Scand J Work Environ Health 1997;23(3):187-192
https://doi.org/10.5271/sjweh.197
Issue date: Jun 1997

Lung cancer incidence among an Icelandic cohort exposed to diatomaceous earth and cristobalit

by Rafnsson V, Gunnarsdóttir H

Key terms: brain cancer; Iceland; Lake Myvatn; loading ships; manufacturing; smoking habit; squamous-cell skin cancer

This article in PubMed: www.ncbi.nlm.nih.gov/pubmed/9243728

Print ISSN: 0355-3140 Electronic ISSN: 1795-990X

Scand J Work Environ Health 1997;23:187—92

Lung cancer incidence among an Icelandic cohort exposed to diatomaceous earth and cristobalite

by Vilhjálmur Rafnsson, MD,[1] Hólmfrídur Gunnarsdóttir MSc[1]

Rafnsson V, Gunnarsdóttir H. Lung cancer incidence among an Icelandic cohort exposed to diatomaceous earth and cristobalite. *Scand J Work Environ Health* 1997;23(2):187—92.

Objectives The objective of this study was to determine the cancer incidence of a cohort exposed to diatomaceous earth and cristobalite with special focus on lung cancer.

Methods The cohort was from a diatomaceous plant in northern Iceland and comprised 919 men and 423 women. Diatomite, when heated, is transformed from amorphous to crystalline silica with a high cristobalite content and traces of quartz. With the use of the identification number of all persons, a link was made with the Cancer Registry. The expected number of malignancies was calculated on the basis of person-years of observation for 5-year age categories during the respective calendar period of the study multiplied by the specific incidence of cancer site for men and women in Iceland.

Results There was no increased overall incidence of cancer in the study population; 5 cases of lung cancer were observed versus 4.4 expected, the standardized incidence ratio (SIR) was 1.14 [95% confidence interval (95% CI) 0.37—2.65]. When the men in the cohort were divided according to their length of employment, there was an excess of lung cancer (3 observed versus 1.28 expected, SIR 2.34, 95% CI 0.48—6.85), nonmelanoma skin cancer (2 observed versus 0.19 expected, SIR 10.53, 95% CI 1.27—38.02), and brain cancer (3 observed versus 0.30 expected, SIR 10.00, 95% CI 2.06—29.23) for those who had worked 5 years or longer. A special investigation of smoking habits among the cohort revealed a smoking pattern similar to that of the general population.

Conclusions The results concerning lung cancer showed an excess risk for workers exposed to diatomaceous earth and cristobalite; the result was not, however, statistically significant. There was a trend towards a higher incidence of lung cancer with longer exposure to crystalline silica, and, in agreement with the results of a previous study from this industry, the findings indicate a causal relation.

Key terms brain cancer, Lake Myvatn, loading ships, manufacture, squamous-cell skin cancer, smoking habits.

The relation between silica exposure and the risk of lung cancer has been studied intensively during the last decade. Epidemiologic investigations have recently focused more on nonsilicotics and those exposed solely to crystalline silica in an attempt to establish the role which silica exposure per se plays and to avoid confounding with other possible carcinogens, such as exposure to radon in mining, diesel exhaust gases in underground mining, and polycyclic aromatic hydrocarbons. Most, if not all, studies have dealt with exposure to quartz dust rather than with other types of crystalline silica, although cristobalite, for example, has been shown to be carcinogenic in experimental systems (1, 2). We are only aware of 1 other study on workers exposed in the diatomaceous earth industry (3, 4). This mortality study showed an excess for lung cancer, and there was indirect control for smoking. The excess risk for lung cancer and an increasing risk gradient with duration of exposure to dust and cumulated exposure to crystalline silica were considered to indicate a causal relationship (3).

The end point in most studies has been mortality from lung cancer, and with only few exceptions it has been cancer incidence (5—8) determined from cancer registers.

This study was intended as a contribution to the evidence on a possible association between silica exposure and lung cancer. The exposure in question was crystalline silica in the form of cristobalite derived from the heating of diatomaceous earth. The exposed cohort was divided into those who had been exposed during the

1 Department of Occupational Medicine, Administration of Occupational Safety and Health, Reykjavik, Iceland.

Reprint requests to: Dr V Rafnsson, Department of Occupational Medicine, Administration of Occupational Safety and Health, Bildshofda 16, PO Box 12220, 132 Reykjavik, Iceland.

production of diatomite and those exposed while handling the finished product when loading ships. The identification of cancer cases was made by means of a nationwide cancer register.

Subjects and methods

The cohort comprised workers from a diatomite plant which had been in operation since 1967 in the northern part of Iceland and also workers who had worked at loading the finished product from the plant onto ships, a total of 1346 subjects. Table 1 shows the characteristics of the cohort and the number of cancer cases. The subjects were identified from employment records available from 1967 to 1981 from the plant and from 1969 to 1980 from the shipping clerk. The entry of the workers was evenly distributed during the study period. Twenty-six persons who had worked at loading ships could not be identified because of errors in the lists. It is difficult to evaluate the effect of the loss of these persons from the cohort as their exposure information was also missing. Each worker's personal identification number, which includes his or her date of birth, was established from the name, date of birth, home address, or a previous identification number and a comparison with the National Register and the Register of Deceased Persons. The subjects entered the study the year they were first mentioned in the employment records. The records also supplied information on which years the subjects had been employed, the number of hours they had worked each year, and their task and occupation. The plant in question is located in a sparsely settled area, and ships were loaded at a nearby fishing village.

Diatomaceous earth is synonymous with diatomite, kieselguhr, and fossil silicon. Diatomaceous earth occurs in the form of deposits of skeletal remains of microscopic, aquatic, single-cell plants and is found in other locations on the bottom of Lake Myvatn in northern Iceland. The mineral forms a layer from 5 to 10 m thick in the lake bed at a depth of $\geq$ 1 m. The diatomite may contain a small amount of quartz but is about 85% amorphous silicon dioxide by weight and the rest is water. Crude diatomite is pumped up from the lake and transferred by pipelines to the plant, where it is filtered and steam-dried with hot water from natural hot springs. Thereafter the diatomite is transferred to a kiln heated by oil-burning to 800—1200°C and flux-calcined (mixed with sodium carbonate) and thus converted to the crystalline form cristobalite. The final product generally contains over 70% cristobalite and less than 2% quartz, measured in bulk by X-ray diffraction. The product is subsequently purified, milled, graded, and packed in paper bags. The handling of bags during transport and shipping was formerly an extremely dusty job.

Records of personal samples of respirable cristobalite showed variation according to a person's type of work and location within the factory (9). The dust measurement of personal samples from 1978 showed comparatively high levels of respirable cristobalite for packers, oven operators, maintenance men, and cleaners, averages being 0.6, 0.3, 0.2 and 0.1 mg/m^3, respectively. The average value for the shiploaders was 0.3 mg/m^3 according to measurements from 1978. Work conditions have improved since then; yet the content of respirable cristobalite in personal samples ranged from 0.03—0.7 mg/m^3 in loading to 0.02—0.5 mg/m^3 in the production during 1978 to 1981 (9).

The employees at the diatomite plant, and, during recent years, those who suffered the heaviest exposure when loading ships, have undergone annual health examinations, and no case of silicosis has yet been found. Records were linked by means of the personal identification number of each subject to the cancer register, which is a nationwide register of cancer cases, more than 92% of which have been histologically verified (10). The Cancer Registry uses the 7th revision of the International Classification of Diseases (ICD). The follow-up was to the end of 1991, and at the end of the study we were able to establish the fate of all the subjects.

Person-years were calculated for each subject starting with the first year on the employment records and ending with the date of death or 1 December 1991. The number of expected cancers was calculated on the basis of the number of person-years for each 5-year age category during the respective calendar years of the study period, multiplied by the specific incidence of cancer site

Table 1. Number of subjects, total number of cancers, and number of lung cancers in the entire cohort and in subcohorts comprised of those who had worked only in the diatomite factory, those who had worked only at loading ships and those who had worked at both.

	Total cohort			Only in factory			Only loading ships			Factory or loading ships		
		Cancers			Cancers			Cancers			Cancers	
	N	All (N)	Lung (N)	N	All (N)	Lung (N)	N	All (N)	Lung (N)	N	All (N)	Lung (N)
Men	920	23	5	196	5	—	690	16	5	34	2	—
Women	426	9	—	20	2	—	404	7	—	2	—	—
All	1346	32	5	216	7	—	1094	23	5	36	2	—

and calendar year for men and women in Iceland (11). The ratio between the observed and expected numbers of cancers, or the standardized incidence ratio (SIR), was calculated with the 95% confidence interval (95% CI) on the assumption of a Poisson distribution (11).

Those who had worked at loading ships only were treated as a separate group, as work at the plant may have involved exposure to other possible carcinogens.

Separate analyses were performed according to accumulated years of employment and accumulated hours of employment. If a person was listed at any time during a particular calendar year, that year was counted as a whole year of employment regardless of the number of hours worked. The exact number of hours each subject had worked each year was added up to determine the accumulated hours of employment. Thus the hours of employment was a more precise indicator of exposure, as part-time work was frequent among the workers. The cut points were arbitrarily chosen as 5 years and 300 h. To eliminate the effect of selection of the subjects into different exposure groups, we allowed 5 and 9 years to elapse before the counting of person-years began, according to McDonald et al (12). No product containing asbestos was manufactured in the plant.

A special survey concerning smoking habits among the cohort members was undertaken in 1993. Data on smoking habits were obtained with a postal questionnaire. The participation rate was 65.0% for all the men and 72.1% for all the women; among those who had worked solely with loading ships, the participation rate was 64.9% for the men and 71.8% for the women. The results of a nationwide survey on smoking habits (participation rate 78.0%) conducted in 1990 by the Committee for Tobacco Use Prevention served as comparison material (13). The smoking data concerned persons aged 15—69 years.

Results

Table 2 shows the results for the total cohort. The standardized incidence ratio for all cancers was 0.79, but the incidence of lung cancer, cervical cancer, cancer of the skin (nonmelanoma), brain, and thyroid gland was higher than expected. There were few cases of cancer of many sites, and the categories with only 1 cancer case are shown for the sake of completeness and to explain why selected cancer sites were subsequently dealt with.

Table 2. Observed and expected numbers of cancers, the standardized incidence ratio (SIR), and the 95% confidence interval (95% CI) for cancer sites among the men (N = 920, 16 399 person-years) and women (N = 426, 7 076 person-years).

Cancer sites[a]	Observed	Expected	SIR	95% CI
All cancers (140—204)	32	40.62	0.79	0.54—1.11
Stomach (151)	1	3.44	0.29	0.01—1.63
Large intestine (153)	1	2.48	0.40	0.01—2.25
Rectum (154)	1	1.01	0.99	0.03—5.52
Liver (155)	1	0.56	1.79	0.05—9.95
Pancreas (157)	1	1.11	0.90	0.02—5.02
Nose (160)	1	0.12	8.33	0.21—46.43
Larynx (161)	1	0.41	2.44	0.06—13.59
Lung (162)	5	4.40	1.14	0.37—2.65
Breast (170)[b]	2	2.85	0.70	0.08—2.53
Cervix uteri (171)	2	0.94	2.13	0.26—7.69
Ovary and adnexa (175)	1	0.71	1.41	0.04—7.85
Prostate (177)	3	4.84	0.62	0.13—1.81
Testis (178)	1	1.40	0.71	0.02—3.98
Kidney (180)	1	1.67	0.60	0.02—3.34
Skin, non-melanoma (191)	2	0.75	2.67	0.32—9.63
Brain (193)	3	1.75	1.71	0.35—5.01
Thyroid gland (194)	2	1.60	1.25	0.15—4.52
Bone (196)	1	0.29	3.45	0.09—19.21
Unspecified sites (199)	1	0.82	1.22	0.03—6.79
Hodgkin's disease (201)	1	0.69	1.45	0.04—8.07

[a] Categories with only one cancer case are shown for the sake of completeness, the code of the International Classification of Diseases, 7th revision appears in parentheses.
[b] Women only.

Table 3 shows the results of the men when the total cohort was classified according to duration of employment, which in this case was measured as the number of years. Those who had worked for 5 years or longer had a higher cancer incidence than those who had worked for a shorter period. Among those who had worked for ≥ 5 years the standardized incidence ratio for lung cancer was 2.34 and 2.70 when 5- and 9-year time intervals, respectively, were allowed before the start of follow-up. These results are based, however, on only 3 cases, and

Table 3. Observed and expected numbers of cancers, the standardized incidence ratio (SIR), and the 95% confidence interval (95% CI) for selected cancer sites, according to length of employment measured in years with a requirement of 5 or 9 years before the start of follow-up.

Cancer sites[a]	Five years' time interval before start of follow-up								Nine years' time interval before start of follow-up							
	Employed ≤ 5 years (N = 754)				Employed ≥ 5 years (N = 160)				Employed ≤ 5 years (N = 752)				Employed ≥ 5 years (N = 159)			
	Observed	Expected	SIR	95% CI	Observed	Expected	SIR	95% CI	Observed	Expected	SIR	95% CI	Observed	Expected	SIR	95% CI
All cancers (140—204)	11	18.13	0.61	0.30—1.09	12	9.02	1.33	0.69—2.32	8	14.19	0.56	0.24—1.11	12	7.76	1.55	0.80—2.70
Lung cancer (162)	2	2.11	0.95	0.11—3.64	3	1.28	2.34	0.48—6.85	2	1.68	1.19	0.14—4.30	3	1.11	2.70	0.56—7.90
Skin cancer (191)	—	0.38	·	··	2	0.19	10.53	1.27—38.02	—	0.30	·	··	2	0.16	12.50	1.51—45.15
Brain cancer (193)	—	0.77	·	··	3	0.30	10.00	2.06—29.23	—	0.58	·	··	3	0.24	12.50	2.58—36.53

[a] Code of the International Classification of Diseases, 7th revision, in parentheses.

Table 4. Observed and expected numbers of cancers, the standardized incidence ratio (SIR), and the 95% confidence interval (95% CI) for selected cancer sites among the men, according to the length of employment measured as the accumulated hours of employment with a requirement of 5 or 9 years before the start of follow-up.

Cancer sites[a]	Five years' time interval before start of follow-up								Nine years' time interval before start of follow-up							
	Employed < 300 h (N = 633)				Employed ≥ 300 h (N = 281)				Employed < 300 h (N = 631)				Employed ≥ 300 h (N = 280)			
	Observed	Expected	SIR	95% CI	Observed	Expected	SIR	95% CI	Observed	Expected	SIR	95% CI	Observed	Expected	SIR	95% CI
All cancers (140—204)	9	16.17	0.56	0.25—1.06	14	10.99	1.27	0.70—2.14	6	12.73	0.47	0.17—1.03	14	9.23	1.52	0.83—2.54
Lung cancer (162)	2	1.93	1.04	0.13—3.74	3	1.46	2.05	0.42—6.01	2	1.55	1.29	0.16—4.66	3	1.24	2.42	0.50—7.07
Skin cancer (191)	—	0.33	·	..	2	0.23	8.70	1.05—31.41	—	0.27	·	..	2	0.19	10.53	1.27—38.02
Brain cancer (193)	—	0.67	·	..	3	0.40	7.50	1.55—21.92	—	0.51	·	..	3	0.31	9.68	2.00—28.28

[a] Code of the International Classification of Diseases, 7th revision, in parentheses

the confidence limits are relatively wide. In the same subgroup there was an excess of skin and brain cancer. There was no case of lung cancer among the women, nor did their cancer pattern differ according to length of employment.

Table 4 shows the standardized incidence ratio for the same cancer sites as in table 3 for all the men in the entire cohort, classified according to accumulated hours of employment. There was an excess of all cancers, lung cancer, and skin and brain cancers among those who had worked 300 h or more and a gradient through increasing time allowed before the start of follow-up.

Table 5. Observed and expected numbers of cancers, the standardized incidence ratio (SIR), and the 95% confidence interval (95% CI) for cancer sites among the men who had been exposed during the loading of ships with the production from the diatomite factory (N = 690, 12 115 person-years).

Cancer sites[a]	Observed	Expected	SIR	95% CI
All cancers (140—204)	16	25.17	0.64	0.36—1.03
Stomach (151)	1	2.67	0.37	0.01—2.71
Large intestine (153)	1	1.74	0.57	0.01—4.15
Liver (155)	1	0.39	2.56	0.06—18.52
Pancreas (157)	1	0.83	1.20	0.03—8.70
Lung (162)	5	3.08	1.62	0.53—3.79
Prostate (177)	1	4.19	0.24	0.01—1.72
Testis (178)	1	1.03	0.97	0.02—7.01
Skin, non-melanoma (191)	1	0.52	1.92	0.05—13.89
Brain (193)	1	1.00	1.00	0.03—7.22
Bone (196)	1	0.17	5.88	0.15—42.50
Unspecified sites (199)	1	0.56	1.79	0.05—12.90
Hodgkin's disease (201)	1	0.41	2.44	0.06—17.62

[a] Categories with only one cancer case are shown for the sake of completeness. The code of the International Classification of Diseases, 7th revision, is shown in parentheses.

Table 5 shows the observed and expected numbers of cancers among the men who had worked only at loading ships. There was a deficit for all cancers, although 5 lung cancers were observed versus 3.08 expected.

Table 6 shows the results for all cancers and lung cancer among men who had worked at loading, classified according to accumulated hours of employment and using 5 and 9 years of latency. There was a deficit of all cancers among those who had worked less than 300 h. Among those who had worked ≥ 300 h there was an excess for all cancers and lung cancer. The standardized incidence ratio for lung cancer was higher the longer allowed before the start of follow-up.

Table 7 shows the results of the survey of smoking habits among the cohort, and the smoking habits of a random sample of the Icelandic population are shown for comparison. The proportion of nonsmokers was higher among the diatomite workers than among the sample of the general population.

Discussion

Our cohort of diatomite workers was exposed to diatomaceous earth and cristobalite and to practically no other

Table 6. Observed and expected numbers of cancers, the standardized incidence ratio (SIR), and the 95% confidence interval (95% CI) for all cancers and lung cancer according to the length of employment measured by accumulated hours of employment with a requirement of 5 or 9 years before the start of follow-up among the men who had been exposed during loading ships with the production from the diatomite factory.

Cancer sites[a]	Five years' time interval before start of follow-up								Nine years' time interval before start of follow-up							
	Employed < 300 h (N = 618)				Employed ≥ 300 h (N = 66)				Employed < 300 h (N = 616)				Employed ≥ 300 h (N = 66)			
	Observed	Expected	SIR	95% CI	Observed	Expected	SIR	95% CI	Observed	Expected	SIR	95% CI	Observed	Expected	SIR	95% CI
All cancers (140—204)	8	15.84	0.51	0.22—1.00	8	5.80	1.38	0.60—2.72	5	12.48	0.40	0.13—0.93	7	4.74	1.48	0.59—6.09
Lung cancer (162)	2	1.89	1.06	0.13—3.82	3	0.81	3.70	0.76—10.82	2	1.51	1.32	0.16—4.78	3	0.67	4.48	0.92—13.09

[a] Code of the International Classification of Diseases, 7th revision, in parentheses.

Table 7. Smoking habits of a random sample of the Icelandic population in 1990 and of the diatomite workers according to a survey in 1993.

Smoking category	Population sample				Diatomite workers							
					All				Loading ships			
	Men		Women		Men		Women		Men		Women	
	N	%	N	%	N	%	N	%	N	%	N	%
Never smoked	478	34.5	642	43.7	224	37.5	137	44.8	173	38.7	128	44.3
Quit smoking more than a year ago	324	23.4	251	17.1	157	26.3	60	19.6	104	23.3	56	12.5
Quit smoking less than a year ago	56	4.0	63	4.3	34	5.7	18	5.9	28	6.3	18	6.2
Smoke, however not daily	65	4.7	48	3.2	22	3.7	20	6.5	14	3.1	19	6.6
Smoke daily	462	33.4	466	31.7	160	26.8	71	23.2	128	28.6	68	23.5

form of crystalline silica. There are no mining activities in Iceland, and quartz is not found in the rocks of the country. No exposure to asbestos occurred in the plant; thus we do not consider asbestos to be a potential confounder in our study, as it was in another study from the diatomite industry (4). To eliminate potential confounding of exposure with that of possible other carcinogens at the processing plant, a restriction was made to those who had never worked in production, but who had been occupied exclusively with transport and the loading of ships.

The diatomite workers smoked less than the general population, and it is thus unlikely that smoking explains the excess of lung cancer. The standardized incidence ratio for lung cancer among those with the longest employment ranged from 2.05 to 4.48 according to varying length of employment in the different subgroups. There is a considerable deficit in the risk of all cancers in contrast to the increased risk for lung cancer.

The weaknesses of this study are obvious but should perhaps be mentioned nonetheless. The cohort was small, the exposure time relatively short but intense, and the period of follow-up barely long enough for the possible development of lung cancer. Therefore further follow-up and a more-detailed analysis of the exposure data could improve the certainty of the results.

The excess of brain and skin cancer was based on only a few cases and, therefore, does not allow any interpretation. However, a Finnish cancer incidence study on silicotic patients has earlier found an excess of skin cancer, both melanoma and nonmelanoma (8).

This study dealt with the association of cristobalite exposure and lung cancer. This is a rare type of exposure and favors a cohort approach. The excess of lung cancer is in concordance with the findings of the mortality study on workers in the diatomaceous earth industry in California (3, 4). The results of our study also agree with findings from previous cancer incidence studies, which have shown excess lung cancer risk among workers exposed to crystalline silica in the form of quartz (5—8).

In light of the indication of less cigarette smoking among the cohort than among the reference population, it is concluded that our results support the suggestion of a causal association between cristobalite and diatomaceous earth exposure and lung cancer.

References

1. Wagner MMF, Wagner JC, Davies R, Griffiths DM. Silica-induced malignant histiocytic lymphoma: incidence linked with strain of rat and type of silica. Br J Cancer 1980;41:908—17.
2. Wagner MMF. Pathogenesis of malignant histiocytic lymphoma induced by silica in a colony of specific-pathogen-free Wistar rats. JNCI 1976;57:509—18.
3. Checkoway H, Heyer NJ, Demers PA, Breslow NE. Mortality among workers in the diatomaceous earth industry. Br J Ind Med 1993;50;586—97.
4. Checkoway H, Heyer NJ, Demers PA, Gibbs GW. Reanalysis of mortality from lung cancer among diatomaceous earth industry workers, with consideration of potential confounding by asbestos exposure. Occup Environ Med 1996;53:645—7.
5. Lynge E, Kurppa K, Kristofersen L, Malker H, Sauli H. Occupational groups potentially exposed to silica dust: a comparative analysis of cancer mortality and incidence based on the Nordic occupational mortality and cancer incidence registers. In: Simonato L, Fletcher AC, Saracci R, Thomas TL, editors. Occupational exposure to silica and cancer risk. Lyon: International Agency for Research on Cancer, 1990:7—20.
6. Tornling G, Hogstedt C, Westerholm P. Lung cancer incidence among Swedish ceramic workers with silicosis. In: Simonato L, Fletcher AC, Saracci R, Thomas TL, editors. Occupational exposure to silica and cancer risk. Lyon: International Agency for Research on Cancer, 1990:113—9.
7. Westerholm P, Ahlmark A, Maasing R, Segelberg I. Silicosis and lung cancer — a cohort study. In: Goldsmith DF, Winn DM, Shy CM, editors. Silica, silicosis and cancer: controversy in occupational medicine. New York (NY): Praeger, 1986:327—33. Cancer research monograph, vol 2.
8. Partanen T, Pukkala E, Vainio H, Kurppa K, Koskinen H. Increased incidence of lung and skin cancer in Finnish silicotic patients. J Occup Med 1993;36:616—22.
9. Reimarsson P. Könnun á kísilsýruryki í andrúmslofti starfsmanna við framleiðslu og flutning kísilgúrs [Concentration of airborne silica dust in the manufacture and shipping of diatomaceous earth]. Reykjavik: Administration of Occupational Safety and Health, 1986.

10. Tulinius H, Ragnarsson J. Cancer incidence in Iceland 1955—1984. Reykjavik: Icelandic Cancer Society and Director General of Health, 1987.
11. Axelson O. Epidemiologi för arbets- och miljömedicin [Epidemiology for occupational and environmental medicine]. Lund: Studentlitteratur, 1981.
12. McDonald JC, Liddell FDK, Gibbs GW, Eyssen GE, McDonald AD. Dust exposure and mortality in chrysotile mining, 1910—75. Br J Ind Med 1980;37;11—24.
13. Ragnarsson J, Blöndal T. Reykingavenjur 1989—1990 [Smoking habits 1989—1990]. Reykjavik: The Committee for Tobacco Use Prevention and Director General of Health, 1990.

Received for publication: 22 July 1996