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Influence of short-term passive smoking on symptoms, lung mechanics and airway responsiveness in asthmatic subjects and healthy controls

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Influence of short-term passive smoking on symptoms, lung mechanics and airway responsiveness in asthmatic subjects and healthy controls. R. Jörres, H. Magnussen.
ABSTRACT: We studied the acute effect of passive smoking on symptoms, lung mechanics and airway responsiveness.

Twenty four patients with mild to moderate bronchial asthma (11 male and 13 female; mean(SD) age 34(15) yrs; forced expiratory volume in one second (FEV_1) 91(17) % pred) were investigated. Sixteen of them had a history of passive smoke-induced respiratory symptoms. For comparison we studied 16 controls (7 male and 9 female; mean(SD) age 31(9) yrs; FEV_1 106(13) % pred).

On two different days, the subjects were exposed in an exposure chamber for one hour to either ambient air (Sham) or environmental tobacco smoke (ETS). During exposure to ETS, the mean concentrations of particles and CO were 3,095 $\mu g \cdot m^{-3}$ and 20.3 ppm, respectively. Before and immediately after exposure, symptoms and lung mechanics were assessed, followed by an inhalation challenge to determine the provocative concentrations of methacholine necessary to increase specific airway resistance (sRaw) by 100%, (PC_{100}sRaw), and to decrease FEV_1 by 20% ($PC_{20}FEV_1$). In the asthmatic subjects, during Sham exposure, mean (SEM) decrease of sRaw and FEV_1 was 0.23(0.22) $cmH_2O \cdot s$ and 0.04(0.03) *l*, respectively, (NS). During ETS, mean(SEM) decrease of sRaw and FEV_1 was 0.55(0.46) $cmH_2O \cdot s$ and 0.13(0.06) *l*, respectively. The significance of this decrease, however, disappeared when taking into account the individual variability of FEV_1. Geometric mean(SEM) PC_{100}sRaw and $PC_{20}FEV_1$ were 0.35(1.32) and 0.23(1.34) $mg \cdot ml^{-1}$ after Sham, and 0.34(1.37) and 0.28(1.36) $mg \cdot ml^{-1}$ after ETS, respectively, with no difference between the two study days. In the controls, the two exposure conditions did not exert any significant effects on sRaw, FEV_1 and airway responsiveness. In all subjects, exposure to ETS was associated with significant discomfort mainly eye irritation but also airways irritation and chest tightness. In the asthmatic subjects, symptoms after ETS exposure were not correlated with the history of complaints caused by passive smoking.

Our observations suggest that in healthy subjects and in patients with mild to moderate asthma, symptoms induced by one hour of passive smoking are not explained by changes in lung mechanics and airway responsiveness.
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Many patients with bronchial asthma report respiratory symptoms related to acute passive exposure to cigarette smoke. However, relatively few studies have investigated whether these symptoms are associated with changes in lung mechanics and airway responsiveness. It has been reported that acute exposure to tobacco smoke induced no impairment [1, 2] or a significant impairment [3, 4] of lung mechanics in all [3, 4] or in only a subgroup [5] of asthmatic patients. The effects on airway responsiveness were not assessed [1, 3, 5], or airway responsiveness was found to be either increased [4] or decreased [2] by passive smoking. The conflicting data generated by these studies prompted us to reinvestigate the occurrence of symptoms and the changes of lung mechanics and airway responsiveness induced by passive smoking in patients with mild to moderate bronchial asthma. These data were compared to a control group of normal volunteers.

Methods

Subjects

We studied 24 patients with bronchial asthma (13 female, 11 male), aged 15–66 yrs (mean (SD) 34 (15)

yrs). The severity of their bronchial asthma was mild or moderate. Individual patient characteristics are given in table 1. Subjects were patients from our department of pneumology or volunteers. In all patients the diagnosis of bronchial asthma was based on typical symptoms, diurnal variation of early morning and daytime peakflow readings of at least 20%, and airway hyperresponsiveness to histamine or methacholine.

The spectrum of the severity of the disease is reflected by baseline forced expiratory volume in one second (FEV_1) in percentage of predicted [6] ranging from 52 to 121% and the intensity of the therapeutic regimen necessary to control the disease (table 1). Eight subjects did not need regular therapy, five subjects were on disodium cromoglycate (DSCG) only, two subjects inhaled, β_2-agonists occasionally, two subjects in combination with DSCG or ipratropium bromide. Six subjects inhaled corticosteroids and two subjects were on theophylline. In all subjects, inhaled bronchodilator aerosols were withheld at least six hours prior to each study session. Theophylline was taken as usual.

Of the 24 patients, 22 were judged to be atopic on the basis of history and a positive skin prick test to at least one common allergen (Allergopharma, Reinbek, Germany). All patients were nonsmokers and 16 complained of respiratory symptoms related to passive smoking (table 1).

During the study period and within the two weeks preceding the study, no subject suffered from an upper respiratory tract infection, experienced an uncommon burden of allergen, or reported on any other trigger which may worsen asthma. Therefore, all subjects were considered to be in a stable clinical condition.

The data obtained in our asthmatic subjects were compared to a group of 16 nonsmoking control subjects who did not complain of asthmatic symptoms (9 female, 7 male), aged 21–51 yrs (mean (SD) 37 (9) yrs). Eight of the controls had positive skin prick tests and four were moderately hyperresponsive to inhaled methacholine as defined by the provocative concentration producing a 20% decrease in FEV_1 ($PC_{20}FEV_1$) and 100% increase in specific airway resistance ($PC_{100}sRaw$) between 1–8 $mg \cdot ml^{-1}$. In the remaining control subjects PC values were >8 $mg \cdot ml^{-1}$ of methacholine. Three of the subjects were ex-smokers and five reported respiratory symptoms from passive smoking.

All subjects were instructed about the design of the study and gave their informed consent.

Exposure conditions

We used a 24 m^3 exposure chamber ventilated to ambient air. The air inside the room was moved by

Table 1. – Individual characteristics of the asthmatic subjects

Subject no.	Sex	Age yrs	VC *l*	FEV_1 *l*	FEV_1 % pred	Atopy	Smoker No/Ex	History of ETS	Therapy
1	F	23	3.01	2.67	100	+	No	+	D
2	M	17	5.60	4.25	89	+	No	+	B
3	M	43	5.46	4.76	106	+	No	+	Ci,B
4	M	42	5.10	3.28	77	+	No	-	-
5	M	46	4.67	3.91	100	+	Ex	+	-
6	F	15	4.41	3.34	86	+	No	+	-
7	F	45	3.70	2.67	92	+	No	+	Ci,B,I
8	F	41	3.36	2.25	80	+	No	+	Ci,B
9	F	31	4.13	2.97	85	+	No	-	D
10	M	34	4.66	3.49	79	+	Ex	-	-
11	F	29	3.91	3.14	96	+	Ex	+	B,I
12	F	31	4.78	4.24	125	+	No	+	D
13	M	34	5.05	3.95	94	+	No	-	Ci,B
14	F	64	3.50	2.75	121	+	No	-	Ci,I,T
15	M	20	5.94	4.66	97	+	No	-	Ci,B
16	M	61	3.93	1.71	52	+	Ex	-	B,T
17	F	66	2.08	1.20	57	-	No	+	-
18	F	16	3.08	2.35	70	+	No	+	-
19	F	22	5.11	4.34	109	+	No	-	-
20	M	27	7.18	4.67	89	+	No	+	D
21	F	54	2.62	2.32	96	+	No	+	D
22	M	21	4.00	3.31	82	+	No	+	B
23	M	20	4.61	3.93	87	+	No	+	B,D
24	F	24	3.88	3.33	105	-	No	+	-
Mean		34	4.32	3.31	91				
SD		15	1.14	0.96	17				

B: inhaled β_2-sympathomimetics; Ci: inhaled corticosteroids; D: disodium cromoglycate; I: ipratropium bromide; T: theophylline; VC: vital capacity; FEV_1: forced expiratory volume in one second; ETS: environmental tobacco smoke exposure.

fans in order to ensure stable and homogeneous concentrations of cigarette smoke. Patients were seated at the same place throughout the exposure. We checked for gradients of gas concentrations and particle density by measuring at different sampling ports inside the room. Cigarette smoke was generated by a smoking machine designed in our laboratory, which took one puff per cigarette per minute (according to DIN 10240). To achieve a target concentration of 20 ppm CO, on average two cigarettes were smoked simultaneously. We used filter cigarettes of a leading brand (nicotine 0.9 mg, tar 13 mg per cigarette).

The concentration of CO was measured continuously by an infrared analyser (Unor 6N, Maihak AG, Hamburg, Germany) and was used to control the level of cigarette smoke in the exposure room. The calibration was checked daily by a certified calibration gas (Linde AG, Unterschleissheim, Germany). The concentration of NO_x was measured by a chemiluminescence nitrogen oxides analyser, which was calibrated regularly by a permeation tube calibrator (Models 8840 and 8550, Monitor Labs Inc., San Diego, CA, USA). Optical particle density was used to check the stability of cigarette smoke and was monitored continuously by an infrared light scattering monitor RAM-1 (GCA/Environmental Instruments, Bedford, MA, USA) using a 4 μm precollector. Repeated calibration of optical particle density was performed gravimetrically by taking filter probes (FALP 03700, Type FA, Millipore GmbH, Eschborn, Germany). Nicotine, acetaldehyde, formaldehyde, acrolein and ammonia were determined using commercially available sample tubes at sampling volumes of 3–100 *l* of air. Sampling flows were continuously controlled (Optiflow 650, Supelco GmbH, Bad Homburg, Germany). Nicotine was analysed by gas chromatography [7]. Acetaldehyde, formaldehyde and acrolein were determined by the high-performance liquid chromatography (HPLC) (dinitrophenylhydrazine method), and ammonia by VDI 2461 (indophenol method). Temperature and relative humidity were measured at the beginning and end of each exposure.

Lung mechanics measurement

Airway resistance during breathing at 1 Hz and thoracic gas volume were measured by a volume-constant body plethysmograph (Bodytest, E. Jaeger, Würzburg, Germany) connected to a Computer (PDP 11/04, Digital Equipment Corp., Maynard, MA, USA). Airway resistance was multiplied by the corresponding thoracic gas volume to obtain sRaw. Airway resistance was averaged from up to four breathing cycles. FEV_1 was assessed by a pneumotachograph immediately after body plethysmography. Measurements were repeated four times. For analysis, the average of the four values of sRaw and the maximum value of FEV_1 were taken. Analysis of COHb using capillarized blood from the ear was performed by a CO-oxymeter (2500 CO-Oximeter, Ciba Corning Diagnostics, GmbH).

Assessment of symptoms

The severity of symptoms induced by exposure was estimated with a questionnaire having an ordinal scale ranging from zero to ten. We determined the severity of eye, nose and throat irritation, and the degree of cough, chest tightness and headache. The subjects were instructed that zero indicated no perceptible symptom and ten an almost intolerable severity of the respective symptom.

Methacholine inhalation challenge

Bronchial challenges with methacholine were performed according to the guidelines of CHAI *et al.* [8] using a breath-synchronized pressure valve. In this method, the aerosol was produced over 0.6 s at the beginning of five slow inspirations from functional residual to total lung capacity. The output was 80 μl of solution per five nebulizations. Solutions of methacholine-chloride (Sigma Chemie, Deisenhofen, Germany) in phosphate buffer were prepared daily. After inhaling buffer solution, the patients inhaled doubling concentrations of methacholine, the starting concentration being adjusted individually according to baseline airway responsiveness. Lung mechanics were measured 1 and 3 min after inhalation. The inhalation was stopped after at least a 100% increase of sRaw and a 20% fall in FEV_1 had occurred as compared to the values after inhalation of the buffer solution, or when the highest concentration (16 $mg \cdot ml^{-1}$) had been reached. Dose-response curves were constructed by plotting sRaw and FEV_1 against log methacholine concentration. By linear interpolation, $PC_{100}sRaw$ and $PC_{20}FEV_1$ were computed as compared to baseline values. We used provocative concentrations instead of cumulative breath units proposed in [8], since they are interpreted more readily and are equivalent to cumulative dosages. We always started at the same concentration of methacholine in Sham and environmental tobacco smoke (ETS) exposures. Based on the correlation between different methods of bronchial challenges [9], hyperresponsiveness was defined by PC values <8 $mg \cdot ml^{-1}$ [10].

Study design

Each subject was studied at the same time of the day on two different days within a two week period. All subjects denied exposure to tobacco smoke at least 12 h before the test. Before the test, subjects rested during 10 min while completing the symptom score. Baseline lung mechanics consisted of four measurements. COHb was determined before the subjects entered the exposure room. The subjects, sitting quietly, were exposed in random order to ambient air (Sham) or cigarette smoke (ETS). Five minutes before the end of exposure, the subjects reassessed their symptoms, and immediately after exposure, lung

mechanics was measured again four times. Twenty minutes after the end of exposure, the methacholine inhalation challenge was started.

Data evaluation and statistics

We computed arithmetic mean values and standard errors of the mean (SEM) of the lung mechanics parameters before and after exposure to Sham or ETS and their changes during exposure. These values were compared by the Wilcoxon matched-pairs signed-ranks test [11]. We took an appropriate Bonferroni correction for the multiplicity of tests into account [12]. Geometric mean values and standard errors of the mean were computed for the PC values measured after Sham or ETS. The Wilcoxon matched-pairs signed-ranks test was used to compare PC values.

Most of our control subjects did not reach a 20% fall in FEV_1 or a 100% increase in sRaw during the methacholine challenge. Therefore, we compared their values of FEV_1 and sRaw after inhalation of the highest concentration of methacholine, which was administered both after Sham and ETS exposure. We evaluated the bronchial responsiveness by computing the absolute and relative changes of these FEV_1 and sRaw with respect to the values obtained after inhalation of buffer solution. These differences were compared by the Wilcoxon matched-pairs signed-ranks test.

Within groups, symptoms, oxygen tension (Po_2) and carbon dioxide tension (Pco_2) in the blood, and COHb were compared by the Wilcoxon matched-pairs signed-ranks test. Between groups, symptoms were compared by the Mann-Whitney U-test [11]. Correlation was assessed by the Spearman rank correlation coefficient [11]. The level of statistical significance was set at p=0.05.

Results

Exposure conditions

During Sham and ETS exposure, mean (SD) temperature was 23.4(1.4) and 23.7(1.6), °C, respectively, and mean relative humidity was 51(5) and 52(5)

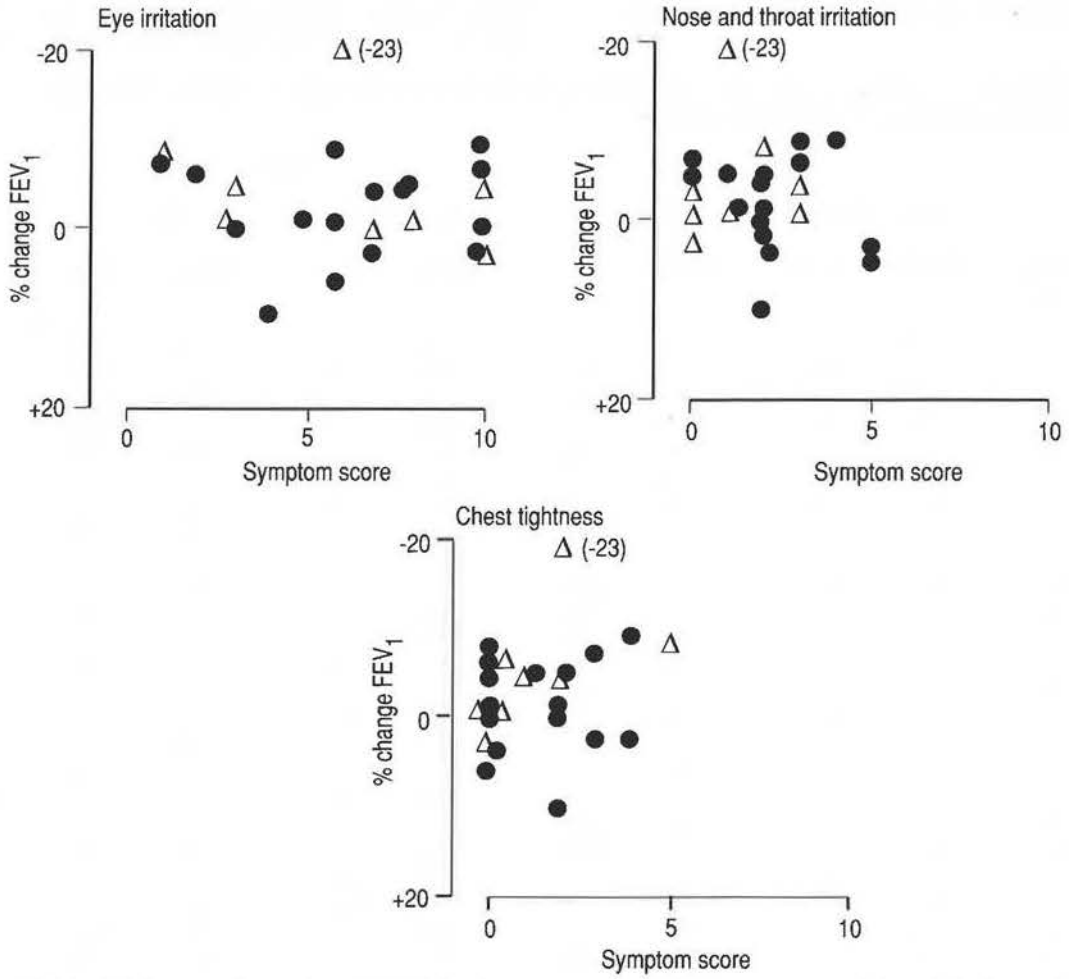

Fig. 1. – Relationship between the severity of ETS-induced symptoms separated for eyes, nose and throat irritation, and chest tightness and the percentage change of pre- and post-ETS exposure FEV_1 in the asthmatic subjects. Before ETS exposure all symptom scores were zero. Subjects with (●) and without (Δ) a history of passive smoke-induced chest symptoms. ETS: environmental tobacco smoke; FEV_1: forced expiratory volume in one second.

%, respectively, with no difference between the study days. Mean(SD) total particle density during Sham and ETS exposure was <7 and 3,095(769) $\mu g \cdot m^{-3}$, respectively, and mean(SD) CO was 0.20(0.35) and 20.3(0.8) ppm, respectively. In repeated determinations, ETS was found to be associated with a mean(SD) nicotine concentration of 397(78) $\mu g \cdot m^{-3}$, NO_x 0.90(0.09) ppm, formaldehyde 0.13(0.01) ppm, acetaldehyde 0.50(0.05) ppm, acrolein 0.08(0.02) ppm, and ammonia 5.7(3.4) ppm.

Symptoms

In the subjects with bronchial asthma, compared to Sham exposure, ETS induced significant increases in irritation of the eyes ($p<0.0001$), nose ($p=0.003$), and throat ($p=0.04$), headache ($p=0.005$), and tightness of chest ($p=0.002$), but no significant increase in cough. The severity of eye irritation, nose and throat irritation and chest tightness is plotted against the percentage changes between pre- and post-FEV_1 associated with ETS exposure in the asthmatic subjects in figure 1. The data demonstrate that symptoms could not be predicted by the history or by the change in FEV_1.

In the control subjects, ETS induced significant increases in irritation of the eyes ($p=0.004$), nose ($p=0.002$), throat ($p=0.03$), and cough ($p=0.008$), but no significant increases in tightness of chest and headache.

The severity of ETS-induced symptoms was not significantly different in the subjects with asthma and the controls and did not differ between subjects with and without history of passive smoke-induced complaints (table 1).

Lung mechanics

Asthmatic subjects. Individual values of sRaw and FEV_1 measured before and after the two exposure protocols are shown in table 2, and mean results are summarized in figure 2.

Baseline sRaw and FEV_1 before Sham and ETS did not differ statistically from each other and showed mean(range) intra-individual coefficients of variation of 16.8(0–64) % for sRaw and 4.4(0–17) % for FEV_1.

With Sham, the mean(range) percentage change from pre- to post-exposure sRaw was -1.5(-21–+20) % (NS) and for FEV_1 -0.5(-8–+12) % (NS).

Table 2. – Effect of one hour exposure to sham or ETS on specific airway resistance (sRaw) and FEV_1 in asthmatic subjects

	Sham				ETS			
	sRaw $cmH_2O \cdot s$		FEV_1 *l*		sRaw $cmH_2O \cdot s$		FEV_1 *l*	
Subject no.	Before	After	Before	After	Before	After	Before	After
1	7.4	8.3	2.58	2.53	5.4	4.9	2.75	2.49
2	7.1	6.4	4.12	4.17	6.6	7.8	4.37	4.15
3	2.9	3.4	4.71	4.33	2.9	3.3	4.80	4.35
4	6.9	7.7	3.18	3.23	6.3	7.0	3.33	3.18
5	7.7	7.2	3.98	3.68	6.3	7.5	3.83	3.84
6	8.5	6.9	3.30	3.29	8.2	8.3	3.37	3.13
7	6.2	5.4	2.71	2.78	5.1	4.6	2.62	2.62
8	9.0	7.6	2.13	2.28	7.8	7.1	2.36	2.50
9	11.5	9.1	3.11	3.29	13.5	13.8	2.83	2.81
10	6.9	6.7	3.51	3.59	9.7	8.8	3.47	3.41
11	9.5	9.0	3.13	3.04	8.0	7.9	3.15	2.91
12	3.7	3.7	4.21	4.07	4.4	4.3	4.27	4.05
13	9.9	9.9	3.90	3.74	11.4	7.6	3.99	3.82
14	5.0	4.8	2.60	2.44	2.4	2.5	2.90	2.65
15	15.1	16.8	4.08	3.94	5.8	8.7	5.23	4.04
16	16.2	14.2	1.56	1.75	10.5	8.3	1.86	1.92
17	11.6	13.0	1.20	1.19	11.0	11.4	1.20	1.24
18	9.7	8.3	2.24	2.29	8.8	7.5	2.45	2.31
19	5.1	5.6	4.42	4.28	4.9	4.7	4.26	4.24
20	6.0	7.2	4.97	4.69	8.0	8.1	4.36	4.32
21	6.2	5.4	2.26	2.11	5.4	4.8	2.38	2.45
22	10.9	10.9	3.42	3.38	11.1	10.7	3.20	3.16
23	8.0	7.7	4.04	4.27	21.3	11.9	3.82	4.21
24	4.7	5.1	3.35	3.40	5.3	5.4	3.31	3.16
Mean	8.2	7.9	3.28	3.24	7.9	7.4	3.34	3.21
SEM	0.7	0.7	0.20	0.19	0.8	0.6	0.20	0.17

For abbreviations see legend to table 1.

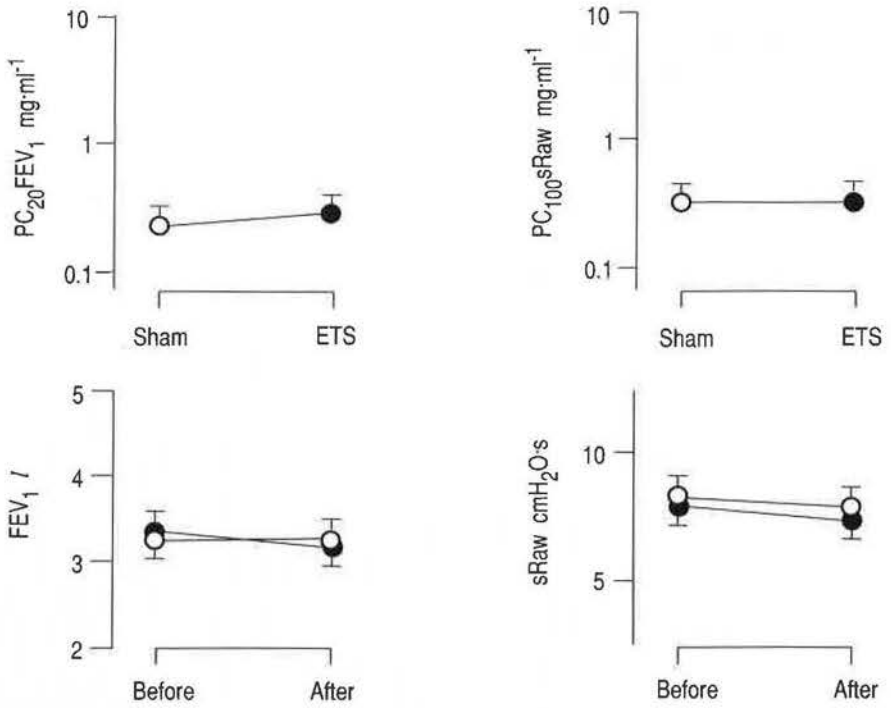

Fig. 2. – Upper panels: $PC_{20}FEV_1$ and PC_{100}sRaw after exposure to Sham and ETS on a log scale. Lower panels: FEV_1 and sRaw before and after exposure to Sham and ETS. Values are geometric mean, bars represent SEM. ○: Sham: ●: ETS; $PC_{20}FEV_1$: provocative concentration of methacholine producing a 20% decrease in FEV_1; PC_{100}sRaw: provocative concentration of methacholine producing a 100% increase in specific airway resistance. For further abbreviations see legend to figure 1.

After ETS, corresponding changes were -1.9(-44–+50) % for sRaw (NS) and -3.1(-23–+10) for FEV_1 (p=0.011). This difference in FEV_1 was not significant taking into account post- *vs* pre-FEV_1 differences after Sham.

COHb increased significantly after ETS (p=0.0002), the mean(SEM) change was 0.43(0.04) %.

Control subjects. Mean(SEM) baseline sRaw and FEV_1 before Sham were 4.8 (0.3) cmH_2O·s and 4.22(0.20) *l* and before ETS exposure were 4.4(0.3) cmH_2O·s and 4.23(0.20) *l*, respectively. There was no significant difference between both exposures. Mean(range) intra-individual coefficients of variation were 10.4(2–30) % for sRaw and 2.5(0–12) % for FEV_1.

After Sham, mean(SEM) sRaw and FEV_1 were 4.8(0.3) cmH_2O·s and 4.22(0.22) *l*, and after ETS exposure were 4.8(0.3) cmH_2O·s and 4.13(0.19) *l*, respectively. With Sham, the mean(range) percentage change from pre- to post-exposure sRaw was 1.6(-30–+25) % (NS) and for FEV_1 -0.2(-11–+10) % (NS). After ETS, corresponding changes were 11.0(-17–+44) % for sRaw (NS) and -2.0(-9–+6) % for FEV_1 (NS).

COHb increased significantly after ETS (p=0.003), the mean(SEM) change was 0.55(0.06) %.

Airway responsiveness

Asthmatic subjects. Individual values of PC_{100}sRaw and $PC_{20}FEV_1$ measured after Sham and ETS are given in table 3. Geometric mean values and SEM are shown in figure 2.

PC_{100}sRaw and $PC_{20}FEV_1$ after Sham exposure were not significantly different from those obtained after ETS exposure. In 5 (2) subjects PC_{100}sRaw ($PC_{20}FEV_1$) after ETS was at least one doubling concentration lower than after Sham; in 5 (5) subjects it was higher by at least one doubling concentration; and in 14 (17) subjects the difference was within one doubling concentration of methacholine.

Control subjects. After Sham, the mean(SD) percentage changes after breathing the highest concentration of methacholine were 122(110) % for sRaw and -17(19) % for FEV_1. After ETS, the changes after methacholine were 103(94) % for sRaw and -18(16) % for FEV_1. These values did not differ significantly between Sham and ETS.

Correlation analysis

In the asthmatic subjects, the individual percentage changes of sRaw and FEV_1 during Sham exposure were significantly correlated (r=-0.46, p<0.025). During ETS, the correlation coefficient was r=-0.39 (p<0.05). There was a significant correlation between the changes in FEV_1 during Sham and ETS (r=0.39, p<0.05). The individual changes of lung mechanics during exposure to ETS and the individual differences of PC values between ETS and Sham did not correlate.

Table 3. – Provocative concentration of methacholine necessary to increase sRaw by 100% (PC_{100}sRaw) and to decrease FEV_1 by 20% ($PC_{20}FEV_1$) after one hour exposure to sham or ETS in asthmatic subjects

Subject no.	PC_{100}sRaw mg·ml^{-1}		$PC_{20}FEV_1$ mg·ml^{-1}	
	Sham	ETS	Sham	ETS
1	0.69	0.12	0.06	0.09
2	1.32	1.41	0.85	1.84
3	0.61	0.40	0.33	0.17
4	1.19	0.28	1.19	1.27
5	2.80	0.96	4.62	2.29
6	0.10	0.38	0.15	0.08
7	3.50	2.70	1.13	2.58
8	0.69	1.04	0.59	0.51
9	0.05	0.05	0.06	0.05
10	0.06	0.09	0.07	0.08
11	0.46	1.66	0.21	1.16
12	1.13	0.68	0.43	0.41
13	0.32	0.40	0.25	0.36
14	2.25	>16.0	2.16	5.94
15	0.07	0.05	0.03	0.04
16	0.11	0.05	0.22	0.14
17	0.35	0.58	0.10	0.16
18	0.10	0.10	0.07	0.10
19	0.21	0.56	0.26	0.35
20	0.09	0.21	0.08	0.29
21	0.21	0.16	0.11	0.09
22	0.11	0.09	0.05	0.08
23	0.09	0.03	0.05	0.02
24	2.61	2.25	2.28	1.42
Mean*	0.35	0.34	0.23	0.28
SEM*	1.32	1.37	1.34	1.36

*: geometric mean values and standard errors of mean. For further abbreviations see legend to table 1.

Symptoms induced by ETS did not correlate with the observed changes in lung function during exposure for asthmatic subjects (see figure 1) or the differences between airway responsiveness after Sham and ETS.

Discussion

In this study we have demonstrated that in subjects with mild to moderate bronchial asthma one hour of passive smoking induced significant discomfort which was mainly based on irritation of the eyes and the upper respiratory tract and produced a small mean decrease in FEV_1 not associated with a corresponding mean increase in specific airway resistance. ETS-induced symptoms could not be predicted from the history of passive smoke-related complaints. Airway responsiveness to methacholine, as estimated from spirometric ($PC_{20}FEV_1$) or body plethysmographic (PC_{100}sRaw) measurements, was not influenced by the passive smoking challenge. In the control group, although symptoms were similar, exposure to cigarette smoke was not accompanied by any significant changes of lung mechanics and airway response to methacholine.

Bronchial asthma is characterized by respiratory symptoms associated with variable airway calibre and airway hyperresponsiveness. Airway hyperresponsiveness can be demonstrated to a whole spectrum of stimuli, and it has been suggested that ETS is one of them [4]. Because many patients with bronchial asthma spontaneously report respiratory symptoms during or immediately after exposure to ETS, a relationship between ETS-induced symptoms, airway calibre, and airway responsiveness would fit into our current understanding. However, only few studies on the acute effect of ETS have been performed, and they have shown conflicting results.

SHEPHARD *et al.* [1] investigated 14 asthmatic subjects during a two hour exposure to ETS (24 ppm CO) and observed no significant changes in pulmonary mechanics. DAHMS *et al.* [3] exposed 10 asthmatic subjects to ETS at 15–20 ppm CO for one hour and found a 22% decrease in FEV_1. No change was seen in normal control subjects. KNIGHT and BRESLIN [4] studied six patients with asthma. After a one hour exposure to ETS at 15–25 ppm CO, FEV_1 had fallen by 11%, and four hours after exposure bronchial reactivity to inhaled histamine was increased. WIEDEMANN *et al.* [2] studied the acute effect of a one hour chamber exposure to a very high concentration of ETS (40–50 ppm CO) on lung mechanics and airway responsiveness in nine asthmatic patients. No significant changes in lung mechanics were detected, however, airway responsiveness to methacholine decreased after ETS. STANKUS *et al.* [5] investigated the effect of a two hour exposure to ETS (9–14 ppm CO) in 21 subjects with asthma, who previously claimed respiratory symptoms from ETS exposure. In 7 of these 21 subjects, a fall in FEV_1 of >20% was found. These findings suggest that there might be a subgroup of "smoke-sensitive asthmatic subjects" who develop acute airway obstruction after breathing ETS.

In our asthmatic subjects we found a significant mean decrease between pre- and post-FEV_1 after ETS. This difference, however, cannot simply be interpreted as airway obstruction induced by ETS exposure, as there was no increase in sRaw. The difference in FEV_1 disappeared when taking into account post *vs* pre changes in FEV_1 after Sham. The changes in lung mechanics could not be predicted by the history of ETS-induced symptoms (fig. 1).

Analysis of the individual data supports the suggestion that this decrease in FEV_1 was not causally related to ETS. The two baseline lung mechanics values measured on the two study days showed a mean coefficient of variation between days of 4.4% for FEV_1 and 16.8% for sRaw, which were within the reported range of reproducibility [11]. Three subjects (nos 14, 15 and 23) showed a more than twofold difference in baseline sRaw and one subject (no. 15) a more than 20% difference in baseline FEV_1 between the study days. Therefore, our results are not explained by weak reproducibility of lung mechanics measurement.

Subject no. 15 showed a decrease in FEV_1 by 23% after ETS compared to 3% after Sham. sRaw increased by 50% after ETS and by 11% after Sham (table 2). Therefore, subject no. 15 might be suspected of being a "smoke-sensitive" patient. The symptoms complained of by subject no. 15 were similar to those of patients who did not show any ETS-induced change in lung mechanics. On the other hand, subject no. 23 showed an increase in FEV_1 by 10% after ETS and 6% after Sham. After ETS and Sham exposure, sRaw fell by 44 and 4%, respectively (table 3). Therefore, lung mechanics improved during ETS exposure, although ETS-induced symptoms were reported. In subjects no. 15 and 23, co-operation was acceptable as in all others. Therefore, analysis of the individual lung mechanics data showed some inhomogeneity in the response of our asthmatic subjects, with one subject possibly sensitive to ETS and another improving during passive smoking despite similarly high levels of airway hyperresponsiveness (table 3).

In the control group, no consistent pattern of the airway response to ETS or Sham exposure could be seen. The maximum changes of FEV_1 during ETS were 9%, and of sRaw 25%.

Airway hyperresponsiveness to inhaled methacholine in terms of $PC_{20}FEV_1$ and PC_{100}sRaw was assessed two times on the two different study days. In most cases, the two challenges showed a difference of ±one doubling concentration of methacholine, which is within accepted limits [13, 14]. In about 20% of the subjects, PC values after ETS were at least one doubling concentration lower than after Sham, and in about as many subjects they were higher by at least one doubling concentration. An ETS-induced increase in airway responsiveness was not associated with more pronounced symptoms or a decrease in FEV_1. The history of ETS-induced symptoms did not predict the pattern of changes in airway responsiveness. The same was true for our control subjects.

We computed the power of our statistical procedures on the basis of a 5% variability in FEV_1, a clinically significant difference in FEV_1 of at least 5%, an error level of 0.05 and a sample size of 24 subjects. The power was larger than 90% for both the separate and the combined evaluation of both exposures. The same values resulted for $PC_{20}FEV_1$ using a reproducibility of ±one doubling concentration of methacholine. It is, therefore, unlikely that we missed, by chance, an effect of ETS larger than the variability of these parameters.

In summary, our data on lung mechanics before and after ETS do not support the hypothesis that inhalation of ETS is followed by airway obstruction. In particular, from our data respiratory symptoms in "smoke-sensitive" subjects are unlikely to be based on airway obstruction. Respiratory symptoms, however, could be observed in all of our asthmatic subjects during the inhalation challenge with methacholine.

The results of the present study in adult asthmatic subjects are very similar to those that we obtained in children using a similar exposure protocol [15].

In both studies, we analysed some of the substances contained in tobacco smoke [16]. The concentrations of single components of ETS (*e.g.* CO, NO_x, formaldehyde, acrolein and aerosolized nicotine) were found to be lower than those effective in single exposure studies (for further discussion see [15]).

We measured airway responsiveness to methacholine 20 min after the end of exposure. This time schedule was chosen because most subjects reported symptoms in direct conjunction to the ETS exposure. There are substances, *e.g.* NO_2, which may already exert their influence on airway responsiveness at short time intervals after exposure [17]. On the other hand, components are known, *e.g.* ozone, which may induce an increase of airway responsiveness over several hours after exposure [18]. Therefore, in principle, by our measuring protocol we might have missed effects of cigarette smoke exposure on airway responsiveness. This possibility should be borne in mind and deserves further investigation.

Most of our asthmatic patients were under therapy with a variety of compounds (table 1). Exposure was started at least six hours after the last inhalation of β_2-agonists or ipratropium bromide to ensure that the effect of these compounds on airway tone and airway responsiveness had ceased [19]. In some subjects, we cannot exclude an attenuating effect of DSCG and inhaled corticosteroids. However, it should be noted that the airways of these subjects were hyperresponsive to inhaled methacholine despite the therapy. In addition, those asthmatic subjects without therapy and with regular therapy did not show different responses to ETS exposure. Thus, it is unlikely that therapy had a major impact on our results.

In conclusion, in the present acute exposure study, we were not able to demonstrate consistent effects of one hour of passive cigarette smoking on lung mechanics and airway responsiveness. These observations in adult asthmatic patients and control subjects are in accordance with our data from asthmatic children [15]. Respiratory symptoms caused by passive smoking exposure in our asthmatic subjects and controls could not be explained by concomitant changes in lung mechanics and airway responsiveness. It should be stressed that our results on the acute effects of passive smoking do not interfere with the increasing bulk of information demonstrating an adverse effect of chronic cigarette smoke exposure in adults and children [20, 21].

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