Oxidative DNA damage in relation to indoor carbon dioxide, volatile organics and tobacco smoke exposures

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Abstract

Purpose: Carbon dioxide (CO_2), volatile organic compounds (VOCs) and environmental tobacco smoke (ETS) are common indoor air pollutants generated from human activities. This study investigated the role of indoor air pollutants in oxidative DNA damage using urinary 8-hydroxydeoxyguanosine (8-OHdG) as the biomarker for employees in office buildings.

Methods: With informed conesnts, urine samples collected from 344 non-smokers and 45 smokers working in eight air-conditioned office buildings for determining urinary 8-OHdG and cotinine concentrations. CO_2 and VOCs in each office unit were continuously measured for 8 hours with portable monitors. Each participant completed a self-reported questionnaire for information on socio-demographic characteristics, life style, health history, and sick building syndromes.

Results: The urinary 8-OHdG levels were significantly associated with urinary cotinine levels and the indoor concentrations of CO_2 and VOCs. The average urinary 8-OHdG level in smokers (11.3 μg/g creatinine) was approximately two times higher than that in never smokers and former smokers (5.07 and 5.65 μg/g creatinine, respectively). The multivariate logistic regression analyses showed that the risk for elevated 8-OHdG was

increased significantly with increasing cotinine and CO_2 independently but moderately with VOCs for both all participants and never smokers. The never smokers in the third quartile levels of CO_2 exposure had a high adjusted odds ratio of 7.73 (95% CI = 3.05-19.6) for the 8-OHdG elevated level, greater than the overall median for 4.99 μg/g creatinine.

Conclusion: The indoor CO_2 and tobacco smoke exposure may contribute independently to the elevated urinary 8-OHdG levels.

Keywords: Volatile organic compounds; Environmental tobacco smoke; Carbon dioxide; Indoor air pollutants; 8-Hydroxydeoxyguanosine; Oxidative DNA damage; Cotinine

1. Introduction

Nitrogen oxides, sulfur oxides, polycyclic arometic hydrocarbons (PAH), volatile organic compounds (VOCs), carbon monoxide, carbon dioxide and particular materials, etc. are important urban air pollutants (Lippmann et al., 1980, 1984; Wolff, 1986; Wixtrom et al., 1992; Barrefors et al., 1993; De Fre et al., 1994; Darral et al., 1998; Pouli et al., 2003; Chuang et al., 2003; Cooper et al., 2004). DNA damage has been conduced from reactive oxygen species (ROS)in the exposure of these pollutants (Vine et al., 2000; Staessen et al., 2001). In the exposure of ROS, 8-hydroxydeoxyguanosine (8-OHdG) is formed by the action of hydroxyl radicals on the C-8 of guanosine as a marker of repairing damaged DNA (Shigenaga et al., 1989; Floyd, 1990; and Fraga et al., 1990). Calderon-Garciduenas et al. (1999) found higher 8-OHdG levels were in the nasal cavity respiratory track epidermic cells for children living in urban area than in rural area, and referred it as the result of air pollution.

Elevated urinary 8-OHdG levels also have been recognized for smokers and occupational drivers due to the formation of oxidative DNA adduct from routine exposure to cigarette smoke and traffic exhaust (Samet et al., 1987; Anderson et al., 1991; Loft et al., 1992; Chuang et al., 2003). Lodovici found the average urinary 8-OHdG concentration in smokers was 2-fold higher than that in never smokers

(Lodovici et al., 2000). Chuang et al. (2003) found the distribution of urinary 8-OHdG levels in male smokers among general population was similar to that in male never smoking taxi drivers. These findings suggested the contribution of occupational exposure to the level of 8-OHdG after taxi driving is outstanding, and smoking among general population contributing DNA damage is as greater as traffic exhaust exposure. Cotinine, the metabolite of nicotine has significant association with the urinary 8-OHdG concentration. It is used to be as a marker of tobacco smoke exposure (Shen et al., 1997).

Both tobacco smoke and environmental tobacco smoke (ETS) may stimulate the activation of the macrophage cells in the human body, leading to the respiratory track oxidative damage (Samet et al. 1987 and Anderson et al., 1991). In addition to chemicals and tobacco smoke, VOCs and ionization radiation can also result the rise of urinary 8-OHdG levels (Tagesson et al., 1995, 1996; Carstensen et al., 1999 and Wilson et al., 1993).

Most of the above studies are related to the exposure in industries and traffic. To our knowledge, little studies have investigated the contribution of indoor air pollution to urinary 8-OHdG levels for employees in office buildings. We conducted a study to evaluate the association between the levels of urinary 8-OHdG and indoor air pollution

for individuals working in high rise office buildings.

2. Materials and methods

Study subjects and data collection

From November 2003 through June 2004, we randomly selected 16 governmental and commercial organizations in Taipei city for subjects recruitment and indoor air pollutants measurement. Five of them declined to participate. Three of the remaining 11 institutions were excluded from this study because urinary specimens were not available. None of the office buildings have the report for indoor air quality issues previously. An invitation letter explaining the study was delivered to potential participants in 87 office units of the rest 8 organizations. With consents, 389 persons responded to our recruitment. Each person returned a spot urine sample and a self-reported questionnaire with information on smoking status and socioeconomic status. Urine samples were transported in a cold box of 4 ℃ to the laboratory stored at –80 ℃ until analysis.

Indoor CO_2 and TVOCs measurement

We used portable monitors (Q-TRAK IAQ Model 8551, TSI Incorporated, Shoreview, MN, USA) at each office to simultaneously detect the levels of CO_2 standardized against a wide range (0-5000 ppm) and delicate resolution (1 ppm), and of

TVOCs (PGM-7240, RAE SYSTEMS, California, USA) standardized against 102 categories of VOCs and acceptable deviation (20 ppb). Monitors were placed, during office hours, in the middle of the office, at 1.2 m height, away from any window or air–conditioner. Standard gas calibration was performed prior to each measurement.

Determination of urinary creatinine

Thawed urine samples were pretreated with centrifuge at 2,000 rpm for 10 minutes to remove the particulate matters. The creatinine value in the urine sample was determined with automatic analyzer (Hitachi 7250, Tokyo, Japan) based on the Jaffe colorimeter reaction (Nerurkar et al. 1960).

Determination of urinary 8-OHdG

Urinary 8-OHdG was determined by OXIS research™ enzyme-linked immunosorbent assay (ELISA) kit (Japan Institute for the Control of Aging, Shizuoka, Japan) because of its highly sensitivity and specificity, and easy operation. At first, all reagents and urinary samples were placed on bench to restore to room temperature (about 25 ℃). Briefly, a 50 µl of primary antibody were added to 50 µl aliquot of each sample or standard in microtiter plates pre-coated with 8-OHdG. The plates were

sealed tightly and inclubated at 37 ℃ for 1 hour with mixing at 100 rpm continuously. Repeatedly washing each well for three times with 250 µl of phosphate buffered saline to remove antibodies unbounded to the 8-OHdG in urine. The horse radish peroxidase (HRP)-conjugated secondary antibody was reconstituted and added 100 µl to each well. The plates were sealed tightly and incubated at 37 ℃ for 1 hour with mixing at 100 rpm continuously. The unbounded secondary antibody was removed by a repeated wash step for three times and continued to add 100 µl of chromogen to each well and incubated in the dark at room temperature for 15 minutes. One hundred microliters of 1 M phosphoric acid was added to each well as reaction terminating solution. The plates were placed in a darkroom for 3 minutes before reading the absorbance with spectrophotometer at 450 nm. Thus, the 8-OHdG concentration in samples could be determined by comparing the absorbance values with a calibration curve generated by 0.5, 2, 8, 20, 80 and 200 ng/ml 8-OHdG. The results were expressed as µg/g creatinine.

Determination of urinary cotinine

For the determination of recent ETS exposure, urinary cotinine was determined by direct barbituric acid (DBA) assay on the basis of rapidly analysis based on the König

reaction (Willers et al., 1995; Benowitz et al. 1996, and Haufroid et al. 1998). At room temperature, 400 µl of each sample or standard solution and 80 µl of 1.5 M KCN in H_2O were added to tube. The 200µl of 4 M sodium acetate buffer (pH 4.7) and 80 µl of 0.4 M chloramines-T in H_2O were added to each tube. Then 400 µl of 78 mM barbituric acid in acetone:H_2O (50% V/V) were added. The tubes were sealed tightly, mixed for 10 minutes and incubated at room temperature for 15 minutes. Eighty microliters of 1 M sodium metabisulphite / metabisulphite in H_2O was added to each tube to terminate the reaction, and read at 550 nm by spectrophotometer after mixing well. The results were expressed as µg/g creatinine against a calibration curve generated by 5, 10, 50, 100, 150, 200 and 250 µmol/l cotinine.

Statistical analysis

The statistical analysis was performed using SPSS for Windows version 10.0. Averages (±standard deviations), medians and ranges for concentrations of urinary cotinine and 8-OHdG were calculated by sex and the smoking status (smokers, former smokers and never smokers). Analysis of variance was performed to evaluate the differences among groups by smoking status for men and women separately. We also presented in figures the cumulative distribution of the cotinine and 8-OHdG levels to differentiate the variations among these groups. Associations between levels of

8-OHdG and ETS, VOCs and CO_2 were estimated with simple correlations. Using the overall median of 8-OHdG levels as the cut-off of elevated concentration, odds ratios (OR) and corresponding 95% confidence intervals (CI) were calculated using logistic regression analyses to identify factors associated with the elevation of urinary 8-OHdG. Probability values less than 5% were considered statistically significant. For never smokers, we further performed comparison in urinary 8-OHdG levels to determine the interaction between ETS and exposure to CO_2 and VOCs. Means and standard deviations of 8-OHdG were calculated by the quartile level of exposure to these three pollutants.

3. Results

The results of 8-hour measures of indoor air pollution exposure revealed an hourly average CO_2 concentration of 1129 ppm with the range between 467 and 2805 ppm in the offices. The hourly average concentration of TVOCs was 1192 ppb with the range between 10 and 55733 ppb.

Urinary Cotinine and 8-OHdG

Table 1 displays the average levels of urinary cotinine and 8-OHdG by sex and smoking status. Most participants were women (77.1%) with a smoking rate much lower than men (6.7% vs. 28.1%). The overall average urinary cotinine in current smokers was much greater (12.9 ± 5.51 μg/g creatinine) than that in former smokers (4.21 ± 2.08 μg/g creatinine) and never smokers (2.39 ± 1.33 μg/g creatinine) ($P < 0.001$). With higher smoking prevalence, men had greater overall average urinary cotinine and 8-OHdG than women had. The average levels for urinary 8-OhdG were also higher in current smokers (10.9 ± 3.96 μg/g creatinine) than in former smokers (5.93 ± 2.75 μg/g creatinine) and never smokers (5.08± 2.84 μg/g creatinine). The cumulative distribution of urinary cotinine in smokers clearly differed from that of the former smokers and never smoking individuals (Figure 1). The 100 percentile cotinine

concentration for none smokers was similar to 20 percentile that for smokers. On the other hand, Figure 2 shows that the 100 percentile urinary 8-OHdG level for former smokers and never smokers were equivalent to the 50 percentile and 90% levels , respectively, for smokers.

Using the overall median 8-OHdG (4.99 μg/g creatinine) among all study participants as the cutoff point of elevated concentration in the logistic regression analysis, the crude OR for the elevated level were significant higher for males, current smokers, and those with the CO_2 exposure at the third quartile level (between 902 and 1689 ppm) and greater, TVOCs exposure at the highest quartile level (greater than 494 ppb), and with the urinary cotinine level at the third quartile level (between 2136 and 3210 μmol/g creatinine) and greater (Table 2). However, in the multivariate logistic regression analysis, the OR of elevated 8-OHdG (8.13; 95% CI=2.57-25.8) was increased for CO_2 exposure, particularly for individuals with the exposure at the highest quartile level. On the other hand the estimated risk decreased for smoking and urine cotinine, and the association with VOCs become non-significant.

Urinary 8-OHdG levels in never smokers

Table 3 showed the average 8-OHdG levels among never smokers by the quartile

exposure levels of CO_2 and VOCs, and cotinine. The average 8-OhdG increased from 3.41 to 6.27 μg/g creatinine as the urinary cotinine level increased from less than 1.33 μg/g creatinine to greater than 3.13 μg/g creatinine, respectively. The results also showed strong dose-response relationships between the urinary 8-OHdG levels and the exposure levels of CO_2 and VOCs. The average 8-OHdG levels increased from 2.33 μg/g creatinine in the lowest quartiles of CO_2 exposure and cotinine to 6.60 μg/g creatinine in the highest quartiles of both variables. The corresponding average 8-OHdG levels were 2.86 and 8.63 μg/g creatinine, respectively, for the interaction relationship between VOCs exposure and cotinine. Table 4 also shows that the urinary 8-OHdG level was more likely response to the CO_2 instead of the VOCs level.

Multivariate logistic regression was also used to identify exposure factors associated with elevated 8-OHdG for never smokers. Results revealed that CO_2 exposure and urinary cotinine remained the significant predictors for the elevated urinary 8-OHdG levels among never smokers. Dose-response trends for their 8-OHdG levels, with both the CO_2 exposure and the cotinine level were both significant at 0.01 level.

4. Discussion

Occupational exposure to chemicals has been associated with the considerable increase of urinary 8-OHdG concentration. Increased excretion of 8-OHdG in urine has been found for engine room personnel with skin contact with engine oil (Nilsson et al., 2004). There is a dose-response effect between workers with benzene exposure and urinary 8-OHdG level (Lagorio et al., 1994). Occupational exposures to styrene and chromium can also induce oxidative DNA damage (Marcznshi et al., 1997; Kuo et al., 2003). Chuang et al. (2003) found that the urinary 8-OHdG levels for non-smoking taxi drivers were almost similar to that for smokers in general population. Heavy industry exposure may confound the contribution of smoking to the oxidative DNA damage (Loft et al. 1998, Toraason et al. 1999). Roofers with coal-tar-pitch dust and/or asphalt fume exposure contribute to the considerable increased urinary 8-OHdG instead of smoking (Toraason et al. 1999).

Indoor air pollution has been of great concern for the sick building syndrome (SBS) (Kreiss et al., 1990; Redlich et al., 1997；Menzies et al., 1997；Teculescu et al., 1998；Seidner, 1999；Tearle et al., 1999; Mahnoudi et al., 2000； Niven et al., 2000; Yassi et al., 2001). Formaldehyde, VOC, carbon dioxide and environmental tobacco smoking have been noticed in the SBS etiologic studies (Skov et al., 1989; Norback et

al., 1990; Lyles et al., 1991; Engvall et al., 2001; Kim et al., 2002; Pommer et al., 2004; Bako-Biro et al., 2004; Sari et al., 2004). CO_2 is thought the major cause to SBS symptoms (Bourbeau et al., 1997; Backman et al., 1999; Seppänen et al., 1999; Apte et al., 2000; Engvall et al., 2001). Seppänen et al. (1999) reviewed 21 studies with a total of 30,000 subjects in more than 400 buildings in North America, Europe and Asia, and found that low ventilation rates or elevated CO_2 levels may lead the significant increase in the prevalence of SBS symptoms. In a study for 41 American official buildings, Apte et al. (2000) have reported the odd ratio was 1.2-1.5 for respiratory symptoms with the increased CO_2 concentration every 100 ppm. Engvall et al. (2001) demonstrated the results similar to the findings in the Stockholm. Among the SBS symptoms studies, no study has been related to CO_2 with the increased of urinary 8-OHdG.

With no industry chemical exposure, there are limited studies investigated the factors associated with 8-OHdG for office building employees. In this study, the results showed that the urinary 8-OHdG levels were the highest in current smokers, for both males and females, approximately 2 times as high as that among former smokers and never smokers. The concentration was significantly correlated with cotinine, reflecting the role of well known tobacco smoking in oxidative DNA damage. The cumulative distribution of urinary cotinine for the study participants showed that the

highest urinary cotinine concentrations in never smokers and former smokers were equivalent to the lowest ends of concentrations, 6 μg/g creatinine, in smokers (Figure 1). In other words, persons who did not smoke had the urinary cotinine levels as high as the 20 percentile of smokers due to ETS. However, the cumulative distribution of urinary 8-OHdG show that the highest level of 8-OHdG in never smokers and former smokers were approximately the 75 percentile (14 μg/g creatinine) and 50 percentile (11.0 μg/g creatinine) of smokers, respectively. It is likely, more than half of urinary 8-OHdG measured among participants with no smoking was contributed from other sources with the effect of oxidation DNA damage. Indoor air pollutants other than ETS might contribute the excessed portions of urinary 8-OHdG.

In our data analysis, we have stratified the urinary cotinine concentrations and indoor air pollutants CO_2 and VOCs into quartiles. It is interesting to note in the univariate logistic analysis that both CO_2 and VOCs were significantly associated with elevated 8-OHdG levels. However, in the multivariate logistic analysis, the association with VOCs diminished. The indoor CO_2 level and urinary cotinine remained as independent predictors of the elevated 8-OHdG levels. The significant dose-response effect on 8-OHdG levels was revealed for both the indoor CO_2 concentration and urinary cotinine concentration. The odds ratio of 8-OHdG greater

than median, 4.99 μg/g creatinine, were 7.34 and 8.13 for higher quartiles of CO_2 exposure, comparing with the lowest CO_2 exposure (Table 2). This association remained significant for never smokers (Table 5).

To our knowledge, this is the first observation on the association between CO_2 and elevated urine 8-OHdG level. For never smokers, the apparent interaction between cotinine and CO_2 in the urinary 8-OHdG pattern indicated a synergistic effect may induce the oxidative stress in the tissue. In fact, CO_2 has been evident in the laparoscopic examination inducing a hypoxic stimulus. Jacobi et al. (1997) investigated the effects of CO_2 and helium on the growth of malignant tumor cells in vitro and found significant increase of tumor cell growth in cultures being incubated with CO_2, compared to those incubated with helium. The involvement of CO_2 enhanced the development of port site metastasis following laparoscopic tumor resection (Jacobi et al., 1998). Wildbrett et al. (2003) found that CO_2 insufflation caused a significant decrease of tissue oxygen partial pressure from 23 mmHg to 5 mmHg, and significant reproducible increases of intracellular free calcium levels in DHD/K12/TRb colon carcinoma cells. Bentes de Souza et al. (2003 a) demonstrated that adhesions in rabbits developed in CO_2-pneumoperitoneum groups but not in the gasless groups. And total adhesion score was correlated with the amount of CO_2

insufflated and intra-abdominal pressure during laparoscopy. Bentes de Souza et al. (2003 b) suggested that CO_2-pneumoperitoneum caused 8-iso-prostaglandin $F_{2\alpha}$ (8-iso-$PGF_{2\alpha}$), one of marker of oxidative stress, during laparoscopy. They also found in vitro exposure to CO_2 can induce significant oxidative stress in mesothelial cells. The 8-iso-$PGF_{2\alpha}$ was significant higher in 24-hour CO_2 exposure group (5.96, 9.33, 7.04 pg/mg phospholipid at immediately, 1 hour, 3 hours after gas incubation, respectively) than 4-hour group (9.87, 12.64, 7.08 pg/mg phospholipid at immediately, 1 hour, 3 hours after gas incubation, respectively) (Bentes de Souza et al., 2004).

This study found that the urinary 8-OHdG concentration in office employees is significantly associated with not only smoking or ETS but also with CO_2 exposure at work. The CO_2 association with urinary 8-OHdG has not been previously reported. This is an association can not be ruled out, and further studies are warranted.

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Table 1. Averages, and ranges of urinary cotinine and 8-OHdG levels measured for office building employees by sex and smoking status

Sex	Cotinine (μg/g creatinine)		8-OHdG (μg/g creatinine)	
Smoke	Mean (S.D.)	Range	Mean (S.D.)	Range
Female (N)				
Never (270)	2.36 (1.29)	0.49 ~ 6.31	5.07 (2.88)	1.06~16.7
Former (10)	3.90 (1.37)	2.10 ~ 6.89	5.65 (2.85)	2.43~11.0
Current (20)	13.7 (6.38)	6.40 ~ 29.0	11.3 (4.54)	4.28~18.8
Total (300)	3.17 (3.49)	0.49 ~ 29.0	5.51 (3.39)	1.06~18.8
P value	＜0.001		＜0.001	
Male (N)				
Never (41)	2.57 (1.60)	0.55 ~ 8.79	5.08 (2.56)	1.06~12.1
Former (23)	4.34 (2.34)	1.14 ~ 8.98	6.05 (2.76)	1.19~10.1
Current (25)	12.3 (4.75)	6.99 ~ 25.4	10.6 (3.49)	4.26~17.6
Total (89)	5.76 (5.11)	0.55 ~ 25.4	6.88 (3.71)	1.06~17.6
P value	＜0.001		＜0.001	
All (N)				
Never (311)	2.39 (1.33)	0.49 ~ 8.79	5.08 (2.84)	1.06~16.7
Former (33)	4.21 (2.08)	1.14 ~ 8.98	5.93 (2.75)	1.19~11.0
Current (45)	12.9 (5.51)	6.40 ~ 29.0	10.9 (3.96)	4.26~18.8
Total (389)	3.76 (4.06)	0.49 ~ 29.0	5.83 (3.51)	1.06~18.8
P value	＜0.001		＜0.001	

S.D., standard deviation

Table 2. Odds ratios of having urinary 8-OHdG greater than overall median, 4.99 μg/g creatinine, by sex, smoking status, CO_2, VOCs and urinary cotinine obtained from univariate and multivariate logistic regression for office building employees (N=389)

	Crude OR	95% CI	Adjusted OR*	95% CI
Sex				
Female	1.00		1.00	
Male	1.74	1.07~2.82	0.88	0.41~1.89
P value	0.017		0.664	
Smoking habits				
Never	1.00		1.00	
Former	2.06	0.99~4.29	1.06	0.41~2.76
Current	18.7	5.68~61.7	5.12	1.24~21.1
P for trend	＜0.001		0.926	
CO_2 (ppm)				
≦745.0	1.00		1.00	
745.1~901.0	1.45	0.79~2.68	2.03	0.92~4.50
901.1~1689.0	7.00	3.71~13.2	7.34	3.05~17.7
＞1689.0	3.37	1.81~6.28	8.13	2.57~25.8
P for trend	0.001		0.001	
VOCs (ppb)				
≦87.0	1.00		1.00	
87.1~190.0	1.76	0.98~3.17	1.17	0.56~2.44
190.1~494.0	1.80	0.99~3.29	0.50	0.19~1.32
＞494.0	5.62	2.95~10.7	1.12	0.39~3.25
P for trend	0.001		0.058	
Urinary cotinine(μg/g creatinine)				
≦1.46	1.00		1.00	
1.47~2.14	1.64	0.87~3.07	1.18	0.59~2.36
2.15~3.21	5.01	2.70~9.32	4.69	2.33~9.41
＞3.21	13.2	6.65~26.2	8.88	3.65~21.6
P for trend	＜0.001		＜0.001	

* Multivariate analysis; CO_2, carbon dioxide; VOCs, volatile organic compounds

Table 3. Means (and standard deviations) of urinary 8-hydroxydeoxyguanosine by quartile levels of indoor CO_2 and VOCs exposure and urinary cotinine for never smokers (N=311)

Exposure Index	Cotinine, μg/g creatinine					
	Total	＜1.33	1.33-2.11	2.12-3.13	＞3.13	P value
Total	5.08 (2.84)	3.41 (2.08)	5.24 (2.93)	5.42 (2.73)	6.27 (2.79)	＜0.001
CO_2, ppm						
≦745.2	3.29 (1.68)	2.33 (1.14)	3.18 (1.09)	3.68 (1.37)	4.95 (2.05)	
745.3~892.0	4.46 (2.26)	4.04 (2.54)	4.39 (1.93)	3.99 (2.20)	5.15 (2.08)	＜0.001
892.1~1690.0	6.76 (2.96)	4.06 (1.49)	6.54 (2.30)	6.88 (2.84)	8.14 (2.74)	
＞1690.0	5.91 (3.00)	4.59 (2.35)	5.55 (3.21)	6.45 (2.73)	6.60 (3.27)	
VOCs, ppb						
≦87.9	3.83 (2.28)	2.86 (1.79)	5.24 (3.11)	3.65 (1.22)	4.74 (1.94)	
88.0~187.9	4.94 (2.46)	3.92 (2.25)	4.76 (2.00)	4.79 (2.19)	6.45 (2.45)	＜0.001
188.0~494.0	4.46 (2.19)	2.90 (1.59)	4.19 (1.94)	4.66 (2.24)	5.09 (2.42)	
＞494.0	7.25 (3.19)	5.07 (2.44)	6.54 (3.59)	7.40 (2.92)	8.63 (2.70)	

CO_2, carbon dioxide; VOCs, volatile organic compounds

Table 4. Means (and standard deviations) of urinary 8-hydroxydeoxyguanosine by quartile levels of indoor VOCs and CO_2 exposure in offices for never smokers (N=311)

Exposure Index	CO_2, ppm					
	Total	≦745.2	745.3~892.0	892.1~1690.0	＞1690.0	P value
Total	5.08 (2.84)	3.29 (1.68)	4.46 (2.26)	6.76 (2.96)	5.91 (3.00)	＜0.001
VOCs, ppb						
≦87.9	3.83 (2.28)	3.00 (1.49)	4.48 (2.33)	5.70 (3.25)	-	
88.0~187.9	4.94 (2.46)	4.07 (1.87)	4.77 (2.53)	6.13 (2.49)	-	＜0.001
188.0~494.0	4.46 (2.19)	3.04 (1.71)	3.79 (1.37)	5.37 (2.47)	4.94 (2.33)	
＞494.0	7.25 (3.19)	-	-	8.06 (2.92)	6.73 (3.27)	

CO_2, carbon dioxide; VOCs, volatile organic compounds

Table 5. Odds ratios of having urinary 8-OHdG greater than overall median, 4.99 μg/g creatinine, by sex, CO_2, VOCs and urinary cotinine obtained from univariate and multivariate logistic regression for office building employees (N=311)

	Crude OR	95% CI	Adjusted OR*	95% CI
Gender				
Female	1.00		1.00	
Male	0.94	0.48~1.83	0.89	0.37~2.13
P value	0.857		0.595	
CO_2 (ppm)				
≦745.2	1.00		1.00	
745.3~892.0	2.65	1.25~5.61	2.30	1.02~5.22
892.1~1690.0	9.90	4.55~21.56	7.73	3.05~19.55
＞1690.0	5.47	2.62~11.42	5.94	1.89~18.74
P for trend	0.001		0.002	
VOCs (ppb)				
≦87.9	1.00		1.00	
88.0~187.9	2.84	1.44~5.61	2.04	0.95~4.38
188.0~494.0	1.79	0.89~3.59	0.63	0.24~1.68
＞494.0	7.35	3.61~14.97	1.80	0.62~5.23
P for trend	0.007		0.059	
Urinary cotinine(μg/g creatinine)				
≦1.32	1.00		1.00	
1.33-2.11	2.78	1.37~5.65	1.97	0.87~4.46
2.12-3.13	3.32	1.64~6.74	2.80	1.23~6.38
＞3.13	6.64	3.23~13.66	6.58	2.91~14.87
P for trend	＜0.001		＜0.001	

* Multivariate analysis; CO_2, carbon dioxide; VOCs, volatile organic compounds

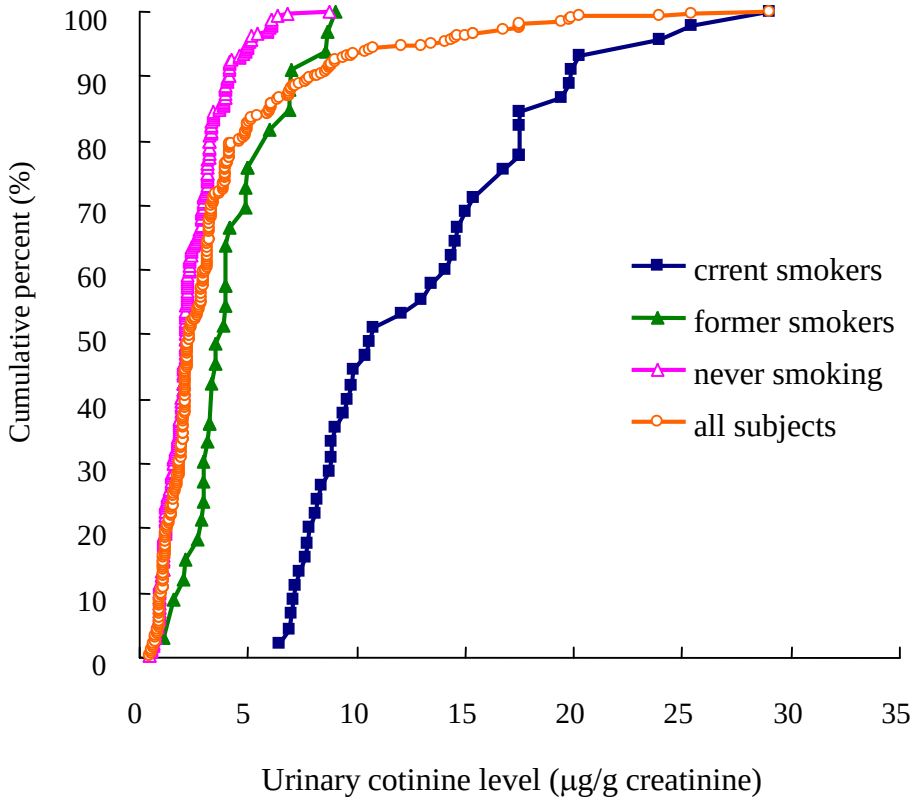

Figure 1. The cumulative distributions of urinary cotinine levels for all smokers, former smokers and never smoking

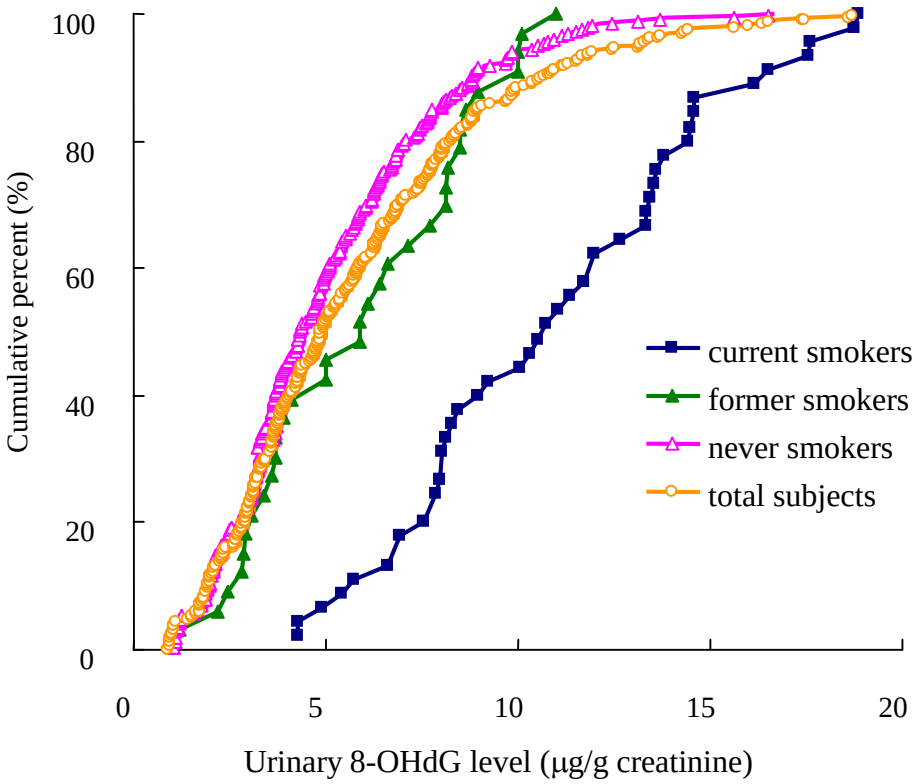

Figure 2. The cumulative distributions of urinary 8-OHdG levels for all smokers, former smokers and never smoking