Oxidative Stress Associated with Indoor Air Pollution and Sick Building Syndrome-Related Symptoms among Office Workers in Taiwan

Chung-Yen Lu, Yee-Chung Ma, and Jia-Min Lin

Institute of Environmental Health, National Taiwan University College of Public Health, Taipei

Chung-Yi Li

Department of Public Health, Fu Jen Catholic University College of Medicine, Taipei

Reuy S. Lin

Institute of Preventive Medicine, National Taiwan University College of Public Health, Taipei

Fung-Chang Sung

Institutes of Environmental Health and Preventive Medicine, National Taiwan University College of Public Health, Taipei, and Institute of Environmental Health, China Medical University College of Public Health, Taichung, Taiwan

This study investigated whether sick building syndrome (SBS) complaints and indoor air pollution for office workers are associated with oxidative stress indicated by urinary 8-hydroxydeoxyguanosine (8-OHdG). With informed consent, 389 employees in 87 government offices of 8 high-rise buildings in Taipei city completed self-reported questionnaires on SBS complaints at work in the past month. Urinary 8-OHdG was determined for each study participant and on-site air pollutants were measured for each office in both indoor and outdoor air. The results showed that urinary 8-OHdG had significant associations with volatile organic compounds and carbon dioxide levels in offices, and with urinary cotinine levels. The mean urinary 8-OHdG level was also significantly higher in participants with SBS symptoms than in those without such complaints (6.16 vs. 5.45 μg/g creatinine, $p = .047$). The mean 8-OHdG increased as the number of SBS symptoms increased. The multivariate logistic regression analyses showed that the adjusted odds ratios (OR) in relation to micrograms per gram creatinine increase in 8-OHdG were statistically significant for eye dryness (1.12), upper respiratory syndrome (1.17) with particularly nose itching (1.25), sneezing (1.51), dry throat (1.21), skin dryness (1.31), and dizziness (1.19). This study indicates that the 8-OHdG level was significantly associated with SBS complaints after controlling for air pollution and smoking. Whether the 8-OHdG can be used as an effective predictor for SBS symptoms deserves further study.

Workers are considered to have sick building syndrome (SBS) when they suffer from symptoms related to eyes, nose, and throat, dry skin, headache, and/or lethargy inside a building, and the symptom complaints may ease when workers leave the buildings (Levin, 1989). Many previous studies were conducted to investigate the etiology of the SBS, but the risk factors causally associated with SBS remain debatable (Kreiss, 1990; Menzies et al., 1997; Redlich et al., 1997; Teculescu et al., 1998; Seidner, 1999; Tearle, 1999; Mahmoudi & Gershwin, 2000; Niven et al., 2000; Yassi et al., 2001). Among findings, insufficient ventilation and uncomfortable temperature and humidity have been thought to be the major factors associated with the SBS (Bourbeau et al., 1997; Backman & Haghighat, 1999; Seppänen et al., 1999; Apte et al., 2000; Engvall et al., 2001; Burge, 2004). Insufficient ventilation in offices may cause indoor air pollutants to accumulate gradually. Previous studies have indicated that both carbon dioxide (CO_2) and volatile organic compounds

(VOCs) are the major air pollutants resulting from insufficient ventilation in offices (Apte et al., 2000; Burge, 2004). Nonetheless, little has been known regarding specific human biomarkers, if any, that may be associated with the occurrence of SBS.

One way to improve the acknowledgment of the occurrence of SBS is to identify a marker that may best reflect the exposure of certain air pollutants as a result of insufficient ventilation. Reactive oxygen species (ROS) are components widely found in many of the air pollutants (van Klaveren & Nemery, 1999; Huang et al., 2005), and can cause oxidative damage to lipids, proteins, and nucleic acids, resulting in oxidative stress (Loft et al., 1992; Wu et al., 2004). We hypothesized that oxidative stress can serve as a predictor of SBS. Urinary 8-hydroxydeoxyguanosine (8-OHdG) has been known to be a biological marker of oxidative stress on DNA. As a result of exposure to ROS, 8-OHdG can be excised with hydroxylation by constitutive enzymatic repair systems and excreted in the urine (Shigenaga et al., 1989; Floyd et al., 1990; Fraga et al., 1990). Urban air pollution, tobacco smoke, environmental tobacco smoke (ETS), VOCs, and ionization radiation have been associated with the rise of urinary 8-OHdG levels (Samet et al., 1987; Anderson et al., 1991; Wilson et al., 1993; Tagesson et al., 1995, 1996; Calderon-Garciduenas et al., 1999; Carstensen et al., 1999).

The investigation of etiology of SBS in office buildings remains an important research issue. To our best knowledge, there have been no previous studies that investigated the association of oxidative stress with SBS symptoms. This study, therefore, was conducted to examine whether poor air quality may be associated with an office worker's oxidative stress, and subsequently with SBS symptoms. The oxidative stress status of individual worker was indicated by the concentration of urinary 8-OHdG. In addition, we used a self-reported questionnaire to assess a worker's SBS complaints.

MATERIALS AND METHODS

Study Design and Study Subjects

From November 2003 to June 2004, we randomly selected 16 government agencies and commercial organizations in high-rise buildings in the city center of Taipei, for recruitment of study subjects and on-site measurements of indoor air pollutants. Five organizations declined to participate. Three of the remaining 11 institutions declined to provide urinary specimens. An invitational letter explaining the study was delivered to potential participants at 87 office units of the rest 8 organizations. With informed consent, 398 persons responded to this study (response rate 61.7%). Each of these office workers was asked to provide a spot urine sample for the measurement of 8-OHdG and completed a self-reported questionnaire on various variables including SBS complaints. The urine sample was collected from each participant at the end of the work day. Samples were transported in a cold box at $4°C$ to the laboratory and stored at $-80°C$ until analysis. This study was approved by an ad hoc review committee organized by the National Science Council, Taiwan.

Questionnaire Survey and Air Quality Examination

This study used a questionnaire to collect the information on typical SBS symptoms adapted from the recommendations of the WHO Regional Office for Europe Report (World Health Organization, 1986). The questionnaire inquired about SBS experienced in the past month, specifically for eyes, upper and lower respiratory tract, skin, and nonspecific complaints. Information on sociodemographic status (sex, age, education, and job), lifestyle (smoking, environmental tobacco smoke), recent airway infections, and medication (asthma, nasosinusitis, atopic rhinitis, and allergy) was also obtained through questionnaire.

On-site measurements of air pollutants for each office were performed for carbon dioxide (CO_2) (inside and outside the office), carbon monoxide, total volatile organics (TVOC), temperature, and humid. CO_2 measures were standardized in the range of 0–5000 ppm (Q-TRAK IAQ model 8551, TSI, Inc., Shoreview, MN), and VOCs were standardized with 102 categories (PGM-7240, RAE System, Sunnyvale, CA). Ventilation efficiency in each office was represented by the 8-h average difference between indoor and outdoor CO_2 levels ($dCO_2 = CO_{2\,indoor} - CO_{2\,outdoor}$).

Determinations of Urinary Creatinine, Cotinine, and 8-OHdG

Specimens of urine were stored at $-80°C$ and assayed within 1 to 2 months. Thawed samples were pretreated with a centrifuge at 2000 rpm for 10 min to remove the particulate matter. The urinary creatinine values in samples were determined with an automatic analyzer (Hitachi 7250, Tokyo) based on the Jaffe colorimeter reaction (Nerurkar & Sahasrabudhe, 1960; Chuang et al., 2003).

Both VOCs and tobacco smoking are potential materials associated with the 8-OHdG levels in urine. We also determined urinary cotinine to assay the levels of smoking and environmental tobacco smoke exposures among the participants. Urinary cotinine was determined by direct barbituric acid (DBA) assay on the basis of rapid analysis based on the König reaction (Benowitz, 1996; Haufroid & Lison, 1998; Willers et al., 2004). At room temperature, 400 μl of each sample or standard solution was used for analysis. The cotinine concentration in the sample was determined by comparing the absorbance values at 550 nm against a calibration curve generated by 5, 10, 50, 100, 150, 200, and 250 μmol/L cotinine, expressed as micrograms per gram creatinine.

Urinary 8-OHdG levels were determined by the OXIS Research enzyme-linked immunosorbent assay (ELISA) kit (Japan Institute for the Control of Aging, Shizuoka, Japan) on the basis of highly sensitivity and specificity, and rapid analysis. At room temperature, 50 μl of 8-OHdG monoclonal antibody and 50 μl of each urine sample or standard solution were loaded onto a microtiter plate that was precoated with 8-OHdG for assay (Yin et al., 1995). The determination ranged from 0.5 to 200 ng/ml, generated using 0.5, 2, 8, 20, 80, and 200 ng/ml 8-OHdG, expressed as micrograms per gram creatinine.

Statistical Analysis

In statistical analyses, we first used Pearson's χ^2 test to test the associations between 8-OHdG levels of study participants and selected covariates, including sociodemographic status, lifestyle, and office environmental status and air quality. The level of 8-OHdG was presented in a tertile distribution (≤ 3.79, 3.80–6.63, >6.63 μg/g creatinine). Mean concentrations of indoor air pollutants and CO_2, temperature, and tobacco smoke exposure (cotinine) were compared, using one-way analysis of variance (ANOVA) by the level of 8-OHdG. We also used Student's t-test to compare the 8-OHdG level in association with the specific SBS symptoms, including eyes (eye dryness and eye irritation), upper respiratory tract (nose itching, runny nose, stuffy nose, sneezing, and dry throat), lower respiratory tract (difficulty in breathing), skin (skin dryness), and nonspecific symptoms (headache, tiredness, difficulty concentrating, angry easily, and dizziness). A study participant was considered to suffer from SBS symptoms if he or she reported having one or more selected symptoms for at least 1–3 days per week at work in the office in the previous month, but the symptoms improved or disappeared at the end of the working day and/or on weekends or vacations. The prevalence rates of SBS symptoms were calculated for the selected symptoms individually and as a group. Finally, simple and step-down multivariate logistic regression (MLR) models were constructed using each of the SBS symptoms as the dependent variables, and the creatinine adjusted 8-OHdG level as independent variable. The odds ratio (OR) and corresponding 95% confidence interval (CI) were calculated. The final MLR analysis was performed controlling for potential confounding factors, including gender, age, presence of carpet in workspace, whether sensitive to tobacco smoke and air pollutants, difference between indoor and outdoor carbon dioxide, and urinary cotinine concentrations. Air pollution and tobacco smoking have been considered the important factors associated with urinary 8-OHdG levels. In this study we found that urinary 8-OHdG levels have a stronger association with CO_2 than with TVOC, and these two groups of substances had a significant collinear relationship. We therefore included CO_2 and urinary cotinine as covariates in the multivariate analysis. Probability values less than 5% were considered statistically significant. All data analyses used SPSS for Windows version 10.0 (SPSS, Inc., Chicago).

RESULTS

Self-Reported Symptoms

Study participants were predominantly women (77.1%). In the tertile distribution of 8-OHdG, 48.3% men versus 28.7% women had their 8-OHdG in the highest tertile, that is, >6.63 μg/g creatinine (Table 1). The urinary 8-OHdG. levels were also higher in active smokers than in nonsmokers and ex-smokers, The study participants who were sensitive to tobacco smoke and air pollutants also tended to have significantly lower level of 8-OHdG.

Urinary 8-OHdG Level

Table 2 shows that the urinary 8-OHdG concentrations were strongly associated with certain indoor air pollutants and urinary cotinine concentrations. The study participants with higher tertiles of 8-OHdG tended to work in offices with higher concentrations of dCO_2 and TVOC. The mean TVOC in the offices exposed by the study participants in the highest tertile of 8-OHdG was approximately 8 times higher than that exposed by the participants with the lowest tertile (2580 vs. 302 ppb). Additionally, the average urinary cotinine concentrations were 1.95, 3.15, and 6.22 μg/g creatinine, respectively, with the corresponding lowest, middle, and highest tertiles of 8-OHdG.

The prevalence rates of SBS symptoms were the highest for nonspecific conditions (29.0% or 111/389), and lowest for skin (1.4% or 6/389) (data not shown). The symptom prevalence rates for upper respiratory tract, lower respiratory tract, skin, and others such as tiredness, difficulty in concentrating, angry easily, and dizziness were estimated at 15.7%, 6.7%, 1.5%, 20.4%, 13.9%, 12.7%, and 6.5%, respectively. Table 3 shows that the means $\pm$ standard deviations of urinary 8-OHdG concentration was greater for study participants with one or more SBS complaints than those without such complaints (6.16 ± 3.81 vs. 5.45 ± 3.10 μg/g creatinine) ($p = .047$). Among specific SBS complaints associated with significantly elevated levels of 8-OHdG, the highest level was observed for skin dryness, followed by headache, sneezing, nose itching, stuffy nose, dry throat, dizziness, angry easily, tiredness, and difficulty concentrating, with a mean ranging from 11.2 (skin dryness) to 7.43 μg/g creatinine (difficulty concentrating). On the other hand, we noted that participants with lower respiratory tract symptoms had a mean 8-OHdG level similar to those without such symptoms ($p = .828$).

To assess the relationship between severity of SBS symptoms and level of 8-OHdG level, Table 4 shows the mean 8-OHdG according to number of SBS symptoms. The study participants with only one SBS symptom had a mean 8-OHdG level of 5.11 ± 3.02 μg/g creatinine, which is somewhat lower than that of participants free from any SBS complaints. The 8-OHdG level concentration then increased monotonically with an increase of number of SBS symptoms (Table 4).

We used both univariate and multivariate logistic regressions models to estimate the relative risk of specific SBS in association with per unit increase of 8-OHdG (Table 5). After controlling for age, gender, presence of carpet, sensitivity to tobacco smoke and air pollutants, difference between indoor and outdoor carbon dioxide, and urinary cotinine concentrations, the highest adjusted OR associated with micrograms per gram creatinine increase in urinary 8-OHdG level was noted for sneezing (OR = 1.51, 95% CI = 1.21–1.87), followed by skin dryness, nose itching, dizziness and eye dryness (OR = 1.12, 95% CI = 1.02–1.23).

TABLE 1
Tertile distribution of 8-hydroxydeoxyguanosine (8-OHdG) according to selected characteristics

Variables	N	≤3.79, n (%)	3.80–6.63, n (%)	>6.63, n (%)	p
		8-OHdG, μg/g creatinine			
Sex					
Male	89	24 (27.0)	22 (24.7)	43 (48.3)	.002[b]
Female	300	108 (27.0)	106 (35.3)	86 (28.7)	
Age, years					
<40	269	84 (31.2)	90 (33.5)	95 (35.3)	.204
≥40	120	48 (40.0)	38 (31.7)	34 (28.3)	
Years at work					
≤4	211	66 (31.3)	77 (36.5)	68 (32.2)	.237
>4	178	66 (37.1)	51 (28.7)	61 (34.3)	
Smoking habits					
Never/former	344	132 (38.4)	121 (35.2)	91 (26.5)	<.001[b]
Current	45	0	7 (15.6)	38 (84.4)	
Dust allergy					
No	291	97 (33.3)	101 (34.7)	93 (32.0)	.413
Yes	98	35 (35.7)	27 (27.6)	36 (36.7)	
Animal allergy					
No	356	117 (32.9)	119 (33.4)	120 (33.7)	.344
Yes	33	15 (45.5)	9 (27.3)	9 (27.3)	
Sensitive to tobacco smoke					
No	122	24 (19.7)	39 (32.0)	59 (48.4)	<.001[b]
Yes	267	108 (40.4)	89 (33.3)	70 (26.2)	
Sensitive to air pollutants					
No	138	35 (25.4)	48 (34.8)	55 (39.9)	.021[b]
Yes	251	97 (38.6)	80 (31.9)	74 (29.5)	
Asthma					
No	375	125 (33.3)	124 (33.1)	126 (33.6)	.196
Yes	14	7 (50.0)	4 (28.6)	3 (21.4)	
Nasosinusitis					
No	360	118 (32.8)	119 (33.1)	123 (34.2)	.182
Yes	29	14 (48.3)	9 (31.0)	6 (20.7)	
Atopic rhinitis					
No	277	95 (34.3)	95 (34.3)	87 (31.4)	.473
Yes	112	37 (33.0)	33 (29.5)	42 (37.5)	
Stress at work					
No	350	119 (34.0)	115 (32.9)	116 (33.1)	.996
Yes	39	13 (33.3)	13 (33.3)	13 (33.3)	
Social support from family					
No	145	79 (32.4)	45 (31.0)	47 (32.4)	.687
Yes	224	79 (32.4)	83 (34.0)	82 (33.6)	
Carpet in workspace					
No	146	65 (44.5)	34 (23.3)	47 (32.2)	.001[b]
Yes	243	67 (27.6)	94 (38.7)	82 (33.7)	
New decoration in workspace					
No	356	117 (32.9)	117 (32.9)	122(34.3)	.227
Yes	33	15 (45.5)	11 (33.3)	7 (21.2)	

TABLE 1
Tertile distribution of 8-hydroxydeoxyguanosine (8-OHdG) according to selected characteristics (*Continued*)

Variables	N	≤3.79, *n* (%)	3.80–6.63, *n* (%)	>6.63, *n* (%)	*p*
		8-OHdG, μg/g creatinine			
Painting recently in workspace					
No	370	121 (32.7)	123 (33.2)	126 (34.1)	.065
Yes	19	11 (57.9)	5 (26.3)	3 (15.8)	
Mold speck in workspace					
No	357	122 (34.2)	118 (33.1)	117 (32.8)	.860
Yes	32	10 (31.3)	10 (31.3)	12 (37.5)	
Exposure to ETS[a]					
No	326	110 (33.7)	107 (32.8)	109 (33.4)	.965
Yes	63	22 (34.9)	21 (33.3)	20 (31.7)	

[a]Environmental tobacco smoke.
[b]Significant difference.

DISCUSSION

This study used the urinary excretion of 8-OHdG as a marker to assess whether it has an association with SBS related symptoms in office workers. The results showed that the 8-OHdG level was positively and significantly associated with concentrations of CO_2 and VOC at offices. The 8-OHdG level was also significantly elevated among workers with sneezing, headache, skin dryness, dry throat, dizziness, nose itching, stuffy nose, runny nose, tiredness, eye dryness, and upper respiratory tract and nonspecific complaints. A positive dose-response effect can also be found between 8-OHdG levels and the number of symptoms. These findings tend to indicate that the occurrence of SBS is likely to be associated with oxidative stress.

To examine the oxidative stress, the measurement of 8-OHdG excretion in urine has been used as a viable noninvasive marker. The formation of 8-OHdG involves environmental exposure (traffic exhaust, sunlight, etc.), lifestyle (smoking, betel nut chewing, etc.), physiological factors (gender, age, body mass index [BMI]), stress (working conditions), and disease (cancer, systemic lupus erythematosus, arthritis, diabetes mellitus, etc.) (Loft et al., 1992; Witherell et al., 1998; van Zeeland et al., 1999; Kasai et al., 2001; Chuang et al., 2003). The present study showed that the risk factors associated with SBS, somewhat similar to factors associated with the formation of 8-OHdG, are complex.

The SBS symptoms first attracted attention in the 1970s associated with ventilation systems in more energy-efficient

TABLE 2
Means and standard deviations (SD) of indoor air pollutants in offices according to tertile levels of urinary
8-hydroxydeoxyguanosine of study participants

Variable	≤3.79, *n* = 132	3.80–6.63, *n* = 128	>6.63, *n* = 129	Total, *N* = 389	*p*
	8-hydroxydeoxyguanosine, μg/g creatinine				
CO[a]	2.59 (0.36)	2.61 (0.33)	2.63 (0.41)	2.61 (0.37)	.731
dCO$_2$[b]	483 (566)	770 (570)	781 (487)	676 (559)	<.001[g]
TVOC[c]	302 (987)	500 (1093)	2580 (8545)	1123 (5086)	<.001[g]
T[d]	24.1 (2.06)	23.7 (1.67)	23.9 (1.65)	23.9 (1.81)	.115
RH[e]	57.5 (7.27)	56.8 (5.56)	56.5 (6.55)	56.9 (6.51)	.486
Cotinine[f]	1.95 (1.28)	3.15 (2.22)	6.22 (5.80)	3.76 (4.06)	<.001[g]

[a]CO, indoor carbon monoxide (ppm).
[b]dCO$_2$, difference between indoor and outdoor carbon dioxide (ppm).
[c]TVOC, indoor total volatile organic compounds (ppb).
[d]T, temperature (°C).
[e]RH, indoor relative humidity (%).
[f]Cotinine, urinary cotinine concentrations in participants (μg/g creatinine).
[g]Significant difference.

TABLE 3
Mean and standard deviation (SD) of urinary 8-hydroxydeoxyguanosine levels of study participants according to SBS symptoms

	Self-rated SBS symptoms		
Symptom $(n/n)^a$	Ever, mean $(SD)^b$ μg/g creat.^{c}	Never, mean $(SD)^b$ μg/g creat.^{c}	p
Eye, any (89/300)	6.32 (3.84)	5.68 (3.39)	.134
Eye dryness (74/315)	6.62 (3.84)	5.64 (3.40)	.029[d]
Eye irritation (22/367)	5.60 (4.24)	5.84 (3.46)	.751
Upper respiratory, any (62/327)	8.32 (4.30)	5.35 (3.13)	<.001[d]
Nose itching (10/379)	8.49 (4.93)	5.76 (3.44)	.015[d]
Runny nose (11/378)	7.73 (4.02)	5.77 (3.48)	.067
Stuffy nose (24/365)	8.88 (4.29)	5.62 (3.36)	<.001[d]
Sneezing (10/379)	9.12 (4.02)	5.74 (3.46)	.003[d]
Dry throat (26/363)	8.61 (4.54)	5.63 (3.34)	<.001[d]
Lower respiratory, any (28/361)	5.69 (3.88)	5.84 (3.48)	.828
Difficulty in breathing (28/361)	5.69 (3.88)	5.84 (3.48)	.828
Skin, any (6/383)	11.2 (4.78)	5.74 (3.43)	<.001[d]
Dryness (6/383)	11.2 (4.78)	5.74 (3.43)	<.001[d]
Nonspecific, any (111/278)	6.91 (4.13)	5.39 (3.13)	<.001[d]
Headache (7/382)	10.9 (2.16)	5.73 (3.46)	<.001[d]
Tiredness (81/308)	7.46 (4.10)	5.39 (3.21)	<.001[d]
Difficulty concentrating (59/330)	7.43 (4.17)	5.56 (3.32)	<.001[d]
Angry easily (50/339)	7.69 (4.95)	5.55 (3.16)	<.001[d]
Dizziness (23/366)	8.44 (4.72)	5.64 (3.33)	<.001[d]
All, any (205/184)	6.16 (3.81)	5.45 (3.10)	.047

[a] (n/n): sample size of Ever/Never.
[b] SD, standard deviations.
[c] creat., Creatinine.
[d] Significant difference.

buildings. Among studies, no single factor or group of factors has been regarded as the specific cause of SBS (Redlich et al., 1997). Burge (2004) has proposed a number of factors related to the increased prevalence of building symptoms; these factors included personal factors (female and working at lower hierarchy in building), individual factors (paper dust, cigarette smoke, office dust, and using computers), and building factors (high indoor temperature, low fresh air ventilation in office, poor control of temperature and lighting, air-conditioned building, poor building service maintenance, poor cleaning or cleanability, and water damage). Attention has been focused on the multiple exposures and sources of common contaminants in the indoor air (Redlich et al., 1997). The office air quality observation with self-reported symptoms by subjects in the present study may strengthen with the association between SBS and urinary 8-OHdG. Volatile organic compounds, environmental tobacco smoke, and carbon dioxide in the building may accumulate from insufficient ventilation rate. Low ventilation rate in room, environmental tobacco smoking (ETS), formaldehyde, carbon dioxide, and VOCs have been noticed in sick building syndrome (SBS) etiologic studies (Skov et al., 1989; Lyles et al., 1991; Norback & Edling,

1991; Engvall et al., 2001; Kim et al., 2002; Bako-Biro et al., 2004; Pommer et al., 2004; Sari et al., 2004). Additionally, exposure to molds inside building has been associated with SBS (Straus et al., 2003; Burge, 2004; Ebbehoj et al., 2005; Laumbach & Kipen, 2005). In this study, we failed to find such kind of association.

TABLE 4
Mean and standard deviation (SD) of urinary
8-hydroxydeoxyguanosine levels of study participants
according to numbers of SBS symptoms

Number of SBS symptoms	n	Mean (SD), μg/g creat.	p Value
0	184	5.45 (3.10)	
1	90	5.11 (3.02)	
2	48	5.79 (3.44)	<.001
3–4	45	7.36 (4.38)	
$\geq$5	22	8.81 (4.52)	

Note. creat., Creatinine.

TABLE 5
Crude and adjusted odds ratio of SBS symptoms associated
with microgram per gram creatinine increase in urinary
8-hydroxydeoxyguanosine level

SBS[a] symptom	Odds ratio (95% CI)[b]	
	Crude estimates	Adjusted estimates[c]
Eye, any	1.06 (0.99–1.13)	1.11[d] (1.01–1.21)
eye dryness	1.08[d] (1.01–1.16)	1.12[d] (1.02–1.23)
eye irritation	0.98 (0.86–1.11)	1.12 (0.93–1.36)
Upper respiratory, any	1.24[d] (1.15–1.34)	1.17[d] (1.05–1.30)
Nose itching	1.18[d] (1.03–1.36)	1.25[d] (1.02–1.53)
Runny nose	1.16[d] (1.01–1.34)	1.22 (0.98–1.52)
Stuffy nose	1.34[d] (1.11–1.35)	1.12 (0.97–1.29)
Sneezing	1.22[d] (1.06–1.40)	1.51[d] (1.21–1.87)
Dry throat	1.22[d] (1.11–1.34)	1.21[d] (1.06–1.38)
Lower respiratory, any	1.00 (0.89–1.11)	0.97 (0.83–1.13)
Difficulty in breathing	1.00 (0.89–1.11)	0.97 (0.83–1.13)
Skin, any	1.34[d] (1.12–1.60)	1.31[d] (1.04–1.65)
Dryness	1.34[d] (1.12–1.60)	1.31[d] (1.04–1.65)
Nonspecific, any	1.13[d] (1.06–1.20)	1.05 (0.96–1.15)
Headache	1.32[d] (1.14–1.53)	1.11 (0.77–1.60)
Tiredness	1.17[d] (1.09–1.25)	1.03 (0.94–1.14)
Difficulty concentrating	1.16[d] (1.08–1.25)	1.03 (0.93–1.15)
Angry easily	1.16[d] (1.08–1.25)	0.99 (0.88–1.12)
Dizziness	1.18[d] (1.08–1.30)	1.19[d] (1.05–1.35)

[a]SBS, sick-building syndrome.

[b]95% CI, 95% confidence interval.

[c]Adjusted for age, gender, presence of carpet in workspace, sensitivity to tobacco smoke and air pollutants, difference between indoor and outdoor carbon dioxide, and urinary cotinine concentrations.

[d]Significantly different.

Low ventilation rate in the room is thought to be the major cause of SBS symptoms (Bourbeau et al., 1997; Seppänen et al., 1999; Backman & Haghighat, 1999; Apte et al., 2000). It has been found that the indoor volatile organic compounds exposure has a significant respiratory effect (Samet et al., 1987). And our further data analysis for nonsmokers did show that the urinary 8-OHdG levels of participants increased as the exposed TVOC and/or CO_2 levels increased in the office (data not shown). We believe some of these common contaminants in offices are associated with oxidative stress leading to the generation of 8-OHdG. Among previous SBS studies, no study has related SBS with increased level of urinary 8-OHdG.

In this study, the urinary 8-OHdG concentrations were significantly associated with volatile organic compounds and carbon dioxide levels measured in the offices. We also found that the 8-OHdG concentration was higher in smokers, with an average of 10.9 ± 4.0 μg/g creatinine, but it was somewhat lower than that observed for community smokers (Chuang et al., 2003). This

study also showed that the concentrations of CO_2 and volatile organic compounds at offices were higher than those in the air outside of the building.

Results of the current analyses suggest significant associations between urinary 8-OHdG levels and risks of certain SBS complaints among office workers, with ORs ranging between 1.11 and 1.51. Additionally, SBS complaints and 8-OHdG are both associated with indoor air pollutants such as carbon dioxide, volatile organic compounds, and tobacco smoke exposure. These findings were evident in adjusted MLR models through adjustment for potential confounders, such as gender, age, sensitivity to tobacco smoke and air pollutants, difference in carbon dioxide between indoor and outdoor, tobacco smoke exposure, the presence of carpet in workplace, and so on. The gradient relationship between number of symptoms and 8-OHdG concentrations in urine has strengthened our research hypothesis, that is, that 8-OHdG can be a predictor for SBS. To our knowledge, this is the first observation of a positive association between SBS and the urinary 8-OHdG level. This study suggested that in urine 8-OHdG, a response to indoor oxidative chemicals, could be considered as a predictor to moderate the risks of certain SBS complaints including eye dryness, nose itching, sneezing, dry throat, dryness of skin and eye, dizziness, and upper respiratory syndromes in office employees. Because the etiology of SBS complaints has not been fully understood, the findings from this analysis cannot be dismissed and warrant further research.

REFERENCES

Anderson, R., Theron, A. J., Richards, G. A., Myer, M. S., and Van Rensburg, A. J. 1991. Passive smoking by human sensitizers circulating neutrophils. *Am. Rev. Respir.* 144:570–574.

Apte, M. G., Fisk, W. J., and Daisey, J. M. 2000. Associations between indoor CO_2 concentrations and sick building syndromes in U.S. office buildings: An analysis of the 1994–1996 BASE study data. *Indoor Air* 10:246–247.

Backman, H., and Haghighat, F. 1999. Indoor-air quality and ocular discomfort. *Am. Optom. Assoc.* 70:309–316.

Bako-Biro, Z., Wargocki, P., Weschler, C. J., and Fanger, P. O. 2004. Effects of pollution from personal computers on perceived air quality, SBS symptoms and productivity in offices. *Indoor Air* 14:178–187.

Benowitz, N. L. 1996. Cotinine as a biomarker of environmental tobacco smoke exposure. *Epidemiol. Rev.* 18:188–203.

Bourbeau, J., Brisson, C., and Allaire, S. 1997. Prevalence of the sick building syndrome symptoms in office workers before and six months and three years after being exposed to a building with an improved ventilation system. *Occup. Environ. Med.* 54:49–53.

Burge, P. S. 2004. Sick building syndrome. *Occup. Environ. Med.* 61:185–190.

Calderon-Garciduenas, L., Wen-Wang, L., Zhang, Y. J., Rodriguez-Alcaraz, A., Osnaya, N., Villarreal-Calderon, A., and Santella, R. M. 1999. 8-Hydroxy-2′-deoxyguanosine, a major mutagenic oxidative DNA lesion, and DNA strand breaks in nasal respiratory epithelium of children exposed to urban pollution. *Environ. Health Perspect.* 107:469–474.

Carstensen, U., Hou, S. M., Alexandrie, A. K., Hogstedt, B., Tagesson, C., Warholm, M., Rannug, A., Lambert, B., Axmon, A., and Hagmar,

L. 1999. Influence of genetic polymorphisms of biotransformation enzymes on gene mutations, strand breaks of deoxyribonucleic acid, and micronuclei in mononuclear blood cells and urinary 8-hydroxydeoxyguanosine in potroom workers exposed to polyaromatic hydrocarbons. *Scand. J. Work Environ. Health* 25:351–360.

Chuang, C. Y., Lee, C. C., Chang, Y. K., and Sung, F. C. 2003. Oxidative DNA damage estimated by urinary 8-hydroxydeoxyguanosine: Influence of taxi driving, smoking and areca chewing. *Chemosphere* 52:1163–1171.

Ebbehoj, N. E., Meyer, H. W., Wurtz, H., Suadicani, P., Valbjorn, O., Sigsgaard, T., and Gyntelberg, F. 2005. Molds in floor dust, building-related symptoms, and lung function among male and female schoolteachers. *Indoor Air* 15:7–16.

Engvall, K., Norrby, C., and Norbäck, D. 2001. Sick building syndrome in relation to building dampness in multi-family residential buildings in Stockholm. *Int. Arch. Occup. Environ. Health* 74:270–278.

Floyd, R. A., West, M. S., Eneff, K. L., and Schneider, J. E. 1990. Mediation of 8-hydroxy-guanine formation in DNA by thiazin dyes plus light. *Free Radical Biol. Med.* 8:327–330.

Fraga, C. G., Shigenaga, M. K., Park, J. W., Degan, P., and Ames, B. N. 1990. Oxidative damage to DNA during aging: 8-hydroxy-2′-deoxyguanosine in rat organ DNA and urine. *Proc. Natl. Acad. Sci. USA* 87:4533–4537.

Haufroid, V., and Lison, D. 1998. Urinary cotinine as a tobacco-smoke exposure index: A minireview. *Int. Arch. Occup. Environ. Health* 71:162–168.

Huang, M. F., Lin, W. L., and Ma, T. C. 2005. A study of reactive oxygen species in mainstream of cigarette. *Indoor Air* 15:135–140.

Kasai, H., Iwamoto-Tanaka, N., Miyamoto, T., Kawanami, K., Kawanami, S., Kido, R., and Ikeda, M. 2001. Life style and urinary 8-hydroxydeoxyguanosine, a marker of oxidative DNA damage: Effects of exercise, working conditions, meat intake, body mass index, and smoking. *Jpn. J. Cancer Res.* 92:9–15.

Kim, W. J., Terada, N., Nomura, T., Takahashi, R., Lee, S. D., Park, J. H., and Konno, A. 2002. Effect of formaldehyde on the expression of adhesion molecules in nasal microvascular endothelial cells: The role of formaldehyde in the pathogenesis of sick building syndrome. *Clin. Exp. Allergy* 32:287–295.

Kreiss, K. 1990. The sick building syndrome: Where is the epidemiologic base? *Am. J. Public Health* 80:1172–1173.

Laumbach, R. J., and Kipen, H. M. 2005. Bioaerosols and sick building syndrome: particles, inflammation, and allergy. *Curr. Opin. Allergy Clin. Immunol.* 5:135–139.

Levin, H. 1989. Building materials and indoor air quality. State of the art reviews. *Occup. Med.* 4:667–694.

Loft, S., Vistisen, K., Ewertz, M., Tjonneland, A., Overvad, K., and Poulsen, H. E. 1992. Oxidative DNA damage estimated by 8-hydroxydeoxyguanosine excretion in humans: Influence of smoking, gender and body mass index. *Carcinogenesis.* 13:2241–2247.

Lyles, W. B., Greve, K. W., Bauer, R. M., Ware, M. R., Schramke, C. J., Crouch, J., and Hicks, A. 1991. Sick building syndrome. *South Med. J.* 84:65–71.

Mahmoudi, M., and Gershwin, M. E. 2000. Sick building syndrome. III. *Stachybotrys chartarum. J. Asthma.* 37:191–198.

Menzies, D., Pasztor, J., Nunes, F., Leduc, J., and Chan, C. H. 1997. Effect of a new ventilation system on health and well-being of office workers. *Arch. Environ. Health* 52:360–367.

Niven, R. M., Fletcher, A. M., Pickering, C. A. C., Faragher, E. B., Potter, I. N., Booth, W. B., Jones, T. J., and Potter, P. D. R. 2000.

Building sickness syndrome in healthy and unhealthy buildings: an epidemiological and environmental assessment with cluster analysis. *Occup. Environ. Med.* 57:627–634.

Nerurkar, M. K., and Sahasrabudhe, M. B. 1960. Synthesis of creatine in x-irradiated rats. *Int. J. Radiat. Biol.* 2:237–246.

Norback, D., and Edling, C. 1991. Environmental, occupational, and personal factors related to the prevalence of sick building syndrome in the general population. *Br. J. Ind. Med.* 48:451–462.

Pommer, L., Fick, J., Andersson, B., Sundell, J., Nilsson, C., Sjöström, M., and Stenberg, B. 2004. Class separation of buildings with high and low prevalence of SBS by principal component analysis. *Indoor Air* 14:16–23.

Redlich, C. A., Sparer, J., and Cellen, M. R. 1997. Sick-building syndrome. *Occup. Med.* 349:1013–1016.

Samet, J. M., Marbury, M. C., and Spingler, J. D. 1987. Respiratory effect of indoor air pollution. *J. Allergy Clin. Jmmunol.* 79:685–700.

Sari, D. K., Kuwahara, S., Tsukamoto, Y., Hori, H., Kunugita, N., Arashidani, K., Fujimaki, H., and Sasaki, F. 2004. Effect of prolonged exposure to low concentrations of formaldehyde on the corticotropin releasing hormone neurons in the hypothalamus and adrenocorticotropic hormone cells in the pituitary gland in female mice. *Brain Res.* 1013:107–116.

Seidner, A. 1999. Sick building syndrome. *Hosp. Pract.* 15:127–129.

Seppänen, O. A., Fisk, W. J., and Merdell, M. J. 1999. Association of ventilation rates and CO_2 concentrations with health and other responses in commercial and institutional buildings. *Indoor Air* 9:226–252.

Shigenaga, M. K., Gimeno, C. J., and Ames, B. N. 1989. Urinary 8-hydroxy-2′-deoxyguanosine as a biological marker of in vivo oxidative DNA damage. *Proc. Natl. Acad. Sci. USA* 86:9697–9701.

Skov, P., Valbjørn, O., and Pedersen, B. V. 1989. Influence of personal characteristics, job-related factors and psychosocial factors on the sick buildibg syndrome. *Scand. J. Work Environ. Health* 15:286–295.

Straus, D. C., Cooley, J. D., Wong, W. C., and Jumper, C. A. 2003. Studies on the role of fungi in sick building syndrome. *Arch. Environ. Health* 58:475–478.

Tagesson, C., Kallberg, M., Klintenberg, C., and Starkhammar, H. 1995. Determination of urinary 8-hydroxydeoxyguanosine by automated coupled-column high performance liquid chromatography: A powerful technique for assaying in vivo oxidative DNA damage in cancer patients. *Eur. J. Cancer* 31A:934–940.

Tagesson, C., Kallberg, M., and Wingren, G. 1996. Urinary malodialdehyde and 8-hydroxydeoxyguanosine as potential markers of oxidative stress in industrial art glass workers. *Int. Arch. Occup. Environ. Health* 69:5–13.

Tearle, P. 1999. The sick building syndrome. *Commun. Dis. Public Health* 2:303–304.

Teculescu, D. B., Sauleau, E. A., Massin, N., Bohadana, A. B., Buhler, O., Benamghar, L., and Mur, J. M. 1998. Sick-building symptoms in office workers in northeastern France: A pilot study. *Int. Arch. Occup. Environ. Health* 71:353–635.

van Klaveren, R. J., and Nemery, B. 1999. Role of reactive oxygen species in occupational and environmental obstructive pulmonary diseases. *Curr. Opin. Pulm. Med.* 5:118–128.

van Zeeland, A. A., de Groot, A. J., Hall, J., and Donato, F. 1999. 8-Hydroxydeoxyguanosine in DNA from leukocytes of healthy adults: Relationship with cigarette smoking, environmental tobacco smoke, alcohol and coffee consumption. *Mutat. Res.* 439:249–257.

Willers, A., Hein, H. O., and Jansson, L. 2004. Assessment of environmental tobacco smoke exposure: Urinary cotinine concentrations in children are strongly associated with the house dust concentrations of nicotine at home. *Indoor Air* 14:83–86.

Wilson, V. L., Taffe, B. G., Shields, P. G., Povey, A. C., and Harris, C. C. 1993. Detection and quantification of 8-hydroxydeoxyguanosine adducts in peripheral blood of people exposed to ionizing radiation. *Environ. Health Perspect.* 99:261–263.

Witherell, H. L., Hiatt, R. A., Replogle, M., and Parsonnet, J. 1998. Helicobacter pylori infection and urinary excretion of 8-hydroxy-2-deoxyguanosine, an oxidative DNA adduct. *Cancer Epidemiol. Biomarkers Prev.* 7:91–96.

World Health Organization. 1986. *Indoor Air Quality Research, EURO reports and studies*, p. 103. Copenhagen, Denmark: WHO Regional Office for Europe.

Wu, L. L., Chiou, C. C., Chang, P. Y., and Wu, J. T. 2004. Urinary 8-OHdG: A marker of oxidative stress to DNA and a risk factor for cancer, atherosclerosis and diabetics. *Clin. Chim. Acta* 339:1–9.

Yassi, A., Kjellström, T., de Kok, T., and Guidotti, T. L. 2001. *Basic environmental health*, pp. 291–292. London: Oxford University Press.

Yin, B., Whyatt, R. M., Perera, F. P., Randall, M. C., Cooper, T. B., and Santella, R. M. 1995. Determination of 8-hydroxydeoxyguanosine by an immunoaffinity chromatography-monoclonal antibody-based ELISA. *Free Radical Biol. Med.* 18:1023–1032.