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Assessment through Environmental and Biological Measurements of Total Daily Exposure to Volatile Organic Compounds of Office Workers in Milan, Italy

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Abstract Personal exposure to total volatile organic compounds (TVOCs), benzene and toluene of 100 Milan office workers was assessed through personal air monitoring at home, in the office, and during commuting. Biological monitoring was performed by measuring blood benzene and toluene concentrations together with urinary trans-trans-muconic acid (t,t-MA) and cotinine at the end of the monitoring period. The geometric means of the total 24-h personal exposure were 514 $\mu g/m^3$ for TVOCs, 21.2 $\mu g/m^3$ for benzene and 35.2 $\mu g/m^3$ for toluene. Daily exposure to the volatile organic compounds was almost totally determined by indoor exposure at home and in the office, with a minor contribution in the transport means. An important factor determining exposure to benzene was found to be tobacco smoke, both for active smokers and for non-smokers exposed to environmental tobacco smoke (ETS). All the mean levels of the biological indicators were significantly higher in active smokers than in non-smoking subjects non-exposed to ETS; urine cotinine and t,t-MA levels were also significantly higher in non-smokers exposed to ETS than in non-smokers non-exposed to ETS.

Key words Volatile organic compounds; Benzene; Toluene; Personal exposure; Biological concentration; Tobacco smoke.

Practical Implications
Daily exposure of Milan office workers to total volatile organic compounds (TVOCs), benzene and toluene was almost totally determined by indoor exposure at home and in the office, with a minor contribution of exposure in the transport means. The major factor determining exposure to the volatile organic compounds was found to be tobacco smoke, both for active smokers and for non-smokers exposed to environmental tobacco smoke (ETS). The finding of an average TVOC exposure level higher in mechanically than in the naturally ventilated offices indicate that mechanical ventilation is often ineffective to improve indoor air quality. Personal exposure to benzene was found to be higher in summer than in winter, while the opposite was found for toluene and TVOCs, thus indicating that indoor exposure to benzene does not follow the seasonal pattern of outdoor VOC pollution levels.

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Introduction

Air pollution is one of the major environmental risk factors to human health (Folinsbee, 1993). Since people spend 80–95% of their time indoors, total human exposure to air pollutants is dominated by indoor air pollution (Clayton, 1993; Wallace, 1989), which is in part caused by indoor penetration of polluted outdoor air and, to a greater extent, by pollution sources located indoors (Maroni, 1995). The overall personal exposure to environmental pollutants depends on the concentrations of pollutants in the various micro-environments where individuals spend their time and the amount of time spent in each of these micro-environments.

The assessment of personal exposure is more reliably obtained through measurements with personal portable samplers than with the fixed monitoring networks, because the former take into account the movement of people across different micro-environments according to their daily individual activities (ECA, 1992).

Data on personal exposure levels of the general population to airborne pollutants are still limited in Europe, as information on population exposure so far is mostly available from measurements provided by outdoor fixed monitoring networks (Jantunen, 1998).

Volatile organic compounds (VOCs) are an import-

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ant class of air pollutants. They consist of hundreds of different organic compounds and their levels in indoor air are usually higher than in outdoor air. They penetrate indoors together with outdoor air by ventilation and can diffuse from polluted soil or be transported into the indoor environment with contaminated drinking water (typically well water) but are mainly generated by indoor sources: man made building materials (e.g. paints, adhesives, floor coverings), consumer products for cleaning and maintenance, and combustion sources (e.g. tobacco smoke). The health effects of different VOCs are quantitatively and qualitatively quite different. Some VOCs are known or suspected human carcinogens (e.g. benzene) and, although few risk assessments are available for VOCs in indoor air, VOCs appear likely to pose a significant cancer risk (WHO, 1989). Some VOCs exhibit neurotoxic effects (e.g. toluene, xylenes). Many VOCs can cause irritation of the eyes and respiratory tract and sensitization reactions which involve the eyes, skin, and the respiratory tract. It has been suggested that there may be an association between total organic volatile compound (TVOC) levels and a complex set of unspecific symptoms called the Sick Building Syndrome (SBS), mucous membrane irritation, decreased tear film stability, and sensation of increased odour intensity and reduced air quality (Maroni, 1995).

This study aimed at assessing total daily personal exposure to TVOCs, benzene, and toluene, of 100 office workers living and working in Milan, through environmental and biological monitoring. Assessment of the contribution to total exposure of each micro-environment, and identification of the major indoor sources or factors determining personal exposure, were among the objectives of the study.

Materials and Methods

Subjects

Since over 75% of the working population in Milan operates in offices or similar micro-environments, it was decided to evaluate the exposure for only this category of workers.

One hundred office workers employed at the Municipality of Milan or at Institutes of the University of Milan, were enrolled for the study. Conditions of admission to the study included an age of 18 to 60 years, a place of residence in Milan, a workplace in a building located in the downtown area of the city, and absence of other jobs in addition to the office work. Two buildings were involved: a large historical building built in 1930s and restored in 1990 with mechanical ventilation system in the lower floors (ground floor and I) and with natural ventilation in the upper floors (II, III and IV); an aluminum-glass 4-story building erected in 1960 with natural ventilation. They had been evaluated in previous studies and can be considered representative of different office building typologies present in Milan (Cavallo, 1993; Carrer, 1996).

Fifty subjects were studied during spring-summer 1995 (May–July) and the other fifty during winter 1996 (January–March). The characteristics of the subjects participating to the study are summarised in Table 1; the groups of subjects studied during the two seasons presented the same characteristics.

All the participants were briefed about the scope and purpose of the study, were requested to express agreement on the environmental and biological sampling programme, and signed an informed consent to participate in the study.

Study Design

All the subjects were studied in working days (Monday to Thursday) and were invited to restrict their activities to home, office and transit on the day of the study.

Personal exposure assessment was performed with sampling sessions at workplace, during commuting back home, at home, and during commuting home-to-office, for a total of 24 consecutive hours, starting at 08:30 a. m. the first day and ending at 08:30 a. m. the next day. The biological samples for the determination of the concentration of benzene and toluene in blood and trans,trans-muconic acid (t,t-MA) and cotinine in urine were collected at the end of the 24-h monitoring period. Benzene in blood and urinary t,t-MA, a metabolite of benzene, were used as biomarkers of low-level exposure to benzene (Ruppert, 1997). Toluene in blood was used as a biomarker of exposure to toluene. Urinary cotinine, a metabolite of nicotine, was used as a biomarker of active and passive tobacco smoke exposure (Haufroid, 1998).

Environmental Air Sampling and Analysis

Personal exposure to VOCs was determined by active and passive sampling using solid sorbent tubes, thermal desorption and gas chromatographic flame ionisation analysis accordingly with methods MDSH 72 and 80 of the Health and Safety Executive, with same modifications (MDSH 72, 1992; MDSH 80, 1996).

Air sampling: VOCs were collected by personal samplers worn by the subjects in the proximity of the respiratory zone. Samplers were stainless steel tubes (Perkin Elmer), filled with 250 mg Tenax TA (60–80 mesh, Alltech). Tubes were conditioned, prior to first use, by heating at 300 °C for 60 min, flowing helium at

Table 1 Characteristics of the subjects and buildings involved in the study

Characteristics		Summer group	Winter group	Total
Subjects				
Number of subjects	(n.)	50	50	100
Gender: Male	(n.)	25	25	50
Female	(n.)	25	25	50
Age–mean±SD	(years)	38.6±10.4	35.9±9.1	37.0±9.8
Smokers	(n.)	16	15	31
ETS exposed	(n.)	13	14	27
Non smokers non ETS exposed	(n.)	21	21	42
Home Building				
Location: Town centre	(n.)	14	12	26
Suburban area	(n.)	36	38	74
Home located in area with high density of traffic	(n.)	23	24	47
Natural ventilation	(n.)	50	50	100
Smokers	(n.)	14	10	24
ETS exposed	(n.)	12	6	18
Non smokers non ETS exposed	(n.)	24	34	58
Office Building				
Office ventilation: Natural	(n.)	25	26	51
Mechanical	(n.)	25	24	49
Smokers	(n.)	17	13	30
ETS exposed	(n.)	13	10	23
Non smokers non ETS exposed	(n.)	20	27	47

50 ml/min. Tubes were routinely cleaned by two thermal cycles at 260°C for 5 min and 280°C for 3 min, flowing helium at 50 ml/min. After cleaning, tubes were randomly tested for the absence of analytes. Helium used for all analytical phases was ultra pure grade (purity >99.996%). Cleaning was performed on batches of 20–30 samples. For personal active sampling (during commuting) pumps (Gillian) set at 100 ml/min were used. Active sampling was performed connecting samplers to the pump by a silicon tube. Passive sampling (home and office) was performed equipping the sampler upper end with a diffusion chamber (Perking Elmer) and capping the lower end with a brass cap sealed with one-piece PTFE ferrule (Swagelok). At the end of air sampling, samplers were closed using the same brass and ferrule above mentioned. Tubes were delivered to laboratory and kept at room temperature in a dry box. Samples were analysed within 60 days, according to their stability (see below).

Analysis: Thermal desorber ATD 400 (Perking Elmer), equipped with Tenax TA trap cryogenically cooled (minimum temperature −30°C) and connected, via silica gel transfer line (0.32 mm internal diameter), to a 8000 series gas chromatograph (Fison) with a flame ionisation detector (FID), was used for analysis. Analytes were separated by a dimethylsiloxane column (DB1 J&W, 0.32 internal diameter, 1.1-μm film thickness, 50 m length). Column was directly connected to the thermal desorber via transfer line by glass connector. The following operative conditions were used: thermal desorber during primary desorption: oven at 260°C for 6 min, helium at 50 ml/min, cryo trap at −30°C; thermal desorber during secondary desorption: cryo trap fast heated at 280°C and held at this temperature for 6 min, helium at 10 ml/min, inlet split off, outlet split 8 ml/min, column flow 2 ml/min, split ratio 4:1. Chromatographic analysis: injection through transfer line at 250°C, initial oven temperature at 40°C, then oven temperature at 250°C at 4°C/min, then 250°C held for 5 min. FID detector was at 300°C. Benzene and toluene were identified based on their retention times in comparison with reference analytes spiked onto calibration tubes.

Calibration: Standard solution EPA TO-1 Toxic Organic Mix (Supelco), containing benzene, toluene and other chemicals at 2000 μg/ml each in methanol, and methanol purge and trap grade (Sigma) were used for preparing calibration solutions. A gas chromatographic injector (set on a Sigma 300 Perkin Elmer gas chromatograph), purged with Helium at 100 ml/min was used for preparing calibration tubes. Clean tubes were connected directly to the injector by a suitable union (Swagelok). One μl of each calibration/standard solution was loaded onto tubes by splitless injection with a 1-μl syringe (Hamilton). Five calibration levels and a blank were prepared for each curve. Each calibration level was repeated 6 times. Calibration curves ($Y=aX + b$) were obtained by least square linear regression using peak area subtracted of blank (mean values of 6 determinations) as dependent variable (Y) and analyte amount loaded on tube as independent variable (X). The analytical limit of detection (ALOD),

as absolute amount of analyte on tube, was estimated to be 1.5 and 1 ng for benzene and toluene, based on the signal to noise ratio (S/N >3).

Calculation: The chromatographic signals of benzene, toluene and TVOCs in the tubes were subtracted of the field blank area (mean value of fields blanks within the same batch, see quality assurance section). The amount of benzene and toluene was obtained from this area using their calibration curves. The amount of TVOCs in the tube was calculated by summing up the peak areas of every individual compounds and using the calibration curve obtained for toluene. For active samples, the concentration was obtained dividing the amount recovered from each tube by its sampling volume. Typical sample volumes were 2 L. Based on sampling volume and ALOD, the detection limit of 0.75 and 0.5 $\mu g/m^3$ were calculated for benzene and toluene during commuting, where active samples were used ($LOD_{commuting}$). For passive samples, the volume of environmental air sampled for benzene and toluene was calculated using the uptake rates previously reported (MDSH 80, 1996), that is 0.41 and 0.44 ml/min for benzene and toluene respectively. For TVOCs, an average uptake rate of 0.44 ml/min was assumed. Typical sampling times were 500 min and 835 min for office and house, respectively. Based on sampling volume and ALOD, the following detection limits in the two micro-environments were calculated: LOD_{house} 4.4 and 2.7 $\mu g/m^3$, and LOD_{office} 7.5 and 4.5 $\mu g/m^3$ for benzene and toluene, respectively.

Quality assurance program: Quality assurance was performed at different phases of the work: tube conditioning and cleaning, tube storage, repeatability of single tube and calibration curve, thermal desorption and gas chromatographic analysis, tube sampling and analysis. The absence of contamination after sorbent conditioning and cleaning was tested by random analysis of 10% tubes in the cleaning batch. Analytes detected in cleaned tubes were generally below the ALOD. For polluted batches, the cleaning procedure was repeated. The stability of the analytes in the tubes was tested in a 60-day trial. Tubes were loaded with 40 ng of each analyte, sealed and stored in a dry box at room temperature. The tubes were analysed (6 each time) at different times. No significant loss of analyte from tube was detected up to 60 days (total mean recovery of 101 and 103% and coefficient of variation of 3.8 and 3.9% for benzene and toluene, respectively). Repeatability was evaluated for single tubes loaded with amounts of analytes of 4, 40 and 400 ng. The coefficients of variation were 7.3, 3.9 and 1.4% for benzene and 4.1, 1.3 and 0.9% for toluene at the three loaded amounts. The calibration curves were repeated along the whole study with minimal changes in the slope value (coefficient of variation of 9.7% and 4.7% for benzene and toluene). Thermal desorber and gas chromatograph were tested for the absence of contaminants before each analytical sequence. A laboratory blank and a short calibration curve were also inserted in the sequence to check for retention times and response factor. Coefficient of variation of retention time was below 1% both for benzene and toluene along the study. To check for contamination in the total procedure, unloaded capped tubes were sent to the field (10 % of sampled tubes). These tubes, identified as field blanks, were kept closed and returned to the laboratory for analysis. The signal of field blank tubes was averaged within the analytical batch and subtracted to each sample in the batch. To check for repeatability of the whole procedure, duplicate samples were collected (10% of sampled tubes). The repeatability of the procedure provided coefficients of variation < 15 % for benzene, toluene and TVOCs.

Biological Monitoring

Sampling and analysis: Blood and urine samples were collected in the morning at the end of the monitored period (usually 8.30). Blood samples for the determination of benzene and toluene were collected from the cubital vein using a disposable syringe previously tested for the absence of analytes. A 2-ml blood sample was immediately transferred onto a 8-ml pre-sealed glass vial containing aqueous EDTA-Na_2 solution as anticoagulant. Proper procedure for cleaning vial and caps was previously described (Fustinoni, 1999). The samples were soon delivered to the laboratory. Blood samples were added with an internal standard solution (benzene-d_6 and toluene-d_8 in methanol), stored at 4 °C, and analysed within 7 days. Urine samples were frozen immediately after collection and stored at −20 °C until analysis.

Determination of aromatic hydrocarbons in blood was performed by dynamic head space sampling followed by gas chromatographic separation and electron impact mass detection, according to Fustinoni, with same modifications (Fustinoni 1995, 1999). The mass detector was used in the single ion monitoring mode, registering the ions m/z: 78 (benzene), 84 (benzene-d_6), 91 (toluene) and 98 (toluene-d_8). The limits of detection of the assay were 25 ng/l for benzene and 35 ng/l for toluene.

Urinary t,t-MA was measured by high performance liquid chromatography according to a method previously reported (Buratti, 1996). Brefly, t,t-MA was extracted from urine by solid-phase anionic exchange chromatography and analysed on a C_{18} reverse phase

Table 2 Time and percentage of day spent in various micro-environments by office workers in Milan, based on the time-activity diary

	Summer group	Winter group	Total
Home			
Mean±SD (min)	849±67	810±65	835±67
Fraction of 24 h (%)	59.1	58.1	58.8
Office			
Mean±SD (min)	497±70	501±48	499±60
Fraction of 24 h (%)	34.6	35.9	35.0
Commuting			
Mean±SD (min)	90±26	84±24	87±25
Fraction of 24 h (%)	6.3	6.0	6.2

column, using formic acid – tetrahydrofurane – water as a mobile phase and ultraviolet (UV) detection at 263 nm. The limit of detection of the assay was 5 μg/l of urine.

Urinary cotinine was determined by reversed-phase high performance liquid chromatography, using a procedure previously described (Lequang Thuan, 1987) with minor modifications. Before analysis, the urine samples were concentrated 100 folds and cotinine was extracted with silica gel columns. The limit of detection of the assay was 20 μg/l of urine.

Time-Activity Diaries and Questionnaires

Information about activities performed by the subjects during the 24-h monitoring period was collected through a time-activity diary (TAD) and a home-office-transfer microenvironment questionnaire compiled by each participant at the end of his/her period of study.

The microenvironment categories considered by the TAD were: Home, Office and Transfer (walk/bike, motorcycle, car/taxi, bus/tram and subway). The subjects had to mark each 15 min of the day the appropriate micro-environment and smoke exposure categories and eventually note special activities (e.g. filling car); smoke exposure considered the self smoking and smoking of others in the same room.

Information about the characteristics of the home and office micro-environments was collected with a standardised form by the investigators through direct inspection during the sampling session set-up. The questionnaire included questions about characteristics related to air quality, namely building location, home or office floor, type of ventilation, occupancy, traffic volume, presence of specific indoor sources, use of chemical or cleaning products. An office-home and home-office transfer questionnaire was also compiled.

Table 3 Personal pollutant exposure levels in microenvironments, daily personal exposure and contribution of each microenvironment exposure to the daily exposure

Pollutant ($\mu g/m^3$)	Home (n=100)	Office (n=100)	Commuting (n=100)	24-h exposure (n=100)
TVOCs				
– Percentiles:				
10th	248	417	74	333.1
25th	286	482	241	407.6
50th	339	609	505	483.6
75th	467	827	911	609.5
90 th	600	1114	1648	850.4
– GM (GSD)	373.2 (1.5)	668.2* (1.5)	420.7 (4.4)	514.0 (1.6)
– Contribution to 24 h exposure (%)	45.7	48.9	5.4	100
Benzene				
– Percentiles:				
10th	5	8	2	7.5
25th	8	14	9	14.0
50th	23	26	21	26.4
75th	40	48	39	39.0
90th	59	94	65	50.2
– GM (GSD)	21.0 (2.6)	28.7* (2.1)	18.2 (3.3)	21.2 (2.6)
– Contribution to 24-h exposure (%)	52.4	42.8	4.7	100
Toluene				
– Percentiles:				
10th	6	10	11	15.6
25th	15	19	27	25.9
50th	31	32	45	37.9
75th	53	48	76	50.1
90th	91	71	136	78.5
– GM (GSD)	30.9 (2.4)	32.5 (2.4)	43.6* (2.6)	35.2 (2.2)
– Contribution to 24-h exposure (%)	52.3	35.8	11.9	100

GM: Geometric Mean
GSD: Geometric Standard Deviation
*=$p<0.05$ (analysis of variance on log-transformed values)

Table 4 Pearson's correlation coefficient among personal exposures to TVOCs, benzene and toluene on log-transformed values

	TVOCs vs. Benzene	TVOCs vs. Toluene	Benzene vs. Toluene
At home	0.22*	0.25*	0.26*
In office	0.17*	0.17*	0.17*
During commuting	0.81**	0.54**	0.62**
24 h exposure	0.21*	0.32*	0.50*

n.s.=not statistically significant ($p > 0.05$)
*=$p<0.05$
**=$p<0.05$

Statistical Analysis

Statistical analysis was performed with the statistical package SPSS/PC^{+}. When the level of the compound in the sample resulted below the limit of quantification, a conventional value equal to half the quantification limit was assigned to the sample for the statistical analysis of the results. Individual total daily personal exposure to each pollutant was calculated as time-weighted average of office, home and commuting concentrations. The mean contribution of each micro-environment to the daily personal exposure was calculated multiplying the mean concentration of each micro-environment by the mean time spent in it and expressing this value as a percentage of the mean 24-h exposure.

Since the pollutant exposure levels were asymmetrically distributed, they were logarithmically transformed. The distribution normalisation was verified by means of the Kolgomorow-Smirnow test. The significance of differences between groups was examined by Student's *t*-test or analysis of variance. The associations between micro-environment characteristics and pollutant exposure levels were assessed by the Pearson's correlation coefficient and the stepwise multiple regression analysis. P-values less than 0.05 were considered statistically significant in all the analyses performed.

Results

Table 2 shows the time spent by the subjects in the micro-environments. On average, they spent 58.8% of their time at home (mean 835 ± 67 min), 35% at workplace (mean 499 ± 60 min), while only 6.2% in daily journeys (mean 87 ± 25 min).

Table 3 summarises the pollutant exposure levels measured in the micro-environments, the daily personal exposure and the contribution of each micro-environment exposure to the daily exposure. No samples were below the limit of detection. The geometric means of the total 24-h personal exposure were 514 $\mu g/m^3$ for TVOCs, 21.2 $\mu g/m^3$ for benzene and 35.2 $\mu g/m^3$ for toluene. TVOCs and benzene levels were significantly higher in office than at home and on commuting; toluene level was significantly higher during commuting than in office and at home. The fractions of total daily exposure accounted by home exposure, workplace exposure, and commuting exposure were respectively: 45.7%, 48.9%, and 5.4% for TVOCs; 52.4%, 42.8%, and 4.7% for benzene; 52.3%, 35.8%, and 11.9% for toluene.

Table 4 shows the correlation among personal exposures to TVOCs, benzene and toluene in the micro-environments and in the total daily personal exposure. High coefficients of correlation were found on commuting and lower coefficients on stay at home and in the office.

The personal exposure levels grouped by season (summer vs. winter) are shown in Table 5. TVOCs and toluene levels were higher in winter than in summer, whereas home and office benzene levels were higher in summer than in winter.

Table 6 shows the personal exposures according to tobacco smoke exposure by grouping the subjects as non-smokers non-exposed to environmental tobacco smoke (ETS), non-smokers exposed to ETS, and active smokers. No differences were found for TVOCs and

Table 5 Personal exposure levels grouped by season ($\mu g/m^3$)

Pollutant		Home		Office		Commuting		24-h exposure	
		Summer (n=50)	Winter (n=50)	Summer (n=50)	Winter (n=50)	Summer (n=50)	Winter (n=50)	Summer (n=50)	Winter (n=50)
TVOCs	GM	323.6	429.5*	622.3	712.8*	311.2	540.8*	461.3	561.0*
	(GSD)	(1.5)	(1.6)	(1.8)	(1.9)	(4.0)	(4.4)	(1.5)	(1.6)
Benzene	GM	22.9*	15.6	37.9*	22.0	14.5	21.9	25.2	18.6
	(GSD)	(2.0)	(1.8)	(2.1)	(1.9)	(1.6)	(2.0)	(2.6)	(2.0)
Toluene	GM	21.5	37.6*	30.9	34.5	34.3	53.7*	29.1	41.8*
	(GSD)	(2.1)	(2.4)	(2.0)	(2.1)	(2.2)	(2.4)	(2.0)	(2.4)

GM: Geometric Mean
GSD: Geometric Standard Deviation
*=$p<0.05$ (Student's *t*-test winter vs summer on log-transformed values)

Table 6 Personal 24 h exposure according to tobacco smoke exposure

Parameter ($\mu g/m^3$)	Non-smokers no ETS			Non-smokers exposed to ETS			Active smokers		
	n.	GM	(GSD)	n.	GM	(GSD)	n.	GM	(GSD)
TVOCs									
Office	47	698.8	(1.6)	23	685.5	(1.4)	30	539.7	(1.6)
Home	58	367.3	(1.5)	18	416.6	(1.4)	24	357.3	(1.5)
24 h	42	510.7	(1.5)	27	503.1	(1.4)	31	450.8	(1.3)
Benzene									
Office	47	20.5	(2.3)	23	36.5*	(2.1)	30	40.4*	(2.3)
Home	58	18.9	(2.5)	18	32.2*	(1.7)	24	24.3	(2.5)
24 h	42	16.5	(2.3)	27	25.4	(2.9)	31	26.0	(2.3)
Toluene									
Office	47	32.0	(2.5)	23	41.6	(2.5)	30	27.5	(2.6)
Home	58	30.1	(2.4)	18	32.0	(2.9)	24	32.8	(2.5)
24 h	42	33.2	(1.9)	27	37.1	(2.9)	31	31.5	(2.0)

GM: Geometric Mean
GSD: Geometric Standard Deviation
*=$p<0.05$ (Student's *t*-test vs. Non-smokers non-ETS exposed on log-transformed values)

toluene levels. Personal exposure to benzene were higher for active and passive smokers than for subjects non-smokers no ETS exposed.

Other factors were investigated for their possible relation to the home and office exposure levels, namely building location, traffic density, floor, type of ventilation, occupancy, presence of papers stored in open shelves, printers or photocopying machines, and use of cleaning products. For TVOC exposure in the office, significant differences were found between natural and mechanical ventilation (geometric mean respectively 610.9 and 743.0 $\mu g/m^3$) and between offices with presence of photocopying machines and offices without photocopying machines (geometric mean respectively 861.0 and 657.6 $\mu g/m^3$). Significant differences were found between natural and mechanical ventilation (geometric mean respectively 20.1 and 28.2 $\mu g/m^3$) also for benzene exposure in the offices. No other factors among those above listed, proved to be significantly associated with exposure.

As commuting is concerned, exposure levels according to the type of transport means are shown in Table 7. TVOCs, benzene and toluene levels were remarkably higher in cars than in all the other means of transport.

Table 8 shows the results of multiple linear regression analyses where TVOC and benzene exposure levels were entered as dependent variable into the model and the factors that resulted to be correlated in the previous analyses were entered as independent variables. Significant relationships were found both with season and mechanical ventilation for TVOCs office levels. A significant negative relationship was found with season for benzene home and office levels and a significant positive relationship was found with smoke exposure for benzene in office only.

Table 9 summarises the concentrations of the bio-

Table 7 Personal exposure levels ($\mu g/m^3$) during commuting according to the transport means

Pollutant	Car (n=11)	Subway (n=12)	Bus/tram (n=25)	Mixed[a] (n=52)
TVOCs GM (GSD)	1042.3* (2.8)	242.1 (3.5)	370.7 (2.5)	388.9 (2.8)
Benzene GM (GSD)	57.8* (2.8)	10.1 (1.6)	16.6 (3.1)	20.2 (2.4)
Toluene GM (GSD)	145.7* (2.4)	39.3 (2.7)	44.1 (3.2)	39.5 (3.1)

[a]=Plus than one transport mean used
GM: Geometric Mean
GSD: Geometric Standard Deviation
*=$p<0.05$ (analysis of variance on log-transformed values)

Table 8 TVOCs and benzene personal exposure levels: stepwise multiple regression analyses

Dependent variable	Independent variables Beta coefficient			Model		
TVOCs air in the office	Season (summer:1-winter:2) 0.20*	Ventilation (natur.:1-mech.:2) 0.23*	Photocop. mach. (n.) 0.09	R^2 0.10	F 3.3	p 0.02
Benzene – air at home	Season (summer:1-winter:2) −0.30*	Smoke exposure (n. active and passive cigarettes) 0.09		R^2 0.11	F 5.3	p 0.007
Benzene – air in the office	Season (winter:1-summer:2) −0.27*	Smoke exposure (n. active and pass.cigar.) 0.29*	Ventilation (natur.:1-mech.:2) 0.12	R^2 0.19	F 6.7	p 0.001

*=$p<0.05$

Table 9 Biological indicator concentrations according to tobacco smoke exposure

Biological indicator	Non-smokers no ETS (n=42)	Non-smokers exposed to ETS (n=27)	Active smokers (n=31)	All subjects (n=100)
Benzene blood (ng/l)				
- n.<LOD	0	0	0	0
- Percentiles:				
10th	34	40	84	41
25th	43	74	124	65
50th	71	82	191	92
75th	102	124	257	150
90th	127	150	416	224
– GM (GSD)	69.2 (1.6)	85.9 (1.6)	203.2*° (1.9)	102.1 (2.0)
Toluene blood (ng/l)				
- n.<LOD	0	0	0	0
- Percentiles:				
10th	179	203	261	204
25th	227	244	396	245
50th	274	348	547	347
75th	356	539	854	572
90th	578	891	1225	891
– GM (GSD)	299.9 (1.6)	383.7 (1.8)	568.8*° (1.8)	390.8 (1.8)
t,t-MA Urine µg/l)				
– n.<LOD	2	0	0	2
– Percentiles:				
10th	10	12	44	15
25th	26	40	68	39
50th	44	63	110	62
75th	63	75	155	111
90th	101	158	193	163
– GM (GSD)	38.9 (2.4)	54.7 (2.9)	102.8*° (1.8)	57.7 (2.5)
Cotinine urine (µg/l)				
– n.<LOD	40	16	0	56
– Percentiles:				
10th	<LOD	<LOD	400	<LOD
25th	<LOD	<LOD	815	<LOD
50th	<LOD	<LOD	1300	<LOD
75th	<LOD	53	1967	550
90th	<LOD	140	2613	1767
– GM (GSD)	11.0 (1.5)	21.2* (2.8)	1069.3*° (2.4)	55.8 (8.9)

GM: Geometric Mean – GSD: Geometric Standard Deviation
<LOD=<level of detection (Benzene blood: 35 ng/l; Toluene blood: 35 ng/l; t,t-MA urine: 5 µg/l; Cotinine urine: 20 µg/l)
*=$p<0.05$ (Student's *t*-test vs. Non-smokers non-ETS exposed)
°=$p<0.05$ (Student's *t*-test vs. Non-smokers ETS exposed)

logical indicators according to tobacco smoke. All the biological indicator levels were significantly higher in active smokers than in non-smokers non-exposed to ETS; t,t-MA and cotinine urinary levels were also significantly higher in non-smokers exposed to ETS than in non-smokers non-exposed to ETS.

Due to the complexity of the kinetics of benzene in the organism, the relation between personal exposure and biological indicators will be the subject of a separate paper (Carrer et al., paper in preparation).

Discussion

The TVOC home and office personal exposure levels observed in this study (373.2 and 668.2 µg/m^3, respectively) are in agreement with those found in other building studies carried out in Milan (Cavallo, 1993; Carrer, 1996). The Milan levels of 1995–1996 are comparable with those found in the European AUDIT project in the UK, Greece and France (range 200–1000 µg/m^3) and higher than those found in Germany, Finland, The Netherlands and Denmark (range 100–400 µg/m^3) (Bluyssen, 1996). In terms of health risk, the majority of the office workers studied resulted to be exposed to TVOC concentrations exceeding the recommended indoor air quality guideline values. A level of 200 µg/m^3 has been proposed from the toxicological data published in indoor air pollution literature (Mølhave, 1991) and a level of 300 µg/m^3 has been recommended based on existing levels and professional judgement about the achievable levels (Seifert, 1990).

Benzene personal levels of this study (daily ex-

posure: 21.2 $\mu g/m^3$) are in line with the urban Italian population exposure (range of daily exposure: 10–30 $\mu g/m^3$) estimated by the Italian National Toxicology Committee (Camoni, 1998). Comparable home levels (average 20 $\mu g/m^3$) were also found in a study of 15 houses in Northern Italy several years ago (De Bortoli, 1985). Our benzene levels, however, are lower than those found in subjects of Turin, Italy (mean during day 51.8 $\mu g/m^3$, mean during night 58.6 $\mu g/m^3$) (Gilli, 1994) and higher than those found in the United States by the TEAM study (mean range 7–13 $\mu g/m^3$) (Wallace, 1989). Personal benzene exposure levels in Milan in 1995 largely exceeded the target level of 10 $\mu g/m^3$ established by the Italian Ministry of Environment for the outdoor air (Ministerial Decree, 1994).

Very high exposure levels to benzene, TVOCs and toluene were found during commuting by cars in this study, like in other studies (Chan, 1991; Nordlinger, 1987; van Wijen, 1995); the pattern of higher levels in cars than in buses is consistent with the findings of the study by Jo et al. (1998). However, commuting exposure to VOCs, due to its short duration, on average accounted for only about 5% of the total 24-h exposure.

The exposure levels found in the different micro-environments in this study emphasise the need for a better control of the indoor VOC sources to reduce exposure of office workers in Milan.

Important information about exposures to VOCs has been provided by the TEAM study (Wallace, 1989) where mean personal exposures to the VOCs were greater than mean outdoor concentrations and the identified specific sources of exposure included active and passive smoking, and use of air fresheners or deodorisers. A further interesting result of the TEAM study was that inhalation provided more than 99% of exposure for the VOCs.

In our study the significant correlations among the exposure levels of the VOCs suggest the presence of a relatively uniform exposure pattern originating from common sources, most represented by tobacco smoke and traffic.

The measured biological indicators confirmed that tobacco smoke is a key factor determining exposure and body levels of benzene (and, to a lesser extent, toluene), both for active smokers and for non-smokers exposed to ETS (Wallace, 1989; IPCS, 1993). However the differences between non-smokers with and without ETS exposure were smaller than the differences with active smokers. Blood benzene concentrations were significantly affected by smoking and in the range reported by other authors for general urban populations (Brugnone, 1992; Ong, 1994; Fustinoni, 1995). In agreement with other studies (Ruppert, 1997; Pezzagno, 1999), the normal background excretion of t,t-MA in non-smokers was found to lower than 50 $\mu g/l$, while higher levels were found in non-smokers ETS-exposed and in active smokers. As concerning urinary cotinine, in agreement with previous studies, the levels in non-smokers are usually less than 20 $\mu g/l$ and the discrimination threshold between active and passive smokers is from 50 to 100 $\mu g/l$ (Haufroid, 1998).

The analysis of the relation between personal exposure and biological indicators has to take into consideration the time of sampling with respect to exposure in the various micro-environments as well the kinetics of benzene distribution and metabolism. Due to the complexity of such analysis, the matter will be the subject of a separate paper (Carrer et al., paper in preparation).

The finding of an average TVOC exposure level higher in mechanically ventilated than in naturally ventilated offices indicates that mechanical ventilation is often ineffective to improve indoor air quality.

In our study, an effect of season on TVOC and benzene exposure was observed; it is interesting to note that, while TVOCs were consistently higher in winter in every micro-environment, benzene exposures at home and in the office showed a reversed pattern, with higher values in summer. Since it is well known that outdoor air pollution in the cities is greater in winter than in summer, the different behaviour of benzene point to the importance of indoor benzene sources as primary determinants of exposure at home and in the office. However a possible greater impact of outdoor air through an increased natural ventilation in summertime in both homes and offices has also to be taken into consideration.

In conclusion, the importance of tobacco smoke on benzene exposure warns that reducing the outdoor air levels of benzene without concomitantly reducing tobacco smoke exposure, will not bring about a remarkable decrease in personal benzene exposure for a large portion of the population; the high VOC levels found in cars suggest that recommending an increased use of public transport would be an effective policy to reduce general urban outdoor pollution and also individual VOC exposure.

The studied group is not fully representative of the general population of Milan because only office workers of two buildings were studied in working days and they were invited to restrict their own activities to home, office and transit. The results of this study have been extended by the EXPOLIS study where Milan was involved with other five European cities (Jantunen, 1998).

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