Respiratory Symptoms and Lung Functional Impairments Associated with Occupational Exposure to Asphalt Fumes

M Neghab¹, F Zare Derisi², J Hassanzadeh³

Abstract

Background: Controversy exists as to the potential of asphalt fumes to induce respiratory symptoms and lung functional impairments.

Objective: To examine the respiratory effects, if any, of occupational inhalation exposure to asphalt fumes.

Methods: In this cross-sectional study, 74 asphalt workers and 110 unexposed employees were investigated. The prevalence of respiratory symptoms among subjects was investigated by a standard questionnaire. Additionally, the parameters of pulmonary function were measured both, prior to exposure and at the end of work-shift. Furthermore, to assess the extent to which workers were exposed to asphalt fumes, total particulate and the benzene-soluble fraction were measured in different worksites.

Results: The mean levels of exposure to total particulate and benzene-soluble fraction in asphalt fumes were estimated to be 0.9 (SD 0.2) and 0.3 (SD 0.1) mg/m³, respectively. Mean values of FEV₁, both prior to the exposure (89.58% [SD 18.69%] predicted value) and at the end of shift (85.38% [SD 19.4%]), were significantly (p<0.05) smaller than those of the comparison subjects (93.88% [SD 13.93%]). Similarly, pre-shift (87.05 [SD 8.57]) and post-exposure (89.95 [SD 6.85]) FEV₁/FVC ratio were both significantly (p<0.01) lower than those of the unexposed employees (107.56 [SD 9.64]). Moreover, the prevalence of respiratory symptoms such as cough and wheezing in exposed employees were 41% and 42%, respectively. The corresponding values for comparison subjects were 10.0% and 3.6%, respectively (p<0.001). The pattern of changes in parameters of lung function in asphalt workers was consistent with that of chronic obstructive lung disease.

Conclusion: Significant decrements in the parameters of pulmonary function as well as, a significant increase in the prevalence of respiratory symptoms in asphalt paving workers compared to their unexposed counterparts provided evidence in favor of a significant association between exposure to asphalt fumes and lung function impairments.

Keywords: Asphalt; Respiratory function tests; Signs and symptoms, respiratory; Occupational exposure; Mastic asphalt; Questionnaires; Benzene; Worksites; Threshold limit values; Air borne disease

Cite this article as: Neghab M, Zare Derisi F, Hassanzadeh J. Respiratory symptoms and lung functional impairments associated with occupational exposure to asphalt fumes. Int J Occup Environ Med 2015;6:113-121.

www.theijoem.com  Vol 6, Num 2; April, 2015

¹Department of Occupational Health and Research Center for Health Sciences, Shiraz University of Medical Sciences, Shiraz, Iran
²Student Research Committee, School of Health, Shiraz University of Medical Sciences, Shiraz, Iran
³Department of Clinical Epidemiology, School of Health, Shiraz University of Medical Sciences, Shiraz, Iran

Correspondence to Forough Zare Derisi, MSc Student of Occupational Health, Student Research Committee, School of Health, Shiraz University of Medical Sciences, Shiraz, Iran
Tel/Fax: +98-71-3627-2045
E-mail: zarederis@sums.ac.ir
Received: Jun 27, 2014
Accepted: Aug 27, 2014
Introduction

Asphalt is produced by heating and drying gravel and mixing it with 4%–5% of hot bitumen. Bitumen is the residue of the distillation of selected petroleum crude oils. Fillers and fibers are also added to modify the properties of the asphalt, and small amounts of aliphatic amines are used to improve the binding between the bitumen and the stone materials.

Asphalt workers are exposed to a wide variety of modulators and modifiers added to the asphalt, such as antioxidants, anticorrosive agents, fillers, fibers, oxidants, plastics, rubber, waste materials and other volatile products that are released from the asphalt.

A major risk associated with exposure to asphalt is being exposed to polycyclic aromatic hydrocarbons and alkyl derivatives, which are byproducts of petroleum processing or combustion. These are highly carcinogenic at relatively low concentrations. Additionally, asphalt workers are exposed to emissions from the exhaust of passing vehicles. Respiratory effects of exposure to asphalt fume have been evaluated in a few studies. However, conclusive results have not been obtained yet.

For instance, many researchers have shown a significant reduction in some parameters of pulmonary function as well as upper respiratory tract irritation and shortness of breath in asphalt workers.

Some studies showed that exposure to asphalt fumes is associated with the incidence of respiratory symptoms. Moreover, bronchitis and emphysema have been reported in asphalt workers. On the other hand, some studies have not found a consistent relationship between exposure to asphalt fumes and decline in the parameters of lung function or increase in the prevalence of respiratory symptoms in asphalt workers. Similarly, Butler, et al., in a study on asphalt workers did not find an increased risk for obstructive pulmonary diseases.

The issue of asphalt fumes-induced respiratory disorders is subject to debate and controversy and requires further investigation. The respiratory effects of asphalt fumes have so far been studied in a few countries such as USA, Germany, and Norway. However, for differences in the chemical structure and composition of asphalt concrete mixtures, the concentration of asphalt fumes to which workers were exposed, air temperature, mechanical rather than manual processing of asphalt, good occupational health practices in these countries and many other differences, the results of these studies are not necessarily comparable with those of other studies. To the best of our knowledge, no study has been conducted on this issue in Iran. We therefore, conducted this study to examine the possible respiratory effects of exposure to asphalt fumes in asphalt workers.

Materials and Methods

This cross-sectional study was carried out to evaluate the respiratory effects of occupational exposure to asphalt fumes in paving workers of Shiraz, southern Iran. The sample size was calculated based on the expected prevalence of respiratory illness of 5% in unexposed employees, and 20% in asphalt workers, a study power of 80%,
and an α of 0.05.4

A total of 74 asphalt paving workers (exposed group) and 110 unexposed employees from governmental departments were randomly selected and served as the comparison group.

The study was conducted in accordance with the Helsinki Declaration of 1964 as revised in 2007.20 Both the exposed and unexposed participants were volunteers. No subject refused to participate in the study. All participants signed an informed consent form before commencement of the study. The protocol of the study was approved by Shiraz University of Medical Sciences Ethics Committee.

None of the exposed subjects had past medical or family history of respiratory illnesses or any other chest operations or injuries. Similarly, none of the subjects in the comparison group had been exposed to asphalt fumes or other chemicals known to cause respiratory symptoms or pulmonary diseases during the course of their employment or prior to it. Only two exposed employees did not meet the criteria to enter the study and were excluded due to pre-existing medical conditions and chest operation.

Measurement of the Study Variables

Respiratory illness

Subjects were interviewed by one of the authors (FZD). A respiratory symptom questionnaire, as suggested by the American Thoracic Society,21 with a few modifications, was administered to the participants.22 This standardized questionnaire included questions regarding respiratory symptoms (presence or absence of regular dry and/or productive cough, wheezing, shortness of breath, etc), nasal and eye symptoms and smoking habits, as well as occupational, medical and family history of each subject. Symptoms of chronic respiratory disorders included cough with sputum at any time during the day or night for at least three months of the year and for at least two consecutive years. Information extracted from the questionnaires were then used to determine the prevalence of symptoms among the exposed and unexposed groups.

Pulmonary function tests

Pulmonary function tests (PFTs) were performed using a portable calibrated Vitalograph spirometer (Model ST-150, manufactured by a joint Japanese-Philippinian company, Fukuda Sangyo Co, Ltd) on-site. The parameters of pulmonary function were measured twice for the exposed group (pre-shift after a 72-hour exposure-free period and post-shift) and once for the comparison group according to the protocol the details of which are described elsewhere.23,24 The measured parameters included mean percentage predicted vital capacity (VC), forced vital capacity (FVC), forced expiratory volume during the first second (FEV1), and peak expiratory flow (PEF).

Measurement of atmospheric concentrations of asphalt fumes

To assess the extent of subjects’ exposure to airborne contaminants, atmospheric concentrations of total particulate (TP) and benzene-soluble fraction (BSF) were measured in different work areas according to the NIOSH analytical method 5042.25 Samples were collected by a personal air sampling pump (Scientific Kit Corporation) equipped with a poly-tetra-fluoro-ethylene (PTFE) membrane filter (2-µm pore size) in a 37-mm cassette filter holder. The samples were re-weighed after sampling; the concentration of TP was calculated based on the weight difference, and the total air volume sampled. After determination of TP, each filter was extracted with benzene for the determination of BSF, which is the gravimetric amount of
the TP that is benzene soluble. Filters were submerged in benzene; the soluble parts were weighed to determine the amount of BSF.

Statistical Analysis

The data were analyzed by SPSS® ver 16.0 for Windows®. Student’s $t$ test for independent samples, $\chi^2$ or Fisher’s exact test, Mann-Whitney U test and logistic and multiple linear regression analysis, were used. A $p$ value $<0.05$ was considered statistically significant. Continuous variables with normal distribution were presented as mean (SD). Variables such as age, weight, height, smoking habits, education, and marital status were considered as potential confounders and their effects on the prevalence of respiratory symptoms and changes in pulmonary function indices were controlled. The initial model was constructed based on the exposure variable as well as all potential confounding variables. Using the backward elimination method and keeping the main exposure variable, asphalt fume, in the model, the final model was obtained.

Results

Demographic characteristics of the studied groups are presented in Table 1. No sig-

### Table 1: Demographic characteristics of the studied groups. Values are mean (SD), median [IQR], or n (%).

| Variable                                | Exposed (n=74) | Comparison (n=110) | p value |
|-----------------------------------------|---------------|--------------------|---------|
| Age (yr)                                | 37.4 (10.9)   | 33.8 (8.1)         | 0.016   |
| Height (cm)                             | 174.0 (7.6)   | 173.3 (6.9)        | 0.538   |
| Weight (kg)                             | 73.5 (12.1)   | 70.2 (11.9)        | 0.074   |
| Length of exposure/employment (yr)      | 10 [15.5]     | 8 [6.5]            | 0.239   |
| Level of education                      |               |                    |         |
| Illiterate                              | 9 (12%)       | 0 (0%)             |         |
| Diploma                                 | 34 (46%)      | 19 (17.3%)         | 0.001   |
| Higher education                        | 31 (42%)      | 91 (82.7%)         |         |
| Marital status                          |               |                    |         |
| Single                                  | 8 (11%)       | 12 (10.9%)         | 0.983   |
| Married                                 | 66 (89%)      | 98 (89.1%)         |         |
| Body mass index (kg/m$^2$)              | 24.3 (3.7)    | 23.4 (3.8)         | 0.122   |
| Smokers                                 | 19 (26%)      | 22 (20%)           | 0.364   |
| Length of smoking (yr)                  | 8.3 (5.7)     | 9.8 (7.5)          | 0.465   |
| Number of cigarettes smoked per day     | 7.8 (6.6)     | 4.7 (3.0)          | 0.058   |
| Air-bone concentration of TP (mg/m$^3$)  | 0.9 (0.2)     | —                  | —       |
| Air-bone concentration of BSF (mg/m$^3$) | 0.3 (0.1)     | —                  | —       |
Significant differences were noted for weight, height, length of employment, number of smokers, duration and intensity of smoking between the two studied groups. Nonetheless, the exposed group, on average, was about 3.5 years older than the comparison group (p=0.016). The mean atmospheric concentration of asphalt fumes did not exceed the current threshold limit value (TLV) of 0.5 mg/m³ set by the American Conference of Governmental Industrial Hygienists (ACGIH).

Pulmonary function test parameters measured in the exposed and unexposed groups are presented in Table 2. VC, FVC, FEV₁, and FEV₁/VC declined significantly after a working day in asphalt workers compared to pre-exposure values (p<0.05). Moreover, FEV₁/FVC and FEV₁/VC measured pre-shift in asphalt workers were significantly (p<0.001) lower than those in the comparison group.

Table 3 shows the prevalence of respiratory symptoms among asphalt workers and comparison group. The prevalence of all respiratory symptoms studied was significantly (p<0.001) higher in the exposed group than in the comparison group.
Binary logistic regression analysis of data, where age, length of exposure, weight, height, education level, and smoking were considered independent variables, significant (p<0.001) association was found between exposure to asphalt fumes and the prevalence of all respiratory symptoms but chest tightness (Table 4).

After adjusting for age, length of exposure, weight, height, education level, and smoking, multiple linear regression analysis revealed a significant (p<0.001) negative correlation between exposure to asphalt fumes and FEV\(_1\)/VC and FEV\(_1\)/FVC ratios. Exposure to asphalt fume reduced the FEV\(_1\)/VC, and FEV\(_1\)/FVC by 20.4% and 20.3%, respectively (Table 5).

Table 4: Association between exposure to asphalt fumes and development of respiratory symptoms (binary logistic regression analysis).

| Outcome                | OR (95% CI)    |
|------------------------|----------------|
| Cough                  | 6.9 (3.1 to 15.4) |
| Phlegm                 | 6.7 (2.9 to 15.5) |
| Productive cough       | 8.5 (3.4 to 21.1) |
| Wheezing               | 18.1 (5.9 to 56.0) |
| Shortness of breath    | 6.9 (2.6 to 18.9) |

Table 5: Association between exposure to asphalt fumes and changes in pulmonary function test indices (multiple linear regression analysis).

| Dependent variable     | β (95% CI)  |
|------------------------|-------------|
| VC                     | −3.1 (−6.9 to 0.7) |
| VC                     | −1.7 (−6.3 to 2.9) |
| FEV\(_1\)              | −3.6 (−8.2 to 1.1) |
| PEF                    | −4.4 (−10.4 to 1.6) |
| FEV\(_1\)/VC           | −20.4 (−24.3 to −16.5) |
| FEV\(_1\)/FVC          | −20.3 (−23.0 to −17.6) |

Discussion

Apart from age and level of education, there was no significant difference between the two studied groups in terms of other variables. There was also no significant difference in the number of smokers and smoking intensity between the two groups. Therefore, it is unlikely that smoking accounted for the differences observed in spirometry results. The significant reduction in FVC, FEV\(_1\), and FEV\(_1\)/FVC, and the significant increase in the respiratory symptoms are therefore, likely to be the result of exposure to asphalt fumes. This conclusion is also supported by the results of the logistic regression analysis (Table 4).

After adjusting for the important founders, a significant association was found between exposure to asphalt fumes and prevalence of respiratory symptoms; exposure to asphalt fumes increased the prevalence of cough and wheezing by 6.9 and 18.1 fold, respectively.

These observations are in agreement with the results of the Randem’s study on 64 asphalt workers. They showed that the risk of wheezing increased by 2.6 times as a result of exposure to asphalt fumes. Similarly, findings from other cross-sectional studies have shown a significant increase in the prevalence of respiratory symptoms following exposure to asphalt fumes.

Measurements of lung capacities before and after the exposure were the basis of assessment for acute and chronic effects of exposure to asphalt fumes. To differentiate the acute and chronic effects of exposure to asphalt fumes in this study, pulmonary function parameters were measured at the beginning (after a 72-hour exposure-free period) and at the end of shift. The average FEV\(_1\)/VC and FEV\(_1\)/FVC ratios in the exposed group (pre-exposure) were significantly lower than those of the comparison group that showed the chronic effect of the
exposure. Furthermore, cross-shift changes in all measured pulmonary function parameters reflected the acute effect of the exposure. These changes could not be attributed to the circadian rhythms considering the circadian rhythms lead to changes in opposite direction. The observed changes could be attributed to asphalt fumes-induced acute partially reversible decrements in pulmonary function tests. This conclusion is further confirmed by the results of multiple linear regression analysis (Table 5) and is consistent with the findings of other studies.

The findings of the current study are not consistent with the findings of some other studies. While the exact reasons for these discrepancies are not clear, factors such as difference in the air concentration of asphalt fumes in different studies, asphalt temperature, the season when the study was conducted, air velocity, direction of wind, the method asphalt was scattered (manual or mechanical), the emission model of asphalt vapors and fumes, study sample size, how confounding variables were controlled, type of statistical analysis, workload, and the personal protective equipment used may explain in part, this issue.

The nature of respiratory disorder associated with occupational exposure to asphalt fumes is consistent with the pattern of obstructive lung disease. In patients with obstructive lung disease, FVC is either normal or increased. The hallmark of this type of disorder is a significant reduction in FEV₁, hence, significant decrease in FEV₁/FVC. This conclusion is in keeping with the results of some other studies where an increased incidence of airway obstruction among asphalt workers has been reported. Other cross-sectional studies have also reported that chronic bronchitis and respiratory symptoms are associated with exposure to asphalt fumes. However, many confounding variables such as smoking, were poorly controlled and the study power was mostly poor.

The significant association between exposure to sub-TLV levels of asphalt fumes and increased prevalence of respiratory symptoms with diminished pulmonary function indices might be interpreted with certain level of skepticism. However, it has to be reiterated that these findings are not only found in this study. Other studies have already shown that exposure of dentists to sub-TLV levels of mercury was associated with sub-clinical symptoms of intoxication. Additionally, it is worth noting that the study was conducted in winter when, due to cold temperature, the concentrations of asphalt fumes were minimal. Therefore, it would plausible to assume that subjects in summer and hot seasons are exposed to higher concentrations of asphalt fumes, and thus, their cumulative exposure is likely to exceed the existing TLV values.

This study had some limitations. Cross-sectional studies cannot establish any cause and effect relationship. For this inherent limitation, one might argue that the significant increase in the prevalence of respiratory symptoms and deteriorated lung function in asphalt workers cannot necessarily be attributed to the exposure to asphalt fumes. While true, a few lines of evidence indicate that these are very likely to be the direct consequences of exposure to asphalt fumes: 1) The exposed group had no medical or family history of chronic lung disease, injuries and surgeries on the chest during the course of their employment, or before it. 2) The exposed workers did not have any exposure to other chemicals causing respiratory disorders. 3) While the pulmonary function in the exposed group partially improved after the exposure ceased, they were still significantly different from those in comparison subjects. 4) There were no significant differences in the number of smokers and smoking intensity.
in two studied groups. 5) Significant association between exposure to asphalt fumes and reduction in lung function parameters was observed. And, 6) after adjusting for confounding variables, significant associations were observed between exposure to asphalt fumes and respiratory disorders in asphalt workers.

Additional longitudinal studies with larger sample size, sufficient follow-up and longer duration of exposure are clearly required to further substantiate our findings.

In conclusion, we found that occupational exposure to sub-TLV levels of asphalt fumes is associated with increased prevalence of respiratory symptoms as well as acute, partially reversible and chronic irreversible changes in some parameters of pulmonary function.

Acknowledgements

The authors sincerely thank Mr. Vahid Dirin and Mr. Sassan Heydari for their technical assistance.

Conflicts of Interest: None declared.

Funding Source

Funding through the Shiraz University of Medical Sciences, Vice Chancellor for Research Affairs, contract #92-6743, partially supported these investigations.

References

1. Ulvestad B, Randem BG, Hetland S, et al. Exposure, lung function decline and systemic inflammatory response in asphalt workers. Scand J Work Environ Health 2007;33:114-21.
2. Roberts F, Kandhal P, Brown E, et al. Hot Mix Asphalt Materials, Mixture Design, and Construction. 2nd ed. Lanham, Maryland: NAPA Education Foundation, 1996.
3. Othmer K. Asphalt Encyclopedia of Chemical Technology. vol 3. Antibiotics (Phenazines) to Bleaching Agents. John Wiley & Sons, US, 1992, pp 299-302.
4. Randem BG. Respiratory symptoms and airflow limitation in asphalt workers. Occup Environ Med 2004;61:367-9.
5. Rauf Heimsoth M, Pesch B, Kendzia B, et al. Irritative effects of vapours and aerosols of bitumen on the airways assessed by non-invasive methods (suppl 1). Arch Toxicol 2011;85:541-52.
6. Karimi H, Mohamadzadeh H. Environmental contamination of a polycyclic aromatic hydrocarbons, (PAHs) in asphalt and bitumen. Fourth Conference and Exhibition of Environmental Engineering, 2010.
7. Marczynski B, Rauf-Heimsoth M, Preuss R, et al. Assessment of DNA damage in WBCs of workers occupationally exposed to fumes and aerosols of bitumen. Cancer Epidemiol Biomarkers Prevention 2006;15:645-51.
8. Rauf-Heimsoth M, Pesch B, Schott K, et al. Irritative effects of fumes and aerosols of bitumen on the airways: results of a cross-shift study. Arch Toxicol 2007;81:35-44.
9. Rauf-Heimsoth M, Pesch B, Spickenheuer A, et al. Assessment of irritative effects of fumes of bitumen on the airways: results of a cross-shift study in mastic asphalt workers. J Occup Environ Hygiene 2007;4(suppl 1):223-7.
10. Kinnes G, Miller A, Burr G. Health Hazard Evaluation Report: The Sim J. Harris Company, San Diego, California, 1996.
11. Sylvain D, Miller A. Health Hazard Evaluation Report HETA 94-0219-2620, Walsh Construction Company, Boston, Massachusetts, 1997.
12. Ma JYC, Barger MW, Kriech AJ, Castranova V. Effects of asphalt fume condensate exposure on acute pulmonary responses. Arch Toxicol 2000;74:452-9.
13. Hansen ES. Cancer mortality in the asphalt industry: a ten year follow up of an occupational cohort. British J Indust Med 1989;46:582-5.
14. Ekstrom L-G, Kriech A, Bowen C, et al. International studies to compare methods for personal sampling of bitumen fumes. J Environ Monitoring 2001;3:439-45.
15. Norseth T, Waage J, Dale I. Acute effects and exposure to organic compounds in road maintenance workers exposed to asphalt. Am J Industrial Med 1991,20:737-44.
16. Maizlish N, Beaumont J, Singleton J. Mortality among California highway workers. Am J Industrial
Med 1988;13:363-79.

17. Hansen ES. Mortality of mastic asphalt workers. Scand J Work Environ Health 1991;17:20-4.

18. Gamble JF, Nicolicli MJ, Barone NJ, Vincent WJ. Exposure-response of asphalt fumes with changes in pulmonary function and symptoms. Scand J work Environ Health 1999;25:186-206.

19. US Department of Health and Human Services, Public Health Service, Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health, Butler MA, Burr G, Dankovic D, et al. Hazard review: health effects of occupational exposure to asphalt, 2000.

20. Goodyear MD, Krleza-Jeric K, Lemmens T. The declaration of Helsinki. BMJ 2007;335:624-5.

21. Ferris BG. Epidemiology Standardization Project (American Thoracic Society). Am Rev Respir Dis 1978;118:1-120.

22. Jahangiri M, Neghab M, Nasiri G, et al. Respiratory disorders associated with occupational inhalational exposure to bioaerosols among wastewater treatment workers of petrochemical complexes. Int J Occup Environ Med 2015;6:41-9.

23. Neghab M, Mohraz MH, Hassanzadeh J. Symptoms of respiratory disease and lung functional impairment associated with occupational inhalation exposure to carbon black dust. J Occup Health 2011;53:432-8.

24. Neghab M, Choobineh A. Work-related respiratory symptoms and ventilatory disorders among employees of a cement industry in Shiraz, Iran. J Occup Health 2007;49:273.

25. Eller P, Cassinelli M. Method 5042, Benzene-soluble fraction and total particulate (asphalt fume). NIOSH Cincinnati, Ohio; 1998, pp 98-119.

26. ACGIH. TLVs and BEIs: Threshold Limit Values for Chemical Substances and Physical Agents and Biological Exposure Indices. Cincinnati, Ohio ACGIH, 2012.

27. Tompa A, Jakab MG, Biró A, et al. Health, genotoxicology, and immune status of road pavers in Hungary. J Occup Environ Hygiene 2007;4:154-62.

28. Baylor C, Weaver N. A health survey of petroleum asphalt workers. Arch Environ Health 1968;17:210-4.

29. Burr G, Tepper A, Feng A, et al. NIOSH Health Hazard Evaluation Report: HETA 2001-0536-2864 Crumb-Rubber Modified Asphalt Paving: Occupational Exposures and Acute Health Effects. National Institute for Occupational Safety and Health, Cincinnati Ohio, 2001:42.

30. Krasniuk E, Cheriuik V, Rossinskia L, Chui T. The effect of manufacturing factors in asphalt-bitumen plants on the health of the workers. Lik Sprava. 2000:106-12. [in Russian]

31. Maintz G, Schneider W, Maczek P. [Chronic obstructive airway diseases caused by long-term occupational exposure to asphalt pyrolysis products]. Z Erkr Atmungsorgane 1987;168:71-6. [in German]

32. Nyqvist B. [Respiratory tract symptoms in asphalt workers--another occupational bronchitis?] Lakartidningen 1978;75:1173-5. [in Swedish]

33. Guberan E, Williams MK, Walford J, Smith MM. Circadian variation of F.E.V. in shift workers. British J Indus Med 1969;26:121-5.

34. Spickenheuer A, Rühl R, Höber D, et al. Levels and determinants of exposure to vapours and aerosols of bitumen. Arch Toxicol 2011;85:21-8.

35. Kumar V CR, Robbin S. Basic Pathology. 6th ed. Philadelphia, WB Saunders Company, 1997, pp 393-425.

36. Surange N, Hoyle J. S4 Occupational asthma: is this the cause of excess respiratory symptoms and COPD described in bitumen exposed workers? Thorax 2011;66:A5-A6.

37. Neghab M, Choobineh A, Zadeh JH, Ghaderi E. Symptoms of intoxication in dentists associated with exposure to low levels of mercury. Industrial Health 2011;49:249-54.