

## Field Study

# Occupational Exposure and Thoracic Malignancies, Is There a Relationship ?

Sevin BASER<sup>1</sup>, Ozlem DUZCE<sup>1</sup>, Fatma EVYAPAN<sup>1</sup>, Beyza AKDAG<sup>2</sup>, Sibel OZKURT<sup>1</sup> and Goksel KITER<sup>1</sup>

<sup>1</sup>Department of Pulmonary Medicine, Pamukkale University Medical Faculty, Turkey and <sup>2</sup>Department Biostatistics, Pamukkale University Medical Faculty, Turkey

### Abstract: Occupational Exposure and Thoracic Malignancies, Is There a Relationship ?

**Sevin BASER, et al. Department of Pulmonary Medicine, Pamukkale University Medical Faculty, Turkey**—The

aim of this study was to evaluate the effect of occupational exposure in the occurrence of lung cancer.

**Method:** Three-hundred lung cancer cases diagnosed between September 1, 1999, and September 31, 2007, and 300 healthy controls were enrolled in this case-control study. Life-long occupational history, gender, age, exposure to asbestos, comorbidities, and smoking status were collected. **Results:** The mean age of the 300 lung cancer cases was 60.3 ± 9.9 year (91.7% male and 8.3% female), and the mean age of healthy control group was 60.4 ± 10.5 year (95.0% male and 5.0% female). The most frequent histological types were squamous (172, 57.3%), adeno (69, 23.1%), and small cell (37, 12.3%). There was an increased risk of lung cancer occurrence among agriculture workers (OR=1.89, 95% CI=1.17–2.98) ( $p=0.009$ ). Inorganic dust exposure (OR=1.81, 95% CI=1.0–3.25) ( $p=0.049$ ) and organic dust exposure (OR=1.89, 95% CI=1.0–3.59) ( $p=0.05$ ) were found to be related with high frequency of having lung cancer. **Conclusion:** Workers who had occupational exposure to organic and inorganic dust, especially in the agricultural field, had higher risk of lung cancer occurrence when compared with office workers.

(J Occup Health 2013; 55: 301–306)

**Key words:** Inorganic dust, Lung cancer, Occupational exposure, Organic dust

Lung cancer is the most common cancer diagnosis worldwide and is the major cause of cancer mortality, particularly among men<sup>1</sup>. Although tobacco smoking is by far the greatest risk factor for lung

cancer, occupational exposures still require attention<sup>1</sup>. It was estimated worldwide in year 2000 that 10% of lung cancer deaths in men (88,000 deaths) and 5% in women (14,300 deaths) were attributable to exposure to selected occupational lung carcinogens (arsenic, asbestos, beryllium, cadmium, chromium, diesel fumes, nickel, and silica)<sup>2</sup>. In the same year in Europe, assuming attributable fractions of 7–15% (men) and 2–9% (women), the estimated number of deaths was over 32,000<sup>2</sup>. The workplace provides an environment in which there is a risk of exposure to carcinogens. In recent years, people know about the damage caused by smoking, and because of quit-smoking policies, occupational exposure to carcinogens will be more important for the etiology of thoracic malignancies in the next decades. The International Agency for Research on Cancer currently lists 19 substances/work situations/occupations that have been proven to be associated with lung cancer (group 1)<sup>3</sup>.

Organic dust consists of particulate matter of microbial, plant or animal origin<sup>4</sup>. The association between occupational exposure to organic dust and its specific constituents and lung cancer risk in the general population is controversial. Increased lung cancer risks have been reported in certain occupations exposed to organic materials, for instance, in meat and wood workers<sup>5,6</sup>. Alternatively, decreased risks among workers exposed to organic dust have also been described<sup>7</sup>. Endotoxin has been proposed to be protective for the development of lung cancer. A recent large pooled case-control study on lung cancer by Peters *et al.*<sup>4</sup> does not seem to support the previous findings, especially among farmers, regarding a possible protective effect of endotoxin. The authors concluded that occupational exposure to organic dust appears to be associated with an increased risk of lung cancer.

In spite of smoking being the etiologically domi-

Received Apr 27, 2013; Accepted May 2, 2013

Published online in J-STAGE Jun 24, 2013

Correspondence to: S. Baser, Pamukkale University Medical Faculty, Department of Pulmonary Medicine, Denizli, Turkey

(e-mail: basersevin@yahoo.com, sevinbaser@pau.edu.tr)

nant factor, lung cancer is quantitatively the most important of work-related cancer. In this study, we evaluated the effect of occupational exposure on the occurrence of lung cancer.

### Materials and Methods

Three-hundred lung cancer cases diagnosed between September 1, 1999, and September 31, 2007, and 300 healthy controls were enrolled in this case-control study. The study was approved by the ethics committee of the University Hospital, and written consent was obtained from all participants. Controls were selected among other patients' relatives who came to hospital with them. The controls were disease free, and the cases had lung cancer.

Data collection was done with a person-to-person questionnaire. The structured questionnaire collected data on age, sex, sociodemographic characteristics, residential history, comorbidities (such as chronic obstructive pulmonary disease, asthma, tuberculosis, diabetes mellitus, congestive heart failure and hypertension and etc.), occupational history, occupational exposures, asbestos exposure and current and past tobacco use. For occupational history, we obtained information on industry name, production type, job title, total work days and work hours in a week, air conditioning status in the workplace, use of a mask or not, description of the workplace (presence of gases, dusts, vapors, or other inhaled agents) and detail occupational exposure materials.

We grouped the cases and controls according to their exposure type by description of the workplace (presence of gases, organic and inorganic dusts, or inhaled agents, production type) and the job they do (industry type). Accordingly, agriculture workers and farmers are grouped separately as group I because they may be exposed to organic dust (particulate matter of microbial, plant or animal origin, hay, grass and field dust), inorganic dust (for example, silica while working with soil), irritants and gases (most of the farmers apply pesticides by themselves). Ceramic and pottery workers, construction workers and mining and quarrying workers were grouped as group II because they were exposed to mainly inorganic dust. Textile workers (not in painting processes, not exposed to irritants), bakers and sugar and sweet production workers were grouped as group III because they were exposed to mainly organic dust. Electrical and electronics equipment assemblers, rubber and plastics product makers, iron and steel foundry workers, house cleaners, painters, and drivers were grouped as group IV because they were exposed to mainly irritants. Cases and controls who work at offices and do not have any exposure were grouped as group V. Cases and controls were categorized according to their

jobs and exposure types as summarized below.

Group I: Agriculture workers and farmers

Group II: Exposure to inorganic dust (ceramic and pottery workers, construction workers, mining and quarrying workers)

Group III: Exposure to organic dust (textile workers, bakers, sugar and sweet production workers)

Group IV: Exposure to irritant (electrical and electronics equipment assemblers, rubber and plastics product makers, iron and steel foundry workers, house cleaners, painters, and drivers)

Group V: No exposure (working in an office)

We also asked agriculture workers how many times they used pesticide in a year to analyze their pesticide exposure.

Histopathologic types of lung cancer were obtained from medical records of the hospital database.

Smoking data included the number of pack-years smoked (the average number of packs of cigarettes smoked per day multiplied by the number of years smoked); smoking status was defined as never-smoker, former smoker, and current smoker. A never-smoker was defined as a patient who had never smoked before or had smoked <100 cigarettes in his/her lifetime and was not a current smoker<sup>8)</sup>. A former smoker was defined as one who had previously smoked >100 cigarettes in his/her lifetime and quit smoking >1 year before diagnosis.

### Statistical analysis

Descriptive statistics are given as frequency, percentage and mean  $\pm$  standard deviation. The SPSS 10.0 package was used for analysis. The data were statistically analyzed by using the independent samples *t*-test, chi-square test and odds ratios and 95% confidence intervals. The statistical significance was set at  $p < 0.05$ .

### Results

Demographic data of cases and healthy controls are presented in Table 1.

The histological types were squamous (172, 57.3%), adeno (69, 23.1%), small cell (37, 12.3%), mesothelioma (10, 3.3%), large cell (5, 1.7%), and others (7, 2.3%).

Occupations of cases and the members of the control group are given in Table 2.

There was an increased risk of lung cancer occurrence among agriculture workers (odds ratio (OR)=1.89, 95 percent confidence interval (95% CI)=1.17–2.98) ( $p=0.009$ ) (Table 2). Inorganic dust exposure (OR=1.81, 95% CI=1.0–3.25) ( $p=0.049$ ) and organic dust exposure (OR=1.89, 95% CI=1.0–3.59) ( $p=0.05$ ) were

**Table 1.** Demographic data of cases and healthy controls

	Cases		Controls		p value
	n	%	n	%	
Male	275	91.7	285	95	NS
Female	25	8.3	15	5	NS
Mean age $\pm$ SD	60.3 $\pm$ 9.9		60.4 $\pm$ 10.5		NS
Never smoked	38	12.7	89	29.1	$p=0.001$
Former smoker	173	57.7	145	48.3	$p=0.001$
Smoker	89	29.7	66	22	$p=0.001$
Asbestos exposure	175	58.3	182	60.7	NS
Mean working days (days/week)	5.94 $\pm$ 0.66		6.17 $\pm$ 3.47		NS
Mean working hours (hours/week)	47.2 $\pm$ 11.3		47.5 $\pm$ 14.6		NS
Existance of airconditioning	248	82.7	238	79.3	NS
Use of a mask	7	2.3	4	1.3	NS

NS=not significant.

**Table 2.** The risk of occurrence of thoracic malignancy among cases and controls

	Cases		Controls		OR	95% CI	p*
	n	%	n	%			
Group I (agricultural workers)	80	26.7	55	18.3	1.89	1.17–2.98	$p=0.009$
Group II (exposure to inorganic dust)	38	12.7	27	9.0	1.81	1.00–3.25	$p=0.049$
Group III (exposure to organic dust)	31	10.3	21	7.0	1.89	1.00–3.59	$p=0.05$
Group IV (exposure to irritant)	84	28	111	37.0	0.97	0.63–1.49	NS
Group V (no exposure)	67	22.3	86	28.7	1.00		

NS=not significant. \*The chi-square test was used.

found to be related to high frequency of having lung cancer (Table 2).

Mean pesticide exposure of the cases was  $0.73 \pm 1.37$  times/year, and the mean pesticide exposure of the control group was  $0.44 \pm 1.01$  times/year. Cases with thoracic malignancies had significantly higher exposure to pesticides ( $p<0.01$ ).

There was no relationship between the histological types of cancer and occupation ( $p>0.05$ ).

The mean working days, mean working hours and use of a mask were not statistically different between the patients and control group (Table 1).

## Discussion

In the present study we found that there was an increased risk of lung cancer occurrence among agriculture workers. Pesticide exposure of these patients was higher when compared with the members of the control group who worked in agriculture. Inorganic dust exposure and organic dust exposure were found to be related to high frequency of having lung cancer.

Several agents encountered in the occupational

setting, such as asbestos, polycyclic aromatic hydrocarbons, arsenic, beryllium, cadmium, chromium, and nickel compounds, are established carcinogens that target the lung<sup>9</sup>. However, despite the knowledge that has been accumulated for decades, establishing occupational causality in cases of lung cancer remains extremely uncommon.

Organic dust is a complex mixture of particulate matter of microbial, plant or animal origin<sup>4</sup>. It is present in many work environments, such as in bakeries, sugar and sweet production, the textile industry, sawmills, and the meat industry. Exposure to organic dust in the workplace is known to lead to an increased risk of occupational respiratory diseases, such as chronic obstructive pulmonary disease (COPD), asthma, hypersensitivity pneumonitis and organic dust toxic syndrome<sup>4</sup>. Much less is known about the risk of lung cancer due to organic dust exposure. Decreased risks among workers exposed to organic dust have also been described. A recent meta-analysis showed a reduction in lung cancer risk among agricultural and (cotton) textile workers who were

exposed to organic dust containing endotoxin<sup>7</sup>). Also, Fritschi *et al.* did not find increased risk of cancer in employees within the textile industry<sup>10</sup>). Stimulation of the immune system, in particular macrophages, by endotoxin has been hypothesized to be the mechanistic pathway<sup>4</sup>). However, many of the epidemiological studies were not adequately controlled for smoking, and therefore residual confounding due to differences in smoking habits between exposed and nonexposed subjects could not be excluded. Besides, a recent study by Peters *et al.* showed that occupational exposure to organic dust was associated with an increased risk of lung cancer, while no effect was observed for endotoxin exposure or contact with animals or animal products<sup>4</sup>). Our findings are concurrent with Peters *et al.* In our study, organic dust exposure was found to be related to high frequency of having lung cancer. An elevated risk of lung cancer was found for men employed in certain food processing occupations (e.g., baking, confectionery making) and food service occupations (e.g., cooks, chefs and bartenders, but only for large-cell carcinoma<sup>11</sup>). This is consistent with epidemiological evidence showing an excess risk in these occupations<sup>12-16</sup>). Cooking fumes are an important common exposure in these occupations. Other suspected carcinogens in bakeries include polycyclic aromatic hydrocarbons (PAH), reaction products of PAH, free radicals, n-nitrosodimethylamine, aflatoxin, sterigmatocystin, and zearalenone<sup>17</sup>). Certain occupations involving exposure to organic dust were associated with an excess risk of lung cancer in our study, in agreement with the literature.

In a population-based case-control study by Menvielle *et al.*, exposure to field dust was associated with lung cancer risk in both sexes, and the risk increased with cumulative exposure level<sup>18</sup>). They also showed that exposure to straw, hay, grass and field dust significantly increased the risk of lung cancer. Similar to their study, we found that there was an increased risk of lung cancer occurrence among agriculture workers in our study. Excessive cancer rates, particularly for prostate, lymphohematopoietic, brain, stomach, and soft-tissue tumors, have been reported among agricultural workers and pesticide applicators and manufacturers around the world<sup>21</sup>). In our study, we also asked agriculture workers how many times they used pesticides in a year to analyze their pesticide exposure. Patients with thoracic malignancies had significantly higher exposure to pesticides when compared with the control group who worked at agriculture. Several epidemiological studies have reported associations between specific pesticides and increased cancer risks<sup>19</sup>).

Silica-containing dusts (quartz dust, cement dust, granite dust), silicate-containing dust, limestone, shale

dust, clay, and asbestos are some types of inorganic dusts<sup>20</sup>). Silica (silicon dioxide) occurs in crystalline and amorphous forms. Of the several crystalline polymorphs of silica found in nature, quartz is by far the most common, being abundant in most rock types, notably granites, sandstones and quartzites, and in sands and soils. Because of the wide usage of quartz-containing materials, workers may be exposed to quartz in a large variety of industries and occupations<sup>21</sup>). Seventeen cohort and five case-control studies have been reported on ore miners potentially exposed to silica dust. The majority of these studies reported an elevated mortality for lung cancer among silica-exposed workers<sup>21</sup>). However, only a few ore mining studies took into account cofounders such as other known occupational respiratory carcinogens. In such studies, consistent evidence for a silica-lung cancer relationship was not found<sup>21</sup>). Stanczyk and Szymczak<sup>22</sup>) showed a fourfold increase in the risk of mortality from lung cancer in workers exposed to inorganic dusts, regardless of smoking habits. Their results also add to the evidence that the risk of lung cancer increases with cumulative exposure to inorganic dusts. Significantly increased lung cancer risk for workers in the ceramics industry and pottery manufacturing<sup>23</sup>) was shown. In ceramic and pottery manufacturing plants, exposures are mainly to quartz, but where high temperatures are used in ovens, potential exposures to cristobalite may occur. In a cohort study of British pottery workers, lung cancer mortality was slightly elevated; a nested case-control analysis of lung cancer did not show an association with duration of exposure, but did indicate a relationship between lung cancer mortality and average and peak exposures in firing and post-firing operations, with relative risks of approximately 2.0<sup>21</sup>). Similar to the studies in the literature, we found higher lung cancer risk for exposure to inorganic dust. An increased risk of lung cancer was noted among men employed as carpenters, insulators, electricians, excavators, pavers, and graders in the construction sector<sup>11</sup>). Although exposure to the dust-containing asbestos and silica seems common in the construction industry, the predominant and the etiologically relevant exposures in the individual occupations are likely different. Construction workers are exposed to many known or suspected carcinogens, including silica, asphalt, fumes, polycyclic aromatic hydrocarbons (PAHs), diesel exhaust, paints, asbestos, lead, metal fumes, and solvents<sup>24</sup>). Polycyclic aromatic hydrocarbons (PAHs) are products of the incomplete combustion or pyrolysis of organic material<sup>25</sup>). Smoking-adjusted increased risks for lung cancer were reported for several industries and for general occupational exposures to PAHs in Germany, Norway and Sweden<sup>25</sup>). The two larger studies (Germany and

Sweden) also found positive exposure–response relationships. A study of lung cancer in Canada found an excess risk for exposure to PAHs from any occupational source among light smokers and nonsmokers only; a Dutch study reported inconsistent results<sup>25</sup>.

Occupational exposure to welding fumes and dusts was associated with a higher relative risk of epidermoid carcinomas than that of other histological types<sup>26</sup>. In one study, there was excessive risk of small cell carcinoma and epidermoid carcinoma in comparison with adenocarcinoma<sup>27</sup>. Therefore, it is possible that there is an association between a given type of exposure and certain cell types of lung cancer. However, in our study, we could not find any relationship between the histological types of thoracic malignancies and type of occupation. Our small patient numbers may preclude definitive conclusions.

In conclusion, our study showed that workers who were occupationally exposed to organic and inorganic dust, especially in the agricultural field, had higher risk of lung cancer occurrence when compared with office workers.

The workplace provides an environment in which there is a risk of exposure to carcinogens. It is difficult to predict the trend for the future incidence of occupational respiratory cancer, but it looks like occupational respiratory cancer has increased during the last 10 to 20 years. Important programs and regulations must be in place to prevent and control occupational cancer, such as banning all forms of asbestos, taking and noting detailed information on workplace production processes, presence of aerosols, gases and vapors, workplace exposure monitoring, and occupational disease surveillance systems.

## References

- Guida F, Papadopoulos A, Menvielle G, et al. Risk of lung cancer and occupational history: results of a French population-based case-control study, the ICARE study. *J Occup Environ Med* 2011; 53: 1068–77.
- De Matteis S, Consonni D, Bertazzi PA. Exposure to occupational carcinogens and lung cancer risk. Evolution of epidemiological estimates of attributable fraction. *Acta Biomed* 2008; 79: 34–42.
- Algranti E, Buschinelli JT, De Capitani EM. Occupational lung cancer. *J Bras Pneumol* 2010; 36: 784–94.
- Peters S, Kromhout H, Olsson AC, et al. Occupational exposure to organic dust increases lung cancer risk in the general population. *Thorax* 2012; 67: 111–6.
- McLean D, Pearce N. Cancer among meat industry workers. *Scand J Work Environ Health* 2004; 30: 425–37.
- Barcenas CH, Delclos GL, El-Zein R, Tortolero-Luna G, Whitehead LW, Spitz MR. Wood dust exposure and the association with lung cancer risk. *Am J Ind Med* 2005; 47: 349–57.
- Lenters V, Basinas I, Beane-Freeman L, et al. Endotoxin exposure and lung cancer risk: a systematic review and meta-analysis of the published literature on agriculture and cotton textile workers. *Cancer Causes Control* 2010; 21: 523–55.
- World Health Organization. WHO guidelines for controlling and monitoring the tobacco epidemic. Geneva (Switzerland): World Health Organization; 1998. p. 77.
- De Matteis S, Consonni D, Lubin JH, et al. Impact of occupational carcinogens on lung cancer risk in a general population. *Int J Epidemiol* 2012; 41: 711–21.
- Fritschi L, Lakhani R, Nadon L. Cancer incidence in textile manufacturing workers in Australia. *J Occup Health* 2004; 46: 493–6.
- Yenugadhati N, Birkett NJ, Momoli F, Krewski D. Occupations and lung cancer: a population-based case-control study in British Columbia. *J Toxicol Environ Health A* 2009; 72: 658–75.
- Richiardi L, Boffetta P, Simonato L, et al. Occupational risk factors for lung cancer in men and women: a population-based case-control study in Italy. *Cancer Causes Control* 2004; 15: 285–94.
- Notani PN, Shah P, Jayant K, Balakrishnan V. Occupation and cancers of the lung and bladder: a case-control study in Bombay. *Int J Epidemiol* 1993; 22: 185–91.
- Zahm SH, Brownson RC, Chang JC, Davis JR. Study of lung cancer histologic types, occupation, and smoking in Missouri. *Am J Ind Med* 1989; 15: 565–78.
- Brüske-Hohlfeld I, Möhner M, Pohlabein H, et al. Occupational lung cancer risk for men in Germany: results from a pooled case-control study. *Am J Epidemiol* 2000; 151: 384–95.
- Spinelli JJ, Gallagher RP, Band PR, Threlfall WJ, Raynor D, Schellekens H. Occupational associations among British Columbia male cancer patients. *Can J Public Health* 1990; 81: 254–8.
- Tüchsen F, Nordholm L. Respiratory cancer in Danish bakers: a 10 year cohort study. *Br J Ind Med* 1986; 43: 516–21.
- Menvielle G, Luce D, Févotte J, et al. Occupational exposures and lung cancer in New Caledonia. *Occup Environ Med* 2003; 60: 584–589.
- Andreotti G, Hou L, Beane Freeman LE, et al. Body mass index, agricultural pesticide use, and cancer incidence in the Agricultural Health Study cohort. *Cancer Causes Control* 2010; 21: 1759–75.
- Baccarelli A, Khmel'nitskii O, Tretiakova M, et al. Risk of lung cancer from exposure to dusts and fibers in Leningrad Province, Russia. *Am J Ind Med* 2006; 49: 460–7.
- Silica, Some Silicates, Coal Dust and para-Aramid Fibrils, IARC Monographs Volume 68. Lyon (France): 1997. p. 204–8.
- Szadkowska-Stańczyk I, Szymczak W. Nested case-

- control study of lung cancer among pulp and paper workers in relation to exposure to dusts. *Am J Ind Med* 2001; 39: 547–56.
- 23) Wünsch-Filho V, Moncau JE, Mirabelli D, Boffetta P. Occupational risk factors of lung cancer in São Paulo, Brazil. *Scand J Work Environ Health* 1998; 24: 118–24.
- 24) Calvert GM, Luckhaupt S, Lee SJ, et al. Lung cancer risk among construction workers in California, 1988–2007. *Am J Ind Med* 2012; 55: 412–22.
- 25) Some Non-heterocyclic Polycyclic Aromatic Hydrocarbons and Some Related Exposures. IARC Monographs on the Evaluation of Carcinogenic Risks to Humans. Volume 92. Lyon (France): 2010. p. 754–9.
- 26) Siew SS, Kauppinen T, Kyyrönen P, Heikkilä P, Pukkala E. Exposure to iron and welding fumes and the risk of lung cancer. *Scand J Work Environ Health* 2008; 34: 444–50.
- 27) Consonni D, De Matteis S, Lubin JH, et al. Lung cancer and occupation in a population-based case-control study. *Am J Epidemiol* 2010; 171: 323–33.