

Pulmonary Changes among Vinyl Chloride Polymerization Workers*

R. Lilis, M.D.; H. Anderson, M.D.; A. Miller, M.D.; and I. J. Selikoff, M.D.

Soon after the emergence of vinyl chloride as a new and potent carcinogen, producing hemangiosarcoma of the liver, clinical studies of three groups of exposed workers were undertaken in order to assess the prevalence of vinyl chloride-induced adverse health effects.

The spectrum of clinical and laboratory tests was broad,¹ with the main focus on a possible hepatotoxic effect and/or portal hypertension, on the abnormalities of peripheral circulation of the extremities with possible associated bone lesions in the distal phalanges (acro-osteolysis), and on the history of pre-narcotic symptoms during overexposure. In the absence of appropriate VC measurements in the past, such acute episodes were interpreted as reflecting significant toxic exposure.

METHODS

Chest x-ray films were included in the examination protocol as a routine procedure, as was a complete smoking history and the chronic bronchitis questionnaire. Pulmonary function tests were also included.² A Systems Research Laboratories predictive pulmonary screener was used for spirometry and a Vertek 3500 Fleisch pneumotachograph for obtaining flow volume curves.

At the time this study was undertaken, there were only a few reports in the literature of lung changes in PVC workers. One case of pneumoconiosis in a 30-year-old worker who had inhaled PVC dust had been reported.³ The lung biopsy had shown granulomatous lesions (foreign body type) to be present. Fibrotic lung changes and altered pulmonary function tests had been reported in 96 workers exposed to polyvinyl chloride dust; the changes were more pronounced in persons with long exposure.⁴

While all three groups of workers had been active in PVC polymerization facilities (vinyl chloride and polyvinyl chloride exposure), there were obvious differences insofar as the degree and pattern of exposure were concerned. The first plant (Group A) was characterized by a very uniform and constant technology, consisting only of the polymerization of vinyl chloride to polyvinyl chloride. VC exposure levels had been significantly elevated in the past, to the point that most of the examined workers had experienced repeated episodes of pre-narcotic symptoms, especially during the reactor cleaning operation. PVC dust had also been abundant, especially in the bagging area. Most of the workers started their activity in this area, and there was no adequate enclosure of the area, so that the entire examined group was practically exposed to vinyl chloride and polyvinyl chloride dust.

The second plant (Group B) was studied because it was the first PVC polymerization facility, so that long exposure effects could be expected. While VC and PVC exposure levels had probably been of the same order as in the first plant in the past, the diversification of the technology introducing copolymers (with vinyl acetate, vinylidene chloride, acrylonitrile) with a relatively low component of vinyl chloride, and the relocation of some production lines in new

*From Mount Sinai School of Medicine, New York City.

Table 1—Chest X-ray Film Abnormalities in VC-PVC Exposed Workers (Group A)*

Duration of Exposure (years)	Total No. Examined	Abnormal Chest X-ray	
		Number	Percent
Less than 2	48	7	14.6
2.1-5	66	12	18.2
5.1-10	54	8	14.8
10.1-20	81	27	33.3**
20.1—	41	12	30.0**
Total	290	66	22.7

*After exclusion of all persons with any past asbestos, silica or coal dust exposure.

**Chi² test showed the difference in prevalence of chest x-ray abnormalities in workers with exposure of more than 10 years to be significantly higher than in those with shorter exposure.

buildings, with modern equipment, had led to a decrease of exposure levels in recent years, for both VC and PVC.

The third plant (Group C) was studied because it was known that industrial hygiene surveys and monitoring of the VC exposure levels had made it possible to achieve a relatively low exposure level.

A panel of five physicians read the chest x-rays. For statistical reporting, a consensus reading was used. The chest x-ray films were read after the completion of each clinical survey. Information on age, job (degree of exposure), length of exposure or any other specifics were not known at the time the x-ray films were read. The only data available to the readers were identification by study number and name.

After the completion of the chest x-ray readings, special attention was given to any other possible occupational exposure which may be associated with abnormal findings. The complete occupational histories, taking into account previous jobs, make it possible to exclude from this analysis all cases in which there had been any asbestos (even slight), silica or coal dust exposure. Most of these cases were clustered in the B group, the plant being located in the vicinity of a coal mining area (West Virginia).

RESULTS

The finding of linear reticular, and less often nodular,

Table 2—Chest X-ray Abnormalities in VC-PVC Exposed Workers (Group B)*

Duration of Exposure (years)	Current Exposure			Past Exposure		
	Total No. Examined	Abnormal Chest X-ray No.	%	Total No. Examined	Abnormal Chest X-ray No.	%
Less than 2	22	3	13.6	12	2	16.6
2.1-10	39	5	13	35	9	25.7
10.1-20	22	5	22.7	15	3	20
20.1—	74	15	20.3	31	5	16.1
Total	157	28	17.8	93	19	20.4

*After excluding all persons with past asbestos, silica or coal dust exposure.

**Chi² test showed the difference in prevalence of chest x-ray abnormalities in workers with current exposure of more than 10 years to be significantly higher than in those with shorter exposure.

Opacities on significant numbers of the VC-PVC exposed workers' chest x-ray films in the first examined group alerted us to the problem (Group A—Table 1). In the absence of a uniform system for classification of chest x-ray abnormality of this type (linear, reticular or rounded opacities) the ILO U/C Pneumoconiosis Classification was used. All readers were experienced in the use of this system. The analysis showed a definite increase of x-ray changes with length of exposure; the prevalence was significantly more elevated in workers with more than ten years of VC-PVC exposure as compared to those with shorter exposure time. The overall prevalence of small linear reticular and/or rounded opacities was 22.7 percent in this group.

In the second examined group (Group B—Table 2), where there had been a more diversified pattern of VC-PVC exposure, with probably a lower level of recent VC-PVC exposure, but with more workers who had been active in the department for over 20 years, some interesting relationships were found.

In workers with current VC-PVC exposure there was again a definite, statistically significant increase in prevalence of the chest x-ray abnormalities with duration of VC-PVC exposure. In separating a subgroup of workers who had worked in the PVC polymerization process in the past, but had since moved to other departments, no relationship with length of exposure was found, but the overall prevalence for this subgroup (past exposure) was slightly more elevated than in the workers with current exposure, probably reflecting the effect of higher levels of exposure in the past.

For the entire Group B the prevalence of chest x-ray changes (small linear reticular and/or rounded opacities) was 19.4 percent, somewhat lower (but not statistically significant) than in Group A. It is of interest to emphasize at this point that there was a difference in age distribution between the two mentioned groups; Group A (with the higher prevalence of chest x-ray changes) being significantly younger than Group B.

The third examined group (Group C) was found to have a much lower prevalence of chest x-ray abnormalities (Table 3). The overall prevalence of 4.3 percent (19

Table 3—Chest X-ray Abnormalities in VC-PVC Exposed Workers (Group C)*

Total No. Examined	Abnormal Chest X-ray	
	No.	%
445	19	4.3

Table 4—Chest X-ray Abnormalities in Three Different VC-PVC Plants

Group	Total No. Examined	Abnormal Chest X-ray	
		No.	%
A	200	66	22.7
B	250	46	19.4
C	445	19	4.3

workers out of 445 examined) made any further analysis irrelevant. Plant C was known to have had relatively low levels of exposure to VC for the last 15 years, when a continuous monitoring system had been instituted.

In evaluating the prevalence of chest x-ray abnormalities in VC-PVC exposed workers in the three mentioned plants (Table 4), two main trends can be identified. First, in the two groups (A and B), where there was a relatively high prevalence of such abnormalities, there was a statistically significant increase with duration of exposure. Second, in comparing the results in the three examined groups, the highest prevalence of chest x-ray changes is found in the plant with highest exposure levels, while the lowest prevalence characterizes workers from the plant with known relatively low exposure levels.

Since the finding of small linear-reticular and/or nodular opacities in VC-PVC exposed workers was rather unexpected and no pathogenic explanation was yet available to suggest an interpretation, several other factors which may have had some relationship to the findings were considered.

Smoking histories had been carefully taken and the overall prevalence of a positive smoking history was strikingly similar in the three examined groups (Group A—75 percent, Group B—75.2 percent and Group C—74.6 percent). The prevalence of positive smoking history was found to be higher in workers with abnormal chest x-ray films, in both Group A and B (Tables 5 and 6). The prevalence of positive smoking history in workers with abnormal chest x-ray films was statistically significantly higher in both groups. This could indicate a

Table 5—Chest X-ray Abnormalities of VC-PVC Exposed Workers and Smoking History (Group A)

Normal Chest X-ray			Abnormal Chest X-ray		
Total No.	Positive Smoking History		Total No.	Positive Smoking History	
	No.	%		No.	%
224	161*	72	66	57*	86

*Prevalence of positive smoking history significantly higher among workers with abnormal chest x-ray ($\chi^2 = 5.734$; $0.01 < P < 0.02$).

Table 6—Chest X-ray Abnormalities of VC-PVC Exposed Workers and Smoking History (Group B)

Normal Chest X-ray			Abnormal Chest X-ray		
Total No.	Positive Smoking History		Total No.	Positive Smoking History	
	No.	%		No.	%
203	151** (71)*	74 (35)	47	42** (12)*	89 (25.8)

*Figures in parenthesis = ex-smokers.

**Prevalence of positive smoking history was significantly higher in workers with abnormal chest x-ray than in those with normal chest x-ray ($\chi^2 = 4.864$; $0.02 < P < 0.05$).

Table 7—Chest X-ray Changes in VC-PVC Exposed Workers and Chronic Bronchitis (by History), (Group A)

Chest X-ray	Total No.	Chronic Bronchitis by History	
		No.	%
Normal	224	41*	18.3
Abnormal	66	18*	27.2
Total	290	59	20.4

*Prevalence of chronic bronchitis in workers with abnormal chest x-ray not significantly different from those with normal chest x-ray.

Table 8—Chest X-ray Abnormalities of VC-PVC Exposed Workers and Chronic Bronchitis (by History), (Group B)

Chest X-ray	Total No.	Chronic Bronchitis by History	
		No.	%
Normal	203	31*	15.3
Abnormal	47	9*	19.2
Total	250	40	16.0

*Prevalence of chronic bronchitis not significantly different in the workers with abnormal chest x-rays, as compared to those with normal chest x-ray.

multiple factor effect of smoking and VC-PVC exposure.

Chronic bronchitis, by history, according to the MRC criteria, was found with an overall prevalence of 20.4 percent in Group A (highest exposure) and of 16.0 percent in Group B, although Group B was significantly older and smoking habits, as mentioned above, were practically identical.

In analyzing the relationship between chronic bronchitis and chest x-ray findings it was found that, although workers with abnormal chest x-ray films had a somewhat higher prevalence of chronic bronchitis, the difference, in both groups, was not statistically significant (Tables 7 and 8).

Finally, since a higher prevalence of chest x-ray abnormalities was found among workers with longer duration of exposure (more than ten years), and since longer duration of exposure generally is associated with older age, the age factor was also looked into (Tables 9 and 10). There was no significant difference between mean ages of workers with abnormal chest x-ray findings as compared to those with normal chest x-ray film findings, when considering the groups with less than ten years and more than ten years' duration of VC-PVC exposure. This was so for both Group A and Group B.

In addition, the group with the higher prevalence of chest x-ray changes (Group A) was significantly younger than the group with the lower prevalence of such abnormalities. These findings would indicate that age is not an important factor in the appearance of small linear-reticular or rounded opacities in VC-PVC exposed workers.

Table 9—Abnormal Chest X-ray in VC-PVC Exposed Workers (Group A)

Duration of Exposure (years)	Normal Chest X-ray	Abnormal Chest X-ray	Total
Less than 10 yrs	31.36* ± 9.7	34.33* ± 9.3	31.9 ± 10.1
More than 10 yrs	44.98* ± 8.9	46.9* ± 9.4	45.4 ± 8.9

*Mean age of workers with abnormal chest x-ray films not significantly different from those with normal chest x-ray, in the less than 10 years exposure group as well as in the more than 10 years exposure group.

Table 10—Abnormal Chest X-ray in VC-PVC Exposed Workers (Group B)

Duration of Exposure	Normal Chest X-ray	Abnormal Chest X-ray	Total
Less than 10 yrs	48.03* ± 7.5	49.4* ± 5.69	48.2 ± 9.9
More than 10 yrs	55.3* ± 7.8	55.7* ± 5.1	55.7 ± 6.0

*Mean age of workers with abnormal chest x-ray films not significantly different from those with normal chest x-ray, in the less than 10 years exposure group as well as in the more than 10 years exposure group.

The pulmonary function tests showed a relatively high prevalence of obstructive changes. FEV₁/FVC was reduced (less than 75 percent) in 43.4 percent of all examined workers in Group A and 46 percent of those in Group B (Tables 11 and 12).

FEV₁ percent of predicted was reduced in smaller proportions of all considered groups; this may be due to

Table 11—Screening Pulmonary Function Tests as Related to Length of Exposure (Plant A)

Duration of Exposure	Total No. Examined	FEV ₁ /FVC		FEV ₁ % of Predicted		FVC % of Predicted	
		<75% No.	<75% %	<80% No.	<80% %	<80% No.	<80% %
Less than 10 years	168	63	37.5	26	16	14	8
More than 10 years	122	63	52	27	23	13	10.6
Total	290	126	43.4	53	18.2	27	9.3

Table 12—Screening Pulmonary Function Tests as Related to Length of Exposure (Plant B)

Duration of Exposure	Total No. Examined	FEV ₁ /FVC		FEV ₁ % of Predicted		FVC % of Predicted	
		<75% No.	<75% %	<80% No.	<80% %	<80% No.	<80% %
Less than 10 years	108	43	39.8	12	11	1	0.9
More than 10 years	115	73	50.3	19	13.1	5	3.4
Total	253	116	46	31	12.3	6	2.3

Table 13—Chest X-ray Changes and Pulmonary Function (Plant A)

	Total	1 or More Abnormal PFT*	
		No.	%
Normal x-rays	222	105	47.3
Abnormal x-rays	68	38	55.9

*FEV₁/FVC ≤ 74%
% Pred FEV₁ ≤ 79%
% Pred FVC ≤ 79%

Table 14—Chest X-ray Changes and Pulmonary Function (Plant B)

	Total	1 or More Abnormal PFT*	
		No.	%
Normal x-rays	207	98	47.3
Abnormal x-rays	46	23	50

*FEV₁/FVC ≤ 74%
% Pred FEV₁ ≤ 79%
% Pred FVC ≤ 79%

the fact that the vital capacity was higher than 100 percent of predicted in one-third of workers. The prevalence of decreased FEV₁ percent of predicted was higher in Group A (although this group was younger) and in this group there was also an increase in prevalence of this abnormality with length of exposure. A decrease of FEV₁ percent of predicted may indicate a more advanced abnormality than the reduction of FEV₁/FVC, and may reflect the specific effect of VC-PVC exposure more accurately.

A restrictive pattern was found in 9.3 percent of Group A and in only 2.3 percent of Group B. Again, it has to be remembered that Group A was significantly younger.

An attempt to evaluate possible correlations between chest x-ray changes and pulmonary function abnormalities did not show any consistent link (Tables 13 and 14). While pulmonary function abnormalities were slightly more prevalent in workers with abnormal chest x-ray film findings, the differences when compared to those with normal chest x-ray films were small, in both groups A and B.

Smoking and age are both related to obstructive pulmonary function changes and, under such circumstances it appears difficult to isolate the specific effect of occupational VC and PVC exposure, although the prevalence of these changes is striking.

It is conceivable that chest x-ray changes and obstructive pulmonary function abnormalities reflect different pathologic processes, the chest x-ray changes being mainly related to parenchymal damage, while the obstructive pulmonary function changes would reflect airway changes.

DISCUSSION

The problem of pulmonary changes developing after

VC-PVC exposure has many implications. First, the possibility of a pathogenic similarity to other VC-induced abnormalities arises. Periportal and capsular fibrosis of the liver, peripheral vascular changes, including Raynaud's syndrome, but also thickening of the arteriolar wall and even complete occlusion of small vessels in some cases, scleroderma-like skin changes with marked increase in collagen formation have all been well documented in VC-exposed workers. The sequence of events at the cellular and subcellular level is not yet completely understood, but such mechanisms may be active in the pulmonary tissue as well.

The number of published reports on VC-PVC induced adverse health effects has markedly increased over the last year, and there were several more, beside those mentioned in the introductory remarks, pointing to pulmonary changes due to VC-PVC exposure. Wegman⁴ reported fine nodular changes on the chest x-ray films of three workers out of 37 in a PVC processing plant (PVC exposure only). Berk et al⁶ found, in a 30-year-old man who had been exposed for eight years, and had characteristic VC induced liver damage, significant restrictive pulmonary disease (forced vital capacity—70 percent of predicted). Prodan and co-workers found in guinea pigs exposed to vinyl chloride (10 percent) over a three-month period, interstitial infiltration, elevated neutral mucopolysaccharides in the alveolar walls, marked pulmonary fibrosis with well organized connective tissue.

Frongia and co-workers³ reported on pathologic changes in guinea pigs and rats exposed 24 hours a day, from two to seven months, to inhalation of PVC dust in the bagging area of a plant. In guinea pigs they found an initial alveolo-lobular macrophagic reaction, with multinucleated giant cells, and with very fine granules in the cytoplasm, which were unchanged by usual coloring techniques. After longer exposure (seven months) granuloma-like foci were identified while the initial alveolar reaction was fading out. In rats there was much less alveolar reaction, but marked thickening of the septa due to histio-macrophagic infiltration was prominent; after seven months, the same granuloma-like changes as in guinea pigs became dominant.

A pathology survey of lung slides from deceased VC-PVC workers is now in progress in our department, and lung specimens from VC-exposed animals are also reviewed.

Pulmonary changes in VC-PVC exposed workers are also of interest from another viewpoint. Waxweiler et al,⁴ in a recent mortality study on VC polymerization workers, found an excess in the mortality due to respiratory cancer (SMR = 156). There was some indication that the large cell undifferentiated type was more prevalent than expected. The same study also found an excess mortality due to "other respiratory diseases" (SMR = 176).

For all these reasons an awareness of the possible lung damage due to VC-PVC exposure is necessary; the purpose of this presentation was to contribute to such a goal.

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Lung Function Profiles in the Chrysotile Asbestos Mines and Mills of Quebec*

Margaret R. Becklake, M.D.; Gisèle Fournier-Massey, M.D.; and Robert Black, M.D.

Because of a clinical impression that it was not uncommon to find lung function profiles other than the classic restrictive one associated with asbestos exposure, we defined the lung function profiles in a sample of over 1,000 Quebec chrysotile asbestos workers. These men had been examined in 1967-68 as part of a comprehensive study of the effects of exposure to asbestos in the chrysotile mines and mills of Quebec.^{1,2} Five standard tests of lung function, expressed as a percent of predicted, were used to establish the function profiles: total lung capacity, residual volume, forced expiratory volume in 0.75 second, forced expiratory volume in 1 second/forced vital capacity, and maximal mid-expiratory flow rate.³ Results were related to dust exposure⁴ and smoking and have been described in full elsewhere.³ Close to half the men (44.3 percent) had normal lung function profiles and a further 26.5 percent had minor function changes only. Among the remainder, restrictive and obstructive function profiles occurred with comparable frequency (12.8 percent and 12.2 percent respectively). Both were associated with radiologic features of asbestosis; both occurred infrequently in the absence of the smoking habit (Table 1.) These findings suggest an association between the smoking habit and the development of an asbestos-related fibrosis in so far as this is reflected in a restrictive function profile. In

Table 1—Effects of Chrysotile Exposure on the Health of 1015 Current Quebec Asbestos Workers*

Dust Index**	>10	10-	100-	200-	400-	800-
Non-Smokers						
Prevalence %†						
a) chronic bronchitis	10	19	19	46	21	49
b) dyspnea	0	14	24	31	13	44
Function profile—‡						
prevalence %						
restrictive	3	3	3	1	1	1
obstructive	0	1	0	—	—	—
% age fall in function†						
VC	0	-10	-16	-18	-19	-23
FEV ₁	0	-9	-9	-13	-15	-22
D _{CO₂} rest	0	-11	-15	-18	-12	-15
exercise	0	-8	-9	-18	-18	-20
Smokers						
Prevalence %†						
a) chronic bronchitis	23	22	30	29	46	45
b) dyspnea	4	15	18	21	30	32
Function profile—‡						
prevalence %						
restrictive	8	14	16	10	4	13
obstructive	12	12	13	12	23	12
% age fall in function†						
VC	0	-3	-7	-10	-13	-14
FEV ₁	0	-3	-8	-10	-15	-15
D _{CO₂} rest	0	+4	+3	+5	-3	0
exercise	0	0	-2	0	-5	-7

*For all measurements, prevalence % has been age-standardized to the total working population as of October 31st, 1966. This was to allow for the smaller number of men for whom function profiles were analyzed.

**Expressed in million particles per cubic foot years†

†Based on a total sample of 1,015 men*, **

‡Based on 995 men†

addition, the data provided some indirect evidence based on a principal component analysis³ that in those Quebec asbestos workers who smoke, the character of the dust-associated function impairment might be either obstructive or restrictive. Further studies are required to establish the extent to which this experience in the primary mining and milling of chrysotile asbestos is directly applicable to secondary industries concerned with the further processing of this fiber.

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*From the Department of Epidemiology and Health, McGill University, Montreal, and l'Université de Sherbrooke, Sherbrooke, Quebec, Canada.

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