The effects of outdoor and indoor nitrogen dioxide (NO₂) exposure on pulmonary function were studied in a cohort of children attending eight elementary schools in Chiba Prefecture. A three-year series of annual pulmonary function tests was conducted from 1989 through 1991. NO₂ concentration in the living room of each child’s home was measured in both the heating period and the non-heating period. Children were classified into four groups according to household annual average NO₂ concentration. The indoor NO₂ concentration varied with the area of residence and type of heating appliance used. Analyses using log-linear models, including interactions among these environmental factors, were performed to evaluate the association of NO₂ exposure with pulmonary function in schoolchildren. Interregional comparison showed that pulmonary function values, adjusted for height and age, were lower among boys living in urban areas, where air pollution levels are high, compared with boys in rural areas. In log-linear models that considered the effect of indoor NO₂ concentration, boys in urban areas showed significantly depressed values of FVC and FEV₀.₇₅. Indoor air pollution was not definitely associated with pulmonary function among boys, after adjustment for the area of residence. Among girls, high indoor NO₂ concentrations were associated with low pulmonary function values, while no significant relationship between area of residence and pulmonary function was shown. Girls in the over-40-ppb group showed significantly depressed values of FVC, FEV₀.₇₅, and V₂₅ in the second testing. In the third testing, V₂₅ was the only parameter that was significantly low. These results suggest that pulmonary function is associated with area of residence among boys and with indoor NO₂ concentration among girls. However, this study could not reveal the long-term effect of indoor air pollution on pulmonary function, since this association became weaker by the third testing. J Epidemiol, 1994; 4: 137-146.

As a result of growing vehicular traffic in recent years, air pollution in urban areas has not been improved substantially, and anxiety has been aroused over the potential impacts of automobile exhaust on the health of inhabitants.

At present, major air pollutants in urban areas include nitrogen dioxide (NO₂) and suspended particulate matter. The former is also generated by indoor combustion apparatus, and indoor concentrations may exceed the environmental air quality standard in some cases. Therefore, in evaluating the effects of outdoor air pollution on human health, the effects of indoor air pollution from sources such as unvented heating appliances and smoking should be studied in parallel.

As an epidemiological method of studying the effects of ambient air pollution on health, pulmonary function tests have long been a popular choice. Recently, some studies have also been conducted on the effects of indoor air pollution on pulmonary function. In investigations of the association between ambient air pollution and pulmonary function, however, few studies have directly measured indoor NO₂ concentrations and assessed their effects.

With the intent of better understanding the effects of various environmental factors on the respiratory health, we have been conducting a series of epidemiological surveys in schoolchildren from various regions of Chiba Prefecture, Japan. Indoor NO₂ concentrations in the homes of these children have been detailed previously.

This report presents an interregional comparison of the
results of pulmonary function tests conducted in 1990 and 1991. We also investigated the association of estimated pulmonary function levels with various environmental factors, including indoor NO$_2$ concentration.

**MATERIALS AND METHODS**

**Subjects**

The study subjects were 1,081 children from eight elementary schools in Chiba Prefecture, the locations of which are shown in Figure 1. The children were in fourth grade as of October 1989.

A total of five schools in Chiba City (A, B), Funabashi City (C, D), and Kashiwa City (E) are located in urban areas; all these school districts contain main regional highways. The school districts containing the two schools in Chiba City are adjacent to one other, as are the school districts containing the two subject schools in Funabashi City. Three schools in Sawara City (F), Ichihara City (G), and Tateyama City (H) are all located in rural areas where ambient air pollution is at low levels.

The annual average NO$_2$ levels in 1991, as measured at the General Air Pollution Monitoring Stations located in close proximity to these schools, were 0.025-0.028 ppm in urban areas and 0.007-0.010 ppm in rural areas.

**Pulmonary function tests**

Pulmonary function tests were performed from October to January of each year for three years, from 1989 (fourth grade) to 1991 (sixth grade). For measurements of pulmonary function, an electrospirometer (DISCOM-21, CHEST Inc., Tokyo) was used. Prior to each day of testing, the spirometer was calibrated using a 3-liter syringe. Testing was carried out by three trained technicians.

On the day of testing, a questionnaire was administered concerning the presence or absence of cough, rhinorrhea, sputum, and fever on the day before and day of testing. The viability of tests on children with such symptoms was left to the judgment of doctors. Each subject was given an adequate explanation on the method of testing, and then submitted to repeated testing, with short pauses interposed between, until at least three but not more than eight reproducible forced expiratory maneuvers were obtained. The height of each subject was measured prior to testing. For all children, testing was conducted in the standing position and with a noseclip.

Only forced expirations that met the criteria recommended by the American Thoracic Society were accepted. For children from whom reproducible forced expiratory maneuvers were obtained, the flow-volume curve used for the analysis was one in which the sum of forced vital capacity (FVC) and forced expiratory volume in one second (FEV$_{1.0}$) was the maximum. Pulmonary function parameters employed for the analysis were FVC, forced expiratory volume in 0.75 second (FEV$_{0.75}$), and maximal expiratory flow rate at 25% of FVC ($V_{25.0}$). Values obtained were expressed in terms of the percentage of measured value to predicted value.

The prediction equations for the standard pulmonary function values were derived on the basis of sex, using data set obtained from tests conducted in 1988 on fourth-sixth grade children in the same three rural schools as those in this study. The apparatus and procedure for measurements are the same as the present study. Only data from children who met the selection criteria for normal individuals (444 boys and 381 girls) was included. Height and age (converted to months of age) were used as variables in the prediction equations according to our earlier study.

**Indoor NO$_2$ concentration measurements**

Indoor NO$_2$ concentrations in each child’s home were measured twice: once during the heating period (January 1991), and once during the non-heating period (June 1991). Measurements were made in the living room using a filter badge NO$_2$ (Toyo Roshi Inc., Tokyo), and 24-hour average concentrations of NO$_2$ were expressed in ppb. Details of the measurement procedure are described elsewhere.

For homes in which valid measurements (i.e., covering an interval of between 22 and 26 hours) were carried out in the both periods, the geometrical mean of the two seasonal NO$_2$ concentrations was calculated according to the method proposed by Neas et al. This geometrical mean was then employed as the annual average NO$_2$ concentration for each home.
**Data analysis**

In autumn 1988 (for F and H schools) or autumn 1989 (for the other schools), a standard respiratory symptom questionnaire, which was a modified Japanese version of ATS-DLD-78-C, was administered to all subjects. The questionnaire was filled out by either of the parents, and replies submitted by households yielding valid indoor NO₂ measurements were analyzed. The following subjects were excluded from further analyses: those with less than 3 years of residence in the current area when this questionnaire survey was conducted, and those with bronchial asthma-like or wheezing symptoms in the 2 years prior to this time.

Pulmonary function values from the second testing (during fifth grade) and the third testing (during sixth grade) were analyzed, because indoor NO₂ measurements were carried out when the subjects were in the fifth grade (January 1991) and in the sixth grade (June 1991). Values obtained for children from urban and rural areas were compared using the Student's t test. Average indoor NO₂ concentrations were classified into the following four groups: 0-19 ppb, 20-29 ppb, 30-39 ppb, and 40 ppb or over. Pulmonary function values were evaluated by trend test using regression for four categories of indoor NO₂ concentrations.

Analyses using a log-linear model were conducted in order to evaluate the effects of multiple factors affecting pulmonary function. Pulmonary function values were arranged in ascending order and classified into three groups: a low-level group, representing the sub-25th percentile; an intermediate group, of the 25th to 75th percentiles; and a high-level group, of the 76th percentile and up. Then the pulmonary function was investigated for associations with area of subject's residence, type of home heating appliance used, and indoor NO₂ concentration. An appropriate model was chosen according to Bishop et al., and odds ratios were estimated using the method described by Yanagawa. The analyses were conducted using the SPSS-X package programs.

**RESULTS**

**Number of subjects**

Table 1 provides the breakdown of subjects. For a total of 972 children, comprising 484 boys and 488 girls, reliable measurements of indoor NO₂ concentration were carried out during the heating and non-heating periods, and completed ATS-DLD-78-C questionnaires were obtained. Of these children, those with less than 3 years of residence (157 children) and those with bronchial asthma-like or wheezing symptoms over the past 2 years (56 children) were excluded from analysis. The final sample size was 759 children, and consisted of 382 boys and 377 girls.

Children who were absent on the day of testing or who produced unacceptable testing results were subsequently excluded from the analysis: such subjects were 75 children at the second testing, and 63 children at the third testing. After the removal of these outliers, 684 and 696 children were submitted to analysis at the second testing and third testing, respectively. There were no differences between rejected and adopted children in terms of respiratory symptoms; residential-housing structure; type of heating appliances; indoor NO₂ concentration; and other factors.

**Indoor NO₂ concentration**

Table 2 shows results for the two measurements of indoor NO₂ concentration, for a sample of 972 children. On the whole, the mean of indoor NO₂ concentrations during the heating period was 34.5 ppb in homes using...
Table 2. Indoor nitrogen dioxide levels by city and type of heating appliance used.

| City   | Type of heating appliance | N   | Household nitrogen dioxide mean (ppb) | Annual | Winter | Summer* |
|--------|---------------------------|-----|---------------------------------------|--------|--------|---------|
| Chiba  | Vented                    | 53  | 28.6                                  | 47.5   | 23.6   | 26.0    |
| (A, B) | Unvented                  | 47  | 40.1                                  | 66.1   |        |         |
| Funabashi | Vented                  | 82  | 29.2                                  | 39.4   | 23.0   | 28.0    |
| (C, D) | Unvented                  | 113 | 37.5                                  | 68.4   |        |         |
| Kashiwa | Vented                    | 72  | 25.5                                  | 33.2   | 23.7   | 25.0    |
| (E)    | Unvented                  | 68  | 38.7                                  | 66.3   | 11.5   | 8.0     |
| Sawara | Vented                    | 122 | 16.4                                  | 30.1   |        |         |
| (F)    | Unvented                  | 159 | 25.8                                  | 60.0   | 10.2   | 10.0    |
| Ichihara | Vented                   | 35  | 17.7                                  | 36.4   |        |         |
| (G)    | Unvented                  | 60  | 24.9                                  | 65.3   |        |         |
| Tateyama| Vented                    | 65  | 20.6                                  | 30.8   | 15.9   | 7.0     |
| (H)    | Unvented                  | 96  | 29.6                                  | 60.0   |        |         |
| Total  | Vented                    | 429 | 22.6                                  | 34.5   | 17.4   |         |
|        | Unvented                  | 543 | 31.7                                  | 63.7   |        |         |

* The mean of nitrogen dioxide concentrations at all subjects' homes in each city, independently of heating appliance used in winter.

ventilated heating appliances, and 63.7 ppb in homes using unvented heaters. The mean of indoor NO₂ concentrations was lower during the non-heating period, at 17.4 ppb. In all cities surveyed, indoor NO₂ concentrations were higher during the heating period than during the non-heating period, and were particularly higher in homes using unvented heaters. Indoor NO₂ concentrations during the non-heating period were higher in urban areas than in rural areas. The household annual average of two seasonal indoor NO₂ measurements was 22.6 ppb in homes using vented heating appliances, and 31.7 ppb in those using vented heaters. The annual indoor NO₂ averages were higher in urban areas than in rural areas regardless of type of heating appliance used.

Pulmonary function tests

Table 3 shows the comparisons of pulmonary function values between children from urban and rural areas. In both the second and third pulmonary function testings, both boys and girls from urban areas showed lower pulmonary function values compared with those from rural areas. All differences between urban and rural boys were significant, except for \( V_{25} \) values obtained at the second testing (hereafter, 2nd \( V_{25} \)). Significant differences in girls were seen in only 2nd FVC and \( FEV_{0.75} \); however, none were seen in any parameters from the third testing.

Comparisons of pulmonary function values based on indoor NO₂ concentrations are shown in Table 4. In both the second and third testings, boys from high indoor

Table 3. Percentage of predicted pulmonary function values in urban and rural children by testing and sex.

|                  | Second testing | Third testing |
|------------------|----------------|--------------|
|                  | Urban          | Rural        | Urban        | Rural        |
| Boys             |                |              |              |              |
| FVC              | 96.88±10.15**  | 99.95±8.87   | 95.82±10.11* | 98.37±9.10   |
| \( FEV_{0.75} \)| 96.66±10.44**  | 99.81±9.37   | 95.47±10.33* | 98.10±9.30   |
| \( V_{25} \)    | 102.46±26.15   | 104.54±26.42 | 100.59±26.40*| 106.41±27.65 |
| (N) (161)        | (196)          | (162)        | (195)        |              |
| Girls            |                |              |              |              |
| FVC              | 95.53±8.50*    | 97.84±10.71  | 94.95±9.33   | 96.68±10.64  |
| \( FEV_{0.75} \)| 95.60±8.99*    | 98.13±10.41  | 95.22±9.45   | 97.15±10.45  |
| \( V_{25} \)    | 99.47±24.62    | 101.10±25.34 | 99.47±25.28  | 102.19±24.95 |
| (N) (137)        | (190)          | (141)        | (198)        |              |

Values are mean±SD.

* \( p<0.05 \), ** \( p<0.01 \) for the difference between children in urban areas and those in rural areas.
Nitrogen Dioxide and Pulmonary Function

NO$_2$ concentration groups showed lower pulmonary function values; those for the over-40-ppb were particularly low. Girls from high indoor NO$_2$ concentration groups also showed low pulmonary function values compared to the under-20-ppb group, except for 2nd $V_{25}$. In trend tests, indoor NO$_2$ concentration was significantly associated with 2nd FEV$_{0.75}$ and $V_{25}$ in boys, and with 2nd FVC and FEV$_{0.75}$ in girls. In the third testing, however, no significant association between indoor NO$_2$ concentration and pulmonary function parameters were obtained in both boys and girls.

Table 5 shows differences in pulmonary function parameters based on presence or absence of past history of respiratory diseases; maternal smoking habits; and type of home heating appliance used. In both the second and third testings, boys with a history of respiratory diseases before 2 years of age showed low FVC values, while girls with such past history showed low FVC and FEV$_{0.75}$, and high $V_{25}$. However, none of these differences were found to be significant. All pulmonary function values were lower in children with maternal smoking than in those with non-smoking mothers, except for FVC in girls. Of these parameters, 3rd $V_{25}$ in girls was the only one that was significantly lower. In terms of the relationship between type of home heating appliance and pulmonary function values obtained, no definite trends were observed in either boys and girls.

### Analyses by log-linear models

Using the log-linear model, the effects on pulmonary function levels of area of residence (A), type of home heating appliance used (H), and indoor NO$_2$ concentration (N) were analyzed. Some possible log-linear models are shown in Table 6. In the abbreviated bracket notation, we describe a hierarchical log-linear model including the highest interaction; e.g., [AHN] means that the interaction among A, H, and N is present in the model. Since indoor NO$_2$ concentration varied with area of residence and type of home heating appliance, the interaction among these factors ([AHN]) was included in all models.

For 2nd FEV$_{0.75}$ in boys (P$_1$), the fit of the log-linear model [AHN] [AP$_1$] [NP$_1$] was satisfactory. Under the condition that this model was the one best fit, the interactive effect between 2nd FEV$_{0.75}$ in boys and area of

### Table 4. Percentage of predicted pulmonary function values in children classified according to the annual average indoor nitrogen dioxide concentrations by testing and sex.

|                | 0-19 ppb | 20-29 ppb | 30-39 ppb | 40 ppb- | p value* |
|----------------|----------|-----------|-----------|---------|----------|
| **Second testing** |          |           |           |         |          |
| **Boys**       |          |           |           |         |          |
| FVC            | 99.26±9.35 | 98.97±9.34 | 97.98±9.50 | 97.16±10.62 | NS       |
| FEV$_{0.75}$   | 99.56±9.77 | 98.64±9.87 | 97.75±10.04 | 96.26±10.35 | <0.05    |
| $V_{25}$       | 106.92±27.39 | 102.99±23.87 | 103.10±28.05 | 97.95±24.58 | <0.05    |
| (N)            | (124)     | (96)      | (82)      | (55)    |          |
| **Girls**      |          |           |           |         |          |
| FVC            | 99.34±10.64 | 95.35±8.98 | 97.20±9.40 | 94.33±9.45 | <0.01    |
| FEV$_{0.75}$   | 99.14±10.25 | 95.98±9.43 | 97.62±9.70 | 94.37±9.52 | <0.01    |
| $V_{25}$       | 99.94±25.21 | 100.34±23.14 | 103.66±25.21 | 97.78±27.07 | NS       |
| (N)            | (109)     | (86)      | (69)      | (63)    |          |
| **Third testing** |          |           |           |         |          |
| **Boys**       |          |           |           |         |          |
| FVC            | 98.42±9.61 | 96.50±8.88 | 97.09±9.73 | 95.92±10.80 | NS       |
| FEV$_{0.75}$   | 97.77±9.29 | 97.01±9.88 | 96.39±10.58 | 95.49±10.04 | NS       |
| $V_{25}$       | 105.73±27.43 | 105.21±26.91 | 102.15±29.84 | 99.10±22.76 | NS       |
| (N)            | (124)     | (98)      | (81)      | (54)    |          |
| **Girls**      |          |           |           |         |          |
| FVC            | 97.43±10.05 | 94.94±9.79 | 95.32±10.88 | 95.19±9.05 | <0.05    |
| FEV$_{0.75}$   | 97.89±10.43 | 95.49±10.24 | 96.13±10.27 | 95.30±8.82 | NS       |
| $V_{25}$       | 102.68±25.67 | 101.98±26.32 | 102.57±24.20 | 95.18±22.78 | NS       |
| (N)            | (106)     | (97)      | (73)      | (63)    |          |

Values are mean±SD.

* p value by trend test for categories of indoor nitrogen dioxide concentrations. NS, not significant.
residence ([AP]) should be significant. Likewise, for 2nd FVC in girls (P2), the fit of the model [AHN] [AP] [NP2] was satisfactory, and the parameter (P2) was shown to be significantly related to indoor NO2 concentration.

Similar results were obtained about the other pulmonary function parameters, indicating that the fits of models were satisfactory when the interactive effects of the area of residence and indoor NO2 concentration on the pulmonary function were included. Using these models, the odds ratios for depressed pulmonary function levels were estimated in terms of area of residence and indoor NO2 concentration.

As shown in Table 7, the estimated odds ratios of boys living in urban areas to those in rural areas were higher than 1 for all parameters except for 2nd V25. The area of residence was significantly associated with 2nd FEV0.75 (odds ratio (OR)=1.55), 3rd FVC (OR=1.63) and 3rd FEV0.75 (OR=1.90). In both the second and third testings, girls showed odds ratios of less than 1 for FVC and FEV0.75, and higher than 1 for V25. None of these were found to be significant, however.

Estimates of odds ratios for depressed pulmonary function levels by indoor NO2 concentration are shown in Table 8. Boys showed odds ratios of over 1 in most cases. However, only the 2nd V25 in the over-40-ppb group (OR=2.21) was significant, and no definite tendencies were noted in relation to indoor NO2 concentration. In girls, most odds ratios were higher than 1, and significantly high odds ratios were obtained for the following parameters: 2nd FVC in the 20-29 ppb group (OR=1.80), FEV0.75 (OR=1.96), V25 (OR=2.08), and 3rd V25 (OR=1.89) in the over-40-ppb group. All odds ratios except for 2nd FVC were highest in the over-40-ppb group.

DISCUSSION

The pulmonary function test has been widely utilized, along with the prevalence of respiratory symptoms, as an epidemiological method of studying the effects of ambient

### Table 5. Differences in percentage of predicted pulmonary function values between children classified according to history of respiratory diseases, maternal smoking, and type of heating appliance used by testing and sex.

|                      | Respiratory diseases before 2 years of age | Maternal smoking | Use of unvented heating appliance |
|----------------------|------------------------------------------|------------------|----------------------------------|
|                      | Second testing | Third testing | Second testing | Third testing | Second testing | Third testing |
| Boys                 |               |              |               |              |               |              |
| FVC                  | -0.76         | -0.76        | -1.21         | -0.91        | -0.55         | -0.73        |
| FEV0.75              | 0.20          | -0.16        | -0.56         | -1.10        | 0.05          | -0.26        |
| V25                  | 4.07          | -1.38        | -1.42         | -3.20        | 2.76          | 3.68         |
| Girls                |               |              |               |              |               |              |
| FVC                  | -3.70         | -3.80        | 0.65          | 0.54         | -0.16         | 0.47         |
| FEV0.75              | -1.29         | -1.20        | -0.78         | -1.21        | 0.34          | -0.11        |
| V25                  | 7.21          | 8.41         | -4.43         | -8.78*       | -0.18         | -2.37        |

* p<0.05 for the difference between children with and those without maternal smoking.

### Table 6. Goodness-of-fit of some log-linear models for the associations of pulmonary function with various factors.

| Model                                      | G^2  | Degrees of freedom | p     | Parameter under test | ΔG^2  |
|--------------------------------------------|------|--------------------|-------|-----------------------|-------|
| 2nd FEV0.75 for boys                       |      |                    |       |                       |       |
| [AHN] [AP] [HP] [NP]                       | 20.91| 20                 | 0.40  | [HP]                 | 1.29  |
| [AHN] [AP] [NP]                            | 22.20| 22                 | 0.45  | [AP]                 | 6.88* |
| [AHN] [NP]                                 | 29.08| 24                 | 0.22  | [NP]                 | 3.83  |
| [AHN] [AP]                                 | 26.03| 28                 | 0.57  |                       |       |
| 2nd FVC for girls                          |      |                    |       |                       |       |
| [AHN] [AP] [HP] [NP]                       | 21.62| 20                 | 0.36  | [HP]                 | 0.22  |
| [AHN] [AP] [NP]                            | 21.84| 22                 | 0.47  | [AP]                 | 2.92  |
| [AHN] [NP]                                 | 24.76| 24                 | 0.42  | [NP]                 |       |
| [AHN] [AP]                                 | 34.73| 28                 | 0.18  | [NP]                 | 12.89*|

G^2: the likelihood ratio chi-squared statistic.

A: area of residence, H: type of heating appliance used, N: indoor nitrogen dioxide concentration.
P1: FEV0.75 for boys in the second testing, P2: FVC for girls in the second testing.
a The abbreviated bracket notation means a log-linear model including the interaction among the variables.

b The adopted model.  c  p<0.05.
Table 7. Estimates of odds ratios (ORs) and 95% confidence intervals (95% CIs) for depressed pulmonary function level by area.

|                | Second testing |            | Third testing |            |
|----------------|----------------|------------|---------------|------------|
|                | OR  | 95% CI    | OR  | 95% CI    |
| **Boys**       |     |          |     |          |
| FVC            | 1.26| 0.90-1.78| 1.63| 1.15-2.31|
| FEV<sub>0.75</sub> | 1.55| 1.10-2.19| 1.90| 1.34-2.69|
| V<sub>25</sub>  | 0.84| 0.60-1.17| 1.23| 0.87-1.74|
| **Girls**      |     |          |     |          |
| FVC            | 0.71| 0.50-1.07| 0.67| 0.46-1.01|
| FEV<sub>0.75</sub> | 0.96| 0.66-1.45| 0.95| 0.65-1.39|
| V<sub>25</sub>  | 1.37| 0.90-1.98| 1.29| 0.88-1.89|

By the model [AHN] [AP] [NP].
A : area of residence, H : type of heating appliance used, N : indoor nitrogen dioxide concentration, P : pulmonary function levels.
* Odds ratios of children living in urban area relative to those in rural areas.

Table 8. Estimates of odds ratios (ORs) and 95% confidence intervals (95% CIs) for depressed pulmonary function level by the annual average indoor nitrogen dioxide concentration.

|                | 20-29 ppb |            | 30-39 ppb |            | 40 ppb- |          |
|----------------|-----------|------------|-----------|------------|---------|----------|
|                | OR  | 95% CI    | OR  | 95% CI    | OR     | 95% CI   |
| **Second testing** |     |          |     |          |        |          |
| Boys           |     |          |     |          |        |          |
| FVC            | 1.01| 0.60-1.70| 1.55| 0.90-2.65| 0.75   | 0.35-1.70|
| FEV<sub>0.75</sub> | 1.13| 0.67-0.89| 1.33| 0.77-2.28| 0.83   | 0.39-1.87|
| V<sub>25</sub>  | 0.95| 0.57-1.60| 1.30| 0.76-2.22| 2.21   | 1.05-4.91|
| Girls          |     |          |     |          |        |          |
| FVC            | 2.13| 1.24-3.63| 1.24| 0.68-2.25| 1.80   | 1.07-3.63|
| FEV<sub>0.75</sub> | 1.70| 0.99-2.91| 1.23| 0.67-2.27| 1.96   | 1.10-3.93|
| V<sub>25</sub>  | 0.78| 0.44-1.36| 1.18| 0.66-2.12| 2.08   | 1.13-5.31|

| **Third testing** |     |          |     |          |        |          |
| Boys             |     |          |     |          |        |          |
| FVC             | 1.27| 0.76-2.13| 1.09| 0.63-1.90| 1.84   | 0.85-4.19|
| FEV<sub>0.75</sub> | 1.21| 0.72-2.03| 1.62| 0.94-2.79| 1.01   | 0.47-2.31|
| V<sub>25</sub>  | 1.47| 0.88-2.46| 1.84| 0.97-3.16| 1.18   | 0.54-2.71|
| Girls           |     |          |     |          |        |          |
| FVC             | 1.34| 0.80-2.26| 1.22| 0.69-2.17| 1.75   | 0.74-4.45|
| FEV<sub>0.75</sub> | 1.56| 0.93-2.61| 1.49| 0.84-2.64| 1.57   | 0.65-4.08|
| V<sub>25</sub>  | 1.18| 0.70-1.99| 0.91| 0.50-1.66| 1.89   | 1.01-4.71|

By the model [AHN] [AP] [NP].
A : area of residence, H : type of heating appliance used, N : indoor NO<sub>2</sub> concentration, P : pulmonary function levels.
* Odds ratios relative to children in homes with indoor NO<sub>2</sub> concentrations of 0-19 ppb.

Air pollution on health7-9). In children, pulmonary function is subject to a number of factors, including host factors such as sex, age, and height, all of which can cause large variations10,11). Compared to the variations caused by host factors, those caused by environmental factors are considered to be relatively small12). Therefore, in order to evaluate precisely the effects of environmental factors such as ambient air pollution on pulmonary function, the involvement of other factors had to be taken into consideration.

In order to eliminate the effects of height and age, some prediction equations for reference standards have been proposed13,14). According to our earlier study15), prediction equations were prepared for each sex using height and age as independent variables. The test results were evaluated in terms of the percentage of measured pulmonary function values to predicted values from these equations.

Additional host factors include respiratory symptoms and past history of respiratory diseases. Individuals with asthma or wheezing symptoms have been reported to have depressed pulmonary function values, even under non-attack conditions16,17). However, many studies indicated that such individuals show no differences from healthy people in cases where 2-3 years have elapsed since the last attack18-20). Therefore, children who had asthma or wheezing symptoms in the 2 years prior to the start of this study, were excluded from present analyses.

While a history of respiratory disease before 2 years of age has been reported to affect pulmonary function during childhood21-23), the degree of adverse effect is considered small compared to that of asthma24). Vedal et al.25) reported that little difference was found in pulmonary function between children with histories of respiratory diseases and...
healthy children after adjusting for asthma and wheezing. In the present study as well, when children with asthma and wheezing were excluded, a past history of respiratory disease before 2 years of age was not associated with depressed pulmonary function.

Among the environmental factors, NO$_2$ is a representative ambient air pollutant, and causes lung injury at high concentrations$^{[5,12,14]}$. Schoolchildren living in areas with high ambient NO$_2$ levels have been reported to show low pulmonary function values$^{[235]}$.

Since NO$_2$ is also generated by the use of combustion apparatus in homes, indoor air pollution has been taken up as an environmental factor$^{[12,39]}$. In the United States and European studies$^{[4-6,10-13]}$, the effects of cooking gas have been investigated as a potentially major source of indoor air pollution. In Japan, however, the use of unvented heating appliances has been frequently assessed as a potential source of indoor air pollution, since gas is normally used for cooking in almost all homes$^{[14,39]}$.

Berkey et al.$^{[13]}$ and Speizer et al.$^{[40]}$ reported that children from homes where gas was used for cooking had slightly lower FVC and FEV$_{1.0}$ values than those from homes using electricity, whereas Dodge$^{[31]}$ and Vedal et al.$^{[36]}$ reported that the use of cooking gas was not associated with pulmonary function in children. In terms of unvented heating appliances, Nitta et al.$^{[35]}$ similarly reported that pulmonary function in children showed no difference with type of home heating appliance used. As the above reports, indoor air pollution has not shown a consistent association with pulmonary function. The present study, similarly, showed no definite relationship between type of home heating appliance used and pulmonary function values in children.

As for passive smoking, many studies have reported that maternal smoking habits decrease pulmonary function levels in children$^{[10,13,26]}$. On the contrary, Dodge$^{[22]}$ and Lebowitz et al.$^{[41]}$ found no relationship between parental smoking habits and pulmonary function among children. In our study, maternal smoking was likely to decrease $V_{25}$ values, but conversely to increase FVC values among girls. This result was in substantial agreement with the results of Nitta et al.$^{[35]}$ and Vedal et al.$^{[36]}$.

In order to evaluate the effects on health of outdoor and indoor air pollution in combination, direct measurements of personal exposure to pollutants should be desirable$^{[39]}$. Some reports have discussed the association between personal NO$_2$ exposure and individual health$^{[39,42,43]}$. However, few of these reports dealt with a sufficiently large number of subjects. Since an epidemiological study on a large number of subjects involves difficulties in measuring personal exposure levels, indoor NO$_2$ concentrations, which are assumed to contribute largely to overall personal exposure$^{[40]}$, have been measured in most cases$^{[5,12,14]}$.

While Fischer et al.$^{[45]}$ found a weak negative association between indoor NO$_2$ concentration and FEV$_{1.0}$ among adult females, the other many studies$^{[20,46-48]}$ found no definite relationship between indoor NO$_2$ concentration and pulmonary function in children. However, these studies have not taken into account the effect of ambient air pollution.

In order to compare pulmonary function values among children living in several regions with different levels of ambient air pollution, Nitta et al.$^{[35]}$ controlled for numerous factors, including indoor air pollution sources, using multiple regression techniques. We previously had measured indoor NO$_2$ concentrations at the homes of schoolchildren from various regions of Chiba Prefecture$^{[44]}$. In the present study, we investigated the relationship of pulmonary function among these schoolchildren to indoor NO$_2$ concentration and area of their residence.

Indoor NO$_2$ concentrations in the homes of schoolchildren were influenced by ambient NO$_2$ concentrations and the type of home heating appliance used$^{[14,49]}$. With this fact in mind, we analyzed the environmental factors that affect pulmonary function using log-linear models$^{[33]}$, which permit systematic analysis of multi-dimensional categorical variables in consideration of the interactions among them.

Both boys and girls living in urban areas with high ambient NO$_2$ concentrations showed lower pulmonary function in all parameters than those living in rural areas. Even after taking into account the indoor NO$_2$ concentration and type of heating appliance, using the log-linear model, boys in urban areas showed significantly elevated odds ratios for depressed values of FVC and FEV$_{0.75}$. On the other hand, girls showed no such significant relationship between pulmonary function and area of residence.

Children from high indoor NO$_2$ concentration groups showed lower pulmonary function values in most parameters. Even after considering the effect of area of residence using the log-linear model, girls from high indoor NO$_2$ concentration groups showed low pulmonary function values. Among girls in the over-40-ppb group, odds ratios were significantly elevated for all parameters at the second testing, but the ratio for only $V_{25}$ was significantly high at the third testing. Boys showed no definite relationship between indoor NO$_2$ concentrations and depressed pulmonary function values, except for $V_{25}$ at the second testing.

Hasselblad et al.$^{[10]}$ reported a significant decline in FEV$_{0.75}$ among girls from homes using cooking gas, but a slight increase among boys from such homes. Neas et al.$^{[50]}$ found a significant association between indoor NO$_2$ concentrations and prevalence of respiratory symptoms among children, which association was stronger among girls than among boys. Melia et al.$^{[4]}$ also reported that the association between use of cooking gas and respiratory symptoms was stronger among girls than among boys, and
suggested that girls would be more likely to subject to increased exposure as they spend more time in the kitchen.

In the present study, girls showed a stronger association between indoor NO\textsubscript {2} concentration and pulmonary function than did boys. This finding appears to correspond to the findings of Hasselblad et al.\textsuperscript{10}. Girls may be more affected by indoor air pollution. The association was the strongest in V\text{25}, which reflects peripheral airway function. By the third testing, however, the number of significant parameters has decreased among girls, which failed to substantiate the long-term effect of indoor NO\textsubscript {2} concentrations. Boys showed different pulmonary function values with varying levels of ambient air pollution, presenting an association between area of residence and pulmonary function. After controlling for indoor NO\textsubscript {2} concentration, the association remained significant in FVC and FEV\textsubscript{0.75}.

Thus, the adverse effects of outdoor and indoor NO\textsubscript {2} may be mediated through different mechanism. The complex mixtures of pollutants present in outdoor and indoor air are clearly distinct under most circumstances. In the urban areas where ambient NO\textsubscript {2} is at high levels, the presence of other pollutants, e.g., suspended particulate matter and ozone, with toxicity for the respiratory health would be anticipated.

In the present study, we carried out indoor NO\textsubscript {2} measurements on only one day each during the heating and non-heating periods, and did not survey the children's time activity patterns during testing. Therefore, the effects of outdoor and indoor air pollution on respiratory health should be studied further, including researches on methods of evaluating these effects.

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