

## The Morbidity and Mortality of Vermiculite Miners and Millers Exposed to Tremolite-Actinolite: Part III. Radiographic Findings

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A study was conducted to estimate the exposure-response relationship for tremolite-actinolite fiber exposure and radiographic findings among 184 men employed at a Montana vermiculite mine and mill. Workers were included if they had been employed during 1975-1982 and had achieved at least 5 years tenure at the Montana site. Past fiber exposure was associated with an increased prevalence of parenchymal and pleural radiographic abnormalities. Smoking was not significantly related to the prevalence of small opacities. However, the number of workers who had never smoked was small, and this prevented measurement of the smoking effect. Under control for smoking and age, the prevalence of small opacities was significantly greater for vermiculite workers with greater than 100 fiber/cc-years exposure than for comparison groups (cement workers, blue collar workers, and coal miners) who had no known occupational fiber exposure. A logistic model predicted an increase of 1.3% in the odds ratio for small opacities at an additional exposure of 5 fiber-years.

**Key words:** tremolite-actinolite, fiber-years exposure, small radiographic opacities

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### INTRODUCTION

In 1978, 12 cases of benign pleural effusion were reported among employees of an Ohio fertilizer plant that had processed vermiculite concentrate from South Africa, and from a mine and mill near Libby, Montana [Lockey et al, 1983].

Lockey et al [1984], noting that the Montana vermiculite concentrate contained asbestiform tremolite, examined 512 workers employed at the Ohio plant. They found an increased prevalence of pleuritic chest pain, shortness of breath, and radiographic pleural abnormalities that they attributed to the tremolite exposure. However, only one worker had parenchymal fibrosis and neither fibrosis nor abnormal pulmonary

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function were found to be associated with tremolite exposure. The authors concluded that their results, which showed an association between asbestos exposure and chest pain, and an increased prevalence of pleural abnormalities, suggested that the cluster of 12 cases of benign pleural effusion in the Ohio plant was due to tremolite exposure.

In 1982, we began studies of environmental exposures, mortality, and morbidity of workers employed at the Montana mine and mill [Amandus et al, 1987a,b]. In addition, McDonald et al [1986a,b] have conducted parallel but separate studies of these miners and millers. The purpose of this paper is to estimate the exposure-response relationship for radiographic findings from estimates of individual cumulative fiber exposure.

## METHODS

Radiographic examinations were administered by the local hospital to all active workers in 1959 and annually since 1964. A questionnaire on cigarette smoking habit and respiratory symptoms was administered by the company staff to most active workers employed after 1975.

Radiographs were unavailable for more than 50% of the workers who were employed less than 5 years at the Libby site, or who terminated prior to 1975. Therefore, the study population was defined to be 191 men employed during 1975-1982 with at least 5 years tenure. Chest radiographs were available for 184 men and questionnaires for 121.

All available radiographs of workers at the Libby site taken since 1959 were independently interpreted by three readers blinded to other data using the ILO classification [ILO, 1981]. Results from each worker's most recent radiograph were evaluated. The most recent film was taken in 1981-1982 for 134 workers, in 1976-1980 for 49 workers, and prior to 1975 for only 1 worker.

Radiographic findings evaluated were (1) the presence of small opacities with a profusion greater than or equal to ILO category 1/0, (2) any unilateral or bilateral pleural change, which included pleural plaque or diffuse thickening on the wall, diaphragm, or other site, but excluded costophrenic angle obliteration, (3) unilateral or bilateral pleural calcification on the wall, diaphragm, or other site, and (4) unilateral or bilateral pleural plaque or diffuse pleural thickening on the wall. A final determination for the profusion category of small opacities was derived from the median of the three readers, and for each pleural finding from a consensus of the readers.

Individual cumulative fiber exposure estimates fiber-years (f-y), tenure, and age were calculated to the date of the most recent radiographic examination. Derivation of estimates of cumulative exposure, i.e. fiber-years, have been described elsewhere [Amandus et al., 1987a,b].

## RESULTS

### Radiographic Findings

The distributions of age, tenure, and f-y are shown in Table I. The average age, tenure, and f-y were similar for the 191 men who met the sample inclusion criteria and the 184 men who had radiographs available. For men with radiographs available,

**TABLE I. The Average and Standard Deviation of Age, Tenure, and Fiber-Years Exposure for All Men in the Study Sample**

		Age at exam <sup>b</sup>	Age in 1982	Tenure	Fiber-years
All workers <sup>a</sup>	Average		46	14	123
	Standard deviation		12	8	281
	Number <sup>c</sup>		190	191	191
Workers with radiographs <sup>b</sup>	Average	44	46	14	119
	Standard deviation	12	12	8	277
	Number <sup>c</sup>	183	183	184	184

<sup>a</sup>All male workers employed from 1975–1982 with at least 5 years tenure.

<sup>b</sup>Most recent radiographic examination.

<sup>c</sup>Number of workers.

**TABLE II. Radiographic Findings by Fiber-Years**

Radiographic finding		Fiber-years				Total
		0–15	16–30	31–85	> 86	
Profusion of small opacities <sup>a</sup>	≥ 1/0	0	1	3	14	18
	< 1/0	63	28	41	34	166
	% > 1/0	0	3	7	29	10
Any pleural change <sup>a</sup>	Yes	4	1	8	15	28
	No	59	28	36	33	156
	% Yes	6	3	18	31	15
Pleural calcification	Yes	1	0	3	3	7
	No	62	29	41	45	177
	% Yes	2	0	7	6	4
Pleural thickening on the wall <sup>a</sup>	Yes	4	1	6	13	24
	No	59	28	38	35	160
	% Yes	6	3	14	27	13

<sup>a</sup>Association with fiber-years is significant ( $p < 0.05$ ).

the average age, tenure, and f-y were 44.4 years, 14.4 years, and 119.4 f-y respectively.

Results of the radiographic reading trial (Table II) indicated that the prevalence of small opacities was 10%, any pleural change was 15%, pleural calcification was 4%, and pleural thickening on the wall was 13%. Fiber-years were significantly related to small opacities, any pleural change, and pleural thickening on the wall ( $p < 0.05$ ), but not to pleural calcification.

Information on the 18 cases of small opacities is presented in Table III. All readers found only small irregular opacities (no rounded) for 9 cases, and two readers found only irregular opacities for 15 cases. All readers agreed that irregular opacities were primarily present for 12 cases, and two readers agreed for 17 cases. Finally, at least two readers reported large opacities on a background of small irregular opacities for two cases.

TABLE III. Cases of Small Opacities

Case	Age at time of radiograph	Median profusion category	Type opacity <sup>b</sup> Reader			f-y	Total tenure (years)	Year of hire
			A	B	C			
1	61	1/2	ST	TS	ST	1013	30	1952
2	64	1/1	ST	TS	SS	407	15	62
3	44	1/0	ST	SS	SS	1231	30	50
4	60	1/2	ST	QT	TS	114	30	50
5	48	2/2	SS	SP	SS	27	15	67
6	69	1/0	TS	TQ	TT	63	29	47
7	67	1/1	ST	TT	ST	352	18	58
8	67	1/0	TS	QT	QT	310	43	37
9	63	2/1 <sup>a</sup>	TU	TQ	PS	124	11	65
10	61	2/2	TT	TT	TU	660	23	53
11	58	2/2 <sup>a</sup>	ST	TT	SS	1796	28	48
12	59	1/2	SS	QT	SS	77	36	46
13	53	2/1	SP	QS	SS	2327	32	45
14	43	1/0	ST	TQ	ST	33	14	66
15	63	3/3	ST	TT	SS	133	16	61
16	66	1/1	SS	TS	SP	130	13	65
17	66	1/0	ST	QT	TT	150	16	60
18	47	1/0	TS	TQ	ST	116	19	63

<sup>a</sup>Large opacity present.

<sup>b</sup>According to the ILO classification scheme, the type of opacity recorded first is that primarily present, and that recorded second is that of secondary predominance.

TABLE IV. Number of Workers by Reader and Radiographic Category of Profusion

Profusion category of small opacities	Reader			Median <sup>a</sup>
	A	B	C	
0/-, 0/0, 0/1	166	151	166	166
1/0	3	14	7	6
1/1	5	9	5	4
1/2	3	3	3	2
2/1	1	4	0	2
2/2	4	1	1	3
2/3	1	0	0	0
3/2	0	1	1	0
3/3	1	1	1	1
3/+	0	0	0	0
Total	184	184	184	184

<sup>a</sup>The median of the profusion categories from readers A, B, and C.

Readers A and C reported a similar prevalence of opacities (category 1/0 or more profusion) (10%), while reader B reported the highest prevalence (16%) (Table IV). In any event, a 6% difference in prevalence is within limits of normal interreader variability for films classified into ILO category 1 [Reger et al, 1973; Amandus et al, 1974].

The association between f-y, small opacities, and pleural change was not found to be significant under joint control for cigarette smoking and age (Table V). However, few cases of small opacities were found among nonsmokers and younger workers with low f-y; 9 of 13 cases were older than age 45, had smoked cigarettes, and had

**TABLE V. Radiographic Findings by Fiber-Years Under Control for Age and Smoking Habits\***

Age	Smoking habit	f-y	Profusion of										Any pleural change				
			Small opacities					Percentage > 1/0					Yes	No	Total	Percentage	Yes
			> 1/0	< 1/0	Total	Percentage > 1/0	Total	Percentage > 1/0	Total								
<45 years	Current smoker	<86	1	33	34	3	3	34	1	33	34	3	1	33	34	3	
		≥86	0	5	5	0	0	5	1	4	5	20	1	4	5	20	
	Ex-smoker	<86	0	41	41	0	0	41	5	36	41	12	5	36	41	12	
		≥86	0	8	8	0	0	8	2	6	8	25	2	6	8	25	
	Never smoker	<86	0	16	16	0	0	16	1	15	16	6	1	15	16	6	
		≥86	1	0	1	100	100	1	0	1	1	0	0	1	1	0	
≥45 years	Current smoker	<86	1	7	8	13	13	8	1	7	8	13	1	7	8	13	
		≥86	5	4	9	56	56	9	4	5	9	44	4	5	9	44	
	Ex-smoker	<86	1	18	19	5	5	19	4	15	19	21	4	15	19	21	
		≥86	4	8	12	33	33	12	3	9	12	25	3	9	12	25	
	Never smoker	<86	0	6	6	0	0	6	1	5	6	17	1	5	6	17	
		≥86	0	2	2	0	0	2	1	1	2	50	1	1	2	50	

\*The association between f-y and radiographic finding within each age-smoking habit group was not significant (p > 0.05).

accumulated greater than 86 f-y. Among 24 cases with any pleural change, 14 were older than age 45, and 21 had smoked cigarettes.

Because it was difficult from these data to measure the association between f-y and radiographic findings under joint control for smoking and age, in the remainder of the analyses, the exposure-response association was internally controlled only for age. However, the effect of smoking will be discussed later.

The exposure-response relationship for f-y and radiographic findings was estimated by fitting a logistic model separately for the entire sample and for workers who had smoked (Table VI). Small opacities, pleural change, pleural calcification, and pleural thickening on the wall were significantly related to age. However, with age in the model, only small opacities were significantly related to f-y ( $p < 0.05$ ). The model for small opacities for the total sample of workers is as follows: percentage of small opacities =  $X/1+X$ , where  $X = \exp(-9.6 + 0.0026 \text{ f-y} + 0.131 \text{ age})$ . The model calculated for current and former smokers is  $X = \exp(-9.4 + 0.0021 \text{ f-y} + 0.131 \text{ age})$ .

For the mean age of the sample (44 years), the estimated prevalence of small opacities from the "total group" model was calculated to be 2.1% at 5 f-y, 2.4% at 50 f-y, and 2.5% at 100 f-y. Estimates of the odds ratio calculated from the model [odds ratio =  $\exp(0.0026 \text{ f-y})$ ] are 1.01, 1.13, and 1.30 respectively.

The exposure-response relationship for small opacities also was evaluated employing an external "control" for smoking. Results were compared to (1) "blue-collar" workers in industries where there was no known risk of pneumoconiosis [Petersen and Castellan, 1984; Castellan et al, 1985, Abrons et al, 1985], (2) workers employed in nonasbestos cement plants [Abrons et al., 1985], and (3) coal miners with less than 5 years employment underground in a coal mine [Hankinson et al, 1975].

Data from studies of the comparison groups were reanalyzed, and workers were excluded from analysis if (1) they had worked in another dusty trade, (2) their radiograph showed a profusion of rounded opacities greater than category 0/1 and no evidence of irregular opacities, or (3) they had never smoked cigarettes regularly. Results for current and former smokers older than age 45 are presented in Table VII.

Results of this comparison indicated that the prevalence of irregular opacities with profusion greater than category 1/0 is greater for the vermiculite than the

TABLE VI. Logistic Models for Radiographic Findings

Radiographic findings	Regression coefficients			Standard error of coefficients		
	Intercept	f-y	Age	Intercept	f-y	Age
Total group						
Small opacities	-9.6 <sup>a</sup>	.0026 <sup>a</sup>	.131 <sup>a</sup>	2.11	.001	.036
Any pl. change	-4.3 <sup>a</sup>	.0008	.051 <sup>a</sup>	0.94	.001	.019
Pl. calc.	-8.0 <sup>a</sup>	-.0010	.097 <sup>a</sup>	2.17	.002	.039
Pl. change on wall	-4.3	.0008	.046 <sup>a</sup>	.99	.001	.020
Current and former smokers only						
Small opacities	-9.39 <sup>a</sup>	.0021	.131 <sup>a</sup>	2.29	.001	.040
Any pl. change	-4.14 <sup>a</sup>	.0005	.052 <sup>a</sup>	1.05	.001	.022
Pl. calc.	-7.25 <sup>a</sup>	-.0021	.087 <sup>a</sup>	2.27	.003	.044
Pl. change on wall	-4.31 <sup>a</sup>	.0005	.052 <sup>a</sup>	1.12	.001	.023

<sup>a</sup>Coefficient is significantly greater than zero,  $p < 0.05$ .

TABLE VII. Current and Former Smokers Age 45–60 Years

	Small irregular opacities	No small irregular opacities	Total	Percentage
Blue collar workers	1	90	91	1.1
Cement workers	12	326	338	3.6
Coal miners	1	318	319	0.3
Vermiculite				
< 50 f-y	1	17	18	5.5
50–100 f-y	1	8	9	11.1
> 100 f-y	4	9	13	30.8

comparison groups; however, the prevalence is significantly different only for the greater than 100 f-y group.

These results should be interpreted cautiously for several reasons. First, the number of vermiculite workers age 45–60 was small. Second, radiographs for workers in the comparison groups were generally of better quality. Third, different readers classified the films in the comparison and study groups. Finally, no cases of small opacities (profusion of category 1/0 or more) were observed among vermiculite workers with less than 30 f-y.

## DISCUSSION

Radiographic findings were consistent with an asbestos etiology. Irregular shaped opacities were found in all cases of small opacities. This was the most predominant type of opacity in 17 of the 18 cases. Category 1 profusion of small opacities was found in 12 of the 18 cases. The prevalence of small opacities with profusion greater than or equal to category 1/0 was 10%, tended to be related to age and fiber-years, but was not significantly related to cigarette smoking. The prevalence of pleural change was 15%. This was related to age but was not significantly associated with fiber-years exposure.

We previously described the results of a study by Lockey et al [1984] of 512 workers at an Ohio fertilizer company that processed vermiculite concentrate from the Libby site. Lockey et al found 1 case of irregular opacities (0.2%), 11 cases of pleural change (2.2%), and 11 cases of costophrenic angle blunting (2.2%). Corresponding results from our study are 18 cases (10%), 28 cases (15%), and 16 cases (8.7%) respectively. Additionally, Lockey et al found seven cases ( $7/512 = 1.4\%$ ) with a history of pleural effusion, and we found one case ( $1/184 = 0.5\%$ ) with a history of radiographic evidence of pleural effusion.

The difference between studies in radiographic findings may be explained by differences in cumulative fiber exposure. To check this we compared results among fertilizer plant workers and vermiculite miners with similar f-y. In the Ohio fertilizer plant, the maximum individual cumulative exposure was reported to be 39 f-y and the average exposure was 3 f-y [calculated from Lockey et al, 1984]. For comparison, we considered 91 vermiculite workers with less than 30 f-y and an average exposure of 13 f-y.

The prevalence of small opacities, pleural findings, and pleural effusions for our 91 workers [sample from Lockey et al, 1984] was 1.1% (0.2%), 8.0% (2.0%),

and 0.0% (1.4%) respectively. Additionally, our logistic models, based on the average age and f-y in the study by Lockey et al [1984], predicted the prevalence of small opacities and pleural change to be 0.9% and 8.0%. Although the prevalence of small opacities and pleural findings was at least four times greater for the vermiculite miners than the fertilizer plant workers, the difference in prevalence was marked only for pleural change. The reason for proportionately more cases of pleural change, and fewer cases of pleural effusion, at the Libby mine and mill than at the fertilizer plant is unclear.

Results on the exposure-response relationship from this and other studies are presented in Table VIII and Figures 1 and 2. For this comparison our exposure measurements were converted to mppcf using a conversion factor of 4.0 f/cc:mppcf [Amandus et al, 1987a]. Exposure estimates from McDonald et al [1986] were converted using a factor of 4.6. Our slope for the exposure response curve for the prevalence of small opacities was similar to the slope reported by McDonald et al [1986b] for Libby workers, Jones et al [1980] for asbestos cement workers (chrysotile and crocidolite), Berry et al [1979] for asbestos textile workers (chrysotile and crocidolite), and Finkelstein et al [1982] for chrysotile asbestos pipe and insulation workers. (Finkelstein reported the prevalence of certified asbestosis based on radiographic, pulmonary function, and clinical findings.) However, the slopes from our study, and the other studies, were higher than the slope reported by Rossiter et al [1972] for Quebec chrysotile miners and millers.

Film quality has been shown to affect the classification of small opacities. Small opacities may be masked in a film that is fogged, overexposed, or has poor contrast [Reger et al, 1972]. In this study, each reader classified film quality according to the

TABLE VIII. Prevalence (%) of Small Irregular Opacities\* by Cumulative Exposure From This and Other Studies\*\*

Jones		Rossiter			This Study			Berry			Finkelstein		McDonald (Libby)	
mmpcf- years	% IR	mmpcf- years	% IR <sup>c</sup>	% IR <sup>f</sup>	mppcf- years <sup>b</sup>	fiber- years	% IR	fiber- years	% OP <sup>c</sup>	% OP <sup>d</sup>	fiber- years	% AS <sup>a</sup>	fiber- years	% OP
0.0	1.8	<10	1.8	6.4	0-3.75	0-15	0						0-15	10.1
5.4	3.1				3.75-7.5	15-30	4	<25	0	0			15-30	18.9
12.1	6.0				7.5-21.5	30-86	7	25-50	0	9.7	<50	0.5	30-86	17.6
17.2	9.6				>21.5	>86	29	50-100	37.5	12.5	50-100	3.4	>86	45.9
30.3	28.6	10-100	3.3	3.7				100-150	27.0	20.8	100-150	6.5		
								>150	34.1	23.5	150-199	7.9		
		100-200	6.3	6.3										
		200-400	8.7	5.0										
		400-800	12.0	6.8										
		>800	17.2	7.0										

\*IR, Irregular opacities; OP, irregular or rounded opacities.

\*\*Jones et al [1980], Rossiter et al [1972], Berry et al [1979], Finkelstein et al [1982], and McDonald et al [1986b].

<sup>a</sup>Asbestosis defined from radiographic findings and other medical data.

<sup>b</sup>Applied conversion factor of 4.0 f/cc per mppcf.

<sup>c</sup>Workers employed before 1951.

<sup>d</sup>Workers employed after 1950.

<sup>e</sup>Thetford mines in Quebec.

<sup>f</sup>Asbestos mines in Quebec.

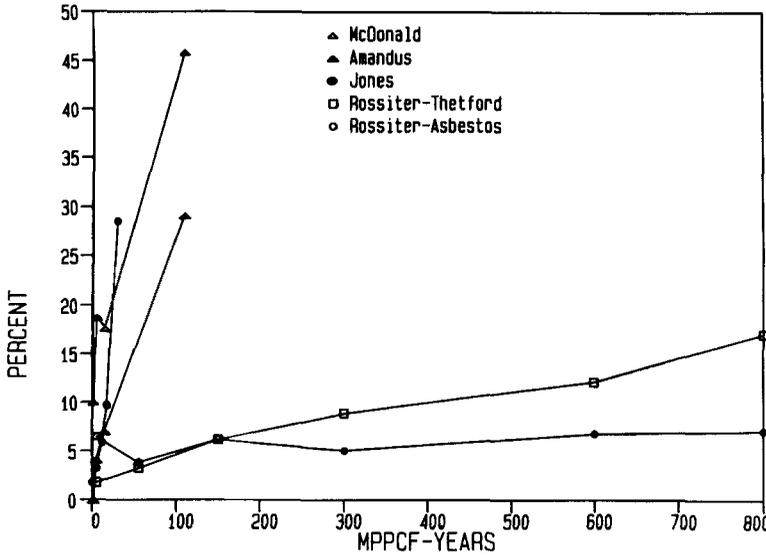


Fig. 1. Prevalence of radiographic opacities by cumulative exposure from asbestos studies.

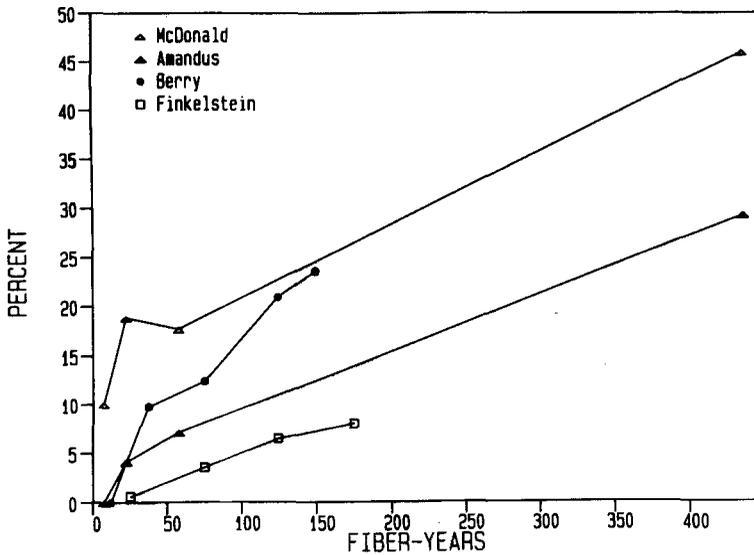


Fig. 2. Prevalence of radiographic opacities by exposure (fiber-years) and asbestos study.

ILO classification as excellent, acceptable (no technical defect impairing the pneumoconiosis classification), poor (some technical defect impairing the pneumoconiosis classification), and unreadable. The proportion of study films rated as acceptable or poor quality was 60.9% and 16.3% for reader A, 60.9% and 14.7% for reader B, and 29.3% and 22.8% for reader C. None of the 184 radiographs was found to be unreadable.

We evaluated the relationship between film quality and cumulative fiber exposure, because poor film quality could lead to an underestimation of the prevalence of radiographic findings, and to confounding of the association with exposure. Film

quality was highly correlated with cumulative fiber exposure (Table IX). The proportion of poor quality films reported by readers A and C was two to three times greater for the greater than or equal to 86 f-y than the less than 86 f-y group.

The reason for poor film quality could not be checked systematically, because the readers did not record this on all of the films. However, reader C reported the reason on 60 films, and 48% were found to be of poor contrast, fogged, or overexposed. Thus, there is a possibility for confounding if these 60 films are representative of the entire film set.

In any event, confounding from film quality would not likely change our conclusions for the increased risk of small opacities at low exposure. Poor film quality would likely lead to underestimation of disease prevalence, and confounding, if any, would likely tend to decrease the slope of our exposure-response curve. However, at low exposure, our logistic model still predicts an increased odds ratio for small opacities.

McDonald et al [1986b] found a higher prevalence of small opacities in a parallel, but separate radiographic study of the vermiculite miners and millers. Differences between studies have been attributed to differences in film quality [Armstrong et al, 1985].

The results of this study must also be interpreted with respect to the possible confounding effect from cigarette smoking. This could not be adequately measured from our data, because of the small number of nonsmokers (25 overall and 8, age 45 or older). Our logistic model predicts the prevalence of small opacities to be 6.6% at 5 f-y and age 53 (midpoint of age group 45-60). This is markedly higher than the 1.9% prevalence of small irregular opacities for 748 coal miners, cement workers, and blue collar workers who were current or ex-smokers and age 45-60. Additionally, the prevalence of small irregular opacities was 0% for 212 blue collar workers, cement workers, and coal miners aged 45-60, who had never smoked.

Thus, the combined effects of fiber exposure and smoking, under control for age, seems to be greater than that from smoking alone. The smoking effect on small irregular opacities seems to be small in the absence of fiber exposure, but confounding and interaction could not be evaluated. Perhaps, if there was no interaction, or if the interaction was small, then the confounding from smoking would be minimal.

In conclusion, if one assumes that (1) smoking is not a confounder, (2) the logistic model is appropriate for the exposure-response curve, and (3) the fiber-year index is applicable whether accumulated in a "high" or "low" average exposure situation, then 5 f-y was found to be associated with a 1.3% increase in the relative

**TABLE IX. The Proportion of Radiographs With Acceptable and Poor Quality by Reader and Fiber/cc-Years**

Reader	Film quality	Fiber/cc-years				Total
		0-15	15-30	31-86	≥86	
A	% Acceptable	26	13	33	28	61
	% Poor	13	24	14	44	16
B	% Acceptable	54	62	59	71	61
	% Poor	11	10	18	19	15
C	% Acceptable	32	18	26	24	29
	% Poor	6	14	11	35	23
Total number of films		63	29	44	48	184

risk of small opacities. Indeed, if the foregoing assumptions are true, an 8-hour TWA fiber exposure of 0.1 f/cc over a working lifetime (approximately 50 years) is not a conservative standard for the prevention of radiographic evidence of small opacities (profusion category 1/0 or more).

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