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IMPACT OF EXPOSURE TO MULTIPLE CONTAMINANTS ON SYMPTOMS OF SICK BUILDING SYNDROME

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ABSTRACT

It has been hypothesized that symptoms of sick building syndrome (SBS) may arise because of the combined effect of exposure to multiple contaminants, when the concentration of each is below levels known to cause health effects. In a randomized double-blind study in four mechanically ventilated office buildings, the outdoor air supply was varied experimentally over a six week period. Volatile organic compounds, formaldehyde, nitrogen oxides, carbon monoxide, as well as airborne fungi and dust were measured each week, at the same time that workers completed questionnaires. Symptoms were associated with increased concentrations of some contaminants in certain buildings, but appeared to be most strongly associated with the combined effect of all contaminants, as estimated by a sum contaminant score. We conclude that this study provides evidence in support of the hypothesis that SBS may be related to combined contaminant exposures. As well, experimental manipulation of outdoor air supply is feasible; the resultant changes in workers exposures in the office environment can provide a powerful tool for further study of the causes of SBS.

INTRODUCTION

In approximately 75% of investigations of apparent outbreaks of building related illness, no cause can be identified - these are termed sick building syndrome (SBS).[1] In these investigations the concentrations of hypothesized causative agents, such as total volatile organic compounds (TVOCs), formaldehyde, nitrogen dioxide (NO_2), carbon monoxide (CO), airborne fungi, and dust, are below levels at which health effects have been previously described.[1] It has been suggested that symptoms of SBS may result from the combined effect of the multiple contaminants typically found in the office environment.[1,2] However, there is very limited data in support of this hypothesis. We have recently completed a study in four mechanically ventilated office buildings, in which workers reported symptoms considered typical of SBS, under conditions of varying outdoor air supply and varying concentrations of a number of hypothesized causative agents. This provided an opportunity to estimate the effect of varying concentrations of these contaminants, both independently and together, on the occurrence of symptoms.

SUBJECTS AND METHODS

Overall Study Design

A randomized double-blind multiple cross-over trial was conducted. For three consecutive two-week blocks, building ventilation systems were manipulated to deliver an intended 20 or 24 litres/second/person of outdoor air to the indoor environment, corresponding to indoor CO_2 concentrations of 1,000 or 600 ppm, respectively.[3] Within each two-week block, the ventilation level was increased for one week and decreased for the other. The order of weekly ventilation level in each block was selected randomly and known only to the study engineers. Two buildings were studied simultaneously in the spring and two in the fall of 1990, with opposite ventilation levels in each pair of buildings, to minimize any potential impact of outdoor conditions, or temporal phenomena.[4]

Study Population

The buildings selected were modern, mechanically ventilated, air-conditioned, office buildings, of 8,9, 23, and 27 stories, with sealed windows, located in downtown Montreal. Within these buildings, a census survey was conducted of all workers who were considered to work full-time at an identifiable worksite. In the 8- and 9-story buildings, all floors were selected, and in each of the other two, 8 floors were randomly selected for study.

Collection of Environmental Data

In each building, in the morning and afternoon of the day of weekly questionnaire completion, carbon dioxide, temperature, relative humidity, and air-velocity were measured using portable direct-reading instruments, at 8-12 sites per floor. In each building, each week, the following contaminants were measured at 1 to 3 sites per floor:

1. Carbon monoxide: portable direct reading instrument.
2. Nitrogen oxides: collected on sampling tubes using volumetric air samplers, operating at 100 ml/minute, over an 8 hr workday, during two consecutive days. Analyzed using NIOSH Method, P and CAM-231.
3. Formaldehyde: collected over 24 hours with passive samplers. Analyzed using NIOSH Method 3500.
4. Total volatile organic compounds: collection on activated charcoal tubes using volumetric air samplers, at 200 ml/minute, for 8 hrs, during 2 consecutive days. Analyzed using: flame ionization detection method.
5. Total airborne particulates: collection by volumetric air pumps, at 1.5 litres/minute, for 8 hrs, on 2 consecutive days. Pre and post dry weights of filters compared.
6. Fungi: airborne colony-forming units sampled with a biotest centrifugal sampler, cultured on rose bengal culture plates.

Questionnaires

All eligible workers were asked to complete a self-administered base-line questionnaire 1 to 3 weeks before the study, providing data on personal, smoking, medical, and work histories. In mid-afternoon of Wednesday or Thursday of each of the 6 study weeks, participants completed a 5 minute questionnaire to rate their office environment and report the presence or absence of symptoms experienced THAT DAY. The symptoms elicited - headache, fatigue, difficulty concentrating, cough, or irritation of the eyes, nose or throat - were those reported most frequently in our pilot study[4] and by others.[2,5]

Data Analysis

All analysis was conducted on personal computers using SAS (SAS Institute, Carey, NC USA), with T-tests for continuous and Chi square for categorical outcomes.
Participants were assigned the mean of the contaminant measures, taken on their floor, in

each week. To analyze the combined effect of all contaminants: Sum Contaminant Score = Sum of $^{CO}/_{Norm\text{-}CO}$ + $^{TVOC}/_{Norm\text{-}TVOC}$ + $^{Form}/_{Norm\text{-}Form}$ + $^{NO2}/_{Norm\text{-}NO2}$ + $^{Dust}/_{Norm\text{-}Dust}$ + $^{Fungal}/_{Norm\text{-}Fungi}$.
Log score sum = Sum of log{ratio of each contaminant to its norms}.
The following norms were used:

- Carbon monoxide: 9 ppm - United States Environmental Protection Agency National Ambient Air Quality Standard - (US EPA NAAQS) (1971).
- Total VOCs: 2.4 mg/M^3 - WHO Working Group (1983)
- Nitrogen dioxide: 0.05 ppm - US EPA NAAQS.
- Formaldehyde: 0.1 ppm - US EPA NAAQS and WHO Working Group.
- Airborne Dust: .26 mg/M^3 - US EPA 24 hour exposure limit
- Airborne Fungi: 1000 CFU/M^3 - ACGIH (1989).

Outcome Variables

Reporting of any symptom was classified as a dichotomous variable (symptom reported vs. not). Additionally, symptoms were grouped as: i) mucosal symptoms (irritation of the nose and throat, as well as cough); and ii) systemic symptoms (headache, difficulty concentrating, and fatigue).

RESULTS

Of 1838 eligible workers in the four buildings, 1546 (84%) participated. Over the six study weeks, on average 82% of participants completed questionnaires each week. Each week approximately half of the participants reported at least 1 of the 7 symptoms elicited. The most commonly reported were mucosal symptoms, particularly those of nasal irritation or congestion. The changes in outdoor air supply were not associated with symptom reporting.[6]
As seen in Table 1, there were substantial differences in the concentrations of contaminants in the four buildings. The high TVOCs in building B may have been because this building was less than three years old, and because of three sources identified on two of the floors selected for study. In Building B, TVOCs exceeded 2,400 mcg/M^3 on more than 10% of instances; more than 50% of all measures taken exceeded 800 mcg/M^3. In building C high TVOCs were recorded in weeks when carpets were reglued. The higher CO and NO_2 concentrations in Building A were at least partly explained by infiltration of exhaust fumes from an underground garage. There was substantial variation in the concentration of TVOCs and formaldehyde each week which were related to the changes in outdoor air supply.[6] Fungal and dust levels were well below norms in all buildings, while formaldehyde exceeded norms only in Building D at a few sites.

Table 1. Mean concentrations of contaminants in the four study buildings.

Contaminant	(Units)	# Measures	BLDG A	BLDG B	BLDG C	BLDG D
CO	(ppm)	59	4.8	2.7	-	-
TVOC	(mcg/M^3)	210	349	1645	1116	164
NO_2	(ppm)	138	.027	.025	.014	.019
Dust	(mcg/M^3)	211	17	26	23	12
Formaldehyde	(ppm)	72	.038	.043	.008	.068
Fungi	(cfu)	257	18	13	6	34
Reporting Symptoms:		Any	50%	40%	53%	65%
		Mucosal	36%	30%	39%	50%
		Systemic	27%	20%	30%	39%

Because of these differences in symptom occurrence, which were associated with differences in population characteristics, between buildings, analysis of the relationship between contaminants and symptoms was conducted within each building. Contaminant concentrations varied between buildings, as seen above, and also within buildings between floors, and sites. As well the changes in outdoor air supply were associated with changes in contaminant concentrations, particularly CO, TVOCs, and formaldehyde.[7] As shown in Table 2, higher concentrations of certain contaminants were associated with reporting of any symptom in some buildings, particularly B, where mucosal symptoms were also significantly associated with TVOCs, systemic symptoms with CO, TVOCs, NO_2, and dust, and eye symptoms were associated with CO, NO_2, and dust.

Table 2. Mean concentrations of contaminants among those with and without symptoms in the four study buildings.

Contaminant	BLDG A		BLDG B		BLDG C		BLDG D	
	Any	None	Any	None	Any	None	Any	None
CO (ppm)	5.0	4.7*	2.8	2.6*	-	-	-	-
TVOC (mcg/M³)	351	347	1827	1523*	1161	1067	163	165
NO_2 (ppm)	.029	.026*	.025	.024*	.013	.014	.019	.020
Dust (mcg/M³)	16	17	28	24*	23	23	12	12
Formald.(ppm)	.037	.040	.041	.045	.009	.008	.070	.065*
Fungi (cfu)	19	18	12	13	7	6	34	32
Sum Score	1.32	1.30	1.85	1.69*	.79	.76	.79	.75*

* $p<.01$ Comparison of means of any versus none within building, using T-Test

Table 3. Percent reporting any symptom by quartiles of individual contaminants.

	Quartiles of contaminant concentrations 1	2	3	4	p value
CO (N = 2017)	36		44	50	****
VOC (N = 7579)	54	52	51	53	NS
NO_2 (N = 6664)	51	52	48	54	NS
Formaldehyde: (N = 4594)	54	49	58	46	NS
Dust (N = 7267)	51	52	52	53	NS
Fungal (N = 6814)	51	51	53	53	NS

**** $p<.0001$ Mantel Hanzel Chi Square

When results from all buildings were combined, the proportion of workers with symptoms was not different between quartiles of individual contaminant concentrations, as shown in Table, except for carbon monoxide which was associated with any, mucosal ($p<.01$), and systemic ($p<.0001$) symptoms. Mucosal and systemic symptoms were not associated with any of the other contaminants.

As shown in Table 4, these sum scores were associated with symptoms, except in Building C. When the results of all buildings were combined, the sum score was highly associated with symptoms. However even at the lowest quartile of combined exposures, symptom prevalence was just under 50%. The log sum score was not associated with any outcome in any building.

Table 4. Percent reporting symptoms by quartiles of sum contaminant scores.

	Quartiles and quartile ranges 1	2	3	4	p value
Building A:	.8-1.1	1.1-1.2	1.2-1.5	1.5-2.1	
Any	43	52	54	51	*
Mucosal	30	38	40	37	*
Systemic	23	29	29	26	NS
Building B:	.8-1.0	1.0-1.5	1.5-2.1	2.1-6.1	
Any	33	43	40	45	****
Mucosal	24	31	30	33	**
Systemic	16	21	19	25	***
Building C:	0-.2	.2-.7	.7-.9	.9-4.1	
Any	56	52	50	53	NS
Mucosal	42	36	36	40	NS
Systemic	35	29	27	28	*
Building D:	.2-.6	.6-.8	.8-.9	.9-1.4	
Any	62	62	65	70	**
Mucosal	47	47	50	54	**
Systemic	38	37	42	41	NS
All Buildings					
Any	49	52	52	56	****
Mucosal	36	38	39	42	****
Systemic	28	29	30	31	*

* $p<.05$ ** $p<.01$ *** $p<.001$ **** $p<.0001$ Mantel Hanzel Chi Square

DISCUSSION

In this study, as the outdoor air supply was manipulated experimentally, concentrations of contaminants varied considerably in four large office buildings, although differences between buildings, floors and sites were greater than differences between weeks. Over 95% of all contaminant concentrations measured were within currently accepted North American norms, yet weekly symptoms reported by the 1546 participants were associated with a number of these contaminants. Symptoms were most strongly associated with combined contaminant exposures, as estimated from a sum contaminant score.

The strengths of the study were that a high proportion of a large population of workers participated, and the buildings selected had similar characteristics to those in which sick building syndrome has been described.[8,9] As well, participants appeared unaware of the changes in environmental conditions, limiting the possibility of reporting bias.[4] Misclassification of exposures should have been reduced by measurement of contaminants at several sites per floor in each building on the same day as questionnaire completion. Inferences from this report are limited because only four buildings were studied, although the number of participants was large. Given the variation in the concentration of contaminants, within and between these buildings, it is possible that measurement at more sites or in more buildings could have resulted in different associations. Calculation of the sum score was arbitrary, and it is possible that calculation with different norms, or different contaminants could alter the sum scores and the associations found. However use of different norms, or measurement of different contaminants could change the sum scores and possibly the associations found.

The combined effect of all contaminants appeared to have a greater effect than each individual agents, although this effect was stronger in the building with higher concentrations of VOCs, dust and nitrogen dioxide. Experimental combined exposure to ozone plus allergens,[10] and formaldehyde plus office air provide supportive data that combined exposures may result in greater health effects.

The evidence from this study that combined exposures are associated with symptoms of SBS can not be considered conclusive, but may offer insight into the pathogenesis of SBS, particularly why concentrations of contaminants in excess of norms are rarely found in investigations of this problem.[1,2] Experimental manipulation of indoor environmental conditions in double-blind randomized fashion, is feasible, and results in significant variation in concentration of contaminants. Further studies using this methodology may provide an understanding of the pathogenesis of sick building syndrome, and provide a scientific basis for standards for indoor air quality to safeguard the health of all those who work in the office environment.

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