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COMBINED EFFECTS OF MINING AND SMOKING IN THE CAUSATION OF LUNG CARCINOMA

A case-control study in northern Sweden

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Lung carcinoma in underground miners is one of the oldest known occupational malignant tumors and its symptoms were already observed centuries ago in Bohemian miners. During the last decades several reports have elucidated the relation between underground mining and respiratory malignancies in both uranium and non-uranium miners in the United States, Czechoslovakia, Canada, England and Sweden (SIKL 1950, WAGONER et coll. 1965, DE VILLIERS & WINDISH 1964, BOYD et coll. 1970, S:T CLAIR RENARD et coll. 1972, CHOVIL & CHIR 1981). Although miners might be exposed to many different agents, radon is now generally thought to be the essential causative factor. In poorly ventilated mines alpha particles from radon daughters may, during years of exposure, give large cumulative radiation doses in the bronchial epithelium. The literature concerning this matter is reviewed in recent UNSCEAR and BEIR reports (1977, 1980), which also contain analyses and discussions as regards possible dose-effect relations.

The radon problems in the Swedish non-uranium mines were recognized at the end of the 1960s. The Swedish Mine Association and the National Institute of Radiation Protection then initiated both radon measurements and epidemiologic surveys. An epidemiologic investigation of all mining districts showed a considerably increased risk for underground miners to develop lung carcinoma (S:T CLAIR RENARD et coll., SNIHS 1974). The risk seemed to be correlated with the retrospectively estimated radon daughter exposure and agreed with similar dose-effect findings in uranium miners in the United States. More detailed reports on lung carcinoma in underground miners also appeared from several local districts, among them the iron ore mines in northern Sweden (JÖRGENSEN 1973, S:T CLAIR RENARD 1974). Lung carcinoma is also strongly associated with smoking and the interaction between smoking and underground mining has been discussed in several reports. ARCHER et coll. (1973) found six to nine times higher rates of respiratory malignancy among smoking and non-smoking uranium miners in the United States than among non-miners with similar smoking habits, which indicates an enhancing effect of the combined exposure. JÖRGENSEN described 13 cases of lung carcinoma in underground workers in iron ore mines in northern Sweden (Kiruna); of these only one was a non-smoker. On the other hand, AXELSON & SUNDELL (1978) found a higher risk for non-smokers than for smokers in a Swedish zinc and lead mine. They suggested that smoking might increase the thickness of the mucus layer and thereby protect the bronchial epithelium from alpha radiation. Not surprisingly, this report was followed by some polemics (FELDSTEIN & BAND 1980, AXELSON & SUNDELL 1980). In a large retrospectively analysed series from an

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iron ore mine in northern Sweden (Malmberget) RADFORD & S:T CLAIR RENARD (1980) found 51 cases of lung carcinoma; 18 of these had never smoked or had given up smoking more than 15 years before death. Preliminary analysis of the cohort data suggested that the combined effects of smoking and radiation exposure were merely additive and not synergistic. Opinions concerning interaction between smoking and underground mining are thus controversial.

The present report is a supplementary investigation on lung carcinoma among workers in the iron ore mines in northern Sweden (Kiruna and Gällivare) with special regard to combined effects of underground mining and smoking. It is part of a large case-control study comprising about 600 males with lung carcinoma from the northern part of Sweden. In a descriptive epidemiologic report large differences, not explainable by random variations, were found between the male lung carcinoma rates in different municipalities of northern Sweden (LARSSON & SANDSTRÖM 1978, DAMBER et coll. 1981). This region contains many fairly well defined population subgroups with different environment concerning for instance industrial activities (mines, smelters, steel factories, coke ovens, paper mills etc.). It was felt that a case-control study might yield valuable information concerning causative factors, particularly occupational ones, and combined effects of smoking and other factors. The collection of data started 1979 and was completed by the end of 1980. The present report is the first one based on these data.

Material and Methods

The present inquiry based case-control study comprised 604 deceased male lung carcinoma cases, 604 deceased and 467 living controls. The cases derived from the three most northern counties in Sweden and had been reported to the Swedish Cancer Registry in 1972 to 1977. Deceased controls were obtained from the National Registry for Causes of Death and matched against the cases according to sex, year of death, age and municipality. Suicide and lung carcinoma as causes of death were not accepted among the controls. From some methodologic aspects a comparison between deceased cases and deceased controls is most adequate since all the questionnaires are answered by relatives. However, since some etiologic factors (e.g. smoking) may cause an increased mortality for other reasons than lung carcinoma, also a living control group was regarded as important. Living controls from the National Population Registry were matched against the cases according to sex, year or birth and municipality. Living controls were only selected for the 467 cases with an age at death not exceeding 80 years.

By questionnaires data concerning municipality, type of residence, occupations, employments and smoking habits were collected. The questionnaires were answered by close relatives to the cases and the deceased controls and by the living controls themselves. Incomplete answers were supplemented by telephone interviews according to defined control criteria. Between 95 and 97 per cent of the questionnaires were answered within the 3 groups. Only a few questions were unanswered in some questionnaires; these were, however, evenly distributed among cases and controls.

Smoking. The information concerning smoking habits included approximate year for start of smoking, daily number of cigarettes, other types of smoking and year for possible cessation of smoking. Individuals who had at least smoked one cigarette daily for one year or more at any time were classified as smokers. From the data the life time consumption of tobacco was estimated and expressed as number of cigarettes. For pipe and cigar smoking 1 g tobacco was regarded as equal to one cigarette.

Occupational exposure. The main part of the occupational period was surveyed for each individual. Occupations and employments, excluding educational periods, time of sick-leave, pension and unemployment, could be mapped out in an average of 38.9 years for the cases, 38.4 years for the deceased controls and 38.1 for the living controls. Further information available was microscopic diagnosis, date of death for cases and deceased controls and causes of death for the latter group. A well defined group such as miners could be specifically analysed. The questionnaire was made in such a way that underground and surface mining could be separated; in this connection only underground mining in iron ore mines was regarded as exposure. Among the cases, only 10 non-iron miners were found distributed on 6 different mines. All iron mines within the region were located in two municipalities (Kiruna and Gällivare) and all non-iron mines were located outside these municipalities. In order to validate the information obtained from the question-

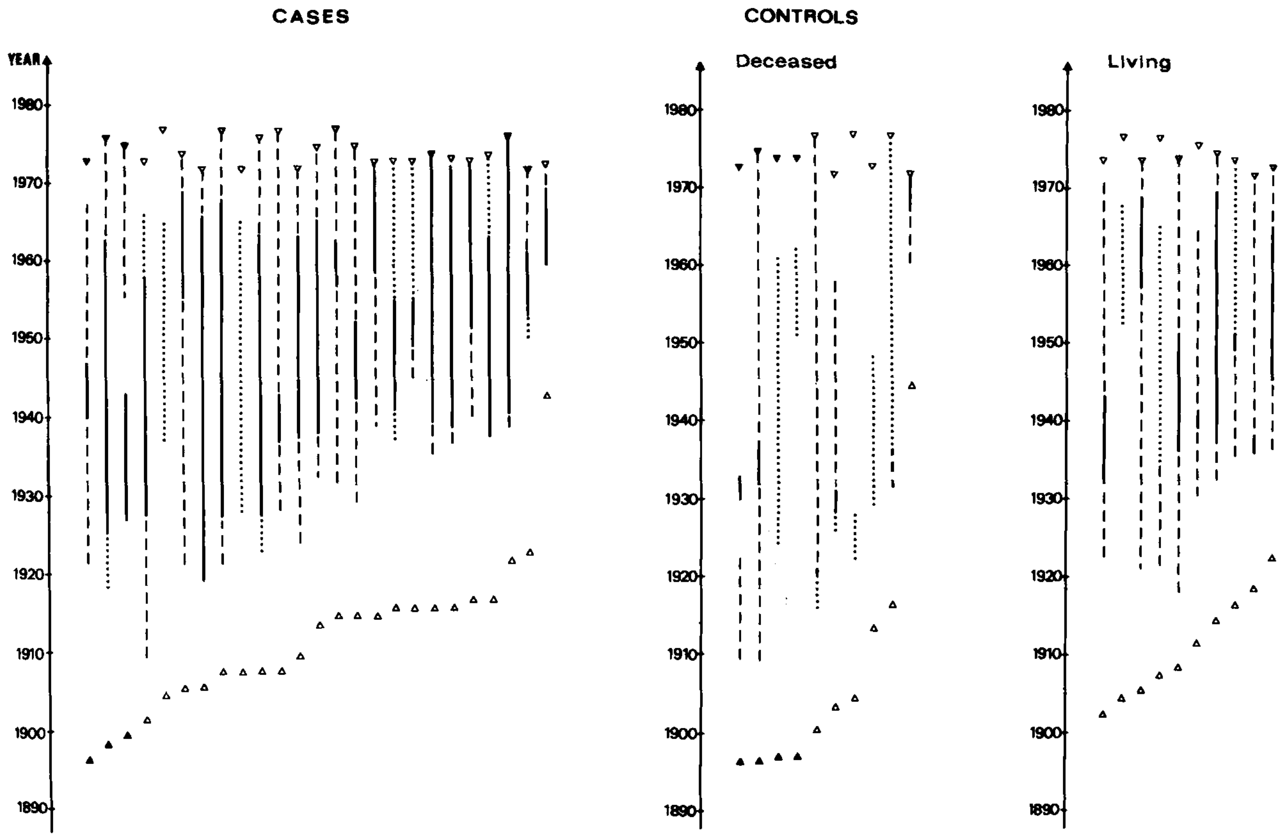

Fig. 1. Smoking (dashed lines), underground mining (dotted lines) and combined smoking and underground mining (solid lines) in all cases and controls exposed to underground mining. The lower triangles mark birth and the upper triangles diagnosis of lung carcinoma. The diagrams for cases and deceased controls can be directly compared as these 2 samples had the same size. If the 3 cases and the 4 deceased controls marked with filled triangles (age>80 years) are excluded, all 3 diagrams can be directly compared. The figure illustrates the strong overrepresentation of underground mining and combined underground mining and smoking among the cases.

naires, the answers concerning non-iron miners, which all had been employed by one company (Boliden), were controlled against the employment register (10 cases, 11 controls). The information from the questionnaires and the register was in good agreement regarding time of underground and surface work and employment periods. Only 2 of the 21 questionnaires were misleading concerning underground work (+ 8 years and − 6 years). In none of the remaining 19 questionnaires the data about underground work deviated more than one year from the register. It seems reasonable to assume that the data concerning iron miners had similar validity. As mentioned only underground work in iron ore mines was defined as exposure, as the aim was to elucidate the effect of smoking in this specific type of miners. Essentially similar results were, however, obtained when also individuals with underground work in non-iron mines were included in the exposed groups.

General radon measurements in the Swedish mines, including the iron ore mines concerned in the present series, were performed in 1969 to 1970. Only two mines have quantitative importance for the present analyses, Kirunavaara in Kiruna and Malmberget in Gällivare. Relatively high concentrations of radon daughters (3 500–7 500 Bq/m^3) were found in several underground areas of Malmberget while in Kirunavaara the concentrations were 350 to 1 000 Bq/m^3 with exception of some poorly ventilated parts (JÖRGENSEN, S:T CLAIR RENARD). Improvements of the ventilation system had been made during the 1960s, why the measurements poorly reflected the exposure during previous years. For this reason and due to the difficulty in defining in which regions of the mines the persons actually had worked, the term 'underground years' was used as a neutral measure of exposure. Most underground years recorded refer to the period before 1965 (Fig. 1), when the underground parts of these mines prob-

Table 1

Crude risk ratio in underground miners

	No. of cases	Controls I	CR̂R	95% conf. interval	No. of cases	Controls II	CR̂R	95% conf. interval
Total	589	582			456	899		
Underground mining≥1 year	25	10	2.5	1.2–5.2	22	16	2.8	1.5–5.3

ably contained higher concentrations of radon daughters. Other agents than radon may also be of importance for the induction of lung carcinoma in miners as dust particles, different metal compounds, asbestos and polyaromatic hydrocarbons from combustion of diesel oil as pointed out by several authors (BOYD et coll., AXELSON & REHN, JÖRGENSEN).

Statistical methods. Most analyses (Tables 1–6) were performed for two sets of cases and controls. In group I all the cases and their matched deceased controls were used. In group II only cases with an age at death not exceeding 80 years and their matched deceased and living controls were used. Thus, in group I each case had one matched control and in group II two matched controls. Estimates based on group II are in the text presented within parentheses after estimates based on group I. The MANTEL & HAENSZEL method (1959) was used for estimation of the overall rate ratio. The relative crude risk for underground mining estimated with individual matching (MIETTINEN 1970) was 3.1 and after dissolving of the matching 2.5. The absolute value of the correlation coefficient was 0.16. The similarity between the estimates and the low correlation coefficient indicates that the matching could be ignored in the analyses. Confidence intervals and the standardized risk ratio were estimated according to MIETTINEN (1972, 1976). Figures for confidence limits are omitted when the number of cases or controls are too small to allow application of these methods. Population etiologic fractions for smoking and underground mining in the 2 municipalities with iron ore mines were estimated according to COLE & MACMAHON (1971).

Results

Underground work in iron ore mines was more than twice as common among the cases than among

Table 2

Time of employment in underground mining

Employment in underground mining (years)	No. of cases	Controls (deceased)	No. of cases	Controls (deceased)	Controls (living)
1–10	5	6	4	4	2
11–20	4	2	3	1	5
>20	16	2	15	1	3
Total No. of cases	25	10	22	6	10
Average employment time	25.8	13.6	26.2	13.3	16.5

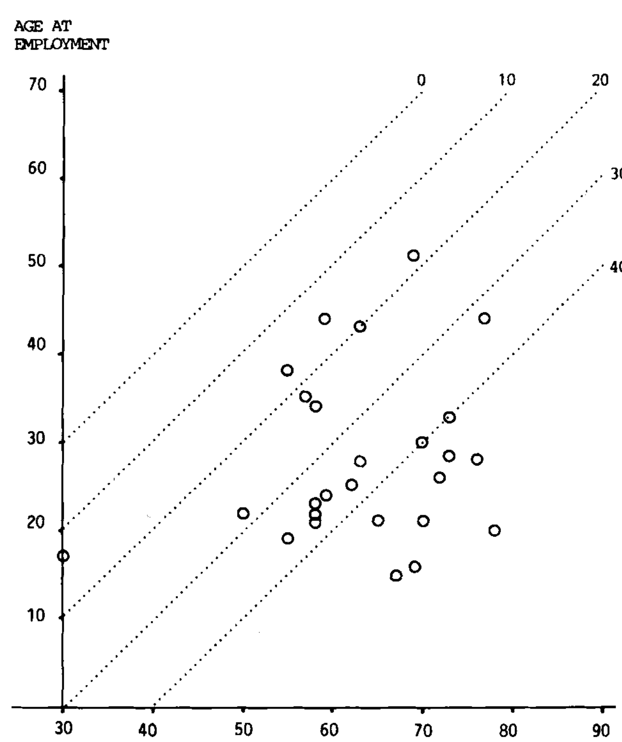

Fig. 2. Year of employment and diagnosis of lung carcinoma in 25 cases with underground mining. The diagonal dotted lines represent time from onset of employment to diagnosis of tumor (years).

Table 3

Cumulative tobacco consumption

Life time tobacco consumption cig. × 10^3	Cases		Controls I		Cases		Controls II	
	No undergr. mining	Undergr. mining	No undergr. mining	Undergr. mining	No undergr. mining	Undergr. mining	No undergr. mining	Undergr. mining
Non-smokers	44	2	209	4	30	2	313	3
<150	58	8	111	5	43	6	200	10
150–299	190	11	133	1	155	10	225	3
⩾300	272	4	119	0	206	4	145	0
Total No.					434	22	883	16
of cases	564	25	572	10				
Average tobacco consumption cig. × 10^3	308.8	182.6	154.7	54.8	303.1	188.8	141.3	88.3

Table 4

Smoking, underground mining

	No underground mining		Underground mining	
	No smoking	Smoking	No smoking	Smoking
Cases	44	520	2	23
Controls I	209	363	4	6
Relative risk	(1.0)	6.8	2.4	18.2
95% conf. interval		4.9–9.4	–	8.5–39.2
Cases	30	404	2	20
Controls II	313	570	3	13
Relative risk	(1.0)	7.4	7.0	16.1
95% conf. interval		5.2–10.5	–	8.4–30.8

the controls (Table 1). The estimated crude risk ratio for underground miners was 2.5 (2.8). In the exposed cases the age group 50 to 59 years was overrepresented but this did not influence the estimated risk ratio. The majority of the exposed cases (64%) had worked underground for more than 20 years. The exposed cases had a much longer average time of employment as underground miners than the exposed controls (Table 2).

The time from employment in underground mining to the diagnosis of lung carcinoma (latency time) was 20 years or more in all but 3 of the 25 cases (Fig. 2). The average latency time was 34.8 years. In the cases with lung carcinoma exposed to underground mining 11 tumors were classified as epidermoid carcinomas, 11 as small cell, undifferentiated carcinomas and 3 as adenocarcinomas. The average latency time was considerably shorter for small cell carcinoma (28.7 years) than for epidermoid carcinoma (40.8 years) and the average age of the small cell carcinoma cases was also lower (58.4 versus 67.0 years).

In Table 3 the smoking habits for cases and controls are described in terms of cumulative tobacco consumption. Referring to the whole case-control material 92 (93) per cent of the cases and 63 (65) per cent of the controls were smokers. The exposed cases (underground miners) had the same proportion of smokers as all the cases but a larger proportion of low tobacco consumers and a considerably lower average tobacco consumption. It was an obvious difference between the smoking habits in cases with small cell, undifferentiated carcinoma and epidermoid carcinoma. In the former group 6 of 11 cases and in the latter group only 2 of 11 cases were low tobacco consumers.

Table 5

Stratification with regard to tobacco consumption

	No smoking		Low tobacco consumption*		High tobacco consumption**	
	No undergr. mining	Undergr. mining	No undergr. mining	Undergr. mining	No undergr. mining	Undergr. mining
Cases	44	2	58	8	462	15
Controls I	209	4	111	5	252	1
Relative risk	(1.0)	2.4	2.5	7.6	8.7	71.3
95% conf. interval		–	1.6–3.9	2.8–21.0	6.3–12.1	22.1–229.6
Cases	30	2	43	6	361	14
Controls II	313	3	200	10	370	3
Relative risk	(1.0)	7.0	2.2	6.3	10.2	48.7
95% conf. interval		–	1.4–3.7	2.4–16.4	7.2–14.5	21.0–113.1

* <150 000 cigarettes.
** ≥150 000 cigarettes.

Table 6

Stratification with regard to tobacco consumption with exsmokers classified as non-smokers

	No smoking*		Low tobacco consumption**		High tobacco consumption***	
	No undergr. mining	Undergr. mining	No undergr. mining	Undergr. mining	No undergr. mining	Undergr. mining
Cases	85	6	43	5	436	14
Controls I	296	7	56	2	220	1
Relative risk	(1.0)	3.0	2.7	8.7	6.9	48.8
95% conf. interval		1.0–8.7	1.7–4.2	2.2–35.0	5.2–9.1	14.3–165.8
Cases	54	6	36	3	344	13
Controls II	452	8	104	5	327	3
Relative risk	(1.0)	6.3	2.9	5.0	8.8	36.3
95% conf. interval		2.4–16.6	1.8–4.6	1.3–18.8	6.6–11.8	15.5–84.7

* Includes ex-smokers of more than 10 years.
** <150 000 cigarettes.
***≥150 000 cigarettes.

In the cases exposed to underground mining a combination of this exposure and smoking was very common as illustrated in Fig. 1. Of 634 underground years 480 were also smoking years. The estimated risk ratio for smoking underground miners compared with non-smokers without underground mining was 18.2 (16.1). The corresponding ratios (Table 4) for non-smoking underground miners and smokers without underground mining were 2.4 (7.0) and 6.8 (7.4). Very high risk ratios were obtained for underground miners with high tobacco consumption (Tables 5, 6).

This report is part of a large case-control study including cases and controls from all the 33 municipalities in the 3 most northern counties of Sweden. If the only purpose had been to analyse the risk of underground work in iron ore mines, which are concentrated to only 2 municipalities, a more natural approach would have been to limit the analysis to residents in just these 2 municipalities. The data can also be used for such an analysis, which is demonstrated in Tables 7 and 8. They include only cases (and their controls) who at the start of the data collection in 1979 were residents of the 2 mentioned municipalities (Kiruna and Gällivare). Due to the low number of cases and controls only analyses with

Table 7

Investigation limited to residents in Kiruna and Gällivare. Tobacco consumption

Tobacco consumption	Cases/ controls	Under-ground mining	No under-ground mining
No smoking	Cases	2	1
	Controls	3	20
Low consumption <150 000 cig.	Cases	6	0
	Controls	7	5
High consumption ⩾150 000 cig.	Cases	12	10
	Controls	3	24
Total	Cases	20	11
	Controls	13	49

Table 8

Investigation limited to residents in Kiruna and Gällivare

	No smoking		Smoking	
	No under-ground mining	Under-ground mining	No under-ground mining	Under-ground mining
Cases	1	2	10	18
Controls	20	3	29	10
Relative risk	(1.0)	13.3	6.9	36.0

the use of both deceased and living controls were performed. The crude risk ratio for underground miners was 6.9. The standardized rate ratio was 7.3, why any essential confounding effect of age could be excluded. The tobacco consumption for cases and controls appears in Table 7. All cases who were not underground miners had high tobacco consumption. The 6 low tobacco consumers were all underground miners with small cell, undifferentiated carcinoma. A very high risk ratio was obtained for smokers exposed to underground mining (Table 8).

Discussion

The main object of the present investigation was the interaction between underground mining and smoking. Most of the data (Tables 4, 5, 6, 8) indicates an enhancing effect of smoking, approximately of multiplicative type. This is in agreement with some previous observations (ARCHER et coll., JÖRGENSEN) but in disagreement with some other reports (AXELSON & SUNDELL 1978), RADFORD & S:T CLAIR RENARD). In the present series the cases with lung carcinoma exposed to underground mining had a considerably lower average tobacco consumption than all the lung carcinoma cases (Table 3). This is exactly what can be expected when two etiologic factors are analysed. Smoking is more dangerous in underground miners than in non-miners and less smoking is therefore needed to induce or promote the development of a lung carcinoma. If low tobacco consumers (smokers with low daily consumption, pipe smokers or former smokers) are classified as non-smokers, data of this type may easily be misinterpreted and the conclusion can be drawn that smoking in underground miners is less important. Exsmokers may require a special comment. It is well known that exsmokers have a decreasing risk of lung carcinoma, which after about 10 years reaches the same low level as in non-smokers (WYNDER & HOFFMAN 1976). It is not known if the same holds true when smoking is combined with another carcinogenic exposure (as radon) but it could be argued that an overrepresentation of exsmokers among the cases exposed to underground mining might have given misleading results. However, no such overrepresentation was found, and when persons who had stopped smoking since 10 years or more were classified as non-smokers a similar synergistic effect was found as in the main series (Table 6).

As in other series, an overrepresentation of small cell undifferentiated carcinoma was found among lung carcinoma cases who had been exposed to underground mining (SACCOMANNO et coll. 1971, KUNZ et coll. 1979). Eleven of 25 cases (44%) were tumors of this type, which in the total series of cases only accounted for about 25 per cent, a figure which is fairly representative for unselected Swedish materials (NOU et coll. 1979). The shorter latency period of these cases compared with the epidermoid carcinomas and the observation that they more often were low tobacco consumers also indicates that underground mining gives an especially large risk for this type of carcinoma.

When the analysis was limited to residents in the 2 municipalities (Kiruna and Gällivare), where the iron ore mines were located, considerably higher risk ratios were obtained than in the larger series which included the 3 most northern counties. The reason for this is probably that the male lung carcinoma rate in these 2 municipalities should have been very low if not exposure to underground mining had existed. This fits well with descriptive epidemiologic data, which show a remarkably low male lung carcinoma rate in most municipalities in the inner (western) part of northern Sweden compared with the coastal (eastern) more densely populated part. For the 2 analysed municipalities the following estimated values for the population etiologic fractions were obtained: smoking 74 per cent, underground mining 55 per cent. Lappland, which constitutes the western part of northern Sweden, contains 12 municipalities, among them Kiruna and Gällivare. During the period 1959 to 1978 the 2 last mentioned municipalities had age standardized incidence rates of male lung carcinoma of 40.2 and 40.4 per 100 000 and year (population of Sweden 1970 used as standard). The corresponding figures for the 10 other municipalities varied from 3.8 to 19.0. Without underground mining also Kiruna and Gällivare should have been low incidence municipalities. Without both underground mining and smoking male lung carcinoma should have been a rare disease.

SUMMARY

Within a case-control study of male lung carcinoma in northern Sweden combined effects of underground mining (iron ore mines) and smoking were analysed. A synergistic effect was found approximately of multiplicative type. Cases with lung carcinoma exposed to underground mining had a considerably lower average cumulative tobacco consumption than other lung carcinoma cases as an expression of the fact that smoking is particularly dangerous in underground miners. Small cell undifferentiated carcinoma was overrepresented among the cases exposed to underground mining and were especially often low tobacco consumers. In the 2 municipalities where the iron mines were located 74 per cent of the male lung carcinoma incidence could be explained by smoking and 55 per cent by underground mining (etiologic fractions).

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