

## Lung cancer in relation to occupational and environmental chromium exposure and smoking

E. HALAŠOVÁ<sup>1</sup>, T. BAŠKA<sup>3</sup>, F. KUKURA<sup>1</sup>, D. MAZÚROVÁ<sup>2</sup>, E. BUKOVSKÁ<sup>1</sup>, D. DOBROTA<sup>4</sup>, I. POLIAČEK<sup>5</sup>, M. HALAŠA<sup>6</sup>

<sup>1</sup>Department of Biology, e-mail: halasova@jfmfmed.uniba.sk, Comenius University, Jessenius Faculty of Medicine, 03601 Martin, Slovak Republic; <sup>2</sup>Department of Oncology, Hospital Dolný Kubín, Slovak Republic; <sup>3</sup>Department of Epidemiology, <sup>4</sup>Department of Medical Biochemistry, and <sup>5</sup>Department of Biophysics, Comenius University Bratislava, Jessenius Faculty of Medicine, Martin, Slovak Republic; <sup>6</sup>Clinic of Surgery, Faculty Hospital in Martin, Slovak Republic

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The increased occurrence of lung cancer in residents of Dolný Kubín, the North-Slovakia district with ferrochromium industry, compared to the general population of Slovakia, led us to the study assessing influence of the occupational and environmental exposure to chromium on the lung cancer incidence, respecting also the risk coming from cigarette smoking. Residents of Dolný Kubín district with the diagnosed lung cancer in 1984–1999 were involved in the study.

The occurrence of lung cancer was significantly higher in people working in ferrochromium industry. The age at the onset of the disease in people exposed to chromium was by 5.5 years lower than in non-exposed.

Smoking was an important risk factor, which has been proved particularly in non-exposed group where 62% were smokers and the onset of the lung cancer in them occurred about 3.4 years earlier than in non-smokers. In exposed groups, no significant effect of smoking was found.

We can conclude, that occupational exposure to chromium was identified as the main risk factor of lung cancer in Dolný Kubín district even overlaying effect of smoking.

*Key words: lung cancer, chromium, cigarette smoking*

Since the 1950s an increased occurrence of lung cancer was reported among workers of ferrochromium industry [2, 14, 16]. The data on occurrence in individual reports was different. The authors did not pay attention either to the smoking habits or to the age-composition of the compared groups.

The conclusion that chromates should be considered as carcinogenic was not generally accepted at that time, but the increase of frequency of lung cancer in relation to the exposure to chromates was in most reports unequivocal.

Due to these findings several research teams started assessing the risk of lung cancer in those exposed to chromium. They concluded that workers in the ferrochromium industry have an excess risk of lung cancer [3, 6, 7, 12, 15, 19, 30, 31, 33, 34, 36].

In 1980 the International Agency for Research on Cancer identified chromium and some of its compounds as human carcinogens [13].

It is now generally accepted that cigarette smoking plays an important role in carcinogenesis of bronchopulmonary tract [1, 9, 11, 29, 43].

In 1953, the ferrochromium works in Istebne (Dolný Kubín district) started its production, and the frequency of bronchogenic carcinomas started to rise in the region [20–28, 37–41]. Particularly, the percentage of lung cancer among all cancers in the study area exceeded the values in Slovak population over the recent 5 years. These findings have prompted us to our current study assessing lung cancer incidence in relation to chromium exposure and smoking with attention to the onset of the illness.

### Subjects and methods

*Subjects and sampling.* The data of the Department of Oncology of Dolný Kubín Hospital over 1985–1999 have been analyzed (574 men and 58 women diagnosed for lung cancer). The occurrence of lung cancer in both sexes was compared separately for every year with the data of National Cancer Registry of Slovakia [20–28, 37–41] and then summarized in Table 1. The numbers of inhabitants in Dolný Kubín district in the period of analyzed years provided us

**Table 1. Number of cases, rate, 95% CI for lung cancer and all cancer and percentage of lung cancers in the Dolný Kubín district and the rest of Slovakia, 1985–1999**

	Dolný Kubín district				Slovak Republic except Dolný Kubín district				Relative	
	Cases	Rate <sup>§</sup>	No of 95% of CI	%	Cases	Rate	No of 95% CI	%	Risk	95% CI
Lung cancer										
Men	574	83.3	79.8–89.3	26.5	32276	72.6	67.3–74.5	21.0	1.26	1.13–1.32
Women	58	7.8	6.7–8.2	3.3	4795	11.7	10.8–12.3	3.4	0.67	0.53–0.78
Both sexes	632	45.6	41.3–47.2	15	37071	42.2	41.3–43.4	13.1	0.92	0.82–1.03
All cancer										
Men	2159	297.5	279.3–301.5		153539	395.6	387.3–401.2		0.76	0.67–0.89
Women	1718	221.5	213.4–242.3		128583	316.1	314.8–318.1		0.70	0.63–0.87
Both sexes	4177	259.5	247.2–265.3		282122	355.9	352.9–363.2		0.73	0.67–0.82

CI – confidence interval, § – per 100,000 person/year, % – percentage of lung cancer of all cancers.

Statistical Institute in Martin (unpublished) to calculate rates. Relative values were used to refer to the onset of the illness in analyzed group.

The group of men was divided into 3 subgroups according to the level of exposure: Exp 0 included residents of the district Dolný Kubín not particularly exposed to chromium; Exp 1 were workers of ferrochromium works not directly exposed to chromium; Exp 2 were workers of ferrochromium works directly exposed to chromium (smelters, tapers and crane operators).

Smoking history and age analysis were an integral part of the study.

*Exposure data.* Chromium analysis in soil and air was made in the vicinity of the plants. The samples taken over 1960–2000 were examined by atomic absorption spectrometry (Varian spectrophotometer AA 30-P). The mean all-shift concentrations of total chromium in the air inside the smelting plant were 0.03–0.19 mg.m<sup>-3</sup>, the values of hexavalent chromium were between 0.019–0.03 mg.m<sup>-3</sup>. The mean concentrations of total chromium in the air in the environment surrounding the works and in the control area (0.013 µg.m<sup>-3</sup>) did not reach the hygienic norm (0.01–0.0117 µg.m<sup>-3</sup>).

In the soil, in a distance of 200 m from the plants, the chromium content was 137 mg.kg<sup>-1</sup>, which is slightly exceeding the hygienic norm (100 mg.kg<sup>-1</sup>). The chromium content in the soil from wider distance and from the control area was below the hygienic norm (60.2 mg.kg<sup>-1</sup> and 46.0 mg.kg<sup>-1</sup>, respectively).

*Statistical analysis.* The found differences were tested by Student's t-test. Relative risk of lung cancer with 95% confidence intervals in relation to chromium exposure was calculated.

## Results

A significant difference was found in the percentage of lung cancer incidence between inhabitants of Dolný Kubín

district and Slovak population (Tab. 1). The relative risk of lung cancer in men (RR=1.26; CI 95%=1.13–1.32) and women (RR=0.67; CI 95%=0.53–0.78) differ between sexes indicating that lung cancer in our study area affects predominantly male population while RR in females is below the rate in the female Slovak population. The relative risks of all cancers were similar in both sexes (0.76; CI 95%=0.67–0.89 in male and 0.70; CI 95%=0.63–0.87 in female) below the values in the general Slovak population.

Table 2 shows the distribution of cases of lung cancer among residents of Dolný Kubín district. The rate (75.2 per 100,000) of lung cancer in the subgroup Exp 0 is close to the rate of general Slovak male population (72.6 per 100,000). This rate in the subgroup Exp 1 was 112.5 per 100,000, which is 1.42 times higher than in non-exposed group. In the directly exposed subgroup Exp 2 (smelters, tapers and crane operators) the rate was 320.1 per 100,000, which is 4.04 times higher than in the non-exposed subgroup.

The results of a detailed analysis of men from different subgroups according to the smoking habits and the age at the onset of cancer are summarized in Table 3. Comparison of the age at the onset of cancer between smokers and non-smokers was tested by Student's t-test. In the group of non-exposed significant difference between the age at the onset of the disease was found between smokers (64.3 years) and non-smokers (67.7 years) (P=0.009). Non-exposed

**Table 2. Number of cases, rate, 95% CI for lung cancer in the Dolný Kubín district, 1985–1999**

Group	Number of cases	Rate <sup>§</sup>	95% CI	Relative Risk <sup>*</sup>
Exp 0	409	79.2	76.3–80.2	
Exp 1	106	112.5	109.0–113.4	1.42
Exp 2	59	320.1	317.9–322.8	4.04

§ – per 100,000 person/year, \*relation between exposed and non-exposed groups.

**Table 3. Number of cases and mean age of onset of lung cancer according to the smoking status in different subgroups**

Group	Number of cases	Mean (in years)	Range (in years)	SD	P- value*
Exp 0	409	65.6	45-75	10.8	
Smokers	254	64.3	45-75	10.8	
Non-smokers	155	67.7	49-70	10.4	0.009
Exp 1	106	63.9	39-72	8.7	
Smokers	73	63.6	39-78	8.1	
Non-smokers	33	64.2	39-82	10.0	0.742
Exp 2	59	61.0	43-87	7.3	
Smokers	45	60.9	39-85	7.3	
Non-smokers	14	61.4	47-87	7.6	0.809

\*comparison between smokers and non-smokers by t-test.

non-smokers had explicitly higher age at the onset of the illness in relation to other groups. In exposed groups (directly and indirectly) significant effect of smoking on the age at the onset of the disease was not found ( $P=0.809$  and  $0.742$ , respectively).

## Discussion

The present study is a logical continuation of our preceding study in which increased cytogenetic parameters were found only in workers directly exposed to chromium, not in the group exposed to its environmental level [10]. Based on these findings and the data of the Slovak National Oncology Register concerning residents of Dolný Kubín district, we focused our attention on this problem. The aim of our current study was to find out if the increased occurrence of lung cancer is typical for all residents of the Dolný Kubín district or for the workers directly exposed to chromium only.

However, it is generally accepted that smoking is one of the main causes of lung cancer, so we analyzed the smoking habit as well.

Our first finding that the occurrence of lung cancer is significantly higher only in the group of workers directly exposed to chromium (despite using respirators) is in accordance with the research results of DAVIES et al [4], GIBB et al [8], MATOS et al [17] and SORAHAN et al [35]. All these authors found an increased risk of lung cancer among workers occupationally exposed to chromium. The finding that chromium exposure decreases the age at the onset of illness is similar to GIBB's findings.

Our results show that occurrence of lung cancer in people living in the neighbourhood of the plants was similar to the general Slovak population.

These results are in accordance with our negative findings of hexavalent chromium in the air and soil in the neighbourhood of the works. A minor amount of chromium, which is ingested or inhaled, can be effectively reduced by de-

toxication mechanisms of the human body [5]. ROWBOTHAM et al [32] who evaluated the impact of environmental exposure to chromium on the human health of the population of UK concluded that there is no clear evidence to relate exposure to environmental levels of chromium with adverse health effects either in the general UK population or in the population of suburbs exposed to chromium around industrialised or contaminated sites. MC CARRON et al [18] used for the evaluation of self-reported health the questionnaire SF 36. He did not find any differences between environmentally exposed group and the control group. Our findings confirm previous supposition that a low-environmental level of chromium itself does not have any negative health effects and does not increase the risk of lung cancer.

There is still little information about combined effect of chromium and smoking. GIBB et al [8] mentioned this problem, but unfortunately in his group of lung cancer patients were only 4 non-smokers, which did not allow reliable statistical analysis. In our study groups of the increased exposure an increase rate of smokers was found. The negative role of smoking was most evident in the group of non-exposed men. Smoking decreases the age of the onset of illness approximately by 3.5 years in comparison with non-smokers. We did not find any significant difference in the age at the onset of illness between smokers and non-smokers in non-directly and directly exposed groups. This finding can lead us to an assumption that smoking and chromium exposure do not have a cumulative effect as we expected according to the findings of WILLIAMS and SANDLER [42]. Our study shows that the final effect of combined action of chromium and smoking is not quantitative but qualitative. In exposed men effect of smoking disappeared. Mean age of onset of the lung cancer among exposed non-smokers is even lower than in not-exposed smokers. It indicates, that chromium exposure has stronger carcinogenic effect and can overlay effects of smoking. We can conclude that occupational exposure as well as smoking significantly increase the occurrence of lung cancer and decrease the age of the onset of the disease. According to our findings general environmental exposure to chromium does not seem to have any negative health effect.

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