A Comparative Study on the Health Effects of Smoking and Indoor Air Pollution in Summer and Winter

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This study was performed by a comparison between summer and winter for the purpose of demonstration the actual conditions of health effects of indoor air pollution with special reference to NO₂ and smoking, on the subjects composed of 820 school children and their 546 mothers in the two areas with different ambient NO₂ concentrations. In either case, examination was carried out with standardized questionnaire test for respiratory symptoms, personal NO₂ exposure measurement using the filter badge by Yanagisawa, and analysis of urinary hydroxyproline and creatinine in two areas with different ambient NO₂ levels.

Personal NO₂ exposure level in winter season was 2–3 times higher than that in summer, particularly NO₂ level among residents living in homes with nonvented stove for space heating was substantially higher from those of residents with vented stove. Wives with vented stove had a moderate exposure level in winter season by the contribution of NO₂ originated from the kitchen and poor ventilation rate. Since the hydroxyproline to creatinine ratio (HOP-ratio) of children increased more, their household location were nearer to any heavy traffic roads in summer, health effects from automobile exhaust were suggested only in summer season. In summer season, personal NO₂ exposure level were almost the same with the ambient NO₂ concentrations over both areas. These results suggest that indoor air pollution in winter season may be separated from outdoor air pollution. It was a matter of course that hydroxyproline to creatinine ratio in winter season was higher than that in summer, in any group and in any area, but the range of variation of hydroxyproline to creatinine ratio was smaller by far than that of personal NO₂ exposure level.

Judging from urinary hydroxyproline to creatinine ratio, health effects of active smoking and passive smoking increased with increasing the number of smoked, dose-dependently in any season. According to stepwise multiple regression analysis, hydroxyproline to creatinine ratio had significant relation to either NO₂ and active or passive smoking, but personal NO₂ exposure level had no relation to cigarette smoking. NO₂ and cigarette smoke were seemed to make hydroxyproline to creatinine ratio increase, independently each other.

(Key words: Urinary hydroxyproline to creatinine ratio, Personal nitrogen dioxide exposure, Seasonal change, Indoor air pollution)

INTRODUCTION

In recent years indoor air pollution may be one of matters of primary concern in the field of epidemiological studies on the health effects of air pollution, because it has gradually become apparent that indoor air pollution especially derived from nitrogen dioxide (NO₂) and passive smoking is related to the health of almost all people.

In most previous epidemiological studies on the health effects of air pollution, the data of the monitoring systems authorized by the Environment Agency were used as the representative values in the district observed. However, it has recently been demonstrated that the indoor levels of air pollutants are different from their outdoor levels (13, 26), especially in winter when ventilation rates are decreased, as a result of improved tightness of houses. Namely, the
indoor levels of NO\textsubscript{2} and suspended particulate matter derived from small indoor sources are much higher than their outdoor levels (21, 51). In order to elucidate the health effect of such indoor NO\textsubscript{2}, it is necessary to determine the amount of NO\textsubscript{2} to which each person is exposed in the local population. The diffusion-type handy personal samplers developed by Palmes (23) and Yanagisawa et al. (30) are useful for this purpose. The filter badge developed by Yanagisawa et al. (30) is particularly excellent, because it is compact (5 \times 4 \times 1 \text{ cm}^3, 15 \text{ g}) and can determine personal exposure for one day to one week.

Increased prevalence rates of respiratory symptoms revealed by MRC and ATS-DLD questionnaires and decreased lung function tests such as flow volume and closing volume have been used as epidemiological indices for elucidating the effects of air pollutants on the respiratory system. However, they can not serve as indices for assessing the health effects of ambient NO\textsubscript{2} in recent years, indoor NO\textsubscript{2} and passive smoking in recent years, and therefore, there has been a growing demand for the development of more sensitive new indices. Kucharcz (17), Kosmider (16), Drozdz (5) and Kleinerman (15) have reported that urinary excretion of hydroxyproline was increased when animals were exposed for extended periods of time. On the other hand, Carp and Janoff (2), Chawdhury (4), Rees (24) and Gadek et al. (9) assessed the effects of smoking on the respiratory organs in terms of changes in serum concentration of alpha-1-antitrypsin, trypsin inhibitor capacity (TIC) and TIC activity ratio. Although no definite conclusion has necessarily been obtained concerning individual determinations, it has generally been accepted that the alveolar wall may possibly be destructed or degenerated by excess protease based on imbalance between protease and antiprotease. Although since Eriksson (6) there have been no papers, but Kosmider's one (16), which dealt with increased urinary excretion of hydroxyproline associated with destruction of the alveolar wall tissue in man, it seems quite reasonable to consider that urinary hydroxyproline may be a useful index. On the basis of the above, we have considered that hydroxyproline, which is a specific imino acid contained in collagen and elastin and is the final product of the these substances, may be useful as an index directly reflecting the effects of low-level NO\textsubscript{2} and smoking, especially passive smoking, on the respiratory organs and performed a series of epidemiological studies since 1977. However, since it is extremely difficult to collect 24-hour urine from many healthy volunteers, we have used random urine specimens and reported that the amount of hydroxyproline in 24-hour urine can be represented by the hydroxyproline to creatinine ratio (HOP ratio) in random urine and this ratio varies to a lesser extent (11). In addition, we have elucidated age- and sex-related changes in this ratio in Japanese (12) and investigated its relationship not only with the health effects of passive smoking and low-level NO\textsubscript{2} but also with those of automobile exhaust fumes and heating and cooking apparatuses as indoor NO\textsubscript{2} sources (18, 19).

The present study was performed for purposes of determining and comparing personal NO\textsubscript{2} exposure and urinary HOP ratio in winter and summer in the same subjects living in the same districts in order to investigate the health effects of NO\textsubscript{2} and passive smoking.

**METHODS**

The districts surveyed are located at Suginami ward in Tokyo and Aikawa town in Kanagawa prefecture. Suginami district is one of typical residential quarters, but a main road goes through it and as many as 40 to 100 thousands of cars travel along it daily. Accordingly, influence of automobile exhaust can not be neglected in areas along the road. On the other hand, Aikawa district is agriculture and mountain village about 60 km distant from the midtown area. There are no factories and main roads as fixed sources of NO\textsubscript{2} in this district. Table 1 summarizes the monthly average values of NO\textsubscript{2}, SO\textsubscript{2} and dust for both districts in 1982.

The winter survey was conducted from December, 1981 to February, 1982, while the summer survey was conducted in July, 1982. In Suginami district, the winter survey was performed on school children from two elementary schools and their mothers, while the summer survey was carried out on school children from one of the two schools and their mothers. In Aikawa district, the summer and winter surveys were performed on school children from the
same three elementary schools and their mothers. ATS-DLD and MRC questionnaires were distributed to school children and their mothers, respectively, through each elementary school. These questionnaires included the number of cigarettes in active and passive smoking, occupation, age and respiratory symptoms as matters for investigation. Determination of personal NO₂ exposure and collection of urine were performed in subjects (820 school children and 546 mothers) who were extracted randomly from school children and their mothers. As a rule, the first urine in the early morning was discarded and the urine one to two hours after it, that is fasting urine was collected. The following analysis was performed on the subjects with complete data on questionnaires, personal NO₂ exposure and urinary HOP ratio.

The filter badge used to determine personal NO₂ exposure consists of an absorption filter paper impregnated with 20% triethanolamine and a prefilter set before the paper. All subjects were asked to wear this badge on the breast of their garments. After 24 hours of exposure, these badges were recovered in tightly sealed aluminium packs. Determination was performed by colorimetry using Saltzman’s reagent.

Determination of hydroxyproline was performed using an autoanalyzer after pretreatment of urine by the modified Parekh and Jung’s method (22). Urinary creatinine determined using an autoanalyzer according to modified Jaffe’s method (28).

Multivariate analysis was performed using BMDP statistical package by the stepwise multiple regression method. In this method, the independent variable whose partial correlation coefficient has already been employed is fixed and any other independent variable showing the highest partial correlation coefficient against the dependent variable is employed. In our case, partial F values were placed at 4.0 or more in the employment of independent variables and 3.9 or less in the removal of independent variables which had already been employed.

RESULTS

1) Distribution of personal NO₂ and urinary hydroxyproline to creatinine ratio

In school children, average personal NO₂ exposure in winter was 37.14 ppb in Suginami district and 32.84 ppb in Aikawa district. In summer, it was depressed to 21.50 ppb in the former and 12.86 in the latter. Namely, average personal NO₂ exposure was significantly higher in winter than in summer (p < 0.01). In mothers, personal NO₂ exposure varied to a large extent from the minimum value of several ppb to the maximum value of 245 ppb in winter. It ranged from 1 to 77 ppb in summer, and average personal NO₂ exposure was also significantly higher in winter than in summer as in school children in both districts (p < 0.01) (Table 2). In mothers, personal NO₂ exposure was higher in winter than in summer (p < 0.01). It showed a logarithmic-normal distribution on both of children and mothers in either winter or summer, and the kurtosis of distribution ranged from 7 to 12 and its skewness from 1.8 to 2.4.

When the subjects were divided into the vented and non-vented stove groups according to the types of heating apparatuses used in winter in order to discuss personal NO₂ exposure for relationship with home environmental factors, it was significantly higher in the non-vented type stove group than in the vented type stove group in winter (p < 0.01). However, there was no difference between the two groups in summer (Fig. 1).

Personal NO₂ exposure was kept below the environmental standard of NO₂ (40 to 60 ppb) in Japan even in winter in both districts, so long as average values were concerned. When the subjects were classified by personal NO₂ exposure into A group (less than 40 ppb), B group (40 to 60 ppb) and C group (more than 60 ppb) in order to examine compliance with the air quality standard in Japan, however, it should be noted that it was kept below the standard in almost all subjects in summer, but was increased beyond it in winter 22.8% of mothers and 8.6% of school children from Suginami district and 22.7% of mothers and 7.2% of school children from Aikawa district.

Urinary HOP ratio, unlike personal NO₂ exposure, varies to a lesser extent with individuals and seasons, and it has been suggested that health effect of exposure to NO₂ at indoor levels is not necessarily large. Urinary HOP ratio showed an almost normal distribution and its skewness ranged from 0.08 to 0.12.
2) Active and passive smoking and urinary hydroxyproline to creatinine ratio

On the basis of the results of MRC questionnaire, the subjects without a smoking habit were classified according to the habit of smoking of their families into the non-passive smoker group and the passive smoker groups of 1 to 10, 11 to 20 and 21 or more cigarettes/day. Urinary HOP ratio was determined in each group and the effect of passive smoking was discussed. In mothers without a smoking habit and school children, urinary HOP ratio was increased with an increase in the number of cigarettes smoked by their families and was significantly higher in the passive smoker group than in the non-passive smoker group in either summer or winter (Table 3 and 4). It was higher in winter than in summer in every group.

When the urinary HOP ratio in the non-passive smoker group was considered 1.00 and the relative ratio (r.r.) against HOP ratio in each passive smoker group was determined, it was assumed that the effect of passive smoking in mothers might be higher in winter than in summer. However, season-related differences in the effect of passive smoking were smaller in school children than in mothers.

When the effect of active smoking was examined, urinary HOP ratio was increased with an increase in the number of cigarettes smoked by mothers themselves in both seasons, and the relative ratio was larger in the active smoker group than in the passive smoker group and was also larger in winter than in summer (p<0.05).

3) Nitrogen dioxide in automobile exhaust and urinary hydroxyproline to creatinine ratio

The dwelling places of subjects in Suginami district were classified by the distance from the main road into the 50 m or less, 51 to 100 m and 101 m or more areas, and NO2 derived from automobile exhaust and urinary HOP ratio were discussed. In winter, no area-related difference was noted in both NO2 and urinary HOP ratio in either school children or their mothers. In summer, however, urinary HOP ratio was increased with a decrease in the distance from the main road and was significantly elevated especially in school children (p<0.01 or 0.05).

4) Correlation among urinary hydroxyproline to creatinine ratio, personal NO2 exposure and the number of cigarettes in active and passive smoking.

In school children, six variables which might influence urinary HOP ratio were employed and discussed for correlation coefficients among them for each season. These were personal NO2 exposure (PN02), age as a variable with growth (AGE), distance from the main road (ROAD), No. of cigarettes in passive smoking (PAS), area-related difference (AREA) and logarithmic values of personal NO2 exposure [log (PN02)] (Table 5). The variables which were highly correlated with urinary HOP were PN02 (winter: 0.565, summer: 0.564), PN02 (0.492, 0.587) and log (PN02) (0.522, 0.382) (p<0.001). It should be noted that urinary HOP ratio and PN02 were not practically correlated with ROAD in winter, but were highly correlated with it in summer (p<0.001).

In mothers, correlation matrices were discussed using the six variables described above and the number of cigarettes in active smoking (ACT) (seven in total) (Table 6). The variables which were highly correlated with urinary HOP ratio were PN02, log (PN02), ACT and PAS in either winter of summer (p<0.001). ROAD was not practically correlated with urinary HOP ratio, PN02 and log (PN02) in winter as in school children, but was significantly correalted with them in summer (p<0.001).

5) Multivariate analysis by the stepwise multiple regression method

In school children, the six variables described above were employed as explanatory variables for urinary HOP ratio and analysis was carried out for each season by the stepwise multiple regression method (Table 7). In winter, the number of cigarettes in passive smoking (PAS) was employed in the first step and the square of its multiple correlation coefficient (R2) was 0.3190. Log (PN02) was employed in the second step and the increment of the square of its multiple correlation coefficient (ΔR2) was 0.2532. These were followed by AGE, AREA and ROAD in the third, fourth and fifth steps, respectively. In summer, PAS was employed in the first place and R2 was 0.3176. Log (PN02) was employed in the se-
cond place and \( \Delta R^2 \) was 0.1456. ROAD was employed in the third place, and no other variables were employed. The coefficients of the distance from the main road (ROAD) were 1.971 in winter, but 6.228 in summer. It is suggested from these results that the influence of ROAD on urinary HOP ratio is larger in summer than in winter.

In mothers, analysis was performed with the six variables described above added with the number of cigarettes in active smoking (ACT) and occupation (OCU). The housewives without occupation accounted for 75.3 and 71.6% of mothers in Suginami and Aikawa districts, respectively. In winter, variables were employed in the following order: \( \log (\text{PNO}_2) \) \( (R^2 = 0.2644) \), PAS \( (\Delta R^2 = 0.2106) \), ACT, AREA, and OCU. In summer, variables were employed in the order: \( \log (\text{PNO}_2) \) \( (R^2 = 0.1481) \), PAS \( (R^2 = 0.1335) \), ACT, ROAD and AREA. It should be noted that ROAD, which was not employed in winter, was employed in place of OCU in summer.

DISCUSSION

1) Seasonal changes in personal exposure to nitrogen dioxide

It is apparent from the results of the present survey that personal NO\(_2\) exposure varies with seasons and is about two times higher in winter than in summer in both school children and mothers in either an urban or a rural district. These results are consistent with those of the survey which was conducted by Yanagisawa et al. (31) to estimate yearly exposure of housewives and suggest that the influence of NO\(_2\) derived from heating apparatuses, especially non-vented type stoves, is large in winter. Personal NO\(_2\) exposure was higher in mothers than in school children in both seasons. This is presumably because mothers stay longer in rooms and are likely to be influenced by NO\(_2\) derived from cooking apparatuses in a kitchen.

Personal NO\(_2\) exposure was almost equal to the ambient NO\(_2\) level in summer, but was much higher than it in winter. These results suggest that indoor pollution with NO\(_2\) is independent of outdoor NO\(_2\) and are consistent with Spengler's report (26) that the probability at which the indoor NO\(_2\) level in winter could be estimated from its ambient level might be as low as 1% in the United States. For this reason, care must be taken when personal NO\(_2\) exposure in a certain district is discussed comparatively, especially in terms of average values in winter. Namely, it has been demonstrated that there is little difference in personal NO\(_2\) exposure in households without non-vented type heating apparatuses.

2) Active and passive smoking and urinary hydroxyproline to creatinine ratio

The effect of passive smoking was discussed in term of an increase in urinary HOP ratio. As a result, this ratio was increased in a dose-effect relationship with an increase in the number of cigarettes smoked by families in school children and their mothers as non-smokers in both seasons. However, it was significantly higher in winter than in summer in mothers, so long as the effect of passive smoking was discussed on the basis of relative ratios. This is probably ascribable to decreased indoor air ventilation rates, prolonged indoor stay time and use of heating apparatuses, especially non-vented type stoves in winter.

In addition, the effect of passive smoking at home was elucidated between husbands as smokers and their wives as non-smokers, mothers as smokers and their school children and fathers as smokers and their school children. Namely, the effect of passive smoking due to smoking by husbands (fathers) was larger in their wives as non-smokers than in their children, regardless of season, and the effect of passive smoking on school children was larger when their mothers were smokers than when their fathers had the habit of smoking. These results are ascribable to difference in contact time at home among family members and reflect close relation between husbands and wives. According to the "Survey of human activity pattern" in the United States (3, 27), they spend about 70% of their living time in rooms, while Japanese housewives without occupation spend about 80% of a day at home as revealed by the "Survey on the Living Time of Nations" (20). Since 70% or more of mothers as the subjects of the present survey were housewives without occupation, it is a matter of course that the effect of passive smoking on school children was larger when not their fathers but their mothers were smokers.
3) Effect of automobile exhaust

In the present survey, one of characteristic differences between winter and summer is the fact that HOP ratio was influenced by the distance of dwelling places from main roads. Namely, it is conceivable that the effect of NO₂ in automobile exhaust (probably suspended particulate matter, too) may be hidden in winter, because indoor NO₂ levels are completely separated from and independent of ambient NO₂ levels, and therefore, the effect of automobile exhaust smaller than that of indoor NO₂ levels. In contrast, the effect of automobile exhaust may be reflected clearly by urinary HOP ratio in summer, especially in school children, while it may not be necessarily reflected directly in mothers, because the effect of cooking apparatuses persists even in summer. However, it is considered that the effect of dust and suspended particulate matter on urinary HOP ratio as well as that of NO₂ in automobile exhaust should be discussed as one of risk factors.

4) Health effects of cigarette smoke and nitrogen dioxide

In the results of correlation matrixes and multivariate analysis, urinary HOP ratio was significantly related to the number of cigarettes in active and passive smoking and personal NO₂ exposure in both seasons, but personal NO₂ exposure was almost unrelated to the number of cigarettes in active and passive smoking. This may be quite reasonable when the fact that NO₂ contents in the mainstream of cigarette smoke are extremely low (29) is taken into consideration, but it can not necessarily be concluded definitely on the basis of these results that the effect of smoking is based on an approach which is different from that for NO₂. Boren (1) noted in animal experiments that the number of damaged alveoli was higher in animals that inhaled carbon particles absorbed with NO₂ than in control animals and test animals that inhaled NO₂ alone and have advanced a theory that carbon particles inhaled together with cigarette smoke may absorb trace amounts of NO₂ contained in the smoke and can serve as "carrier mechanism" to keep local NO₂ levels elevated in alveoli. Freeman (7, 8) and Heuter (10) reported that cigarette smoke containing low levels of NO₂ inhibited protein metabolism and suggested the possibility of "carrier mechanism". Rylander (25) reported that cigarette smoke elicited increased macrophages and neutral polynuclear leukocytes, while cigarette smoke after removal of small particles through a Cambridge filter did not elicit these changes in animal experiments. Kiburn et al. (14) also carried out experimental study on neutral polynuclear leukocytes and reported similar results.

Occurrence of chronic obstructive respiratory diseases can rationally be explained by Eriksson's (6) "protease antiprotease imbalance theory", and this imbalance may be induced by atmospheric polluting oxides represented by NO₂ and oxides, metal cadmium, suspended particulate matter, etc. in cigarette smoke. Accordingly, to the results of experiments on exposure to cigarette smoke, protease derived from neutral polynuclear leukocytes and alveolar macrophages in increased to cause imbalance with alpha-1-antitrypsin estimated from serum levels or its trypsin inhibitor capacity, resulting in destruction of collagen and elastin in the alveolar wall. Accordingly, it must be elucidated in the future whether increased urinary HOP ratio due to NO₂ and cigarette smoke is based on trace amounts of NO₂ transported to alveoli by the carrier mechanism, or whether NO₂ and cigarette smoke affect pulmonary tissues through different approaches, for example, cadmium and suspended particulate matter.

ACKNOWLEDGEMENT

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Table 1 Monthly average concentration of air pollutants in Suginami and Aikawa Area

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Table 2 Average of Hydroxyproline to creatinine ratio and Personal NO\textsubscript{2} Exposure in each area and in each season

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<th>Summer</th>
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<td>Mean</td>
<td>S.D.</td>
<td>Mean</td>
<td>S.D.</td>
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<td>Aikawa</td>
<td>Suginami</td>
<td>Aikawa</td>
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<tr>
<td>Wives</td>
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<td>S.D.</td>
<td>Mean</td>
<td>S.D.</td>
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Table 3 Smoking effects revealed by urinary HOP ratio measurement in winter

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<th>Active smoking effects by smoking of wives themselves</th>
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<td>Smoking habits of husbands</td>
<td>Smoking habits of wives</td>
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<tr>
<td></td>
<td>Non-S 1-10 cig./day 11-20 cig./day 21-40 cig./day</td>
<td>Total Ex-S 1-10 cig./day 11-20 cig./day</td>
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<tr>
<td>Non-S</td>
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</tr>
<tr>
<td>M</td>
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<td>1.29</td>
</tr>
<tr>
<td>S.D.</td>
<td>5.52</td>
<td>5.71</td>
</tr>
<tr>
<td>r.r.</td>
<td>1.00</td>
<td>1.22</td>
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Wives          |                                                                 |                                                                 |      |
| Non-S          |                                                                 |                                                                 |      |
| M              | 108 | 104 | 103 | 103 | 107 | 103 | 103 | 103 |
| S.D.           | 5.12 | 5.68 | 5.48 | 5.48 | 5.48 | 5.48 | 5.48 | 5.48 |
| r.r.           | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |

Schoolchildren |                                                                 |                                                                 |      |
| Non-S          |                                                                 |                                                                 |      |
| M              | 158 | 164 | 163 | 163 | 163 | 163 | 163 | 163 |
| S.D.           | 10.76 | 11.49 | 11.50 | 11.50 | 11.50 | 11.50 | 11.50 | 11.50 |
| r.r.           | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |

Passive smoking effects by smoking of wives

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<tr>
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<td>Non-S 1-10 cig./day 11-20 cig./day</td>
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<td>Schoolchildren</td>
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<td>Wives</td>
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Table 4  Smoking effects revealed by urinary HOP ratio measurement in summer

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<th>Smoking habits of wives</th>
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<td>S.D.</td>
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<tr>
<td>N</td>
<td>131</td>
</tr>
<tr>
<td>M</td>
<td>89.12</td>
</tr>
<tr>
<td>r.r.</td>
<td>1.00</td>
</tr>
</tbody>
</table>

Table 5  Correlation coefficients among dependent and predictor variables about school children in winter ( ) : summer data

<table>
<thead>
<tr>
<th>HOP:C</th>
<th>PNO2</th>
<th>AGE</th>
<th>ROAD</th>
<th>PAS</th>
<th>AREA</th>
<th>Log</th>
<th>(PNO2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HOP:C</td>
<td>1.000</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PNO2</td>
<td>0.492 ***</td>
<td>1.000</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(0.387)***</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AGE</td>
<td>0.046</td>
<td>−0.065</td>
<td>1.000</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(0.036)</td>
<td>(0.124)*</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ROAD</td>
<td>0.067</td>
<td>−0.063</td>
<td>0.091 **</td>
<td>1.000</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(0.295)***</td>
<td>(0.328)***</td>
<td>(0.090)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PAS</td>
<td>0.565 ***</td>
<td>0.044</td>
<td>−0.033</td>
<td>−0.024</td>
<td>1.000</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(0.564)***</td>
<td>(0.015)</td>
<td>(0.011)</td>
<td>(0.057)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AREA</td>
<td>0.128 **</td>
<td>0.092 **</td>
<td>0.027</td>
<td>0.299 ***</td>
<td>−0.045</td>
<td>1.000</td>
<td></td>
</tr>
<tr>
<td>(−0.285)***</td>
<td>(−0.722)***</td>
<td>(−0.062)</td>
<td>(−0.388)***</td>
<td>(0.057)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Log(PNO2)</td>
<td>0.522 ***</td>
<td>0.924 ***</td>
<td>−0.058</td>
<td>−0.044</td>
<td>0.033</td>
<td>0.140 ***</td>
<td>1.000</td>
</tr>
<tr>
<td>(0.382)***</td>
<td>(0.973)***</td>
<td>(0.111)**</td>
<td>(0.319)***</td>
<td>(0.001)</td>
<td>(−0.726)***</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

HOP:C: urinary hydroxyproline to creatinine ratio,
PNO2: daily average in personal NO2 exposure,
AGE: age of subject,
PAS: number of cigarettes in passive smoking,
AREA: Suginami Ward = 1,
ROAD: near the heavy traffic roads = 1

*p<0.05  **p<0.01  ***p<0.001
Table 6  Correlation coefficients among dependent variable and predictor variables about wives in winter ( ): summer data

<table>
<thead>
<tr>
<th></th>
<th>HOP:C</th>
<th>PNO$_2$</th>
<th>ACT</th>
<th>PAS</th>
<th>AGE</th>
<th>AREA</th>
<th>ROAD</th>
<th>Log (PNO$_2$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HOP:C</td>
<td>1.000</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PNO$_2$</td>
<td>0.526***</td>
<td>1.000</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>(0.398)***</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ACT</td>
<td>0.293***</td>
<td>-0.009</td>
<td>1.000</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>(0.506)***</td>
<td>(-0.039)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PAS</td>
<td>0.483***</td>
<td>0.054</td>
<td>0.211***</td>
<td>1.000</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>(0.354)***</td>
<td>(-0.038)</td>
<td>(0.354)***</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AGE</td>
<td>-0.085*</td>
<td>-0.075</td>
<td>-0.109*</td>
<td>-0.069</td>
<td>1.000</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>(-0.031)</td>
<td>(0.125)**</td>
<td>(-0.020)</td>
<td>(-0.068)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AREA</td>
<td>-0.154**</td>
<td>-0.037</td>
<td>0.020</td>
<td>-0.065</td>
<td>0.141**</td>
<td>1.000</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>(0.083)</td>
<td>(0.371)</td>
<td>(0.022)</td>
<td>(0.034)</td>
<td>(0.192)***</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ROAD</td>
<td>-0.028</td>
<td>-0.041</td>
<td>0.023</td>
<td>0.057</td>
<td>0.098</td>
<td>0.283***</td>
<td>1.000</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(0.272)***</td>
<td>(0.283)***</td>
<td>(-0.059)</td>
<td>(0.021)</td>
<td>(0.132)**</td>
<td>(0.394)***</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Log (PNO$_2$)</td>
<td>0.582***</td>
<td>0.890***</td>
<td>0.002</td>
<td>0.039</td>
<td>-0.063</td>
<td>-0.051</td>
<td>-0.031</td>
<td>1.000</td>
</tr>
<tr>
<td></td>
<td>(0.385)***</td>
<td>(0.892)***</td>
<td>(0.046)</td>
<td>(0.030)</td>
<td>(0.122)**</td>
<td>(0.424)***</td>
<td>(0.252)***</td>
<td></td>
</tr>
</tbody>
</table>

HOP:C: urinary hydroxyproline to creatinine ratio,
PNO$_2$: daily average of personal NO$_2$ exposure,
ACT: number of cigarettes in active smoking,
PAS: number of cigarettes in passive smoking,
AGE: age of subject,
AREA: Suginami Ward = 1,
ROAD: near the heavy traffic roads = 1

* $p<0.05$  ** $p<0.01$  *** $p<0.001$
Table 7  Equations by stepwise multiple regression

School children

Winter

HOP:C = 51.503 + 0.382 PAS + 28.693 Log(PNO₂) + 0.576 AGE - 1.543 AREA + 1.971 ROAD

( R = 0.770 )

Summer

HOP:C = 59.482 + 0.414 PAS + 27.735 Log(PNO₂) + 6.228 ROAD

( R = 0.697 )

Wives

Winter

HOP:C = 4.809 + 11.680 Log(PNO₂) + 0.149 PAS + 0.235 ACT + 0.139 AREA + 1.145 OCU

( R = 0.817 )

Summer

HOP:C = 9.740 + 10.775 Log(PNO₂) + 0.097 PAS + 0.346 ACT + 3.149 ROAD + 1.914 AREA

( R = 0.748 )

HOP:C: urinary hydroxyproline to creatinine ratio,
AGE: age of subject,
PNO₂: daily average of personal NO₂ exposure,
AREA: Suginami Ward = 1,
ACT: number of cigarettes in active smoking,
PAS: number of cigarettes in passive smoking
ROAD: near the heavy traffic roads = 1,
OCU: Housewife = 1

Fig. 1  Seasonal and regional variation of personal NO₂ exposure level with filter badge in wives by the type of space heating