysis adjusting for age, sex, parental education, environmental tobacco smoke (ETS), and visible mould.

addition, the relationship with O_3 levels indicates that photochemical air pollution contributes to adverse health effects.

Authors' affiliations

B-F Hwang, Department of Health Care Administration, Diwan College of Management, Tainan, Taiwan; and Department of Environmental and Occupational Health, College of Medicine, National Cheng Kung University, Tainan, Taiwan
Y-L Lee, Y L Guo, Department of Environmental and Occupational Health, College of Medicine, National Cheng Kung University, Tainan, Taiwan; and Department of Internal Medicine, National Cheng Kung University Hospital, Tainan, Taiwan
Y-C Lin, College of Dental Medicine, Kaohsiung Medical University, Kaohsiung, Taiwan
J J K Jaakkola, Institute of Occupational and Environmental Medicine, University of Birmingham, Birmingham, UK

This study was partially supported by grant #NSC92-2302-B-006-028 from the National Science Council and grant #DOH90-TD-1138 from the Department of Health. Yung-Ling Lee was also a recipient of the Taiwan National Health Research Institute MD-PhD Predoctoral Fellowship (DD9102N). Jouni Jaakkola was partly supported by The Yrjo Jahnsson Foundation.

REFERENCES

1 **International Study of Asthma and Allergies in Childhood (ISAAC) Steering Committee**. Worldwide variation in prevalence of symptoms of asthma, allergic rhinoconjunctivitis and atopy eczema: ISAAC. *Lancet* 1998;**351**:1225–32.
2 **Kauffmann F**, Dizier MH, Annesi-Maesano I, *et al*. EGEA (Epidemiological study on the Genetic and Environment of Asthma, Bronchial Hyperresponsiveness and Atopy)—descriptive characteristics. *Clin Exp Allergy* 1999;**29**(Suppl 4):17–21.
3 **D'Amato G**. Outdoor air pollution, climate and allergic respiratory disease: evidence of a link. *Clin Exp Allergy* 2000;**32**:1391–3.
4 **Yu O**, Sheppard L, Lumley T, *et al*. Effects of ambient air pollution on symptoms of asthma in Seattle-area children enrolled in the CAMP study. *Environ Health Perspect* 2000;**108**:1209–14.
5 **Ross MA**, Persky VW, Scheff PA, *et al*. Effect of ozone and aeroallergens on the respiratory health of asthmatics. *Arch Environ Health* 2002;**57**:568–78.
6 **Delfino RJ**, Gong H Jr, Linn WS, *et al*. Asthma symptoms in Hispanic children and daily ambient exposures to toxic and criteria air pollutants. *Environ Health Perspect* 2003;**111**:647–56.
7 **Studnicka M**, Hackl E, Pischinger J, *et al*. Traffic-related NO_2 and the prevalence of asthma and respiratory symptoms in seven years olds. *Eur Respir J* 1997;**10**:2275–8.
8 **Brauer M**, Hoek G, Van Vliet P, *et al*. Air pollution from traffic and development of respiratory infections and asthmatic and allergic symptoms in children. *Am J Respir Crit Care Med* 2002;**166**:1092–8.
9 **Pikhart H**, Bobak M, Gorynski P, *et al*. Outdoor sulphur dioxide and respiratory symptoms in Czech and Polish school children: a small-area study (SAVIAH). *Int Arch Occup Environ Health* 2001;**74**:574–8.
10 **von Mutius E**, Martinez FD, Fritzsch C, *et al*. Prevalence of asthma and atopy in two areas of West and East Germany. *Am J Respir Crit Care Med* 1994;**149**:358–64.
11 **Shima M**, Motoaki A. Effect of outdoor and indoor nitrogen dioxide on respiratory symptoms in schoolchildren. *Int J Epidemiol* 2000;**29**:862–70.
12 **Zhang J**, Hu W, Wei F, *et al*. Children's respiratory morbidity prevalence in relation to air pollution in four Chinese cities. *Environ Health Perspect* 2002;**110**:961–7.
13 **Guo YL**, Lin YC, Sung FC, *et al*. Climate, traffic-related air pollutants, and asthma prevalence in middle-school children in Taiwan. *Environ Health Perspect* 1999;**107**:1001–6.
14 **Dominici F**. Air pollution and health: what can we learn from a hierarchical approach? *Am J Epidemiol* 2002;**155**:11–5.
15 **Greenland S**. Principles of multilevel modeling. *Int J Epidemiol* 2000;**29**:158–67.
16 **Asher MI**, Keil U, Anderson HR, *et al*. International study of asthma and allergies in childhood (ISAAC): rationale and methods. *Eur Respir J* 1995;**8**:483–91.
17 **World Medical Assembly**. Declaration of Helsinki: Recommendations guiding physicians in biomedical research involving human subjects. *Bull Pan Am Health Organ* 1990;**24**:606–9.
18 **Witte JS**, Greenland S, Kim LL, *et al*. Multilevel modeling in epidemiology with GLIMMIX. *Epidemiology* 2000;**11**:684–8.
19 **Lee YL**, Lin YC, Hsiue TR, *et al*. Indoor/outdoor environmental exposure, parental atopy and childhood asthma. *Pediatrics* 2003;**112**:e389–95.
20 **Kramer U**, Koch T, Ranft U, *et al*. Traffic-related air pollution is associated with atopy in children living in urban areas. *Epidemiology* 2000;**11**:64–70.
21 **Ramirez-Aguilar M**, Cicero-Fernandez P, Winer AM, *et al*. Measurements of personal exposure to nitrogen dioxide in four Mexican cities in 1996. *J Air Waste Manag Assoc* 2002;**52**:50–7.
22 **Cyrys J**, Pitz M, Bischof W, *et al*. Relationship between indoor and outdoor levels of fine particles mass, particle number concentrations and black smoke

under different ventilation conditions. *J Expos Anal Environ Epidemiol* 2004;**14**:275–83.
23 **Partti-Pellinen K**, Marttila O, Ahonen A, *et al*. Penetration of nitrogen oxides and particles from outdoor into indoor air and removal of the pollutants through filtration of incoming air. *Indoor Air* 2002;**10**:126–32.
24 **Rojas-Bracho L**, Suh HH, Oyola P, *et al*. Measurement of children's exposures to particles and nitrogen dioxide in Santiago, Chile. *Sci Total Environ* 2000;**287**:249–64.
25 **Ko YC**. Air pollution and its health effects on residents in Taiwanese communities. *Kaohsiung J Med Sci* 1996;**12**:657–69.
26 **Lee YL**, Shaw CK, Su HJ, *et al*. Climate, traffic-related air pollutants and allergic rhinitis prevalence in middle-school children in Taiwan. *Eur Respir J* 2003;**21**:964–70.
27 **Wang JH**, Devalia JL, Duddle JM, *et al*. Effect of six-hour exposure to nitrogen dioxide on early-phase nasal response to allergen challenge in patients with a history of seasonal allergic rhinitis. *J Allergy Clin Immunol* 1995;**96**:669–76.
28 **Matsumura Y**. The effect of ozone, nitorogen dioxide, and sulfur dioxide on the experimentally induced allergic respiratory disorders in guinea pigs. *Am Rev Respir Dis* 1970;**102**:430–47.
29 **Peden DB**. Pollutants and asthma: role of air toxics. *Environ Health Perspect* 2002;**11**(Suppl 4):565–8.
30 **Brunekreef B**, Holgate ST. Air pollution and health. *Lancet* 2002;**360**:1233–42.
31 **Dockery DW**, Cunningham J, Damokosh AI, *et al*. Health effects of acid aerosols on North American children: respiratory symptoms. *Environ Health Perspect* 1996;**104**:500–5.

LUNG ALERT

Further evidence on the dangers of exposure to second hand tobacco smoke

▲ Vineis P, Airoldi L, Veglia F, *et al*. Environmental tobacco smoke and risk of respiratory cancer and chronic obstructive pulmonary disease in former smokers and never smokers in the EPIC prospective study. *BMJ* 2005;**330**:277–80

▲ McGhee SM, Ho YS, Schooling M, *et al*. Mortality associated with passive smoking in Hong Kong. *BMJ* 2005;**330**:287–8

Vineis *et al* report a prospective case-control study examining 123 479 ''healthy'' never smokers or former smokers. Over 7 years of follow up, cases were defined as ''respiratory cancers'' or deaths from COPD. Controls were well matched. Information about tobacco smoke exposure and a thorough list of confounders was obtained by questionnaire at recruitment. This strengthens the study by cutting out recall bias. Follow up data were from multiple sources. A subset of subjects and controls were tested for the presence of genetic polymorphisms implicated in carcinogenesis.

Exposure to tobacco smoke was associated with increased risk of death from respiratory cancers/COPD (hazard ratio (HR) 1.30, 95% CI 0.87 to 1.95) and lung cancer alone (HR 1.34, 0.85 to 2.13). The effect was significantly greater for exposure at work (HR for lung cancer 1.65, 1.04 to 2.63) than at home (HR 1.03, 0.60 to 1.76) and for former smokers than for never smokers. Work exposure may have been higher than at home but exposure was not quantified and only measured at one point in time. The authors postulate that the greater effect in former smokers may be due to genetic mutations already accrued. The case for causality is strengthened as genetic polymorphisms increase the susceptibility to smoke: odds ratio (OR) for lung cancer increased from 1.33 to 2.86 between the presence of one or two versus three or more risk polymorphisms. Self-reported exposure to smoke in childhood showed a clear dose-response effect in never smokers. Daily exposure for many hours as a child increased the HR for lung cancer in adulthood from 1.0 to 3.63 (1.19 to 11.11).

McGhee *et al* report a retrospective case-control study. Cases were identified from all deaths reported amongst never smokers, and those reporting the death completed a questionnaire about the deceased. Second hand smoke exposure was classified by the number of smokers who lived with the deceased (0, 1, 2 or more). There was no attempt to further quantify exposure. This retrospective nature risks recall bias and the only confounder controlled for was education, a proxy of social class. There was a 34% increase in all cause mortality with any exposure to second hand smoke. Importantly, there was a significant dose-dependent association between second hand smoke and mortality from lung cancer (OR 1.74, 1.06 to 2.86 comparing no exposure to living with >2 smokers). There was a similar association between exposure and mortality from COPD (OR 2.51, 1.22 to 5.18), stroke (OR 2.08, 1.33 to 3.25) and ischaemic heart disease (OR 1.68, 1.05 to 2.68).

These studies add impetus to the demand for restrictions on smoking in public places. In the Hong Kong study deaths from poisoning were also analysed, as a control measure, and showed no relation to tobacco smoke exposure. Perhaps now there is an argument for reclassifying some of the other environmental tobacco related deaths as ''poisoning''?

E Cetti
Specialist Registrar, Princess Royal Hospital, Haywards Heath, UK;
ed_cetti@hotmail.com