DUST EXPOSURE INDICES AT THE EARLIEST APPEARANCE OF PNEUMOCONIOSIS

EDWARD MOORE, Ph.D.* • John R. Martin, M.D.* • Alison C. Edwards, B.Sc.* • Henry A. Anderson, M.D.† • Edward A. MacLaughlin, M.B.‡

*Division of Community Medicine and Behavioural Sciences and
‡Discipline of Radiology, Health Sciences Centre, Memorial University of Newfoundland, St. John's, A1B 3V6, Canada
†Section of Environmental and Chronic Disease Epidemiology, Wisconsin Division of Health, Madison WI 53701, USA

INTRODUCTION

In 1981 a number of workers with a radiologic appearance compatible with pneumoconiosis were identified in a cross-sectional survey of an iron ore mine and beneficiation plant in Labrador West, designated as the Labrador West Dust Study (LWDS).[1] In some, pneumoconiosis had been diagnosed in the years preceding the survey but in the case of others, the LWDS marked the first appearance of radiologic abnormality. Various indices for exposure to dust have been calculated for each of these workers at the point in time when pneumoconiosis was first suspected or diagnosed from their periodic surveillance chest radiographs. These indices were compared for their power to predict pneumoconiosis (ILO category ≥ 1), using workers placed in ILO category 0 in the LWDS as a comparison group. One of the indices, cumulative quartz, has been used to assess the validity of ACGIH recommendations for exposure to silica.[2]

METHODS

Case Selection

One thousand nine hundred and fifty workers (1950) completed all phases of the LWDS. Forty-four (44) qualified for inclusion in category 1 or higher in the ILO classification (1980) of radiographs for pneumoconiosis by the method described elsewhere.[1,3]

Exclusions

1. For workers in all ILO categories.
   a. Exposure to rock dust at previous places of employment in excess of 25% of employment with present company.
   b. Location in administrative or "not dusty" jobs as defined elsewhere.[1]
2. For workers scoring $\geq$ ILO category 1 LWDS.
   a. Presence of confounding factors in radiographic interpretation.
   b. Absence of antecedent normal chest radiographs.

The 36 workers remaining in ILO category ≥ 1 comprised two groups. The first Group A—were workers where the LWDS confirmed a diagnosis of pneumoconiosis made for the first time between 1972–79. The second Group B, were workers where the diagnosis was made for the first time in the LWDS (1981). In both groups periodic surveillance chest films had been read by a single observer without reference to the ILO classification. Consequently, in Group A the earliest appearance of pneumoconiosis has been defined as the first mention of radiographic changes compatible with or suspicious of this diagnosis. In Group B however, the first manifestation of changes suggestive of pneumoconiosis occurred in the LWDS film which had been read to the ILO classification. For this group the earliest appearance of pneumoconiosis refers to a score of 1/0 or higher on the ILO scale.

Exposure Indices

Five exposure indices were created for each worker as described elsewhere.[4,5] In brief, they were years of exposure to detectable amounts of dust and four quantitative dust exposure indices. The latter were functions of years of exposure and dust concentrations (based on Harvard nylon cyclone measurements) at all the locations where a worker had been employed. The four measurements were cumulative and "peak" respirable dust and quartz indices. "Peak" indices, were devised to take account of periods in a worker's dust concentration-time profile when dust levels were much higher than usual. These elevations would receive no special weighting in calculating cumulative indices. Hence these special "peak" parameters were computed to assess their importance.

For each index of exposure, the 1709 workers were analyzed and the observed prevalence values i.e. (number of diagnosed cases)/(number in workforce) were calculated and tabulated for a set of sub-intervals appropriate to each index of exposure. Multivariate logistic regression analysis was performed on all of the five indices to give predicted prevalence figures.

RESULTS AND ANALYSIS

The characteristics of the workers scoring ILO category 1 or higher in the LWDS, and who were included in this analysis, are listed in Table I by group. In the combined groups, when radiologic abnormality was first noted, the mean months of exposure at the present company of employ-

Table I
Worker Characteristics at Appearance of Radiologic Abnormality

	Max	Min	Mean	Median
Months of Exposure Present Company				
Group A	224	85	135	135.5
Group B	211	61	150	156.0
Group A & B	224	61	147	138.5
Months Since Previous Normal X-ray				
Group A	26	2	13	12.0
Group B	96	5	33	15.5
Group A & B	96	2	23	12.5
Age				
Group A	52	27	38	35.5
Group B	61	24	40	37.0
Group A & B	61	24	39	36.0

LWDS ILO Classification (1981)

	Subcategory (n)	Shape	n	%
Group A	1/0 (4); 1/1 (5); 1/2 (4); 2/1 (2); 2/2 (5); 2/3 (2); 3/3 (2)	Round	17	71
Group B	1/0 (11); 1/1 (1)	Round	4	33
Group A & B	1/0 (15); 1/1 (6); 1/2 (4); 2/1 (2); 2/2 (5); 2/3 (2); 3/3 (2)	Round	21	58

Group A: Diagnosed as pneumoconiosis prior to LWDS n = 24

Group B: Diagnosed as pneumoconiosis at LWDS n = 12

Group A & B: n = 36

ment was 147 months with a maximum of 224 and a minimum of 61 months. The mean of the interval between the normal and the abnormal chest radiographs was 23 months with a maximum of 96 and a minimum of 2 months. The explanation for this wide spread was that five workers, all in Group B, had moved from "dusty" jobs where surveillance films are customary to locations where they are not. At the time of the LWDS, the profusion of the small opacities ranged from 1/0 to 3/3 and the shape of the primary small opacities was described as round in 58% of the 36 diagnosed cases.

A stepwise multivariate logistic regression analysis was performed on the five exposure indices. This gives the logistic response function which is the probability that an employee is in ILO category ≥ 1. The most important variable chosen by the regression analysis was "peak" quartz (PQ)—in fact, this was the only variable chosen if a p-value of 5% is kept as the criterion for the 'improvement chi-square'. This gave the function:

$$\text{Probability (Category} \geq 1) = \frac{\exp[-5.12 + 0.00343(PQ)]}{1 + \exp[-5.12 + 0.00343(PQ)]}$$

The observed and predicted values for this function are shown in Table II. If the 5% value is relaxed to 6%, then cumulative quartz (CQ) and years of exposure (YRS) are included as the next variables in the response function.

$$\text{Probability (Category} \geq 1) = \frac{\exp[-4.87 + 0.003(PQ) + 0.18(CQ) - 0.11(YRS)]}{1 + \exp[-4.87 + 0.003(PQ) + 0.18(CQ) - 0.11(YRS)]}$$

However, further analysis does not allow the inclusion of the remaining two indices—cumulative and "peak" respirable dust—for an acceptable response function. This is in accord with our Case-Control Study where quartz was identified as the dominant differentiating mineral index for exposure between category 0 and categories 1, 2 and 3.[4]

The rest of this present analysis concerns only the three significant indices; viz, years of exposure, cumulative quartz and "peak" quartz. Figures 1–3 show the distributions for the healthy workers as opposed to the "cases' for each of the three indices. These figures along with the median values in Table III show that "peak" quartz is the index which distinguishes best between the distributions of the 'healthy' worker and the 'cases'.

Values for the ratio: (number of cases)/(number of total workers) for sub-intervals of the three significant exposure indices are shown in Figures 4–6. The ratios rise with increasing exposure, but for reasons which are not apparent, this rise was not sustained in years of exposure after 12 years.

DISCUSSION

The workers scoring ILO category 1 or higher in the LWDS comprised two groups—one diagnosed prior to, and the other during the LWDS. The groups differed in the method used for determining the earliest manifestation of pneumoconiosis; the significance of this is being examined.

Table II
Observed and Predicted Values for Logistic Response Function

PQ	200	400	600	800	1000	1200	1400
Obs%:	0.5	4.0	7.5	8.5	20.0	15.1	38.1
Pred%:	1.1	2.0	4.0	7.8	14.3	24.5	38.8

PQ: "Peak" Quartz; $(mg/m^3)^3.yr$

Table III
Median Values for Exposure Indices for 'Healthy' Workers and 'Cases'

	Years of Exposure	CQ	PQ
Healthy Workers n = 1673	5.9	1.8	34.2
Cases n = 36	11.4	7.6	912.0

CQ: Cumulative Quartz; mg/m^3yr

PQ: "Peak" Quartz; $(mg/m^3)^3.yr$

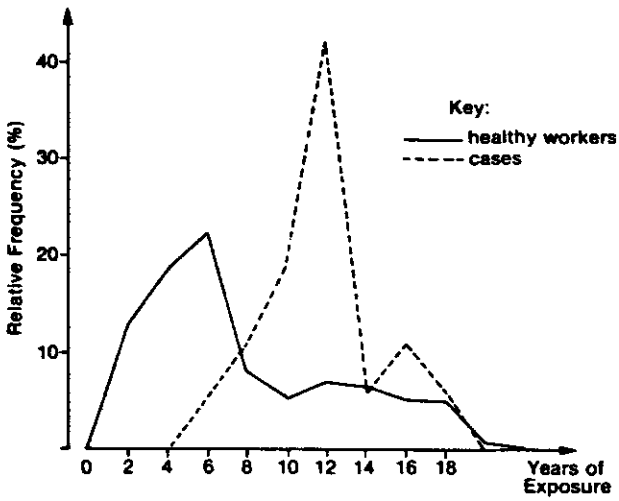

Figure 1. Relative frequency polygons for healthy workers and cases—years of exposure.

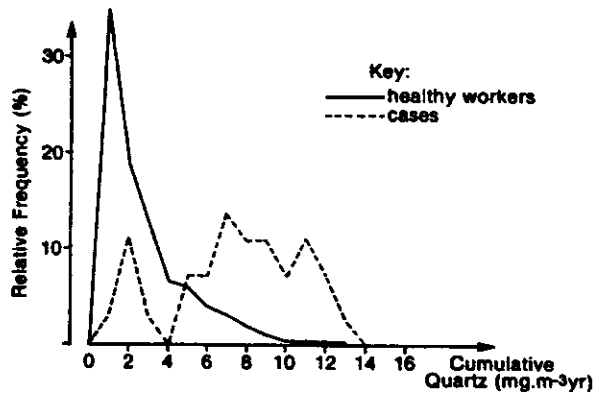

Figure 2. Relative frequency polygons for healthy workers and cases—cumulative quartz.

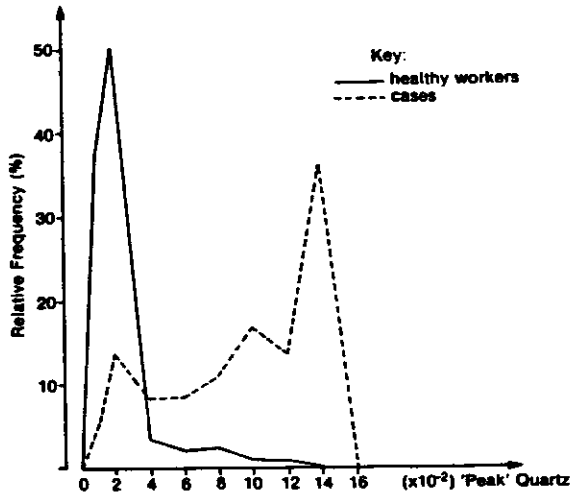

Figure 3. Relative frequency polygons for healthy workers and cases—"Peak" quartz.

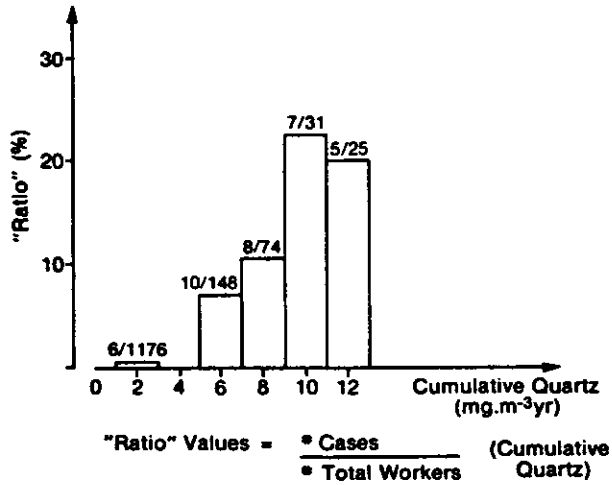

Figure 5. Ratio values for cumulative quartz.

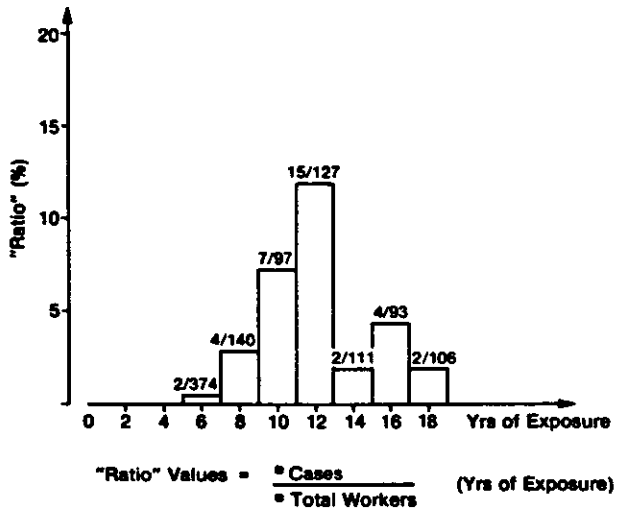

Figure 4. Ratio values for years of exposure.

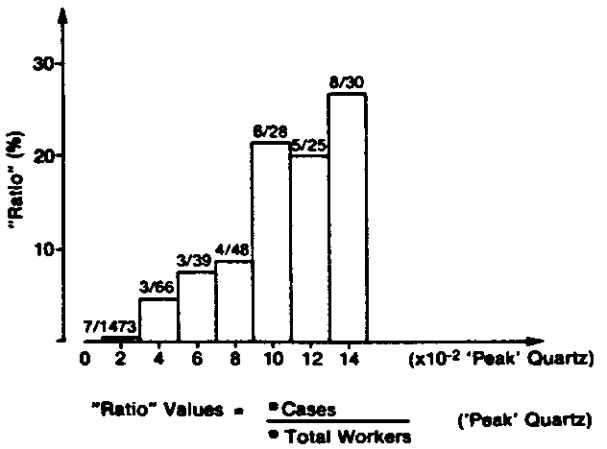

Figure 6. Ratio values for "Peak" quartz.

Dividing the workforce into two populations—those with pneumoconiosis (cases) and those without pneumoconiosis (healthy workers)—"peak" respirable quartz is the index which most clearly separates the two (Figure 3). This is substantiated by the logistic regression which singles out only this same index for prediction purposes at the 5% level. Thus the "peak" exposure index is a better predictor for pneumoconiosis than the cumulative exposure index evaluated on the same dust concentration time profile. This result is further confirmation of our previous observation that short lasting periods or "peaks" when dust levels are much higher than usual, contribute significantly to the development of pneumoconiosis.[4]

"Threshold limit values ... represent conditions under which it is believed that *nearly all* (our emphasis) workers may be repeatedly exposed day after day without adverse effect."[2] The ACGIH Threshold Limit Value—Time Weighted Average (TLV—TWA) for exposure to silica is 0.1 mg/m^3. Assuming that a worker is exposed to this TLV-TWA for say forty years, about the maximum duration of employment that could be expected for such workers, then his cumulative quartz index would be $40 \times 0.1 = 4$ mg/m^3 yr. In our study, for workers with cumulative quartz indices of 4 mg/m^3 yr or less, the average number of years of exposure was 7 years and as Figure 5 shows, the prevalence of pneumoconiosis was 6/1176 cases or 0.5%. Thus, to date, in the conditions prevailing at this mining complex, 99.5% of those workers who have been exposed to silica concentrations resulting in a cumulative quartz index of ≥ 4 mg/m^3 yr, appear to have suffered no adverse respirable effects.

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SILICA DUST, RESPIRATORY DISEASE AND LUNG CANCER —RESULTS OF A PROSPECTIVE STUDY

M. NEUBERGER • M. Kundi • A. Rutkowski • W. Gründorfer

Department of Preventive Medicine, Institute of Environmental Hygiene
University of Vienna, A-1095 Vienna, Kinderspitalgasse 15, Austria

INTRODUCTION

Mineral particles are not generally considered to be carcinogenic, except for a few specific species such as asbestos, and the carcinogenicity of crystalline silica to humans has been a matter of controversy[2,4] since results of retrospective studies and results on persons selected for silicosis have been questioned.[6] Our investigation was initiated by the hypothesis that chronic irritation of the bronchial mucosa by inspirable particles increases lung cancer incidence. Meanwhile other and more detailed pathogenetic mechanisms have been discussed in this context, considering respiratory clearance, carrier effects and other combined effects.[2] Our contribution will be new results on the first cohort of dust exposed workers which has been followed prospectively from a preventive checkup in the 1950s, during the second part of life up to death (and in about 50% up to autopsy). Details of the source population,[10] setting up of cohorts[5] and first results of follow-up[8,9] have been given earlier.

METHODS

A mobile team of the occupational health care unit started screening examinations in 1950 which included an occupational and a smoking history.[10] All persons with a history of dust exposure were chest X-rayed and are the source of our exposed cohort. 1630 men given the first chest X-ray in 1950–1960 because of silica and/or heavy "inert" dust exposure were born before 1911 and resident in Vienna. An equal number of Viennese men without occupational dust exposure was selected from the occupational health care examination files by matching year of birth, year of first examination and smoking.[5] At a later control of exposure histories at the pension insurance board 5 men were found not to meet the eligibility criteria and were therefore eliminated from the study together with their matched counterparts (dustworkers: 1 because of confounding asbestos exposure, 1 because of lack of dust exposure, 1 because of being born 1911; references: 2 because of dust exposure). Thus we followed 1925 workers exposed to non fibrous dust in the metal, glass, ceramics, stone, construction, cleaning agent and a few other industries and 1625 non-dust-exposed workers from a great variety of branches (publishing and printing, chemical, construction, textile, leather, food, electrical industry, etc.).

Diagnoses at death were traced and encoded without knowledgement of the exposure. Death certificates in Vienna are based on autopsy in more than 50%,[3] but a small proportion of diagnoses had to be clarified with the reporting hospital or physician. The best available informations were used for comparison on dust and non-dust-exposed. The official diagnosis was used for comparison with the general population of Vienna, which gives conservative estimates of standard mortality ratios (SMR), because mortality (especially cancer mortality) is higher in Vienna than in Austria, and some of the cohort members moved to rural districts after retirement.

RESULTS

1621 dust-exposed (DUST) and 1621 reference subjects (NO DUST) = 99,8% could be traced up to the end of 1986. 1442 DUST (89%) and 1384 (NO DUST) (85,4%) died. The underlying cause of death is given in Table I for 1439 (99,8%) DUST and 1379 (99,6%) NO DUST. Observed cases (0) in DUST divided by expected cases in NO DUST are given under Relative Risk (RR). This age-adjusted relative risk of DUST was significantly raised ($p < 0,001$, Poisson, two-sided) for lung cancer, stomach cancer, chronic obstructive lung disease (emphysema, bronchitis, asthma) and silicosis/fibrosis/tuberculosis of the lung. Gastrointestinal diseases (mainly liver cirrhosis) were found more frequent, too ($p < 0,05$).

Respiratory diseases were also found increased in OUST as secondary cause on death and additional diagnoses on death certificates (mainly silicosis and chronic obstuctive lung disease, but also pneumonias).

Table II shows official diagnoses of underlying cause of death and standard mortality ratios. In DUST overall mortality, lung cancer, stomach cancer, chronic obstructive lung disease, silicosis/fibrosis/tuberculosis and acute/infectious respiratory diseases was found higher ($p < 0,001$, Poisson, two-sided) than expected in Viennese men of same age. In NO DUST overall mortality was the same as in the general population; silicosis/fibrosis/tuberculosis, cardiovascular diseases and accidents were lower than expected and lung cancer was slightly higher ($p < 0,05$).

For 775 foundry workers, 475 grinders and other metal workers, 191 glass and ceramic workers, 87 stone cutters and construction workers and 65 other dust-exposed workers observed lung cancers and stomach cancers are given in Table III (32 workers could not be included in this stratification because the main branch of occupational dust exposure was

Table I
Main Causes of Death: Dust Exposed Compared to Reference Cohort

Best available diagnose	DUST 0	NO DUST 0	RR
cancer of lung	183	142	146***
" other respirat.o.	4	4	114
" stomach	80	48	190***
" intestine	37	50	88
" other digestive o.	50	45	125
" other sites	67	84	92
" not localised	1	2	
chron. obst. lung dis.	83	47	202***
tuberculosis, silicosis	78	15	513***
acut, infect. respir.d.	50	55	110
heart disease	362	404	106
cerebrovascular dis.	125	157	97
other vascular dis.	132	145	107
gastrointestinal dis.	93	84	127*
accidents, suicide	41	39	109
other disease	55	58	112
unknown, ill-defined	3	5	111

* $p < 0,05$, ** $p < 0,01$, *** $p < 0,001$

ill-defined on entry file). Table III shows increased lung cancer mortality in all subgroups of DUST with the highest SMR in stone and glass/ceramics ($p < 0, 001$). The SMR for stomach cancer was above 100 in all strata, but significantly only in those employed in foundries and other metal industries.

Life table analyses showed reduced survival of DUST not before 7 years of observation and 58 years of age (Figure 1). At the median the survival difference between DUST and NO DUST was 3 years. Survival probability from lung cancer at age 70 was 91,4% in DUST (95% confidence interval: 89,9–92,9) and 71,7% in NO DUST (95% confidence interval: 93,2–95,6) which is significant (Figure 2).

DISCUSSION

In Viennese workers we found a relation between exposure to respirable particulates and mortality from lung cancer and chronic diseases of the lung. The rate of chronic obstructive lung deseases was 2-times higher and the rate of lung cancer was 1,5-times higher than in non-dust-exposed workers with comparable smoking habits. The 17% lung cancer increase in

Table II

Main Causes of Death: Dust Exposed and Reference Cohort Compared to General Population

OFFICIAL DIAGNOSE (ICD, 9.REV.)	DUST		NO DUST	
	O	SMR	O	SMR
CANCER OF LUNGS (162)	180	168***	142	117*
" OTHER RESPIRATORY O.(161, ETC.)	4	67	4	60
" STOMACH (151)	78	167***	47	89
" INTESTINE (152-154)	36	84	50	100
" OTHER DIGESTIVE (140-150, 155-159)	48	115	44	92
" OTHER	70	92	85	95
CHRON.OBSTR.LUNG DIS. (490-493)	77	205***	45	101
TUBERCULOSIS, SILICOSIS, FIBROSIS (011, 502, ETC.)	75	299***	17	63*
ACUTE, INFECT.RESPIRAT.D.(460-487)	52	135*	55	120
CARDIOVASCULAR D. (390-459)	628	97	707	92*
GASTROINTESTINAL D. (520-579)	95	109	85	87
ACCIDENTS, SUICIDE (800-999)	42	86	42	76*
ALL CAUSES	1442	123***	1384	100

+ $P<0,05$, ** $P<0,01$, *** $P<0,001$

Table III

Lung and Stomach Cancer in Dust Exposed Industries Compared to General Population

CANCER DEATHS	FOUNDRY		METAL		GLASS/CERAMICS		STONE		OTHER	
	O	SMR	O	SMR	O	SMR	O	SMR	O	SMR
LUNG	85	163***	44	135*	28	236***	15	293***	6	153
STOMACH	40	176***	21	149*	6	116	4	173	3	172

* $P<0.05$, ** $P<0.01$, *** $P<0.001$

non-dust-exposed workers compared to the general population could be due to smoking and occupational exposures (vapours etc.) except dust. In dust-exposed the increased lung cancer rate was found in all subgroups, which have very different confounding exposures (e.g. polycyclic aromatic hydrocarbons in foundries, possibly arsenic in glass industry, nitrosamines in some metal grinders, etc.). We discussed elsewhere[8,9] the minor importance of confounding exposures for our study, such as the very limited use of asbestos in Vienna and its metal industry (no signs of asbestos exposure were found on chest X-rays of dust-exposed and no mesotheliomas occurred), the lack of sources of radiation in the plants investigated (only in a few stone- and tunnel-workers radiation might have been a co-factor) and the negligible use of carcinogenic metals and compounds in iron foundries at the time of the cohort recruitment. Confounding exposures after registration seem to be of minor importance, too, because work histories obtained in 1982 from the national pension insurance board showed a low inter-industry and interplant mobility of dust-exposed (because of registration after age 40) and no second jobs with exposure to accepted carcinogens (one lung cancer case was exposed to glass wool as an insulator and a few other cases with suspected confounding exposure such as a sepiolite grinder are still alive or died from nonmalignant diseases).

Most earlier studies on lung cancer in dust workers have been biased by selection and competing causes of death (silicosis). In coal workers a protective effect of coal dust has been discussed.[7] The seemingly conflicting results on lung cancer in silica and "inert" dust-exposures could perhaps be explained by a multistage model of carcinogenesis: Genotoxic substances (from tobacco smoke as well as from foundry air or other sources) could function as initiators and particles as adsorbens and promotors. In this case it would not be surprising if lung cancer increases with total dust load and not necessarily e.g. with PAH-concentrations, even though both might be involved. From available measurements in our study[8] we cannot decide whether silica or total respirable or inspirable dust was responsible for the increase of lung cancer, but we suspect that also "inert" dust exposure (if heavy and long lasting) can promote chronic obstuctive lung diseases and lung cancer. Bombardment of airways by dust particles, even "inert" ones, could eventually sustain high levels of polymorphonuclear recruitment, alveolar macrophage activation and finally result in a disturbed balance of protease and antiprotease activity.[1]

From the age in which we observed excess lung cancer deaths (Figure 2) we conclude that screening examinations should be continued after retirement from a job with heavy dust exposure. Screening for chronic obstructive lung disease must begin much earlier. Most important, however, is primary prevention by reduction of dust exposures, even "inert" ones.

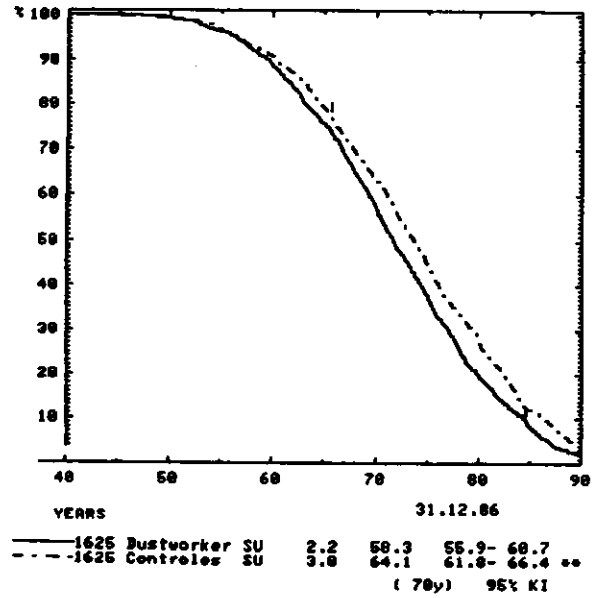

Figure 1. Survival of dust-exposed (solid line) and reference subjects (dashed line).

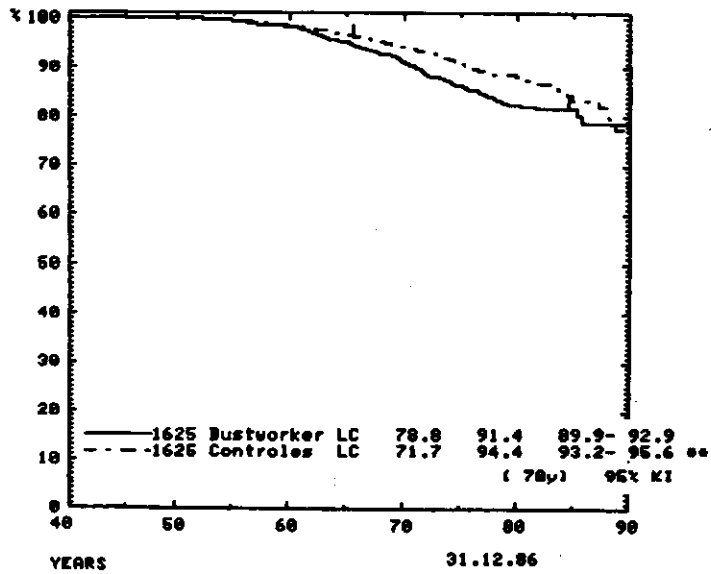

Figure 2. Survival from lung cancer (dust-exposed: solid line, reference subjects: dashed line).

SUMMARY

From 1625 men examined in 1950–1960 with a history of occupational exposure to silica and other non-fibrous particulates in foundries, other metal, glass, ceramic, brick, stone and some other dusty industries 1621 were traced up to 1986, 1442 died, 183 from lung cancer (SMR 168), 80 from stomach cancer (SMR 167), 83 from chronic obstructive lung disease (SMR 205) and 78 from silicosis/fibrosis /tuberculosis (SMR 299).

From 1625 non-dust-exposed workers from the same source population, matched in 1950–1960 to dust exposed workers for age, smoking and begin of observation, 1621 were traced, 1384 died, 142 from lung cancer (SMR 117), 48 from stomach cancer (SMR 89), 47 from chronic obstuctive lung disease (SMR 101) and 15 from tuberculosis/fibrosis (SMR

63). Life table estimates show that primary and secondary prevention should not be focused on pneumoconioses alone.

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EPIDEMIOLOGIA DE LA SILICO-TUBERCULOSIS EN MINEROS ASTURIANOS: TASA DE NUEVOS CASOS BACTERIOLOGICAMENTE POSITIVOS. PERIODO 1971-1985.

J. A. MOSQUERA

Jefe del Servicio de Neumologia del INSTITUTO NACIONAL DE SILICOSIS (INS). Oviedo. SPAIN.

ABSTRACT

La población diana la forman 50.470 ± 7.454 mineros—del carbón de Asturias. La muestra estudiada prospectivamente abarca a 3.612.2 ± 1.779 primeras visitas que son estudiados en el Instituto Nacional de Silicosis cada año. A todo sospechoso de tuberculosis se le practica sistematicamente: 4 extensiones de esputo (Método Ziehl-Nielsen) y 3 cultivos (Medio de Lowenstein) y si precisan, otros tests diagnósticos más invasivos. Durante el periodo 1971-1985, 1.136 pacientes fueron diagnosticados de tuberculosis por presentar positivos los tests bacteriológicos. Durante los 7 primeros años de observación, entre los 508 tuberculosos, la distribución de la categoria de neumoconiosis (ILO 1971) y edades era 7.8% tenian Categoria 0 y 51.1 ± 13.6 años; 9.8% con Categorias 1,2,3 y 54.3 ± 13.3 años; 82.3% con Fibrosis Masiva Progesiva y 53.5 ± 10.6 años. Entre 1978-85, la distribución de neumoconiosis y edades eran respectivamente: 33.3% y 48.7 ± 14.7 años; 14.1% y 55.5 ± 10.5 años; 62.6% y 58.4 ± 10.2 años. La tasa de nuevos casos bacteriologicamente positovos fué de 150.1 ± 30.9 por 10^5 mineros y año, no modificándose significativamente a lo largo de los 15 años, a pesar de la eficacia de los tratamientos. Esta tasa es 3 veces superior a la de la población no minera de la zona, pero no es diferente a la encontrada en otras poblaciones ocupacionales similares.

INTRODUCCION

La Tuberculosis Pulmonar es responsable en en nuestra región de la evolución de las categorias simples de neumoconiosis (1,2,3) a Fibrosis Masiva Progresiva (FMP) en el 9.7% de los casos.[1] Por ello el control de la Silicotuberculosis reduciria la morbilidad y mortalidad que condiciona la FMP.

METODOS

El periodo de estudio comprende desde el 1 de Enero de 1971 hasta el 31 de Diciembre de 1985, dividido en dos periodos 1971-1977 y 1978-1985.

La población diana, objeto de este estudio, es la población minera de Asturias. Esta región, localizada en el Norte de España tiene yacimientos de hulla y antracita. La cuantia media anual, con una desviación standard (±1SD), de esta población se compone, a lo largo de estos años de 50.470 ± 7.454 mineros.

La población muestreada anualmente (±1SD) asciende a 3.612.2 ± 1.779.1 mineros.

Los diagnósticos de neumoconiosis se realizaba en base a exposición laboral y presencia de opacidades redondas de profusión igual o mayor a P 1/1 (Clasificación ILO 1970).[2] La lectura radiológica se efectuó por 3 lectores con experiencia en neumoconiosis, usando la escala de profusiones ampliada.[3] Las discrepancias de lecturas eran promediadas.

El diagnóstico de tuberculosis pleuro-pulmonar se hacia al observar cuadro clinico-radiológico compatible y presencia de material alcohol-acido resistente con el método de ziehl Nielsen y/o identificación del Mycobacterium Tuberculosis en medio de Lowenstein-Jensen. A todo sospechoso de tuberculosis se le practicaba sistematicamente 4 extensiones de esputo con el método Ziehl y 3 cultivos sucesivos en medio de Lowenstein; si era preciso, el paciente era sometido a otros métodos diagnósticos, (broncoscopia, punción transpulmonar, etc.).

A efectos epidemiológicos eran excluidos los casos en que el diagnóstico se sustentaba solo por métodos histológicos.

Las resistencias "in vitro" del Mycobacterium Tuberculosis eran estudiadas mediante el método de Canetti, modificado.[4,5]

Todos los pacientes tuberculosos eran seguidos por una sección especifica de Neumologia del INS, que los trataba y controlaba su evolución. Durante el periodo 1971-1977, el tratamiento antituberculoso era el "standard" de 18 meses, con seguimiento, clinico, radiológico y bacteriológico cada 3 meses hasta 2 años después de finalizado el tratamiento Desde 1978 a 1985 los tratamientos usados fueron 2 regimenes de curso corto; a) Hidracida (I) 300 mg./dia, Rifampicina (R) 600 mg./dia, Etambutol (E), 1200 mg/dia, durante 9 mg./dia, Rifampicina 600 mg./dia y Pirazinamida (Z) 1500 mg./dia, durante 2 meses, seguido de Hidracida y Etambutol durante 7 meses más. (SIZR)2, (IE)7. (6). Se practicó el mismo tipo de seguimiento pero a intervalos de

1 mes. También durante este periodo se hizo chequeo de contactos intimos.

En caso de retratamientos en enfermos tuberculosos, se usaba el régimen standard de 18–24 meses, intentando que la combinación de drogas útiles, conocidas por antibiograma, sumase 1.5. Esto se hacia adjudicando valor 1 a I,R y 0.5 a Z y aminoglicosidos.[7]

La cuantificación de la enfermedad tuberculosa, se hacia midiendo la tasa anual de los nuevos casos bacteriológicamente positivos. Esta se obtenia refiriendo el número de nuevos enfermos, hallados por cultivo y/o estensión, a la población diana que existia a 31 de Diciembre del año correspondiente.

RESULTADOS

1.136 pacientes fueron diagnosticados de tuberculosis pulmonar después de excluir 2 casos en que creció una Mycobacteria no tuberculosa.

Durante 1971–77, entre los 507 tuberculosos la distribución de las categorias de neumoconiosis y edades eran: 7.8% tenian categoria 0 y 51.1 ± 13.6 años; 9.8% con categorias 1,2 y 3 y 54.3 ± 13.3 años; 82.3% con FMP y 53.5 ± 10.6 años. Entre 1978-85, la distribución de neumoconiosis y edades eran respectivamente de 33.3% y 48.7 ± 14.7 años para la categoria 0, 14.1% y 55.5 ± 10.5 años para las neumoconiosis simples y 62.6% y 58.4 ± 10.2 años para la FMP.

La tasa de resistencias primarias a las drogas antituberculosa fueron para los mineros sin neumoconiosis (categoria 0) del 12.9% y 11.9% para las categorias 1,2 y 3.

Las cifras de curación para los pacientes que completan los tratamientos, al finalizar los mismos eran:

a) Tratamiento standard 121/123 (90.9%).
b) Tratamiento curso corto (EIRZ)2 (IE)7 26/27 (96.2%).
c) Tratamiento curso corto (IRE)9 39/40 (97.5%).
d) Retratamiento con "standard" en pacientes sin resistencias: 48/49 (97.9%).
e) Retratamiento con "standard" en pacientes con resistencias a 1 droga: 25/28 (89.2%).
f) Retratamiento con "standard" en pacientes con resistencias a 2 drogas 14/17 (82.3%).
g) Retratamientos con "standard" en pacientes con resistencias a multiples drogas 9/10 (90.0%).

DISCUSION

La tasa de neuvos casos bacteriologicamente positivos se ha mantenido estable a lo largo del periodo de observación, con un valor medio (± 1SD) de 150.1 ± 30.9 por 10^5 mineros y año. Esta cifra triplica a la de la población no minera de la zona. Las tasas registradas en otras poblaciones mineras han variado desde cifras de 49.6 × 10^5 y año[8] hasta las encontradas por Popovac et al[9] que alcanzan valores de 8000 × 10^5 y año. Nuestros resultados son casi coincidentes con la cifra de 146 × 10^5 y año encontrada por Lander en Dinamarca.[10] La persistencia de la tuberculosis ocurre a pesar de la alta eficacia de los tratamientos y la no excesiva alta prevalencia de resistencias primarias.

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EPIDEMIOLOGICAL STUDY OF SILICOSIS IN HARDROCK MINERS IN ONTARIO

D. C. F. MUIR • A. Sebestyen • J. Julian • C. Bernholz • D. K. Verma • H. Shannon
McMaster University, Hamilton, Canada

ABSTRACT

An epidemiological survey of silicosis in hardrock miners in Ontario was undertaken. Radiographs had been taken annually, and these were classified by 5 readers for silicosis. The point in time at which miner's radiographs were considered to have passed the 1/1 category for small round opacities was taken as identifying the onset of silicosis. A side-by-side comparison of konimeter and gravimetric dust sampling was carried out in both gold and uranium mines, the resulting relationship being used to convert historical konimeter data from the mines to equivalent respirable quartz concentrations. By using work records, a cumulative respirable quartz exposure index was calculated for each miner. A Kaplan-Meir survival curve analysis was used to derive risk estimates for the development of silicosis in relation to cumulative respirable quartz exposure.

No Paper provided.

RADIOGRAPHIC ABNORMALITIES IN VERMONT GRANITE WORKERS EXPOSED TO LOW LEVELS OF QUARTZ

WILLIAM G. B. GRAHAM • Sheila Weaver • Taka Ashikaga • David Hemenway • Robert O'Grady

Depts. of Medicine, Biostatistics, and Engineering, University of Vermont, and the Vermont State Health Department. Burlington, VT, USA

ABSTRACT

Whether exposure to levels of granite dust below the current OSHA limits leads to radiographic abnormalities after a lifetime of exposure has not been settled. In 1953, we carried out an X-ray survey of the Vermont granite industry. Quarry and stone shed workers who had been exposed to the low dust levels prevailing in the Industry since 1940 were offered chest X-rays. Films were read by three "B" readers, and were considered abnormal if 2 or 3 of the readers assigned a profusion score of 1/0 or greater. 976 workers out of a total of approximately 1400 participated. 65 (6.9%) of the films were judged abnormal, but the profusion scores were low, only 4 of the films being assigned scores of 6/1 or greater. Only 7 (0.7%) had "pqr" or rounded opacities as the major abnormality. The remaining 61 had irregular opacities, largely lower lobe in location, which are of doubtful significance, but may be related to smoking and aging. In addition, total dust concentrations were measured using personal samplers; dust levels were similar to previous measurements. Mean concentrations were 601 ± 365 micrograms/cuhic meter. Using previously estimated values for percentage quartz of 10%, the mean quartz concentration was below the current OSHA standard of 100 micrograms/cubic meter, although 11% of the samples were above this value. If exposure levels have remained approximately the same over the past 45 years, we conclude that current dust controls, which conform to OSHA standards, have essentially eliminated silicosis.

BACKGROUND

Studies of workers' health in the Vermont granite industry have provided a great deal of information on the health effects of quartz dust inhalation since 1969, when the first comprehensive study of the industry was published.[4] Based on a high incidence of silicotuberculosis, control measures which reduced granite dust levels below 10 million parts per cubic foot (mppcf) were accomplished between 1935 and 1940. At that time, the Vermont Division of Industrial Hygiene (DIH) began annual radiographic surveys to assess the effect of dust reduction on the prevalence of silicosis. Subsequent studies showed that as workers with established silicosis retired or left the industry because of illness, and as new workers were hired, the percentage of the work force with radiographic abnormalities declined.[1,3] In 1964, it was stated that no new cases of silicosis had been detected in workers exposed only to the lower dust levels prevailing after 1940.

In 1974, a study analyzing the results of the DIH radiographic survey of 1970–1 suggested that radiographic abnormalities were present in approximately 30% of the workforce.[7] Most of these were of low grades of profusion and comprised both irregular and rounded shadows. However, 67 films (5% of the total) were assigned profusion scores of 6 or 3, which was believed to be consistent with definite silicosis.

Three possible criticisms might he made of this study. First, the films were interpreted only by a single non-certified reader. Second, workers who were exposed only to the low dust levels prevailing after 1940 were not analyzed as a separate group. It was therefore not possible to know whether levels less than 10 mppcf had eliminated silicosis, or were, on the contrary responsible for some of the radiographic abnormalities. Finally, a certain percentage of the films were interpreted as showing opacities in workers with zero dust years of exposure.

The present study attempts to clarify the issue whether the dust levels present in the industry since 1940 have caused radiographic abnormalities, and if so, of what type and extent. We present the results of an industry-wide radiographic survey done in 1953, which includes only workers exposed to granite dust after the institution of dust controls in 1935. Results of dust sampling for total respirable dust will also be mentioned briefly.

METHODS

All workers employed in 1953, including quarry and stone shed workers, were offered 14×17 chest radiographs taken in a mobile van provided by the Appalachian Laboratory for Occupational Safety and Health (ALOSH). Work histories were recorded or updated on all participants, including oc-

cupational category, the shed where employed, duration of employment and smoking histories. Forced spirometries were also carried out. The chest radiographs were interpreted by three "B" readers using the ILO format (1980). The definition of an abnormal film was that either 2 or 3 of the readers assigned a profusion scores of 1/0 or greater, either of the rounded (pqr) or irregular (stu) type. One worker with definite silicosis was excluded because his major work experience occurred in Canada. Gravimetric dust sampling of respirable size particles were collected using personal breathing zone samplers at flow rates of 6 liters/minute.

RESULTS

972 workers out of a total work force of approximately 1400 were x-rayed. Of those workers not having X-rays, 102 were absent on the day of the survey and the remainder (326 or 23% of the work-force) refused. Only 28 (2.88%) of those x-rayed were interpreted by 2 or 3 of the three readers as showing abnormalities consistent with pneumoconiosis. In only 7 films did all 3 readers agree that an abnormality was present. 21 of the 28 films judged abnormal had as the primary abnormality an irregular or stu type of opacity; this was true of the secondary readings as well. Only 7 (0.7% of the total cohort) showed rounded opacities (pqr) of the type typically seen in early silicosis. The grades of profusion were extremely low, only four films being judged as have profusion scores of 2/1 or higher and these films showed irregular (stu) types of opacities. The location of the stu changes, even at low grades of profusion, tended to be in the lower lung zones. No large opacities or egg shell calcifications were observed.

Comparison of the workers with abnormal radiographs compared to the remainder of the workforce showed that the former were older on average (53.6 yrs vs. 41.5 yrs.), and spent longer in granite (30.9 yrs vs. 17.5 yrs.), had smoked longer (27.9 yrs. vs. 19.2 yrs.), and more heavily (32.3 yrs. vs 26.99 yrs.) P values for the first three variables show significant differences at the .001 level. Several of the workers with abnormal films had notably low exposures to dust: one was a lumper for 6 years, and for the remainder of his 37 years had been a draftsman with little exposure. Another had worked exclusively in an office as a draftsman without any exposure.

Average dust concentrations of 417 samples was 601 $\pm$ 368 micrograms/cubic meter, which is similar to values observed by previous workers.[5]

DISCUSSION

These results indicate that radiographic abnormalities consistent with silicosis have occurred at a very low level (0.7% of cohort) at quartz exposures which are in conformance with the current OSHA limit of 100 micrograms/cubic meter.,This is particularly surprising inasmuch as approximately 10% of the samples, using the 10% quartz value of previous workers, were over 100 micrograms/cubic meter. Further, the changes observed tend to be a very low grades of profusion. The predominant type of opacities judged to be present were of the stu or irregular type, seen in 21 of the 28 workers judged to have abnormal films. The significance of these changes is uncertain, but may be associated with peribronchial fibrosis associated with pathological changes of chronic bronchitis which has been described in older, heavily smoking patients.[6]

In summary, this study provides an overview of the prevalence and type of radiographic abnormalities which have developed in Vermont granite workers over a 45 year period of observation, when dust controls were effectively maintained. This essential elimination of radiographic silicosis has occurred at quartz levels which are in conformance with current OSHA standard.

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A STUDY OF SILICOTIC CHINESE GRANITE QUARRY WORKERS IN SINGAPORE

W. H. PHOON, MBBS, M Sc (Occ. Med.), DIH, MFOM, AM • S. E. Chia, MBBS, M Sc (Occ. Med.)
Department of Industrial Health Ministry of Labour Republic of Singapore

SYNOPSIS

Although silicosis is less prevalent today than in the past owing to better dust control at workplaces, cases still occur in a number of countries. In Singapore, the greatest hazard of silicosis is in the granite quarries.

In 93 Chinese granite quarry workers diagnosed as having silicosis and followed up, there was an increased prevalence of chest X-rays with large opacities for category 3 profusion compared to category 1 although this was not statistically significant. The duration of exposure to silica dust did not seem to affect the extent of opacities in the chest X-rays as workers with more than 20 years exposure in the quarries did not have a higher category of profusion of opacities on chest X-ray than those with shorter exposure. There was no statistical significance in the difference in prevalence of cyanosis, clubbing and crepitations among the 3 profusion categories of chest X-ray. Although nearly 25% of the cases had pulmonary tuberculosis, this did not seem to be related to the profusion category on chest X-ray. 58% of the cases had FVC results which were less than 80% of the predicted values, including all the 6 cases with category 3 profusion on chest X-ray, compared with about 52% of those in category 1. This was statistically significant ($p = 0.002$).

INTRODUCTION

It is well-established that occupational exposure to silica dust can cause silicosis.[1] Although the disease is less prevalent today than in the past owing to better dust control at workplaces, new cases still occur in a number of countries.[2]

This paper describes the radiological, clinical and ventilatory function findings in silicotic workers on followup in Singapore.

MATERIALS AND METHODS

Silicosis is a notifiable and compensable occupational disease in Singapore. Confirmation of the diagnosis is made by the Department of Industrial Health, Ministry of Labour, after due investigation. The diagnosis is made mainly on:

a) a confirmed history of occupational exposure to dust containing free silica

b) a chest X-ray picture consistent with silicosis, with a grading of at least category 1/1 of the ILO international classification

c) a clinical picture consistent with the disease, and exclusion of other similar diseases.

Silicosis cases are followed up 3 yearly by the Department of Industrial Health. A clinical examination, full size postero-anterior chest X-ray and ventilatory function tests (FEV_1 and FVC) are done. The ventilatory function tests are done on the Autospiror HI-498. The best of 3 readings is taken and corrected to BTPS. Each reading is compared to the predicted value for the local population, specific for ethnic group, sex, age and height of the subject.[3]

The chest X-rays were read by one of the authors together with a consultant radiologist. The films were compared to the standard ILO films and graded according to the ILO international classification of radiographs of pneumoconioses.[4] Although the workers were asked for respiratory symptoms (cough, breathlessness, sputum), this study has excluded them because the authors felt that the replies might be too subjective for reliable analysis. Instead, this study has included the objective clinical findings of cyanosis, clubbing and crepitations.

All cases were asked for a history of pulmonary tuberculosis. This was then checked with the tuberculosis registry of the National Tuberculosis Control Unit to confirm the history.

The period of 1984 to 1986 was taken. As the silicosis cases are followed up 3 yearly, this period would cover all the cases on followup. New cases during this period were also included. However, the final number included in this study has excluded 82 who had died, and 63 others who were unable to come for examination, were unable to cooperate sufficiently for the FEV_1 and FVC tests, and those who were lost to followup. Four of the cases whose latest chest X-rays were graded as category 0 were also excluded. Thus a total of 140 were included in this study.

In the analysis of the data, Pearson chi-square test was used, with the significance level set at 0.05. Fisher's Exact Test was used where cell values were less than 5.

RESULTS

A total of 140 cases were followed up in the period 1984 to 1986. Most of them were men. Chinese male workers

comprised by far the largest single group (Table I). Of the 115 Chinese men, 93 were granite quarry workers, 22 of whom were still working in the quarries at the time of the follow-up. Seventeen had been exposed to a powder containing a high percentage of free silica which was used as a "filler" in the milling of rubber (Table II). Two of the workers worked in a quarry where such powder was obtained; the others worked in rubber factories which used the powder.

Since the vast majority of the cases were Chinese men who had worked or were still working in the granite quarries, it was decided to study them as a fairly homogeneous group. Table III shows that their mean exposure duration as at the date of follow-up was 22.8 years, with a standard deviation of 9.9 years. Their average age was 59.1 years with a S D of 10.2 years.

In nearly 68% of this group, the profusion grading of opaci-

Table I
Distribution of Silicotic Workers Followed-Up 1984–86, by Ethnic Group and Sex

Ethnic Group	Male	Female	Total
Chinese	115	15	130
Malay	7	-	7
Indian	3	-	3
Total	125	15	140

Table II
Distribution of Chinese Male Silicotic Workers by Type of Exposure

Type of Silica Exposure	Still Exposed	Ceased Exposure	Total
Granite quarry	22	71	93
Rubber filler	2	15	17
Others	1	4	5
Total	25	90	115

ties on their chest X-rays was category 1, with only 6 out of 93 with category 3 (Table IV). The average age of the workers in the 3 categories was similar. Workers with more than 20 years of dust exposure did not have a higher category of profusion of opacities than those with shorter exposures (Table V).

Table III
Duration of Exposure of Chinese Male Silicotic Granite Quarry Workers

Duration of exposure* (years)	No.
1 -	5
6 -	6
11 -	7
16 -	23
21 +	52
Total	93
$\bar{x}$	22.8 yrs
SD	9.9 yrs

(*as at date of followup)

Table IV
Chest X-ray Category and Age of the Chinese Male Quarry Workers

Chest X-ray Profusion	n	Age (years)	
		$\bar{x}$	SD
Category 1	63	59.6	10.2
Category 2	24	58.0	11.0
Category 3	6	58.2	7.8
Total	93	59.1	10.2

A total of 11 out of the 93 cases showed large opacities on their followup chest X-ray films (Table VI). There was an increasing prevalence of chest X-rays with large opacities from the category 1 profusion group to category 3. However this was not statistically significant at the 0.05 level. As the symptoms of cough and dyspnoea were subjective, we analyzed for the more objective signs of cyanosis, clubbing of nails, and crepitations on clinical examination. There was no statistical difference in the prevalence of these signs among the 3 profusion categories of chest X-ray (Table VII).

Table VIII shows an apparent increasing prevalence of past occurrence of pulmonary tuberculosis with profusion category. But this was not statistically significant at the 0.05 level. There was no statistical significance in the prevalence of "abnormal" FEV_1[5] results among the 3 chest X-ray categories (Table IX). But the difference in the prevalence of "abnormal" FVC[5] results was significant between categories 1 and 3 ($p = 0.002$). All the 6 workers with category 3 chest X-rays had FVC values which were less than 80% of those predicted for their age and height.

Table V
Duration of Exposure in Quarries and Chest X-ray Category

Chest X-ray Profusion	Exposure in Quarries		
	< 20 years	> 20 years	Total
Category 1	26	37	63
Category 2	13	11	24
Category 3	2	4	6
Total	41	52	93

Table VI
Prevalence of Large Opacities on Chest X-ray

Chest X-ray Profusion	No.	With large opacities	
		n	%
Category 1	63	5	7.9
Category 2	24	4	16.7
Category 3	6	2	33.3
Total	93	11	11.8

Table VII
Clinical Signs and Chest X-ray Category

Chest X-ray Profusion	No.	Clinical signs		
		Cyanosis	Clubbing	Crepitations
Category 1	63	2	6	10
Category 2	24	1	5	2
Category 3	6	0	0	1
Total	93	3	11	13

Table VIII
History of Pulmonary Tuberculosis and Chest X-ray Category

Chest X-ray Profusion	No.	Pulmonary tuberculosis	
		No.	%
Category 1	63	12	19
Category 2	24	8	33.3
Category 3	6	3	50
Total	93	23	24.7

All the 6 persons in category 3 had stopped smoking compared with 9 out of 20 smokers in category 2, and 15 out of 52 smokers in category 1.

DISCUSSION

In Singapore, the greatest hazard of silicosis is in the granite quarries where the blasting and crushing of granite are very dusty operations. The second commonest type of exposure was to powder containing a high percentage of free silica which was used in the milling of rubber. Such exposure is much less common now.

Of the 93 Chinese granite quarry workers with silicosis followed up, 68% had a chest X-ray profusion grading of category 1, with only 6 in category 3. Eleven showed large opacities. This compares with the 9 out of the 144 silicotics who had large opacities in the followup study reported by Koskinen.[6] There was an increasing prevalence of chest X-rays with large opacities from the category 1 profusion group to category 3 but this was not statistically significant.

Theriault et al.[7] were able to obtain a dose-response curve of granite dust on roentgenograms by plotting the percentage of people with opacities on their chest X-rays against an increasing exposure expressed in dust-years. In our study, the duration of exposure to silica dust did not seem to affect the extent of opacities in the chest X-ray. Workers with more than 20 years exposure in the quarries did not have a higher category of profusion of opacities on chest X-ray than those with shorter exposure.

The pathogenesis of silicosis involves the interaction between

Table IX

FEV_1 and FVC Results, and Chest X-ray Category

Chest X-ray Profusion	No.	FEV_1		FVC	
		normal*	abnormal**	normal*	abnormal**
Category 1	63	22	41	30	33
Category 2	24	7	17	9	15
Category 3	6	1	5	0	6
Total	93	30	63	39	54

* normal is ≥ 80% of the predicted value.

** abnormal is < 80% of the predicted value.

silica dust and pulmonary macrophages. Inflammatory and fibrotic reactions involved in cell-mediated and humoral immune responses also participate in the pathogenesis.[8] The immunological basis for the development of silicosis, which would have contributed to our findings, could also explain the well-documented wide variation among individuals in the way workers respond to the same exposure to silica dust.[9]

As the symptoms of cough and dyspnoea were largely subjective, we analyzed for the more objective signs of cyanosis, clubbing and crepitations on clinical examination. There was no statistical significance in the prevalence of these signs among the 3 profusion categories of chest X-ray. This could be because the physical signs associated with generalized pulmonary fibrosis, including asbestosis, i.e. clubbing of nails and basal inspiratory crepitations, are less frequent findings in silicosis.[10]

Twenty three (or nearly 25%) of the 93 cases had pulmonary tuberculosis. This compares with 23 (16%) of 144 cases in the series reported by Koskinen.[6] However, tuberculosis is endemic in Singapore. It has been said that the risk of contracting tuberculosis increases with the severity of silicosis, and that previous tuberculosis, whether treated or not, probably increases the risk and severity of silicosis.[11] But although our cases showed an apparent increasing prevalence of past occurrence of pulmonary tuberculosis with profusion category on chest X-ray, this was not statistically significant at the 0.05 level.

Ventilatory function may be affected in silicosis. This is mainly restrictive in nature, and is indicated by a FVC reading which is less than 80% of the predicted value for the age and height.[6] Fifty-four or about 58% of our cases had FVC readings which were less than 80% of the predicted values (Table 10). In the series reported by Koskinen, 46% of 144 followup cases were in this category.[6] The decrease in lung function may be greater with the coalescence of shadows on the chest X-ray.[11] In our series, those with category 3 profusion on chest X-ray all had abnormal FVC readings, compared with about 52; of those in category 1. This was statistically significant ($p = 0.002$). Smoking could be a potential confounder although it is less likely to affect the FVC results. Category 3 chest X-rays also showed more large opacities than category 1.

It was interesting to note that all the 6 persons in category 3 had stopped smoking on followup, compared with only 15 of the 52 smokers in category 1, although their mean ages were similar. This might have been partly due to the increasing respiratory difficulty experienced by those in category 3.

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REVISED ESTIMATES OF PULMONARY FUNCTION LOSS IN VERMONT GRANITE WORKERS: RESULTS OF A LONGITUDINAL STUDY

W. GRAHAM • T. Ashikaga • S. Weaver
University of VT Burlington, VT, USA

ABSTRACT

Previous studies have suggested that excessive losses of FVC and $FEV_{1.0}$ were occurring in Vermont granite workers despite the fact that quartz levels existing in the industry were below the current OSHA standards. We re-examined these losses in granite workers over an eight year period, testing the workforce from 1979 to 1987 on alternate years. All workers including stone shed, quarry and office were offered forced spirometry using a 10 L. Collins water-sealed spirometer. In the peak year of participation (1983), 887 workers out of a total of approximately 1400 were tested. Estimates of longitudinal loss were based on 711 workers who participated in at least 3 of the semi-annual surveys. The mean age of this group was 42.9 years, and the mean years employed was 19.3 yrs. 21.4% were non-smokers (NS), 34.2% ex-smokers (ES) and 44.4% current smokers (CS). Average annual losses of FVC were .025 ± .055 L. (CS: .032 L.; NS: .014 L.; ES: .024 L.). Average annual losses of $FEV_{1.0}$ were .036 ± .040 L. (CS: .044 L.; NS: .027 L.; ES: .033 L.). Analysis of covariance indicated that losses were related to the initial values for FVC or $FEV_{1.0}$, height, age, and smoking history. The losses of both FVC and $FEV_{1.0}$ were not correlated with years employed in the granite industry. The losses of pulmonary function were significantly smaller than those estimated previously, e.g., .070–.080 L. in FVC, and .050–.070 L. in $FEV_{1.0}$. We conclude that current dust levels in the Vermont granite industry do not accelerate pulmonary function loss.

See Table of Contents, Part II, for Paper.

LUNG FUNCTION WITH ASBESTOS-RELATED CIRCUMSCRIBED PLAQUES

EDWARD A. GAENSLER, M.D. • Peter J. Jederlinic, M.D. • Theresa C. McLoud, M.D.

Departments of Medicine and Surgery, Boston University School of Medicine and
Department of Radiology, Harvard Medical School, Boston, MA, USA

Early studies of asbestosis made no mention of plaques, and pleural calcifications were not identified with asbestos exposure until 1955.[10,12,22] In 1965 Selikoff[36] found a long latent period of 20 years and a high prevalence of 44%. Thereafter, pathologic studies showed no difference between plaques with and without calcification, and often plaques were found without microscopic asbestosis.[20,23] Radiographs showed plaques in only a small proportion of cases who had such lesion at autopsy.[20,37] Epidemiologically, it emerged that plaques can be caused by relatively slight household and neighborhood exposure.[8] Clinically, plaques early on were described as "harmlos-skurriler Schönheitsfehler," that is, a harmless beauty mark,[5] since they were neither precancerous lesions nor caused symptoms or loss of function.[5,7,23]

A number of studies since 1968[24] have dealt with the functional consequences of asbestos-related pleural disease but most often no clear distinction was made between circumscribed plaques and diffuse pleural thickening. Because fibrothorax of whatever cause may have serious physiologic consequences,[13,16,27,29,38] in this study we made a strict distinction between plaques and diffuse thickening. Also, we addressed the confounding effect of smoking; and for controls we used both normal subjects studied by the same protocol and employees matched for age and years of employment but without plaques.

METHODS

Clinical Material

We studied 1,764 persons during annual industrial surveys between 1966 and 1988 at two large shipyards, three papermills and one asbestos plant. Details of employment and type of exposure have been described elsewhere.[9,15,27]

Control subjects included two groups: *100 Normal unexposed males (group I)* 40 years or older without discernable lung disease and without prior asbestos exposure, who presented for pre-employment examination (Table I). The second group consisted of *154 persons exposed for 15 or more years* (group II) who had normal roentgenograms and who were selected from our survey group by matching for age and years since first exposure with group III which had plaques only and no diffuse thickening or asbestosis.

Survey Studies

On-site examination included a medical and detailed occupational history, a physician-administered respiratory questionnaire and chest physical examination.

Lung function studies included forced vital capacity (FVC), the forced expiratory volume in one second (FEV_1) and other flow derivatives, and the single breath diffusing capacity (D_L) with alveolar volume (VA) calculated from single-breath helium dilution. Instrumentation, unchanged over the years, has been described in detail.[17] FVC and FEV_1 were selected from the best of 3 efforts[2] and DL values were accepted if VA (BTPS) was at least 90% of FVC (BTPS). Predicted values were calculated from Morris et al.,[31] and for D_L from our own data.[18]

Chest roentgenograms, PA, lateral, and on at least one occasion oblique views, were obtained within one week of examination. Reading was according to the 1980 ILO scheme[21] by two "B" readers, one of whom was unaware of the nature and type of exposure. Films were read prospectively without recourse to other films ("apart reading"), and were reviewed later by display of the entire series of each case in order of date ("side-by-side" reading).

Definitions for this Study

Excluded were persons with significant non-asbestos intrathoracic disease, most often chest surgery, trauma, extensive pleural and parenchymal scarring from tuberculosis or residuals from infarction or pneumonia. Persons with heart disease we excluded only with marked cardiomegaly and/or evidence of chronic passive congestion.

Chronic obstructive lung disease (COLD) was diagnosed for this study only when the ratio of FEV_1 /FVC was more than 2 SD below the normal predicted.[1] We ignored lesser degrees of COLD and evidence of "small airways disease" which was observed in virtually all smokers and ex-smokers.

Circumscribed plagues were distinguished from *diffuse thickening* by detailed study of routine and oblique films aided by review of history, outside records, and CT scans in some cases.[27] Descriptions of Fletcher and Edge[11] were useful, but the ILO Film was of no help because we believe that the single example of "diffuse thickening" also represents a circumscribed plaque.[21] *Large plaques* were bilateral with width "b" and extent "2" or larger. *Large diffuse thickening* could be unilateral but had to be of width and extent 2b or larger. Asbestosis was graded according ILO major categories 0,1,2 and 3.[21] *Years since first exposure* included prior asbestos exposure. *Nonsmokers* had

Table I
Clinical Material for Plaque Study

Group	Definition	No COLD	Also COLD	Also Diffuse
I	Normal Unexposed, age over 40	100	0	0
II	Exposed > 15 Yrs, Normal X-ray (Matched For Age & Exposure With Group III)	129	25	0
III	Circumscribed Plaques Only	197	21	12
IV-VI	Plaques and Asbestosis 1,2 or 3	151	25	50

smoked less than 2 pack-years and had stopped at least 20 years earlier.

RESULTS

Among 1,764 persons in the survey we found 218 (12.3%) with circumscribed pleural plaques as the only abnormality (Group III), and there were 176 (10.0%) who had plaques and asbestosis (Groups IV–VI) (Table I). Additionally, 158 exposed persons with normal roentgenograms were matched for age and years since first exposure with the group with plaques (Tables I, II). COLD was found in 16.2% of those with normal X-rays, 9.6% with plaques only, and 14.2% among those with plaques and asbestosis. For some comparisons with normal unexposed persons the COLD group was excluded (Tables I–III, Figure 2). Mean age was similar for all exposed groups, but the 100 unexposed controls were 3 years younger. First exposure was 27 years ago for groups II–VI, and in this study this figure was virtually the same as total years exposed.

Lung function tests for the 100 controls were about 4% lower than predicted (Table II) because the Morris equations are for nonsmokers.[31] For the 40 nonsmokers in this group all function tests averaged almost exactly 100% (Table III). Mean values for the exposed controls (Group II) were slightly lower ($p < .05$).

With circumscribed plaques as the only abnormality (Group III) all three screening tests actually were slightly higher than the normal subjects ($p < .05$) or exposed persons without plaques ($p < .01$) (Table II). With progressing asbestosis there was the predictable precipitous decline, with D_L most severely affected. Inclusion of persons with COLD reduced mean function by only 2%–3% (Table II) because there were few such persons (Table I) and usually their obstructive disease was slight. COLD was no more common among persons with plaques than those without them (Table I). However, among all smokers and ex-smokers, including "normal" controls, both FEV_1 and D_L were significantly worse ($p < .01$) than among nonsmokers (Table III).

The fact that circumscribed plaques have no measurable effect on function was further documented by separation according to width and extent. Table IV and Figure 2 indicate no functional difference between large and small plaques.

Calcified plaques were seen in 80 persons (17.5%). This group was older and had longer employment by about 4 years. Nevertheless, the screening tests were virtually identical compared to the group with uncalcified plaques.

Diffuse pleural thickening initially was recorded from apart readings in 158 cases (Table V). Subsequent detailed study led to exclusion of 96 cases. Among these, subpleural fat pads were recognized more often following publication of the beautiful illustrations by Sargent et al.[35] Among the included 62 cases (3.5%) diffuse thickening was most often the residue of a benign effusion (Table V).

Diffuse thickening, unlike plaques, caused a significant loss of lung function and, unlike plaques, this loss was strongly related to extent and thickness, with bilateral cases most markedly impaired (Figure 2). Lung volume (FVC) was most severely affected, and D_L/VA often was larger than predicted as has been noted by others.[26,29,38]

DISCUSSION

The prevalence of asbestosis is declining rapidly, and most of the 254 cases (14.4%) in this series were the result of first exposure more than 38 years ago.[15] Circumscribed pleural plaques were more frequent (23.6%), and many were recognized among persons first exposed less than 38 years ago. This was, in part, because plaques can arise from lesser exposure and, in part, because of improved recognition of early lesions. Therefore, clinical and functional implications of plaques have become of increasing interest.

Published material does not provide a good overview of the physiologic effects of circumscribed plaques because, initially, attention was focused on calcifications,[24] and later the effect of plaques was obscured by inclusion of diffuse pleural thickening under the general term of "pleural changes."[3,6] This is not surprising because neither the 1958 nor the 1971 ILO schemes provided for separate quantification of these pleural reactions.[27].

Initial physiologic and pathologic studies of benign asbestos effusion showed that these often bilateral and often recurring bloody effusions frequently result in marked functional impairment and fibrothorax, sometimes so severe as to require decortication.[16,29] An epidemiologic study of effusions showed persisting radiographic changes: Among 34 persons there remained a blunted costophrenic angle in 91.4% and measurable diffuse thickening in 54.3%.[9] The serious con-

sequences of imprisoned lung, so well described in the days of tuberculosis and empyema,[13] have now been rediscovered in the asbestos-exposed under such fancy terms as "lung en currasse," "lung entrapment,"[29] "pleural hyalinosis complicata,"[32] or "squashed lung."[38] However, unlike pleural thickening after empyema or trauma, in asbestos cases the cortex may increase over the years,[28,38] probably from recurring subclinical effusions. Rounded atelectasis from effusion is also described in the asbestos exposed[4,30] and also may be associated with functional impairment. In all of these cases there was marked dyspnea, severe reduction of all lung volumes and D_L, and sometimes ventilatory failure. However, in contrast to pulmonary fibrosis, D_L/VA (sometimes called KCO) was normal, indi-

Table II

Pleural Plaques: Age, Years Since First Employment and Lung Function

Group	No.	Age	Years Since First Empl.	FVC % Predicted	FEV_1 % Predicted	D_L % Predicted
Excluding Obstruction, and Excluding Diffuse Thickening						
I	100	51.8 ± 10.7	0	94.5 ± 12.6	96.9 ± 13.3	95.3 ± 17.4
II	129	55.3 ± 8.1	27.9 ± 7.5	91.0 ± 13.6	97.3 ± 13.3	93.8 ± 17.9
III	197	53.8 ± 7.6	27.4 ± 5.9	96.1 ± 11.4	101.8 ± 13.6	101.6 ± 13.9
IV	112	56.1 ± 7.6	27.4 ± 6.1	82.3 ± 11.3	87.5 ± 12.5	80.2 ± 16.5
V	31	59.5 ± 8.1	29.0 ± 7.0	73.6 ± 16.7	77.6 ± 17.7	58.1 ± 13.6
VI	8	56.8 ± 6.6	23.4 ± 7.9	53.9 ± 16.8	58.7 ± 20.1	45.8 ± 11.1
Including Obstruction, Excluding Diffuse Thickening						
I	100	51.8 ± 10.7	0	94.5 ± 12.6	96.9 ± 13.3	95.3 ± 17.4
II	154	55.5 ± 7.7	28.3 ± 7.4	90.5 ± 14.3	93.6 ± 17.2	91.0 ± 19.1
III	218	54.0 ± 7.5	27.4 ± 6.3	94.5 ± 12.7	98.7 ± 16.8	100.4 ± 14.7
IV	128	56.3 ± 7.3	27.4 ± 6.8	81.6 ± 12.5	84.9 ± 15.4	78.4 ± 17.0
V	40	59.5 ± 7.3	28.9 ± 7.1	74.4 ± 17.1	75.2 ± 19.1	58.4 ± 14.0
VI	8	56.8 ± 6.6	23.4 ± 7.9	53.9 ± 16.8	58.7 ± 16.8	45.8 ± 11.1

Table III

Pleural Plaques: Effect of Smoking

Excluding Diffuse Thickening, Including Obstruction

Group		No.	Smokers	No.	Nonsmokers
I	FVC %	60	92.4	40	97.8
II		110	90.5	44	90.5
III		163	93.8	55	96.8
IV		107	82.4	20	77.6
V		36	75.6	4	63.8
VI		7	55.3	1	44.0
I	FEV_1 %	60	93.4	39	102.4
II		110	91.1	44	99.7
III		163	97.4	55	102.6
IV		107	84.9	20	84.6
V		36	75.4	4	73.0
VI		7	60.1	1	49.0
I	D_L %	60	91.6	39	101.0
II		110	86.5	44	102.2
III		163	98.8	55	105.0
IV		107	77.3	20	86.3
V		36	57.8	4	64.1
VI		7	47.7	1	32.4

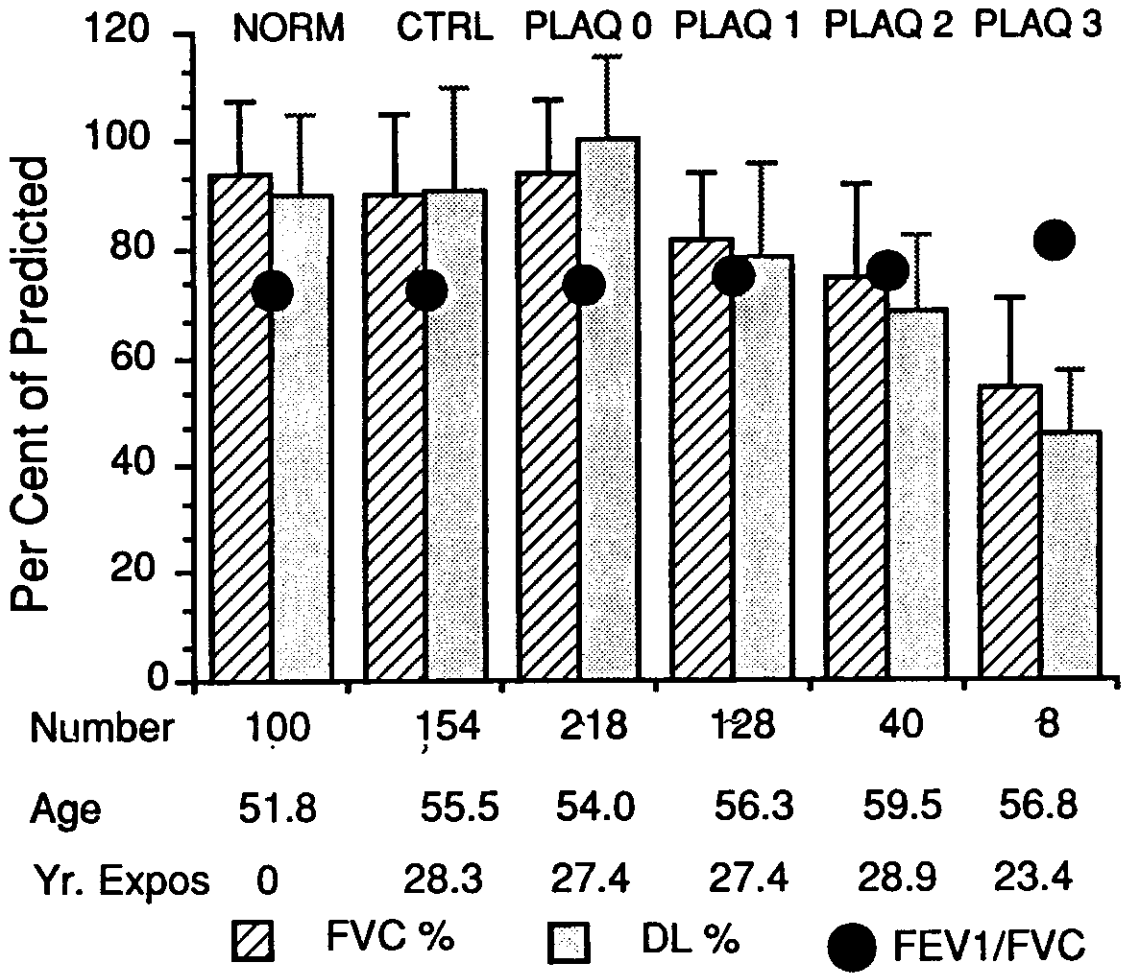

Figure 1. Lung function with plaques and asbestosis. Forced vital capacity (FVC) and diffusing capacity (D_L) as percent of predicted, and the FEV_1/FVC ratio of 100 normal unexposed males over age 40 (NORM), exposed males with normal roentgenograms matched for age and years since first exposure (CTRL), 218 males with circumscribed hyaline pleural plaques only (PLAQ 0), and 176 persons with plaques and varying degrees of asbestosis (PLAQ 1,2,3). This representation includes persons with chronic obstructive lung disease while persons with diffuse pleural thickening have been excluded.

cating that reduced D_L was the result of reduced lung volume and not of impaired respiratory gas exchange. From the foregoing it is evident that inclusion of but a single case of this nature in a group largely with circumscribed plaques would have a significant effect on average values of lung function.

A larger series of diffuse thickening was reported by McGavin and Sheers.[26] They, like Britton[6] before them, devised a grading scheme to measure radiographic extent of diffuse thickening and found impairment of FVC and D_L closely related to severity score. Calcifications alone had no significant effect on function.[24,25]

SUMMARY AND CONCLUSIONS

In 218 persons with circumscribed pleural plaques, but without diffuse thickening or apparent asbestosis, we found lung function with respect to volume, flow and gas exchange no different than that of 154 persons matched for age and years since first exposure who had no visible plaques, and no different than that of 100 unexposed normal subjects. Inclusion of persons with chronic obstructive lung disease in the exposed groups did not alter results significantly. There was no difference among persons with and without calcification of plaques, and no difference between large and small plaques. With plaques and increasingly severe asbestosis there was the predictable progressive functional impairment.

Diffuse pleural thickening, unlike plaques, caused significant functional loss, especially with regard to lung volumes. This is because pleural plaques involve only the parietal pleura, do not cause adhesive pleuritis, and are patchy and interrupted structures that do not interfere with thoracic motion. Diffuse thickening, on the contrary, involves both visceral and parietal pleurae forming an uninterrupted fibrous peal with granulation tissue that extends to involve cortical interlobar septa, and seriously interferes with motion of both

Table IV

Circumscribed Plaques: Effect of Size and Extent (Cases with Diffuse Thickening or Obstruction Excluded)

Group	No.	Age	Years Since First Empl.	FVC % Predicted	FEV_1 % Predicted	D_L % Predicted
Small Plaques (< 2b)						
III	100	53 6 ± 6.9	27.5 ± 5.5	96.0 ± 11.6	102.5 ± 13.1	101.0 ± 14.4
IV	27	55.9 ± 7.5	28.5 ± 7.2	81.3 ± 9.0	89.4 ± 8.8	75.1 ± 17.8
V	7	62.4 ± 6.8	31.4 ± 6.9	74.7 ± 23.2	74.3 ± 16.7	58.8 ± 9.5
VI	4	59.3 ± 5.1	26.5 ± 8.5	58.8 ± 18.7	65.8 ± 22.6	47.5 ± 10.7
Large Plaques (≥ 2b)						
III	97	54.0 ± 8.3	27.4 ± 6.4	96.3 ± 11.1	101.2 ± 14.1	102.2 ± 13.4
IV	35	56.4 ± 5.9	27.9 ± 5.3	80.3 ± 10.6	86.5 ± 12.0	84.7 ± 17.2
V	11	58.4 ± 9.5	29.5 ± 7.0	71.4 ± 19.3	76.0 ± 19.3	49.2 ± 12.1
VI	4	54.3 ± 7.7	20.2 ± 6.9	49.0 ± 15.7	51.8 ± 17.2	44.0 ± 13.0

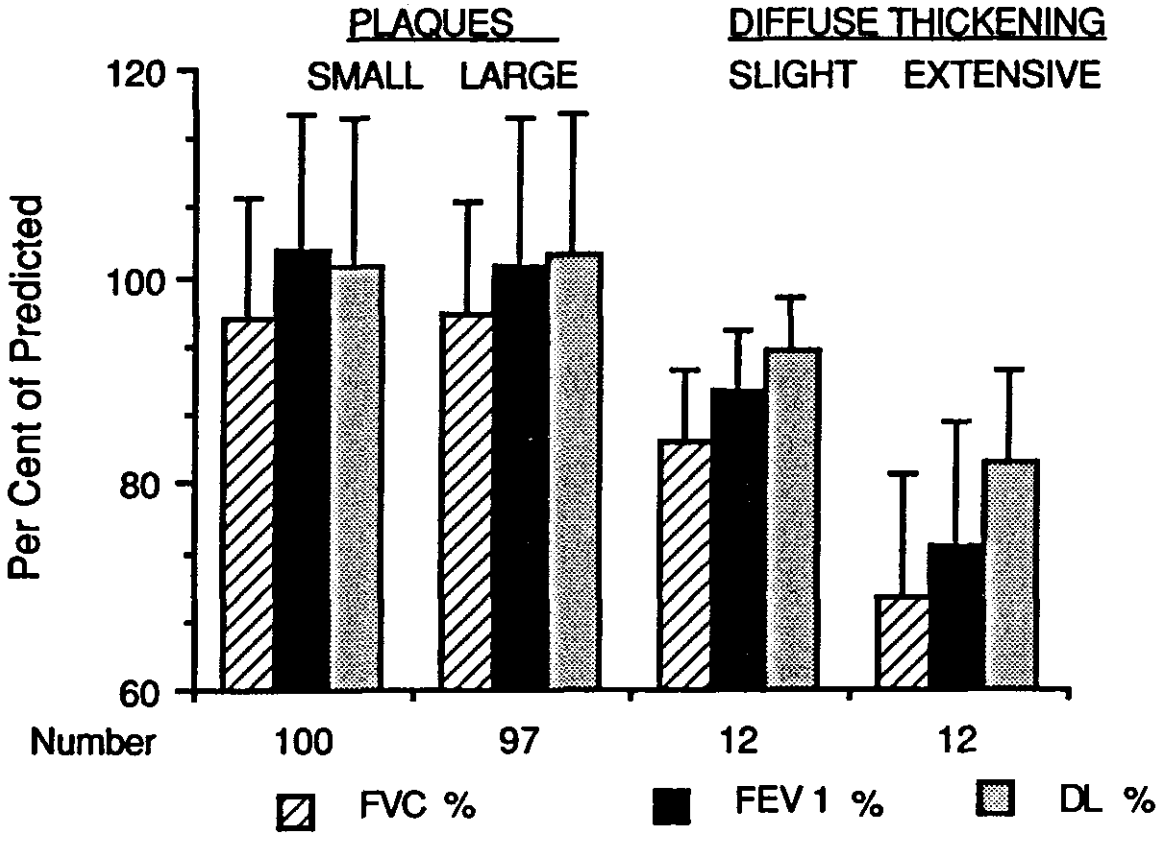

Figure 2. Lung function: plaques and diffuse thickening. The effect on lung function of asbestos-related pleural disease. Forced vital capacity (FVC), forced expiratory volume in one second (FEV_1) and diffusing capacity (D_L) were all in the normal range for persons with circumscribed plaques, and there was no difference between small plaques (<2b) and large plaques (>2b). Persons with diffuse pleural thickening had a significant functional deficit, and this was greater with extensive diffuse pleural disease.

Table V
Causes of Diffuse Thickening

Initial Coding from Apart Readings	158
Excluded After Further Study	96
Actually Confluent Plaques	40
Malignancy	5
Infection, Trauma, Surgery	22
Subpleural Fat Pads	18
Included as Diffuse Thickening	62
After Benign Effusion	41
Related to Asbestosis	15
Unexplained	6

lungs and thorax. The cause of diffuse thickening in most cases could be traced to one or more episodes of benign asbestos effusion. Our studies confirm the old dictum of Bohlig et al[5] that plaques are an epidemiologic leading fossil for asbestos exposure, but otherwise are merely a beauty mark and without functional consequences. We also agree with McGavin and Sheers[26] that diffuse thickening at times may lead to significant pulmonary insufficiency and then represents an industrial injury even when there is no asbestosis.

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PREDICTIVE SIGNIFICANCE OF LESSER DEGREES OF PARENCHYMAL AND PLEURAL FIBROSIS. PROSPECTIVE STUDY OF 1,117 ASBESTOS INSULATION WORKERS, JANUARY 1, 1963–JANUARY 1, 1988. MORTALITY EXPERIENCE

IRVING J. SELIKOFF, M.D. • Herbert Seidman, MBA • Ruth Lilis, M.D. • Yehuda Lerman, M.D.

Division of Environmental and Occupational Medicine, Mt. Sinai School of Medicine of the City University of New York and the Department of Epidemiological Research of the American Cancer Society, New York, NY, USA

ABSTRACT

In 1963, 1,117 asbestos insulation workers were examined. X-ray findings were categorized according to the Saupe classification and reported. Subsequently, the films were recategorized when the International Labour Office Classification was introduced, using the 1980 Classification. The entire cohort has been maintained under observation. We have investigated all deaths that have occurred in the 25 years and will present the mortality experience of this group in relation to the radiological findings in 1963, with particular reference to 0/0, 1/0, 0/1, 1/1 interstitial, as well as the presence or absence of pleural fibrosis.

No Paper provided.

SPIROMETRIC ABNORMALITIES IN 2573 ASBESTOS INSULATORS WITH LONG TERM EXPOSURE: EFFECTS OF SMOKING HISTORY AND RADIOGRAPHIC ABNORMALITIES

ALBERT MILLER, M.D. • Ruth Lilis, M.D. • James Godbold, Ph.D. • Eva Chan, Ph.D. • Irving J. Selikoff, M.D.

Divisions of Environmental and Occupational Medicine
(Community Medicine) and Pulmonary Disease (Medicine)
Mount Sinai School of Medicine, City University of New York
New York, NY USA

INTRODUCTION

The 2573 insulators who are the subjects of this report comprise one of the largest reported populations occupationally exposed to asbestos. They were selected on the basis of a long duration from onset of exposure (DURON; 87% were ≥ 30 years) in order to provide sufficient time for evolution of disease, whether it be pleuropulmonary fibrosis caused by asbestos or chronic airways obstruction attributable to smoking and perhaps to occupational dusts. This population is therefore well suited to provide information concerning:

1. The prevalence of the various pulmonary function impairments in a large well defined group occupationally exposed to asbestos.
2. The effect of such influences as radiographic abnormalities, DURON and smoking on pulmonary function. In this regard, the large number of lifetime nonsmokers (n = 506) allows characterization of the effects on pulmonary function of asbestos inhalation alone, unconfounded by cigarette smoking.

METHODS

Details concerning subject selection, medical evaluation and radiographic reading are given in a companion paper.[1] Subjects were studied in 19 cities in North America over a two year interval. Spirometric tests adhered to current guidelines;[2] at least 3 acceptable efforts were obtained on each subject, who was standing and wore a noseclip. A computerized rolling seal spirometer was used; efforts were monitored by maximum expiratory flow-volume curves recorded in real time and all data, including the flow volume arrays, were stored on digital tape.

Predicted values were those published by this laboratory using the same equipment in a random sample of the population of a large industrial state, adjusted for the effects of smoking in current smokers (which were significant on all tests except FVC).[3]

"Nonsmokers" (NS) smoked less than one cigarette a day, had smoked ≤ ten cigarettes a day for ≤ six months or smoked only cigars and pipes, which are not inhaled. Current smoker (SM) exceeded these limits. "Ex-smokers" (XS) exceeded these limits and had discontinued smoking ≥ two years previously.

Impairments were defined as follows:

Normal (Nl): Nl. FVC, FEV_1/FVC and MMF;

Restrictive (Rest): FVC <95% lower confidence interval (CI)

Restrictive (Rest): FVC <95% lower confidence interval (CI), ↓FEV_1/FVC nl (≥0.65 age ≥60, ≥0.70 age 30–59);

Overt Obstructive (Obs): FVC nl, FEV_1/FVC below limits defined above;

Small Airways Dysfunction (SAD): FVC nl, FEV_1 /FVC normal, $FET_{25-75\%}$ (also called mid-expiratory time) ≥0.78 sec;[5]

Combined, primarily restrictive (Comb Rest): Both FVC and FEV_1/FVC ↓ ; ↓ FVC ≥ ↓ FEV_1/FVC;

Combined, primarily obstructive (Comb Obs): ↓ FEV_1/FVC > ↓ FVC.

RESULTS

Mean Values

Table I shows mean demographic, exposure and pulmonary function variables for NS and those with a smoking history. There is no difference in age, DURON or years exposed. FVC and FEV_1 are reduced in the NS, but not FEV_1/FVC or the flows $FEF_{25-75\%}$ or $FEF_{75\%}$. FVC and FEV_1 are reduced to a greater extent in the smokers but FEV_1 /FVC and flows are only minimally reduced using smoking specific predicted values.

Prevalences of Functional Impairment

By Smoking History (Table II):

Of the 2573 workers studied, 506 (19.7%) were NS, 861 (33.5%) SM and 1206 (46.9%), XS. This last group, which includes only those who have discontinued smoking for at least 2 years, reflects the effect of educational efforts to discontinue smoking among asbestos workers.

Table I

Demographic, Exposure and Pulmonary Function Variables by Smoking History (Mean and SD)

	Nonsmokers (n = 506)	Current and Ex-Smokers (n = 2067)
Age (yrs)	58.6 (8.6)	57.3 (8.0)
Height (cm)	173.2 (6.9)	174.0 (6.6)
Duron (yrs)	36.3 (7.6)	34.9 (7.0)
Yrs exposed	32.0 (8.3)	31.6 (7.5)
Dur smoking (yrs)	0	31.6 (12.0)
Pack years	0	40.6 (26.1)
FVC (% pred)	86.5 (16.6)	82.0 (17.3)
FEV_1 (% pred)	85.5 (17.4)	82.3 (20.6)
$FEF_{25-75\%}$ (% pred)	96.6 (36.2)	86.6 (40.1)
$FEF_{75\%}$ (% pred)	101.2 (45.5)	97.7 (49.3)
FEV_1/FVC x 100	79.2 (7.6)	73.4 (10.5)
FEV_1/FVC (% pred)	100.6 (9.5)	97.1 (13.5)

Table II

Spirometric Impairments in 2573 Asbestos Insulators ≥20 Years from Onset of Exposure (by Smoking History)

	NS (19.7%)*	SM (33.5%)	XS (46.9%)	All Smoking Categories
Normal pf	222 (43.9)*	146 (17.0)	376 (31.2)	744 (28.9)
Restrictive	156 (30.8)	270 (31.4)	413 (34.2)	839 (32.6)
Obstructive	17 (3.4)	144 (16.7)	92 (7.6)	253 (9.8)
Small Airways	98 (19.4)	145 (16.8)	204 (16.9)	447 (17.4)
Combined	13 (2.6)	156 (18.1)	121 (10.0)	290 (11.3)
Combined, rest	11 (2.2)	110 (12.8)	92 (7.6)	213 (8.3)
Combined, obst.	2 (0.4)	46 (5.3)	29 (2.4)	77 (3.0)
All Impairments	506	861	1206	2573

* Percentages are shown in parentheses. Percentages after each smoking category are of the total population (e.g., 19.7% of the population were NS). Percentages within each smoking category are of each impairment within that smoking category (e.g., 43.9% of NS had nl pf).

The prevalence of several impairments varies by smoking history. Normal pulmonary function was most likely in NS (43.9%) and least in SM (17.0%); XS were intermediate (31.2%). Overt obstruction was most likely in SM (16.7%) and least in NS (3.4%). While restrictive impairment by itself did not vary in frequency by smoking category, combined impairment was far more common in SM (18.1%), again with XS intermediate. Frequency of small airways dysfunction was similar in all smoking categories.

By radiographic abnormality (Table III):

Normal pulmonary function was most likely (43.4%) when the chest radiograph was normal and least likely (21.2%) when both parenchymal and pleural disease was present. While frequencies of small airways dysfunction did not vary by radiographic abnormality, restrictive and combined impairments were most common when parenchyma and pleura were both abnormal and obstruction was more likely when only the parenchyma was abnormal. Interestingly, when frequency of restriction was compared in *isolated parenchymal* vs. *isolated pleural* disease, it was greater in the latter (34.4% vs. 22.3%).

Despite the greater frequency of normal function when the radiograph was normal (43.3%), 21.3% of those with a normal film had restriction and 7.7% had combined impairment, meaning that 29% had a reduced FVC. Similarly, while a normal film was more likely when pulmonary function was normal (25.1%), 10.4 percent of workers with restriction had a normal film.

Table III

Spirometric Impairments in 2573 Asbestos Insulators ≥20 Years from Onset of Exposure (by Radiographic Abnormality)

	"Normal" (16%)*	Parenchymal Only (11.7%)	Both (Parpleu) (48.2%)	Pleural Only (24.1%)	All Radiograph Categories
Normal pf	187 (43.3)*	105 (34.9)	263 (21.2)	189 (30.5)	744 (28.9)
Restrictive	88 (21.3)	67 (22.3)	471 (38.0)	213 (34.4)	839 (32.6)
Obstructive	36 (8.7)	37 (12.3)	121 (9.8)	59 (9.5)	253 (9.8)
Small Airway	77 (18.6)	64 (21.3	202 (16.3)	104 (16.8)	447 (17.4)
Combined	25 (7.7)	28 (9.3)	182 (14.7)	55 (8.9)	290 (11.3)
All Impairments	413	301	1239	620	2573

* Percentages are shown in parentheses. Percentages after each radiographic abnormality are of the total population (e.g., 16% of the population had normal films). Percentages within each radiographic abnormality are of each impairment within that radiographic abnormality (e.g., 43.3% of subjects with normal films had normal pulmonary function).

The percentage of NS was relatively greater in subjects with normal pulmonary function no matter in which radiographic category they fell whereas the percentage of SM was increased in those with obstructive or combined impairments within each radiographic category.

By Duration from Onset of Exposure (Table IV): Frequency of normal pulmonary function fell with increased duration of exposure while frequency of restriction and of combined impairment increased. Small airways dysfunction did not change and obstruction actually decreased.

Regression Analysis of Pulmonary Function

FVC (analyzed as percent predicted, to adjust for age and height) and the actual ratio FEV_1/FVC were analyzed for the contributions of such independent variables as radiographic category (any par, any pleu and parpleu interaction), DURON and pack years (Table V). Parenchymal involvement was not significant for FVC, although pleural and combined parenchymal-pleural involvements were. Pleural involvement (alone or combined) was not significant for FEV_1/FVC: The predominant influence on FEV_1/FVC was pack years, each pack year diminishing the FEV_1/FVC (x 100) by 0.11 so that 41 pack years (the mean of all subjects with a positive smoking history) would diminish the FEV_1/FVC (x 100) by 4.5. By contrast, DURON 35 years (the mean of all subjects in the study) would diminish FEV_1/FVC (x 100) by two-thirds of the smoking effect (2.9) and the presence of parenchymal disease on chest film would diminish the ratio negligibly (0.013).

Each year from onset diminished the FVC by 0.436 percent of predicted, so that DURON 35 years would diminish FVC by 15.3 percent of predicted, whereas each pack year diminished FVC by 0.096 percent of predicted. Cumulative decrement for 41 pack years was 3.9 per cent of predicted or 25% of the effect of DURON. The presence of pleural involvement on radiography diminished the value by 4.7 percent of predicted and the presence of parenchymal plus pleural involvement diminished the value by 7.8 percent of predicted.

DISCUSSION

The 2573 asbestos insulators are a large enough group to allow analysis of the effects on lung function of such independent variables as years from onset of exposure, cigarette smoking (pack years) and radiographic abnormalities. We used percent predicted FVC, the most easily and universally measured single test of pulmonary function, as our index of restrictive impairment. The largest effect was that of DURON, followed by combined pleuropulmonary involvement, smoking and isolated pleural involvement. As expected, smoking was the predominant influence on FEV_1/FVC, used as an index of airways obstruction. The effect of DURON is probably attributable to aging (which obviously parallels duration) since the FEV_1/FVC ratio is not adjusted for age as is percent predicted FVC.

In computing the prevalence of impaired pulmonary function, common practice has been to use as the numerator the number of subjects with abnormal values for *any* of the major pulmonary function parameters, e.g., FVC or FEV_1. This tends to obscure differences in the types of impairments and the relationship of these impairments to various exposures, e.g., asbestos vs. cigarette smoking. A reduced FVC is not necessarily indicative of restriction (airways obstruction with air trapping and an elevated RV may reduce

Table IV

Spirometric Impairments in 2573 Asbestos Insulators ≥20 Years from Onset of Exposure (by Duration from Onset of Exposure)

	≤ 29 Yrs. n = 331 (12.9%)	30-39 Yrs. n = 1593 (61.9%)	≥ 40 Yrs. n = 649 (25.2%)
Normal	127 (38.4)	470 (29.5)	147 (22.7)
Restrictive	84 (25.4)	487 (30.6)	268 (40.3)
Obstructive	39 (11.8)	171 (10.7)	43 (6.6)
Small Airways	56 (16.9)	287 (18.0)	104 (16.0)
Combined	25 (7.6)	178 (11.2)	87 (13.4)

Table VA

Regression Analysis of Percent Predicted FVC
Percent Predicted FVC (n = 2667)

Intercept	106.19
Duron	-0.436 (p0.0001, F 92.4)
Pack Yrs.	-0.096 (p0.0001, F 74.2)
Any pleu	-4.676 (p0.0001, F 28.1)
Parpleu interact	-3.091 (p0.0001, F 14.8)
Any par	NS
R^2	11.7

Table VB

Regression Analysis of FEV_1/FVC
$FEV_1/FVC \times 100$ (n = 2573)

Intercept	81.949
Pack Yr.	-0.111 (p0.0001, F 265.8)
Any par	-0.013 (p0.0018, F 9.73)
Duron	-0.084 (p0.002, F 9.56)
Any pleu	NS
Parpleu interact	NS
R^2	11.1

the FVC as well) nor are reduced FEV_1 and flow rates specific for obstruction (restrictive disease will generally result in a reduction in FEV_1 and flow rates proportional to the reduction in FVC).

Instead, a mutually exclusive classification of impairments based on a *combination* of spirometric measurements, including the FEV_1/FVC ratio, was employed. We have published the prevalence of these impairments in 351 patients with chronic pulmonary sarcoidosis.[4] Preliminary results from our sampling of the population of the state of Michigan[5] show far lesser frequencies of restriction (7% NS, 9% XS, 12% CS) and combined impairment (0% NS, 5% XS, 5% CS) but similar or greater frequencies of obstruction (13% NS, 17% XS, 21% CS).

Not surprisingly, normal pulmonary function was most likely in NS (44%) and least likely in SM (17%) while obstruction was most likely in SM (17%) and least in NS (3%). FREQUENCY OF RESTRICTIVE IMPAIRMENT DID NOT VARY BY SMOKING HISTORY, consistent with the predominant effects on FVC of asbestos exposure (measured as years from onset) and radiographic evidence of pleuropulmonary or pleural fibrosis. However, combined impairment was far more frequent in SM (18%) than NS (2.6%), with XS intermediate. This pattern results from the addition of obstruction (attributable to smoking) to the restriction of pleuropulmonary fibrosis. Such combined impairment is frequently seen in advanced sarcoidosis, bronchiectasis, cystic fibrosis or silicosis (progressive massive fibrosis).[6,7]

It is of interest that the most common impairment in both SM and XS (as well as NS) was restriction. It is recognized that what we call combined impairment can also result from reduction in FVC secondary to air trapping in severe obstruction. True combined impairment and air trapping can be distinguished only by full lung volumes. These obviously cannot be measured using physiologic methods on such large numbers of subjects under survey conditions. (We hope to measure full lung volumes using a planimetric method[8] on the posteroanterior and lateral chest films of these workers). We attempted to separate combined impairments into "predominant restrictive," and "predominant obstructive" by the relative decreases in FVC vs. FEV_1/FVC.

RESTRICTION WAS IDENTIFIED AS THE PREDOMINANT ELEMENT IN THE COMBINED IMPAIRMENT IN ALL SMOKING CATEGORIES (Table II)

The large number of NS in our study permits us to characterize the pulmonary function patterns attributable to inhalation of asbestos fibers alone. The 3 percent prevalences each of overt obstruction and of combined impairment do not provide strong evidence for obstructive impairment resulting from such inhalation (Table II). Half of the patients with these impairments (14 of 30) did not show radiographic evidence of pulmonary fibrosis. These 30 (of 506) NS may well have an independent cause of obstruction (e.g., asthma).

The decrease in frequency of obstruction with increasing

duration of exposure is the reciprocal of the increase in combined impairment, resulting from the superimposition of restriction in subjects with obstruction.

The greater contribution of radiographically identified pleural fibrosis (by itself) than of interstitial fibrosis (by itself) to restrictive impairment is seen in the regression analysis (Table V) and in the higher frequency of restrictive and combined impairments in those with isolated pleural vs. isolated parenchymal involvement (Table III). These findings concerning pulmonary function are similar to those concerning dyspnea in this population[1,9] and demonstrate the important effect of pleural fibrosis on lung function. These conclusions concerning pleural vs. parenchymal fibrosis may not be generalizable to other exposed populations for the following reasons:

1. This population was selected for long duration from onset and for heavy occupational exposure.
2. It is to a certain extent a survivor population in which those with the most severe interstitial fibrosis may have died (either of respiratory insufficiency or of bronchogenic carcinoma).
3. The largest proportion of subjects (48.2% of all subjects and 52.4% of those with abnormal films) had pleuropulmonary disease.

However, pleural disease is more prominent than interstitial fibrosis in many occupations with less intense exposure, and in family exposures. The important effect of pleural disease on lung function may be relevant to these groups.

Pulmonary function tests are used not only to *quantify* and *characterize* impairment in asbestos-related disease but to *detect* evidence of disease which is not apparent clinically or radiologically. In this regard, it is noteworthy that 21.3% of those with a normal film had restriction and an additional 7.7% had combined impairment and that of those with only pleural disease, 34.4% had restriction and an additional 8.9% had combined impairment. Further testing, especially of gas exchange (D_L, V_D/V_T) would undoubtedly uncover additional individuals with intrinsic lung disease despite normal lung fields on chest radiograph.

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MORTALITY AND CANCER INCIDENCE AMONG SWEDISH CERAMIC WORKERS WITH SILICOSIS

GÖRAN TORNLING*† • C. Hogstedt*‡ • A. Gustavsson‡ • P. Westerholm§

*Departments of Occupational Medicine and †Thoracic Medicine
Karolinska Hospital, S-104 01 Stockholm
‡National Institute of Occupational Health, Solna
§The Swedish Trade Union Confederation, Stockholm. Sweden

The question whether quartz exposure increases the risk for lung cancer was raised 50 years ago by Anderson & Dible.[1] More recently two literature reviews considering both animal experiments and epidemiological investigations have been published, one talking for[3] and the other against[4] such an association. In most published epidemiological investigations the subjects have, beside quartz, been exposed to known lung carcinogens such as polycyclic aromatic hydrocarbons in the foundry industry and ionizing radiation in mining, which make the interpretation difficult.[5] This investigation, which has become a part of a multicenter initiative by IARC, was undertaken in order to study the risk for lung cancer in the Swedish ceramic industry, where no confounding lung carcinogens are known to occur.

MATERIAL AND METHODS

The Swedish Pneumoconiosis Registry has compiled case notifications from 1931 and onwards. The study population consists of those 314 males from the ceramic industry who had been accepted as compensated cases of silicosis. Since there were only 36 females they were excluded from analysis.

The vital status of the study persons was established by linking the ten-digit identification number based on time of birth for each person with the census register for all living persons in Sweden, the death register of all deceased persons in Sweden, and the emigration register. By these procedures all but one of the persons could be identified as alive or deceased during the study period.

During the study period (1951–1985) for the mortality analysis the study population has accumulated 5695 person-years. Cause of death from the death certificates was recorded on all deceased persons in the study population.

The Swedish Cancer Registry was established in 1958 and receives notifications on more than 95% of all malignancies. During the study period (1958–1983) for the cancer incidence calculations the study population had accumulated 4247 person-years. The cancer morbidity was established by linking the identification numbers of the individuals in the study population with the National Cancer Register.

The expected number of deaths and malignancies was calculated by multiplying person-years of observation within five-year age categories during each year of the study periods by site- and gender-specific national rates. The calculations of standardized mortality/morbidity rates (SMR) with 95% confidence intervals (CI) based on a Poisson distribution was performed by a computer program developed at the University of Linköping (EPILIN program package).

RESULTS

The overall mortality in the study population was increased (SMR=138; CI 120–157) due to an excess in mortality from respiratory tuberculosis (SMR=1932; CI 1144–3054) and other non-malignant respiratory diseases (SMR=746; CI 577–947).

There was no overall increased incidence of malignant diseases in the study population (SMR=94; CI 67–126). However, nine cases of lung cancer were observed vs. 4.8 expected (SMR=188; CI 85–356). With a latency time requirement of 10 years from discovery of silicosis SMR was 236 (CI 107–448), and with a latency time of 20 years there was a further increase (SMR=267; CI 98–582). Lung cancer was diagnosed 36–72 years after first quartz exposure and 11–32 years after that silicosis had been detected.

DISCUSSION

The results from this study on Swedish ceramic workers with silicosis demonstrate an increased mortality in non-malignant, but not in malignant, respiratory diseases. However, the lung cancer incidence was doubled.

The size of the cohort is small, and we have no data on smoking habits in the study population. The results are, however, in accordance with other studies on silicotics from the ceramic industry. An increased risk among pottery workers of dying from lung cancer has been reported, especially if they had been exposed to talc,[7-9] but also in individuals with no talc exposure.[8] Talc was, however, only used in four of the 19 factories in our study, and the lung cancer cases were not accumulated to these factories. A recent Italian case-referent study among ceramic workers controlling for age, period of death and smoking did also show an increased lung cancer risk, especially among individuals with silicosis.[2]

The mechanism for a carcinogenic effect of quartz is not clear. A direct carcinogenic effect is supported by the cytotoxic effect of quartz *in vitro*.[6] It has been shown

among ceramic workers that silicotics have a greater risk for lung cancer than non-silicotics.[2] This could be due to a higher quartz exposure, but a causal relationship between the silicotic lesions and the cancer should be considered. Fibrotic lesions in the lung might impair the pulmonary clearance mechanisms for various carcinogenic substances, and a high incidence of bronchial carcinoma has been reported among individuals with various fibrotic lung diseases without relationship to dust exposure.[10]

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