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Clinical Science

Chronic Obstructive Pulmonary Disease in Never-Smoking Bricklayers

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Key words: airflow limitation; bronchodilator reversibility testing; occupational exposure; questionnaire; spirometry.

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Abstract

Background: Chronic obstructive pulmonary disease (COPD) due to occupational exposures remains an important public health problem taking significant toll on the global burden of the disease.

Aim: In order to assess chronic prevalence and characteristics of COPD in bricklaying we performed a cross-sectional study including 47 never-smoking male bricklayers (aged 34 to 57 years) and an equal number of never-smoking male office workers studied as a control.

Methods: Evaluation of examined subjects consisted of completion of a questionnaire, baseline spirometry, and bronchodilator reversibility testing.

Results: We found higher prevalence of respiratory symptoms in bricklayers with significant difference for cough and phlegm. Majority of the chronic respiratory symptoms in bricklayers were work-related. The mean values of all measured spirometric parameters in bricklayers were significantly lower than in office workers. The prevalence of COPD was significantly higher in bricklayers than in office workers (14.9% *vs.* 4.3%, P = 0.034). COPD in both examined groups was close related to age over 45 years, while in bricklayers significant association was registered for duration of occupational exposure longer than 20 years and work-related respiratory symptoms.

Conclusion: Our findings support data about relationship between occupational exposure to inorganic dust and fumes in construction workers and persistent airflow limitation.

Introduction

There is strong evidence that chronic obstructive pulmonary disease (COPD) due to occupational exposures have markedly increased during the last decades becoming a major cause of morbidity in many occupations, as well as a relevant public health problem [1-3].

Despite that tobacco smoke is undoubtedly the main cause of COPD, results from epidemiological studies indicates that population attributable fraction for COPD related to workplace exposures to dusts, gases, vapors, and fumes may be 15-20% in overall population and about 30% in never smokers (4, 5). Epidemiological studies have indicated increased risk for COPD in a number of occupations, including rubber, plastics, leather, textile, and paper manufacture, wood industry, transportation, mining, and construction [6, 7]. In regard to the occupational exposures, statistically significant association with COPD was demonstrated with exposure to asbestos, silica, welding fumes, cement dusts, and some tasks associated with exposures to paints, solvents, and removal of paints [8]. Furthermore, Bergdahi et al. [9] demonstrated an increased mortality from COPD in construction workers exposed to inorganic dust that was more expressed in never smokers. In addition, the experimental studies have demonstrated that several agents (e.g., mineral dusts, vanadium, endotoxin, ozone, and sulphur dioxide) are capable of inducing chronic bronchitis (CB) in animal models [10-13]. The list of agents that can cause emphysema in animal model includes several ones for which there is also epidemiological evidence in exposed occupational cohorts (e.g., cadmium, coal, silica, and endotoxin) [14].

In opposite to occupational asthma (OA), COPD does not have a clinical subcategory that is clearly identified as occupational, because the persistent and progressive airflow limitation does not reverse when exposure is discontinued, so the clinical diagnosis of occupational COPD using methods similar to those used for OA diagnosis is not feasible. Epidemiological identification of occupational COPD is based on documenting excess occurrence of COPD among exposed workers in certain occupations [15, 16].

In the present study we aimed at assessment of prevalence and characterstics of COPD in never-smoking bricklayers.

Methods

Study design and setting

A cross-sectional study was carried out in the Department of Cardiorespiratory Functional Diagnostics at the Institute for Occupational Health of R. Macedonia, Skopje - WHO Collaborating Center for Occupational Health and GA^{2}LEN Collaborating Center in the period September 2012 – April 2013. Prevalence of chronic respiratory symptoms, mean values of spirometric parameters, and prevalence of COPD was compared between a group of never-smoking male bricklayers and a group of never-smoking male office workers. The study protocol was approved by the ethics committee of the institution and each subject gave an informed consent before entering the study.

Subjects

We examined 47 male bricklayers aged 34 to 57 years, employed in a big company for surface construction with duration of employment 12 to 28 years. They worked in one working shift lasting 8 hours and their working tasks included building of structures from individual units laid in and bound together by mortar. The common materials of their work include brick, concrete, stone, whitewash, granite, travertine, marble, man-made mineral fibres etc. Brick and concrete block, either weight-bearing or a veneer, were the most common types of bricklaying in use in their day-to-day work. Their work activities included outdoor works, as well as working at heights. The process control provided keeping of the exposures at the permissible levels. The protective equipment during the working included protective clothing, gloves, and masks (i.e., disposable non-woven dust masks without valve). According to the classification of occupational muscular work the bricklaying was classified as a heavy-to-very heavy muscular work [17]. All examined bricklayers were never smokers, i.e. non-smokers who have never smoked at all, or have never been daily smokers and have smoked less than 100 cigarettes in their lifetime [18, 19].

In addition, an equal group of never-smoking male office (administrative) workers matched to construction workers by age was studied as a control. According to the classification of occupational muscular work their work was classified as a sedentary work.

In either group there were no subjects with chronic respiratory disease diagnosed by physician (i.e. asthma, COPD, bronchiectasis, etc.), neither subject treated with bronchodilators and/or corticosteroids. In either group also there were no subjects in whom spirometry or bronchodilator reversibility testing was contraindicated [20, 21].

Questionnaire

An interviewer-led questionnaire was completed by all study subjects. The questionnaire included questions on work history (e.g., chronological list of jobs; description of job activities at the actual workplace; type, extent and duration of exposure; and use of protective equipment), respiratory symptoms in the last 12 months and their relatedness to the workplace, chronic respiratory diseases diagnosed by physician, family history of COPD and CB (taking into account the first-degree relatives), environmental exposure to tobacco smoke (ETS), accompanying disease, and medication use.

Respiratory symptoms in the last 12 months (cough, phlegm, dyspnea, wheezing, and chest tightness) were documented using the European Community for Coal and Steel questionnaire (ECCS-87), and the European Community Respiratory Health Survey (ECRHS) questionnaire [22, 23]. The work-relatedness of the respiratory symptoms was defined as more than usual cough, phlegm, dyspnea, wheezing, and chest tightness during daily work [24].

ETS or passive smoking or second-hand smoking was defined as an exposure to tobacco combustion products from smoking by others (at home, workplace, etc.), i.e. as a presence of at least one smoker in the household and/or in the workplace [25, 26]. In addition, passive smokers were divided in two groups regarding the number of hours per day they were exposed to ETS (less or more than four hours per day).

Baseline spirometry

The baseline spirometry, including measures of forced vital capacity (FVC), FEV_1, FEV_1/FVC, and maximal expiratory flow at 50%, 25%, and 25-75% of FVC (MEF_{50}, MEF_{25}, and MEF_{25-75}, respectively), was performed in all subjects using spirometer Ganshorn SanoScope LF8 (Ganshorn Medizin Electronic GmbH, Germany) with recording the best result from three measurements the values of FEV_1 of which were within 5% of each other. The results of spirometry were expressed as percentages of the predicted values according to the actual recommendations of European Repsiratory Society (ERS) and American Thoracic Society (ATS) [20, 21]. The combined reference equations for people aged 18 to 70 years, with a height range of 155-190 cm in males, published in the 1993 ERS statement [27] were used for deriving predicted values.

Bronchodilator reversibility testing

Bronchial reversibility testing was performed according to the actual GOLD spirometry guide [20]. Spirometric measurements were performed before and 20 minutes after administration of 400 μg salbutamol by metered dose inhaler through spacer. Fixed airflow narrowing characteristic for COPD was considered if post-bronchodilator FEV_1/FVC remained less than 0.70. The degree of FEV_1 reversibility was expressed as % FEV_1 reversibility ([post-bronchodilator FEV_1 – pre-bronchodilator FEV_1] / pre-bronchodilator FEV_1 x 100). Significant FEV_1 improvement (a change more than 12% and more than 200 mL) in the presence of fixed airflow limitation did not negate a diagnosis of COPD.

COPD diagnosis

The diagnosis of COPD was established according to the actual GOLD recommendations [28], i.e., COPD was considered by the presence of a post-bronchodilator FEV_1/FVC less than 0.70 suggesting persistent airflow limitation in the subjects who had dyspnea, chronic cough or sputum production, and/or a history of exposure to risk factors for the disease (tobacco smoke, smoke from home cooking and heating fuels, and/or occupational dusts and chemicals).

Statistical analysis

Continuous variables were expressed as mean values with standard deviation (SD), and the nominal variables as numbers and percentages. Analyses of the data involved testing the differences in prevalence, comparison of the means, and testing the association between COPD and studied variables. Chi-square test (or Fisher's exact test where appropriate) was used for testing difference in the prevalence. Comparison of spirometric measurements was performed by independent-samples *T*-test. Chi-square test was used for testing association between COPD and studied variables. A *P*-value less than 0.05 were considered as statistically significant. Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS) version 11.0 for Windows.

Results

Results

Demographic characteristics of the study subjects were similar in both examined groups (Table 1).

Table 1: Demographics of the study subjects.

Variable	Bricklayers (n = 47)	Office workers (n = 47)
Age (years)	46.2 ± 4.9	45.3 ± 6.2
Less than 45 years	21 (44.7%)	24 (51.1%)
More than 45 years	26 (55.3%)	23 (48.9%)
BMI (kg/m^2)	25.7 ± 3.8	26.1 ± 3.4
BMI less than 25	25 (53.2%)	22 (46.8%)
BMI more than 25	22 (46.8%)	25 (53.2%)
Duration of employment (years)	20.8 ± 5.7	18.9 ± 7.2
Duration of employment less than 20 years	23 (48.9%)	26 (55.3%)
Duration of employment more than 20 years	24 (51.1%)	21 (44.7%)
Former employment in dusty trades	11 (23.4%)	/
Family history of COPD or CB	5 (10.6%)	3 (6.4%)
Environmental ETS	19 (40.4%)	17 (36.2%)
Exposed less than 4 hours	11 (23.4%)	8 (17.0%)
Exposed more than 4 hours	8 (17.0%)	9 (19.1%)
Accompanying diseases		
Arterial hypertension	6 (12.8%)	8 (17.0%)
Diabetes mellitus type 2	2 (4.3%)	3 (6.4%)
Peptic ulcer	5 (10.6%)	3 (6.4%)

Numerical data are expressed as mean value with standard deviation; frequencies as number and percentage of study subjects with certain variable.
BMI: body mass index; kg: kilogram; m: meter; COPD: chronic obstructive pulmonary disease; CB: chronic bronchitis; ETS: exposure to tobacco smoke.

Prevalence of overall respiratory symptoms in the last 12 months was higher in bricklayers but statistical significance was not reached. Significantly higher prevalence in bricklayers was registered for cough and phlegm (Table 2).

Table 2: Prevalence of respiratory symptoms in the last 12 months in the study subjects.

Respiratory symptoms in the last 12 months	Bricklayers (n = 47)	Office workers (n = 47)	*P*-value*
Overall respiratory symptoms in the last 12 months	21 (44.7%)	14 (24.8%)	0.108
Cough	16 (34.0%)	7 (14.9%)	0.041
Phlegm	9 (19.1%)	2 (4.3%)	0.017
Dyspnea	7 (14.9%)	4 (8.5%)	0.094
Wheezing	8 (17.0%)	5 (10.6%)	0.139
Chest tightness	5 (10.6%)	6 (12.8%)	0.248

Data are expressed as number and percentage of study subjects with certain variable.
*Tested by Chi-square test (or Fisher's exact test where appropriate).

Work-relatedness of respiratory symptoms in the last 12 months in bricklayers and office workers is shown on Figure 1. The majority of respiratory symptoms in the last 12 months in bricklayers were reported as work-related symptoms (80.9%). The highest relatedness with workplace in bricklayers was reported for cough (72.9%) and phlegm (88.9%). Work-relatedness of respiratory symptoms was reported by three office workers (21.4%) with respiratory symptoms in the last 12 months, i.e., work-related cough was reported by one office worker with cough (14.3%), work-related dyspnea was reported by one office worker with dyspnea (25.0%), and work-related chest tightness was reported by one office worker who reported this symptom (16.7%).

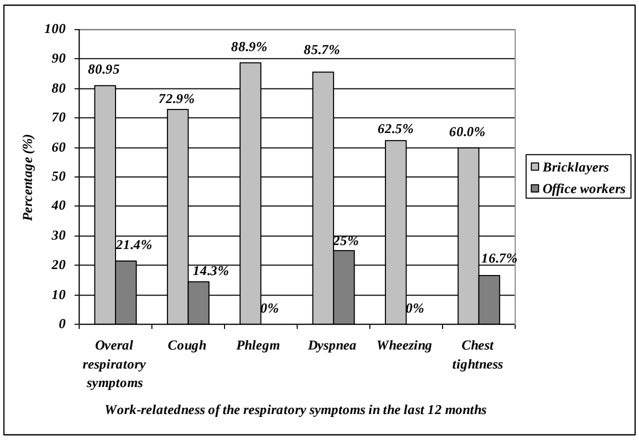

Figure 1: Work-relatedness of respiratory symptoms in the last 12 months in the study subjects.

The mean baseline values of all spirometric parameters were significantly lower in bricklayers (Table 3).

Table 3: Mean baseline values of spirometric parameters in the study subjects.

Spirometric parameter	Bricklayers (n = 47)	Office workers (n = 47)	*P*-value*
FVC (%pred)	88.1 ± 10.4	96.4 ± 9.2	0.037
FEV_1 (%pred)	81.7 ± 8.9	88.1 ± 11.2	0.031
FEV_1/FVC	0.73 ± 0.04	0.78 ± 0.07	0.026
MEF_{50} (%pred)	68.1 ± 15.3	77.4 ± 12.9	0.009
MEF_{25} (%pred)	62.9 ± 14.8	71.6 ± 11.3	0.010
MEF_{25-75} (%pred)	64.5 ± 15.1	73.6 ± 16.7	0.008

Data are expressed as mean value with standard deviation. FVC: forced vital capacity; FEV_1: forced expiratory volume in one second; MEF_{50}, MEF_{25}, MEF_{25-75}: maximal expiratory flow at 50%, 25% and 25-75% of FVC, respectively; % pred: % of predicted value. *Compared by Independent-samples *T*-test.

The mean post-bronchodilator values of all spirometric parameters also were significantly lower in bricklayers (Table 4). The mean FEV_1 reversibility (%FEV_1 reversibilty) was significantly higher in bricklayers (10.8% *vs.* 4.9%, *P* = 0.028; Independent-samples *T*-test).

Seven subjects among bricklayers and two subjects among office workers met criteria for diagnosis of COPD (14.9% *vs.* 4.3%, *P* = 0,034; Fisher's exact test) (Figure 2). All bricklayers with COPD and none of the office workers with COPD reported work-relatedness of their symptoms. According to the GOLD 2010 classification of COPD severity [29], five subjects with COPD among bricklayers and all subjects with COPD among office workers can be categorized as a mild COPD (FEV_1/FVC < 0.70; FEV_1 ≥ 80% predicted) and two subjects with COPD among bricklayers can be categorized as a moderate COPD (FEV_1/FVC < 0.70; 50% ≤ FEV_1 < 80% predicted).

Table 4: Mean post-bronchodilator values of spirometric parameters in the study subjects.

Spirometric parameter	Bricklayers (n = 47)	Office workers (n = 47)	*P*-value*
FVC (%pred)	90.2 ± 12.9	98.8 ± 10.4	0.034
FEV_1 (%pred)	83.3 ± 9.6	89.9 ± 12.7	0.042
FEV_1/FVC	0.74 ± 0.02	0.79 ± 0.06	0.029
MEF_{50} (%pred)	71.4 ± 18.6	78.7 ± 14.7	0.021
MEF_{25} (%pred)	63.6 ± 16.3	73.1 ± 13.9	0.009
MEF_{25-75} (%pred)	65.8 ± 17.4	75.1 ± 15.2	0.007

Data are expressed as mean value with standard deviation. FVC: forced vital capacity; FEV_1: forced expiratory volume in one second; MEF_{50}, MEF_{25}, MEF_{25-75}: maximal expiratory flow at 50%, 25% and 25-75% of FVC, respectively; % pred.: % of predicted value. *Compared by Independent-samples *T*-test.

COPD was significantly associated with age more than 45 years in both bricklayers (*P* = 0.027; Chi-square test) and office workers (*P* = 0.043; Fisher's exact test). Significant association in bricklayers was registered between COPD and duration of employment more than 20 years (*P* = 0.018; Chi-square test) and work-related respiratory symptoms (*P* = 0.038; Chi-square test). Associations between COPD and other variables (e.g., BMI, family history of COPD or CB, and environmental ETS) were statistically non-significant in both bricklayers and office workers. Association between COPD and former employment in dusty trades in bricklayers was also statistically non-significant.

Figure 2: Prevalence of COPD in the study subjects.

Discussion

COPD is one of the leading causes of morbidity and mortality worldwide, with smoking being the most important predisposing factor, followed by occupational and environmental exposures. In the present study we assessed the impact of specific occupational exposure in never-smoking bricklayers on developing of COPD. A group of never smoking male office workers with similar age to bricklayers were studied as a control.

The examined groups included subjects with similar demographic characteristics. In either group there was a large proportion of passive smokers that is similar to its prevalence among workers in R. Macedonia documented in our previous studies [30, 31] and indicate still insufficient nationwide smoking cessation activities.

Occupational exposure in bricklayers included inorganic dust, i.e., exposure to silica, sand, concrete, and cement dust. Diseases caused by inhalation of free crystalline silica include silicosis, pulmonary tuberculosis, lung cancer, COPD, and several extra-pulmonary diseases [32, 33]. Development of pulmonary silicosis requires exposure to high dust levels for prolonged periods [34, 35]. There is a limited data supporting the quantitative relationship between silica exposure and COPD at dust levels that appear not to cause radiologically detectable silicosis and there is still not clear whether the threshold limit values for protecting silicosis adequately protects workers from developing COPD that may have significant public health relevance [33, 35].

We found higher prevalence of respiratory symptoms in the last 12 months in bricklayers than in office workers with significantly higher prevalence of cough and phlegm. An excess of acute and chronic respiratory symptoms in workers exposed to similar occupational exposure is reported in a number of studies [36-39]. The majority of respiratory symptoms in bricklayers were work-related, reaching more than 80% for cough, phlegm, and dyspnea. Over the last years, several studies indicated that chronic cough is one of the most prevalent work-related respiratory symptoms and the best-known examples of occupations related to the development of cough are coal miners, hard-rock miners, tunnel workers, and concrete manufacturing workers [40].

The mean values of all measured spirometric parameters in the present study (FVC, FEV_1, FEV_1/FVC, MEF_{50}, MEF_{25}, and MEF_{25-75}) were significantly lower in bricklayers than in office workers. Similarly, significantly lower mean values of FVC, FEV_1, and FEV_1/FVC was found in the workers exposed to cement dust as compared to non-exposed controls in the study conducted by Al-Neaimi et al [41]. According to the findings from studies performed in the last decades [42, 43], exposure to inorganic dust is associated with chronic airflow obstruction independent of cigarette smoking and separate from other effects of exposure such as pneumoconiosis, asthma or hypersensitivity pneumonitis. The changes in lung function are dose-related but individual susceptibility is also important. According to the results of the study carried out by Seixas et al. [44], estimated decline in FEV_1 in coal miners exposed to relatively low levels of coal mine dust was 5.7 mL for each mg x m^3/year of exposure over their working life. In addition, Hnizdo et al [45] indicated that the estimated effects of cumulative silica dust exposure in gold miners has been 10 times greater than those seen in coal mining cohorts being more pronounced in non-smokers.

We performed bronchodilator reversibility testing in order to detect subjects with the presence of a post-bronchodilator FEV_1/FVC less than 0.70, i.e., to confirm the diagnosis of COPD. According to the actual GOLD recommendations, the post-bronchodilator spirometry is required for diagnosis and assessment of severity of COPD, but the degree of reversibility of airflow limitation (e.g., FEV_1 measurements before and after administration of bronchodilator) is no longer recommended. The degree of reversibility has not be shown to add to the diagnosis, differential diagnosis with asthma, or to prediction of the response to long-term treatment with bronchodilators or corticosteroids [28]. We found significantly higher COPD prevalence in bricklayers than in office workers that confirms the increased risk for developing COPD in construction jobs. COPD in both examined groups was close related to age over 45 years probably reflecting the sum of cumulative exposures throughout the life in susceptible subjects. We found significant association between COPD and duration of occupational exposure in bricklayers. Similar findings were reported in several studies that investigated the dose-response relationship between occupational exposure to inorganic dist and developing of COPD [35-37]. COPD in bricklayers was strongly linked to the work-related respiratory symptoms. In the study conducted by Meijer et al. [24] aimed at creation of a validated and structured medical questionnaire for occupational lung disease, the work-related respiratory symptoms, besides shortness of breath, wheeze, and heavy smoking, were identified as a significant independent determinant of COPD.

The findings in this study are subjects to at least three limitations. First, relatively small number of the subjects in the study groups could have certain implications on the data obtained and its interpretation. Second, environmental measurements were not performed, so we could not document the effect of the type and the level of exposure on COPD. Third, as in the case of any cross-sectional study, the impact of healthy workers' effect on the data obtained could not be excluded. The healthy-workers' effect (HWE) is the most common selection bias in occupational studies occurring because relatively healthy individuals are likely to gain employment and to remain employed and it may partially or completely mask excess mortality and morbidity caused by harmful exposure. The strength of the study is the investigation of respiratory effects of occupational exposure on never-smoking workers performing one of the specific construction jobs.

In conclusion, in a cross-sectional study including never-smoking bricklayers we found a higher prevalence of respiratory symptoms in the last 12 months, significantly highly mean values of spirometric parameters, and significantly higher prevalence of COPD than in matched office workers. COPD in bricklayers was significantly associated with age over 45 years, duration of occupational exposure longer than 20 years, as well as with work-related respiratory symptoms. Our findings support data from other studies about relationship between occupational exposure to inorganic dust and fumes in construction workers and persistent airflow limitation and indicate the need of reduction of adverse occupational exposures via proper engineering controls and/or respiratory protective equipment.

Ethical Approval

The Ethical Committee of the Institute of Occupational Health of R. Macedonia, Skopje – WHO Collaborating Center and GA^{2}LEN Collaborating Center gave approval for performing the study and publishing the results obtained (03-133/2-03.2013).

Authors Participations

JM participated in the study design, writing the protocol, data collection, managing the analyses of the study, and writing all versions of the manuscript. JKB participated in the study design, writing the protocol, managing the analyses of the study, as well as writing all versions of the manuscript. KV performed the statistical analysis and participated in the managing of the analyses of the study. SS, DM and SRK participated in the data collection and in the managing of the analyses of the study. All authors read and approved the final manuscript.

References

1. Beclacke MR. Chronic airflow limitations: its relationship to work in dusty occupations. Chest. 1985; 88: 608-617.
2. Meredith SK, Taylor VM, Mc Donald JC. Occupational respiratory disease in the United Kingdom: a report to the British Thoracic Society and the Society of Occupational Medicine by the SWORD project group. Br I Ind Med. 1991; 48: 292-298.
3. Blanc PD. Occupation and COPD: a brief review. J Asthma. 2012; 49 (1): 2-4.
4. Balmes J, Becklake M, Blanc P, Henneberger P, Kreiss K, Mapp C, Milton D, Schwartz D, Toren K, Viegi G. American Thoracic Society Statement: Occupational contribution to the burden of airway disease. Am J Respir Crit Care Med. 2003; 167: 787-797.
5. Trupin L, Earnest G, San Pedro M, Balmes JR, Eisner MD, Yelin E, Katz PP, Blanc PD. The occupational burden of chronic obstructive pulmonary disease. Eur Respir J. 2003; 22: 462-469.
6. Hnizdo E, Sullivan PA, Bang KM, Wagner G. Association between chronic obstructive pulmonary disease and employment by industry and occupation in the US population: a study of data from the Third National Health and Nutrition Examination Survey. Am J Epidemiol. 2002; 156: 738-746.
7. Blanc PD, Menezes AM, Plana E, Mannino DM, Hallal PC, Toren K, Eisner MD, Zock JP. Occupational exposures and COPD: an ecological analysis of international data. Eur Respir J. 2009; 33 (2): 298-304.
8. Dement JM, Welch L, Ringen K, Bingham E, Quinn P. Airways obstruction among older construction and trade workers at Department of Energy nuclear sites. Am J Ind Med. 2010; 53: 224-240.
9. Bergdahi IA, Toren K, Eriksson K, Hedlund U, Nilsson T, Flodin R, Jarvholm B. Increased mortality in COPD among construction workers exposed to inorganic dust. Eur Respir J. 2004; 23: 402-406.
10. Churg A, Hobson J, Wright J. Functional and morphological comparison of silica- and elastine-induced airflow obstruction. Exp Lung Res. 1989; 151: 813-822.
11. Shore S, Kobzik L, Long NC, Skornik W, Van Staden CJ, Boulet L, Rodger IW, Pon DJ. Increased airway responsiveness in a rat model of chronic bronchitis. Am J Respir Crit Care Med. 1995; 151: 1931-1938.
12. Harkema JR, Hotchkiss JA. Ozone- and endotoxin-induced mucous metaplasias in rat airway epithelium: novel animal models to study toxicant-induced epithelial transformation in airways. Toxicol Lett. 1993; 68: 251-263.
13. Bonner JC, Rice AB, Moomaw CR, Morgan DL. Airway fibrosis in rats induced by vanadium pentoxide. Am J Physiol. 2000; 278: L209-L216.
14. Shapiro SD. Animal models for COPD. Chest. 2000; 117: 2235-2275.
15. Becklake MR. Occupational exposures: evidence for a causal association with chronic obstructive pulmonary disease. Am Rev Respir Dis. 1989; 140: S85-S91.
16. Boschetto P, Quintivalle S, Miotto D, Lo Cascio N, Zeni E, Mapp C. Chronic obstructive pulmonary disease (COPD) and occupational exposures. J Occup Med Toxicol. 2006; 1: 11.
17. Brown JR, Crowden GP. Energy expenditure ranges and muscular work grades. Br J Ind Med. 1963; 20: 277-283.
18. World Health Organization. Guidelines for controlling and monitoring the tobbaco epidemic. Geneva: WHO, 1998.
19. Leffondre K, Abrahamowicz M, Siemiatycki J, Rachet B. Modelling smoking history: A comparison of different approaches. Am J Epidemiol. 2002; 156: 813-823.
20. Spirometry Guide: 2010 Update. *http://www.goldcopd.org/uploads/users/files/GOLD_Spirometry_2010.pdf*.
21. Miller MR, Hankinson J, Brusasco V, Burgos F, Casaburi R, Coates A, Crapo R, Enright P, van der Grinten CPM, Gustafsson P, Jensen R, Johnson DC, MacIntyre N, McKay R, Navajas D, Pedersen OF, Pellegrino R, Viegi G, Wanger J. Standardisation of spirometry. Eur Respir J. 2005; 26: 319-338.
22. Minette A. Questionnaire of the European Community for Coal and Steel (ECSC) on respiratory symptoms. 1987 - updating of the 1962 and 1967 questionnaires for studying chronic bronchitis and emphysema. Eur Respir J. 1989; 2:165-177.
23. European Community Respiratory Health Survey. Variations in the prevalence of respiratory symptoms, self-reported asthma attacks, and use of asthma medication in the European Respiratory Health Survey (ECRHS). Eur Respir J. 1996; 9:

687-695.

24. Meijer E, Grobbe DE, Heederik DJJ. Health surveillance for occupational chronic obstructive disease. J Occup Environ Med. 2001; 43: 444-450.

25. U.S. Department of Health and Human Services. The health consequences of smoking: chronic obstructive pulmonary disease. A report of the Surgeon General. US Department of Health and Human Services, Public Health Service, Office of the Assistant for Health, Office of Smoking and Health. DHHS Publication No. 84-50 205, 1984.

26. Janson C, Chinn S, Jarvis D, Zock JP, Toren K, Burney P, for the European Community Respiratory Health Survey. Effects of passive smoking on respiratory symptoms, bronchial responsiveness, lung function, and total serum IgE in the European Community Respiratory Health Survey: a cross-sectional study. Lancet. 2001; 358: 2103-2109.

27. Quanjer PH, Tammeling GJ, Cotes JE, Pedersen OF, Peslin R, Yernault JC. Lung volumes and forced ventilatory flows. Report Working Party Standardization of Lung Function Tests, European Community for Steel and Coal. Official Statement of the European Respiratory Society. Eur Respir J. 1993; 6 (16): 5-40.

28. Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Pulmonary Disease: 2011 Update. Available at: *http://www.goldcopd.org/uploads/users/files/GOLD_Report_2011_Feb21.pdf*

29. Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Pulmonary Disease: 2010 Update. Available at: *http://www.goldcopd.org/Guidelines/guideline-2010-gold-report.html*

30. Minov J, Karadzinska-Bislimovska J, Vasilevska K, Risteska-Kuc S, Stoleski S. Exposure to environmental tobacco smoke in the workplace in Macedonia: Where are we now? Arh Hig Rada Toksikol. 2008; 59: 103-109.

31. Minov J, Karadzinska-Bislimovska J, Vasilevska K, Nelovska Z, Risteska-Kuc S, Stoleski S, Mijakoski D. Smoking among Macedonian workers five years after the anti-smoking campaign. Arh Hig Rada Toksikol. 2012; 63: 207-213.

32. Weill H, Jones RN, Parkes WR. Silicosis and related diseases. In: Parkes WR, ed. Occupational lung disease. Oxford: Butterworth-Heinemann, 1994:pp 285-339.

33. American Thoracic Society (ATS). Adverse effects of crystalline silica exposure. Am J Crit Care Med. 1997; 55: 761-765.

34. Steenland K, Brown D. Silicosis among gold miners: exposure-response analyses and risk assessment. Am J Public Health. 1995; 85: 1372-1377.

35. Ng TP, Chan SL. Lung function in relation to silicosis and silica exposure in granite workers. Eur Respir J. 1992; 5: 986-991.

36. Zuskin E, Mustajbegovic J, Schachter EN, Kern J, Doko-Jelinic J, Godnic-Cvar J. Respiratory findings in workers employed in brick-manufacturing industry. J Occup Environ Med. 1998; 40: 814-820.

37. Meijer E, Krombout H, Heederik D. Respiratory effects of exposure to low levels of concrete dust containing crystalline silica. AM J Ind Med. 2001; 40: 133-140.

38. Barber CM, Fishwick D. Chronic cough – occupational considerations. Chron Respir Dis. 2008; 5 (4): 211-221.

39. Rodriguez E, Ferrer J, Marti S, Zock JP, Plana E, Morell F. Impact of occupational exposure on severity of COPD. Chest. 2008; 134 (6): 1237-1243.

40. Groneberg D, Nowak D, Wussow A, Fischer A. Chronic cough due to occupational factors. J Occup Med Toxicol. 2006; 1:3.

41. Al-NeaimiYI, Gomes J, Lloyd OL. Respiratory illnesses and ventilatory function among workers at a cement factory in a rapidly developing country. Occup Med. 2001; 51: 367-373.

42. Love RG, Miller BG. Longitudinal study of lung function in coal miners. Thorax. 1982; 37: 193-197.

43. Oxman AD, Muir DCF, Shannon HS, Stock SR, Hnizdo E, Lange HJ. Occupational dust exposure and chronic obstructive pulmonary disease. Am Rev Respir Dis. 1993; 148: 38-48.

44. Seixas NS, Robins TG, Attfield MD, Moulton LH. Longitudinal and cross-sectional analyses of coal mine dust and pulmonary function in new miners. Br J Ind Med. 1993; 50: 929-937.

45. Hnizdo E, Baskind E, Sluis-Cremer GK. Combined effect of silica dust exposure and tobacco smoking on the prevalence of respiratory impairment among gold miners. Scan J Work Environ Health. 1990; 16: 411-422.