



Prolonged occupational exposure leads to allergic airway sensitization and chronic airway and systemic inflammation in professional firefighters



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ARTICLE INFO

Article history:

Received 21 January 2016

Received in revised form

7 July 2016

Accepted 7 July 2016

Available online 13 July 2016

Keywords:

Firefighters

Airway inflammation

Systemic inflammation

Allergic sensitization

ABSTRACT

Background and objectives: Little data exist on short- and long-term effects of occupational exposure on airway and systemic inflammation in professional firefighters. We aimed to characterize airway and systemic inflammation in training firefighters with a maximum occupational exposure of 1 year compared to the long-term exposure of professional firefighters.

Methods: A questionnaire for symptoms and exposure, pulmonary function, atopy, bronchial hyper-responsiveness, and markers of inflammation in induced sputum, serum, bronchoalveolar lavage (BAL) fluid and bronchial biopsies were assessed in a total of 92 firefighters (63 full-time professionals and 29 trainees).

Results: Professional firefighters showed allergic bronchial sensitization documented by the presence of atopy, and eosinophilia in induced sputum, BAL and bronchial biopsies. IL-8, ECP, VEGF, and TNF- α levels were statistically significantly higher in the sputum supernatants of professional firefighters compared to the trainees ($p = 0.04$, $p = 0.02$, $p = 0.04$, and $p = 0.02$, respectively). Serum IL-8 and TNF- α levels were also statistically significantly higher in the group of professional firefighters ($p = 0.04$, $p = 0.03$, respectively). Finally, there was a linear correlation between the duration of the occupation in Service and the degree of airway and systemic inflammation.

Conclusions: These results indicate a "dose-response" effect of chronic exposure to a polluted environment on bronchial and systemic inflammation in professional firefighters.

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1. Introduction

Professional firefighters have prolonged and direct exposure to smoke and to a wide variety of inhaled particles and particulates [1,2] which are inhaled into the respiratory tract. Several epidemiological and toxicological data show the adverse effects of inhaled smoke from the burning of wood and biomass on cardiopulmonary morbidity [3–5]. Exposure to air pollutants (combustion products) may lead to increased sensitization to airway

Abbreviations: FEV₁, forced expiratory volume; FVC, forced vital capacity; TLC, total lung capacity; RV, residual volume; KCO, CO transfer coefficient; PD20meth, provocative dose of methacholine producing a 20% fall in FEV₁; ECP, Eosinophilic cationic protein; IL-8, Interleukin-8; IL-4, Interleukin-4; IL-13, Interleukin-13; TNF- α , tumor necrosis factor-alpha; VEGF, vascular endothelial growth factor; BALF, bronchoalveolar lavage fluid.

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allergens [6,7]. Studies examining respiratory symptoms and pulmonary function in professional firefighters have found increased symptoms, and airways hyper-responsiveness, and declined lung function during fire fighting periods and seasonally [5,8–12].

These observations suggest that firefighting is associated with upper and lower airways inflammation and raise concern about the potential risk of long-term respiratory effects, including asthma, chronic obstructive pulmonary disease (COPD), and upper airways conditions, such as sinusitis [3,13–15]. Furthermore, apart from the inflammatory responses locally in the airways [16–19] a measurable systemic inflammatory response is also induced [20–25], which in turn is associated with an elevation of several cytokines (Interleukin (IL)-6, IL-1b) in the bloodstream [25], as well as increased production and release of polymorphonuclear leukocytes (PMN) and monocytes from the bone marrow [22–25].

Data from the firefighters involved in rescue operations during the World Trade Center attack showed that there is an association between the intensity of the exposure and the decline rate in pulmonary function parameters [8] as well as the persistence of airway hyper-responsiveness [12,26]. Aim of this study was to assess respiratory health and airway and systemic inflammation in young firefighters (trainees) with a part-time occupational exposure in firefighting for a year the most and compare it to that of professional firefighters with chronic occupational exposure.

To address this question we assessed symptoms, pulmonary function, atopy, bronchial hyper-responsiveness, and markers of inflammation in induced sputum, serum, bronchoalveolar lavage (BAL) fluid and bronchial biopsies.

2. Methods

2.1. Study population

A total of 92 male firefighters were included in this study (63 full-time professional firefighters, 29 trainees that had been working on a part-time basis for a year the most and 18 healthy subjects who served as a control group). All firefighters (professional and trainees) participated in similar operations and there was no difference in the use of respiratory protection equipment between the groups.

Firefighters were administered a standardized questionnaire assessing lifetime chronic respiratory conditions, history of tobacco use, history of upper and lower respiratory symptoms during fire fighting and during the interval periods, volunteer firefighter status, and lifetime occupational history.

Subjects underwent spirometry, sputum induction, methacholine provocation test and skin prick tests. Each subject attended the laboratory in two separate visits within one week. On visit one sputum induction was performed after reversibility test. On visit two, patients underwent methacholine provocation challenge and skin prick tests. Bronchoscopy was performed in a subgroup of 20 firefighters who volunteered, after signing an informed consent. There was no interest from the healthy subjects to undergo bronchoscopy.

All subjects gave informed consent for the participation in the study, which was approved by the Ethics Committee of Sotiria Hospital, IRB number: 16750.

2.2. Reversibility test

Lung function (FEV_1 , FEV_1/FVC) was measured with a dry wedge spirometer (Masterscreen, Jaeger, Hoechberg, Germany) according to standardized guidelines [27]. Reversibility test was performed 20 min after inhalation of 200 µg salbutamol via a metered dose inhaler.

2.3. Bronchial responsiveness to methacholine

BHR was measured as PD_{20} of methacholine using the dosimeter method by a commercially available system (APS; Viasys Healthcare, Jaeger, Hoechberg, Germany), according to ATS guidelines [28].

2.4. Skin prick tests

Atopic status was measured by skin-prick tests using 13 common aeroallergens applied to the fore-arm. The allergens tested (HAL allergen Lab B. V. Harlem) were house dust mites (*Dermatophagoides pteronyssinus* and *Dermatophagoides farinae*), household pets (cat and dog), pollens (mixed grass, olive, mixed weed, and *Parietaria judaica*) and molds (alternaria, and *Aspergillus fumigatus*). Histamine and glycerinated saline solution were used as positive and negative controls. Atopy was defined as having at least one positive skin prick test. A skin-prick test result was considered positive if the mean wheal diameter was at least 3 mm.

2.5. Sputum induction and processing

Sputum was induced by inhalation of hypertonic saline aerosol and processed as described previously [29], by using an ultrasonic nebulizer (ULTRA-NEB 2000, DeVilbiss Healthcare INC, Somerset, USA). Sputum samples containing >20% of squamous cells and with cell viability <70% were excluded from analysis as indication of poor quality. Sputum supernatants were stored at -80°C for subsequent assay for interleukin (IL)-4, IL-8, IL-13, TNF- α , vascular endothelial growth factor (VEGF), and eosinophil cationic protein (ECP) concentration.

2.6. Measurement of inflammation biomarkers

IL-8, IL-4, IL-13, VEGF, TNF- α , and ECP concentrations were measured in both serum and sputum supernatants. The concentrations of TNF- α , IL-8, IL-13, VEGF, and IL-4 were determined by ELISA using kits purchased from R & D Systems (Minneapolis, Minnesota, USA). The sensitivities of the assays used were 1.6 pg/ml, 3.5 pg/ml, 32 pg/ml, 9 pg/ml, and 10 pg/ml, respectively. ECP was measured using Unicap ECP kit (Pharmacia Diagnostics; Uppsala, Sweden) with a detection limit of 0.5 ng/ml. In all cases, the assays were carried out according to the manufacturer's recommendations.

2.7. Bronchoscopy

After local anesthesia of the throat, larynx, and bronchi which was achieved with 2% lidocaine, a flexible bronchoscope (BF 1T200; Olympus Optical; Tokyo, Japan) was introduced into the bronchial tree and gently wedged into the segmental bronchi of the right middle lobe. Four to six bronchial biopsies were obtained from segmental divisions of the main bronchi at the end of the bronchoscopic procedure. Collection, processing and microscopic evaluation of histological and cytological specimens were performed according to standard procedures.

2.8. Statistical analysis

Continuous variables are expressed as mean $\pm$ SD and categorical variables are expressed as relative frequencies and percentages. Fisher's exact test expanded with the use of linear regression was used for testing differences in the prevalence of respiratory symptoms, the provocative dose of methacholine, and atopy between groups. Differences in markers of inflammation between

study groups were initially assessed by Kruskal-Wallis test, and if significant by the Mann-Whitney rank test. Spearman's correlation was used to demonstrate the relation between years in Service and measures of inflammation. Comparisons were adjusted for age, smoking pack-years and pre-existing diagnosed asthma.

3. Results

General characteristics of study population are shown in Table 1.

Professional firefighters had atopy and allergic rhinitis in a statistically significantly higher percentage in comparison to trainees and healthy subjects ($p = 0.013$, and $p < 0.001$, respectively). Furthermore, in four of them a history of asthma was not previously acknowledged, and was documented through the protocol assessment. None of the participants reported a diagnosis of chronic obstructive pulmonary disease, bronchiectasis or any other chronic condition of the lung.

General respiratory symptoms such as cough, dyspnea, and sneezing were statistically significantly higher in the group of professional firefighters compared to trainees (Table 2). There were no significant differences in respiratory symptoms between trainees and healthy subjects (Table 2).

There were no significant differences in the mean values of pulmonary function test parameters between the groups (Table 1).

Thirteen (21%) professional firefighters had a positive methacholine challenge test based on a fall of $FEV_1 \geq 20\%$ compared to 1 (3%) in the trainees' group ($p = 0.042$) (Table 1).

3.1. Markers of inflammation

The analysis of the sputum samples revealed a significant increase of eosinophils in the group of the professional firefighters as compared to the trainees' and healthy subjects' groups (Table 3). Similarly, the analysis of BAL showed a significantly higher percentage of eosinophils in the group of professional firefighters compared to the trainees' group (Table 4). There were no significant differences between the study groups regarding the other cell types.

IL-8, ECP, VEGF, and TNF- α levels were found statistically significantly higher in the sputum supernatants of professional

firefighters as compared to the trainees and healthy subjects (Table 4, Fig. 1). Furthermore, serum IL-8 and TNF- α levels were statistically significantly higher in the group of professional firefighters (Table 4, Fig. 1). Trainees had significantly higher levels of sputum and serum IL-8 and TNF- α compared to healthy subjects (Table 5).

Finally, the longer duration of the occupation in Service correlated with higher number of cells in sputum and BAL, higher percentage of eosinophils, neutrophils and lymphocytes in sputum (Table 5). A linear correlation was also observed between the years in Service and sputum levels of ECP, as well as sputum and serum levels of VEGF.

3.2. Histological findings

Seventeen out of twenty specimens were eligible for histology. In the group of professional firefighters the most interesting histological finding was the atrophy of the bronchial epithelium and the squamous metaplasia (Fig. 2: A, B, C, D). There was a mild thickening of the basal membrane in all cases and focal increase of mucus production. Alterations in the number of eosinophils were observed ranging from rarity in 5 cases, mild in 7 cases and moderate in 1 case. In the cases of firefighters with histological findings of atrophy of bronchial epithelium a polymorphonuclear predominance was observed.

In all cases of trainees a mild thickening of the basal membrane was observed, with small increase in mucus production in almost all the samples, while the presence of eosinophils was rare, without obvious presence of lymphocytes or polymorphonuclears. (Fig. 2: E, F).

4. Discussion

Our study shows that prolonged occupational exposure of municipal and professional firefighters leads to allergic bronchial sensitization, a high incidence of chronic respiratory symptoms, and chronic airway and systemic inflammation, which deteriorate along with the exposure years. The major novelty of this study lies on the objective documentation of allergic sensitization in professional firefighters by all measurable means, namely markers of

Table 1
Subjects' characteristics.

	Healthy subjects n = 18	Trainees n = 29	Professional firefighters n = 63	p
Age	30 $\pm$ 0.8	27 $\pm$ 0.8	33 $\pm$ 0.6	<0.001*
Smokers	9 (50%)	11 (38%)	21 (33%)	0.5
Ex-smokers	0	0	0	
Pack – Years	8 $\pm$ 4	6 $\pm$ 3	14 $\pm$ 2	0.09
Years in Service	–	1 $\pm$ 0.1	9 $\pm$ 1	<0.001**
Atopy#	3 (17%)	2 (10%)	27 (43%)	0.013**
History of asthma	1 (5%)	0	4 (6%)	0.035*
Allergic rhinitis	1 (5%)	2 (10%)	13 (20%)	<0.001**
FEV ₁ , % pred	103 $\pm$ 5	104 $\pm$ 4	103 $\pm$ 2	0.343
FVC, % pred	108 $\pm$ 9	104 $\pm$ 4	108 $\pm$ 2	0.326
FEV ₁ /FVC	93 $\pm$ 4	90 $\pm$ 3	86 $\pm$ 1	0.08
FRC, % pred	108 $\pm$ 5	110 $\pm$ 6	94 $\pm$ 3	0.09
TLC, % pred	98 $\pm$ 4	90 $\pm$ 3	95 $\pm$ 2	0.277
RV, % pred	96 $\pm$ 10	116 $\pm$ 13	92 $\pm$ 5	0.08
KCO, % pred	102 $\pm$ 6	103 $\pm$ 4	103 $\pm$ 2	0.321
Methacholine challenge (+)	1 (5%)	1 (3%)	13 (21%)	0.042**
PD20meth	425 $\pm$ 23	343 $\pm$ 58	463 $\pm$ 64	0.630

The bold values represents the statistically significant differences in the table.

All values are expressed as mean values $\pm$ SE, unless otherwise stated.

FEV₁: forced expiratory volume; FVC: forced vital capacity; TLC: total lung capacity; RV: residual volume; KCO: CO transfer coefficient; PD20meth: provocative dose of methacholine producing a 20% fall in FEV₁.

* $p < 0.05$ as compared to trainees; ** $p < 0.05$ as compared to trainees and healthy subjects; # at least one skin prick test positive to one of the tested antigens.

Table 2
Respiratory symptoms in trainees and professional firefighters.

	Healthy subjects N (%)	Trainees N (%)	Professional firefighters N (%)	p
Wheezing %	1 (5)	2 (10)	6 (9.5)	0.899
Cough %	2 (11)	2 (10)	41 (65)	<0.001
Nocturnal dyspnea %	1 (5)	1 (5)	8 (13)	0.07
Dyspnea %	1 (5)	1 (5)	14 (22)	0.01
Chest tightness	1 (5)	1 (5)	5 (8)	0.462
Chronic bronchitis	2 (5)	1 (5)	7 (11)	0.458
Chronic expectoration	2 (5)	1 (5)	6 (10)	0.642

The bold values represents the statistically significant differences in the table.

Table 3
Total and differential cell counts in sputum and bronchoalveolar lavage fluid (BALF).

	Healthy subjects n = 18	Trainees n = 29	Professional firefighters n = 63
Induced sputum			
Total no. of cells $\times 10^4$	38 $\pm$ 5	33 $\pm$ 3	42 $\pm$ 3
Macrophage %	38 $\pm$ 3	37 $\pm$ 3	43 $\pm$ 2
Neutrophils %	13 $\pm$ 6	19 $\pm$ 4	30 $\pm$ 2
Eosinophils %	0.4 $\pm$ 0.1	0.6 $\pm$ 0.7	2.1 $\pm$ 1.2*
Lymphocytes %	13 $\pm$ 8	13.5 $\pm$ 2	18.6 $\pm$ 62
BALF			
Total no. of cells $\times 10^4$		20 $\pm$ 3	28 $\pm$ 4
Macrophage%		83 $\pm$ 3	82 $\pm$ 2
Neutrophils%		1.6 $\pm$ 0.4	2.8 $\pm$ 0.7
Eosinophils%		0.4 $\pm$ 0.7	1.9 $\pm$ 0.8*
Lymphocytes%		11 $\pm$ 2	15 $\pm$ 2

All values are expressed as mean values $\pm$ SE, unless stated otherwise; *p < 0.05 as compared to trainees and healthy subjects.

Table 4
Markers of inflammation in induced sputum and serum.

	Healthy subjects n = 18	Trainees n = 29	Professional firefighters n = 63	p
Sputum IL-8 (pg/ml)	103 (9–256)	318 (53–423)	587 (131–1835)	0.04
Sputum TNF- α (pg/ml)	16 (1–123)	37 (10–88)	44 (23–760)	0.02
Sputum VEGF (pg/ml)	198 (5–325)	204 (8–368)	251 (104–693)	0.04
Sputum IL-4 (pg/ml)	3 (2–28)	4 (3–37)	4 (4–38)	0.74
Sputum IL-13 (pg/ml)	175 (143–305)	190 (175–322)	192 (173–1405)	0.49
Sputum ECP (pg/ml)	17 (3–84)	21 (3–91)	57 (3–95)	0.02
Serum IL-8 (pg/ml)	26 (9–160)	137 (8–342)	207 (126–549)	0.04
Serum TNF- α (pg/ml)	32 (2–256)	78 (6–531)	289 (90–813)	0.03
Serum VEGF (pg/ml)	28 (2–258)	33 (1–351)	47 (12–531)	0.16
Serum IL-4 (pg/ml)	5 (3–28)	7 (6–37)	7 (6–68)	0.94
Serum IL-13 (pg/ml)	287 (248–459)	390 (327–493)	378 (307–603)	0.5
Serum ECP (pg/ml)	16 (13–58)	20 (17–113)	19 (15–45)	0.09

Values are expressed as median values (inter-quartile range); ECP: Eosinophilic cationic protein; IL-8: Interleukin-8; IL-4: Interleukin-4; IL-13: Interleukin-13; TNF- α : tumor necrosis factor- α ; VEGF: vascular endothelial growth factor. The bold values represents the statistically significant differences in the table.

Table 5
Spearman's correlations between years in Service and airway and systemic inflammation.

	r	p
Total number of cells in sputum	0.728	0.026
Total number of cells in BALF	0.841	0.036
Sputum lymphocytes (%)	0.675	0.016
Sputum neutrophils (%)	0.886	0.019
Sputum eosinophils (%)	0.580	0.048
Sputum ECP	0.489	0.02
Sputum VEGF	0.434	0.05
Serum VEGF	0.325	0.024

BALF: bronchoalveolar lavage fluid; VEGF: vascular endothelial growth factor; ECP: Eosinophilic cationic protein.

inflammation in induced sputum, BAL, bronchial biopsies, pulmonary function tests, bronchial hyperresponsiveness, skin prick tests, and history.

Several epidemiological studies have demonstrated the association between occupational exposure and respiratory symptoms and pulmonary function in professional firefighters, especially after the World Trade Center (WTC) incident [3,5,8–15]. However, there are few data on airway and systemic inflammation as a result of occupational exposure in firefighters [20,21,30–35], especially in newly hired professionals. Our study provides evidence that occupational exposure in firefighters leads to airway and systemic inflammation early in their professional life. Even one year's exposure in the group of trainees led to measurable airway and systemic inflammation compared to healthy subjects. Furthermore, it was shown that airway and systemic inflammation become more intense as the exposure years in occupation increase. Professional fire fighters had a higher degree of airway inflammation compared to trainees, as reflected by the significantly higher levels of IL-8, TNF- α , and VEGF in induced sputum, as well as, the higher number of total cells, and the elevated counts of neutrophils and lymphocytes in sputum and BAL. Interestingly, a linear correlation was

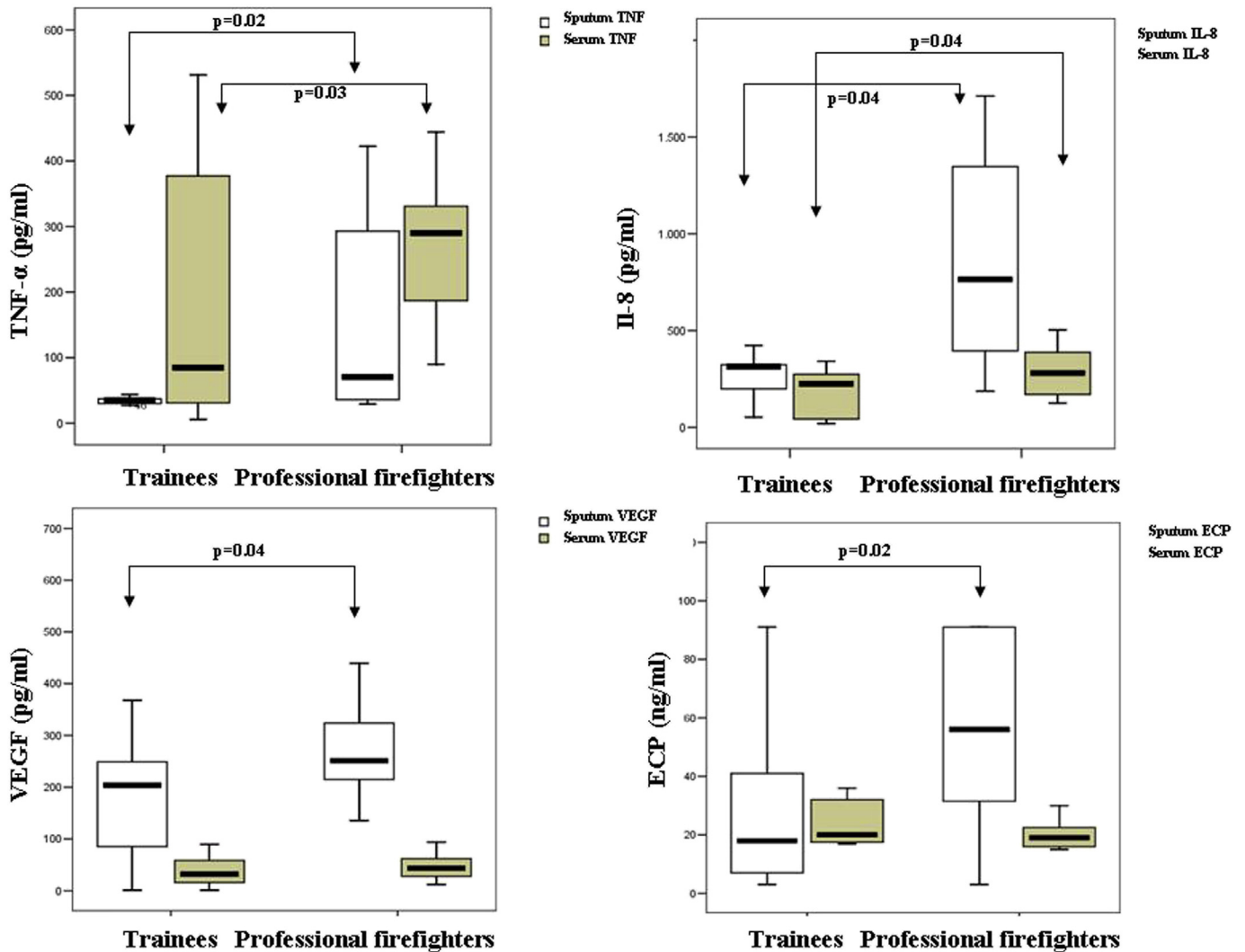


Fig. 1. Serum and sputum levels of TNF- α , IL-8, VEGF, and ECP in trainees and professional firefighters.

found between years in Service and total number of cells in sputum and BAL, as well as, lymphocytes' and neutrophils' counts in sputum. The more profound airway inflammation in professional firefighters was also documented in bronchial biopsies, where the more the years in Service the more the neutrophilic infiltration and the alterations in bronchial epithelium. The inflammatory response is not surprising after exposure to noxious particles [26,36]. Few studies in the past have shown increased neutrophil counts in BAL and induced sputum following exposure to particulate matter [20,30]. The induced sputum of firefighters with WTC exposure had increased percentages of granulocytes compared to healthy non firefighters, with a significant dose-response relationship [20]. Furthermore, Holgate et al. [37] demonstrated that modest concentrations of diesel exhaust have clear-cut inflammatory effects on the airways of non asthmatic subjects, suggesting a direct effect of diesel exhaust on IL-8 production leading to upregulation of neutrophil recruitment.

A dose response effect on systemic inflammation was demonstrated after continuous acute exposure to smoke during firefighting. Acute airway inflammation has been described after exposure to ambient particulate matter (PM) and WTC-PM [16–18]. Greven et al. [38] showed that acute exposure to fire smoke induces acute neutrophilic airway and long-lasting systemic inflammation

in healthy firefighters. Serum IL-8 concentrations were higher 24 h post-exposure compared to pre-exposure and elevated levels lasted up to 3 months. Swiston et al. [20] showed increased levels of serum IL-8, IL-6 and MCP-1 following firefighting. The elevated levels of circulating cytokines in our study following smoke exposure in firefighting are consistent with the findings of previous studies indicating the stimulation of the bone marrow [22,24,25] and the initiation of a systemic inflammatory response as a result of smoke inhalation. IL-8 is a potent stimulator of bone marrow promoting the sequestration of neutrophils in the lung [39] that possibly enhances or perpetuates the neutrophilic inflammation seen in the bronchi, and initiates the systemic inflammatory response as a result of smoke inhalation.

Allergic airway sensitization has been previously reported on the basis of the presence of atopy and symptoms from upper and lower respiratory system [5,10,12,15]. Exposure to combustion products can lead to increased sensitization to airway allergens [6,7], however scarce data are available regarding sensitization to common airway allergens and allergies in firefighters, who are also at increased risk of exposure to air pollutants [10]. This study documents the allergic airway sensitization based not only on the prevalence of atopy, but also on the significant increase of eosinophils in induced sputum, BAL fluid, and bronchial biopsies, and the elevated ECP levels in the

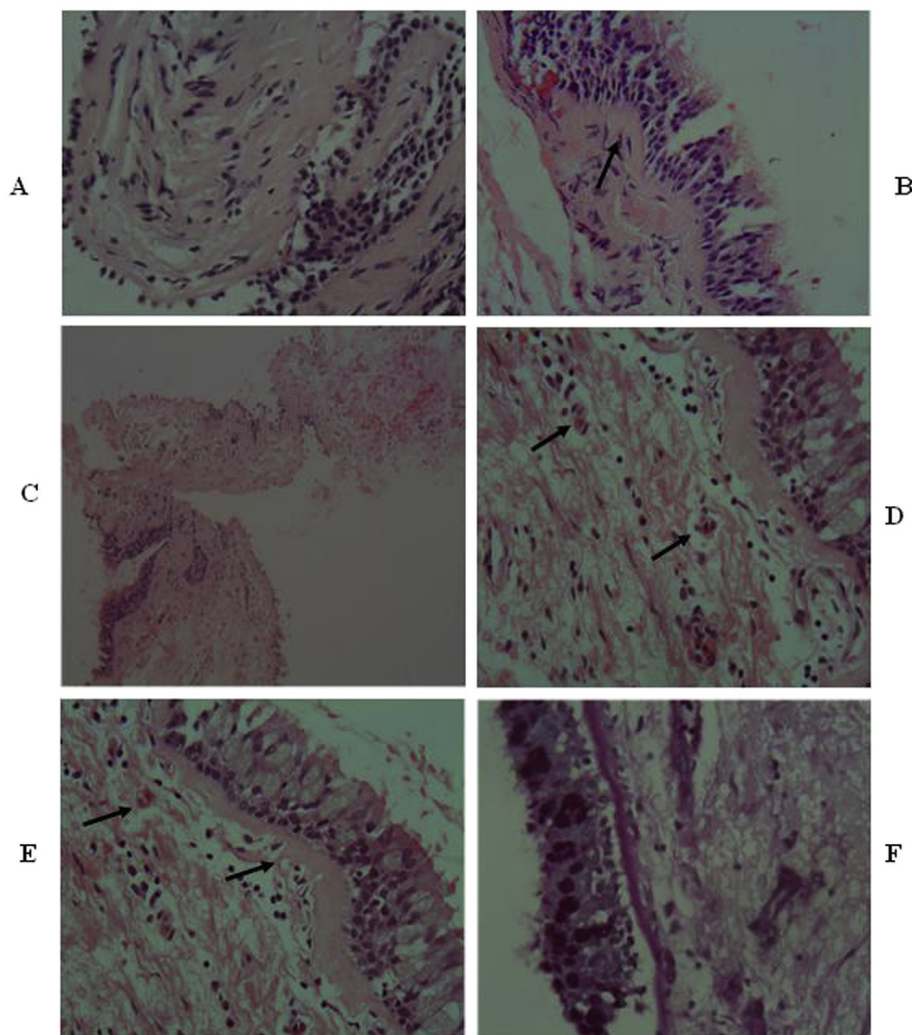


Fig. 2. Bronchial histological findings of professional firefighters and trainees. A: Focally squamous metaplasia of bronchial epithelium (professional firefighter). H-E stain. Image is shown at magnification $\times 400$. B: Moderate thickening of basal membrane with squamous metaplasia of bronchial epithelium. H-E stain (professional firefighter). Image is shown at magnification $\times 100$. C: Areas of bronchial atrophy, focally increase of mucus production. H-E stain. Images are shown at magnification $\times 400$. D: In high magnification the presence of eosinophils. H-E stain. E: Increased mucus production of goblet cells, presence of few eosinophils and mild thickening of basal membrane. H-E stain, in a trainee. Image is shown at magnification $\times 100$. F: Increase of mucus production from goblet cells. PAS-D stain in a case of a trainee.

sputum of professional firefighters, findings not observed in the fire fighters with minor exposure (trainees). After chronic occupational exposure, increased eosinophil counts have been seen in the induced sputum of sensitized asthmatics and in asbestos workers [40]. It has been proposed that inhaled pollutants may damage the airway mucosa, impairing the mucociliary clearance, resulting thus in an easier penetration of inhaled allergens that interact with nitrogen dioxide and carbon particles, eventually leading to an allergic immune response [41]. Several studies have shown that persistent exposure to particulate air pollution poses a significant factor responsible for the observed increased prevalence of atopy [6–8,41–44]. Experimental studies examining the challenge with diesel exhaust particles in combination with allergens have shown a significantly higher allergen specific IgE induction compared to the challenge with the allergen alone [44]. Dong et al. [44] demonstrated that exposure to diesel exhaust particles prior to ovalbumin sensitization in rats exacerbates the allergic responses to the subsequent challenge with OVA in OVA-sensitized rats. Moreover, studies in people living in areas with high traffic have shown increased sensitization to outdoor allergens [45,46].

In our study, a linear correlation was found between years in Service and eosinophils and ECP concentrations in sputum. In line with this finding, firefighters in the WTC exposure had increased percentages of eosinophils compared to healthy non firefighters, with a significant dose-response relationship [47].

The group of professional firefighters had a higher prevalence of atopy (defined as at least one skin prick test to an allergen tested) compared to trainees and the control group (43% vs 10%, and 17%, respectively), while they also had a significantly higher prevalence of allergic rhinitis (20% vs 10%, and 5%, respectively). This prevalence is significantly higher compared to the prevalence of atopy and allergic rhinitis in the general population of Greece [48]. The high prevalence of atopy among firefighters is well established in many studies and our percentages are comparable to the published data [10–15]. Prolonged occupational exposure is related to higher exposure to pollutants and this may justify why trainees have similar prevalence with the control group.

In our study, professional firefighters had a four-fold percentage of bronchial hyperreactivity compared to trainees. Banauch et al. [26] revealed persistent hyperreactivity (and respiratory

symptoms) for at least 6 months in firefighters engaged in rescue operators during the World Trade Center attack that was significantly associated to exposure intensity. Firefighters can be expected to show an increase in airway responsiveness after exposure to products of pyrolysis, such as ozone, oxides of nitrogen that have been shown to increase airway responsiveness in some subjects [2,3,9,10,16,49]. After smoke inhalation bronchial hyperreactivity may occur within hours and it seems to be confined to those subjects with a long history of firefighting activity [9,10,12,16,49]. The higher bronchial hyperreactivity was associated with more symptoms of lower respiratory tract irritation during work and at rest in the professionals' group, and this is in line with previous studies [10,49]. In only four subjects among the professionals the history of asthma was documented, while an overall higher incidence of cough and dyspnea was observed. Although the prolonged occupational exposure could justify the severity of symptoms in professional firefighters we should not neglect the merely contribution of smoking as well, since a considerable proportion of them were heavier smokers than trainees and healthy subjects. Smoking should also be accounted when interpreting the degree of inflammation in between the groups.

In the present study a decline of lung function was not documented. Similarly, Miedinger et al. [10] found no significant decrease of pulmonary function in professional firefighters, and Gaughan et al. [5] observed recovery of FEV₁ from post fire to post season, without cross-season FEV₁ decline. This differs from the findings of previous studies that reported a small but persistent post-season decrement of FEV₁ among wildland firefighters [9,50].

In summary, the findings of this study support the evidence that inhalation of particulate matter and smoke during firefighting induces a local inflammatory response within the lungs and allergic sensitization, which subsequently initiates a systemic response resulting in the adverse health consequences associated with air pollution exposure. Our findings show that a short time of low intensity exposure is adequate in order to generate this inflammatory procedure. Although, this effect may be of minor clinical significance for young healthy firefighters, it is inevitable that susceptible subjects establish chronic cardiopulmonary disease. Awareness should be heightened among firefighters to avoid exposure and to adequately use the self-contained breathing apparatuses during operations.

Author contributions

NR planned the study. NG, PK, ED, GC, KM, SV, TR, KA, BP, ME, LE, and NR collected, assembled, analyzed, and interpreted the data. NG and NR drafted the manuscript. TA, PC planned the firefighters' recruitment. RC, KN, and NR revised the manuscript and approved its final version. NR supervised the study.

Funding

The study was supported by "Thorax" Foundation and funded by a grant from Chiesi Hellas.

Conflict of interest

Authors declare no conflict of interest.

Acknowledgments

Authors would like to thank the firefighters of the Hellenic Fireforce Dpt. for their participation in this study, and the nurses L. Stoubi and F. Zikopoulou for their valuable assistance and support in the endoscopic laboratory.

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