CHANGES IN PULMONARY FUNCTION IN WORKERS EXPOSED TO VINYL CHLORIDE AND POLYVINYL CHLORIDE*

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INTRODUCTION

The hazards of vinyl chloride (VC) which have received recent attention have been hemangiosarcoma of the liver, functional and histologic changes in the liver, and acroosteolysis. Since VC is a volatile small molecule and many workers are also exposed to a fine dust of polyvinyl chloride (PVC), pathogenic effects on the lungs might be anticipated. However, except for two limited East European studies,[1,2] pulmonary alterations have not been reported. To determine whether exposure to an occupational environment containing VC and PVC is associated with an increased risk of respiratory impairment, pulmonary function was investigated in 348 workers in a polymerization plant in Niagara Falls, New York.

MATERIALS AND METHODS

The entire current work force (267 workers) of the Goodyear plant in Niagara Falls and approximately 40 percent of those previously employed for more than one year (87 workers) were examined. Clinical, occupational, and smoking histories, complete physical examinations, and chest roentgenograms were obtained. The clinical and roentgenographic findings will be presented in a separate report. Spirometry was performed by all but 6 subjects. In addition, maximum expiratory flow-volume curves were obtained from 159 workers. These included the first 94 subjects (a random 28 percent of the total group) and 65 others selected because of abnormal spirometric findings. All examinations were made at the headquarters of the local union during a 3-day weekend.

For spirometry, a Systems Research Laboratories predictive pulmonary screener (model M-12) was used. The flow signal obtained by a heated-wire anemometer was integrated, then displayed digitally and graphically recorded against time. Flow-volume curves were obtained using a Vertek 3500 Fleish pneumotachygraph and recording both flow and integrated volume signals on a Houston X-Y plotter. Each instrument was calibrated in the laboratory before and after the survey and in the field against the other instrument as well as by using a calibrating syringe and known normal subjects. Subjects were standing

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and nose clips were placed. The best of at least three forced expirations was used unless the initial spirographic or flow-volume curve was normal or the first two curves agreed within 10 percent of each other.

If the forced vital capacity (FVC) was decreased but indices of air flow were normal, several slow vital capacity (SVC) maneuvers were performed. Predicted values for vital capacity and maximum midexpiratory flow (MMF) were those of Morris *et al.*;[3] the MMF was considered normal if it was $\geq$75 percent of predicted and the vital capacity if it was $\geq$80 percent of predicted. The 1-sec forced expiratory volume (FEV_1) was considered normal if it was $\geq$75 percent of FVC. The forced expiratory flow (in liters per second) after all but 25 percent of the FVC (in liters) had been expired (FEF_{25}) was considered normal if it was $\geq$0.30 FVC.[4,5]

The following definitions were used:

Nonsmokers—never smoked, smoked less than 1 cigaret a day, had smoked $\leq$10 cigarets a day for $\leq$6 months >2 years ago or smoked only cigars and pipes.

Ex-smokers—had discontinued smoking at least 1 year before; current smokers and ex-smokers were generally analyzed together.

Chronic bronchitis—cough and sputum production for at least 3 months of 2 consecutive years (definite) or for most of 1 year (suspect).

Emphysema—the presence on physical examination of two of the following signs: diminished breath sounds, prolonged expiratory phase, diminished diaphragmatic excursion, and depressed diaphragm; emphysema was suspected if only one of these was present. Most patients also had increased anteroposterior diameter of the thorax and distant heart tones.

Positive clinical finding—chronic bronchitis or recurrent wheezing by history and/or emphysema or wheezing on physical examination.

Impairment of air flow—decrease in MMF, FEF_{25}, or FEV_1.

Impairment of lung volume—SVC $\leq$79 percent of predicted without impairment of air flow.

Results

Age

The mean age for all 348 workers was 38.8 years (range, 19–68 years); 182 (52.3 percent) were $\leq$39. With advancing age, the prevalence of air flow impairment increased from 41 percent ($\leq$29 years) to 55 percent (30–39 years) to 69 percent ($\geq$40 years; Table 1). The prevalence of volume impairment, which was much lower (16 subjects or 4.6 percent) did not increase with age. It is likely that these 16 values were merely the lower limits of a normal distribution of vital capacity, since only 5 were less than 75 percent of predicted and the lowest was 66 percent.

Smoking

In all, 76 workers (21.8 percent) had never smoked cigarets and 78 (22.4 percent) had discontinued. Younger workers ($\leq$29 years) were twice as likely never to have smoked. There was no difference in prevalence of air flow impairment between current (119 of 194 or 61 percent) and previous (44 of 78 or 57 percent) smokers; both groups were considered as one category for further analysis.

Mean values for the three tests of air flow are shown in Table 2, related to

TABLE 1
CHANGES IN PULMONARY FUNCTION RELATED TO AGE AND SMOKING

Age Group	Flow Impairment			Volume Impairment			No Abnormality		
	Smokers and nonsmokers	Smokers	Nonsmokers	Smokers and nonsmokers	Smokers	Nonsmokers	Smokers and nonsmokers	Smokers	Nonsmokers
<29 yr	35/92 (38%)	26/63 (41%)	9/29 (31%)	5/92 (5.4%)	3/63 (4.7%)	2/29 (6.8%)	52/92 (57%)	34/63 (54%)	18/29 (62%)
30–39 yr	50/90 (56%)	47/76 (62%)	3/14 (21%)	3/90 (3.3%)	3/76 (4.0%)	0/14	37/90 (41%)	26/76 (34.2%)	11/14 (78.5%)
>40 yr	115/166 (69%)	94/133 (71%)	21/33 (64%)	8/166 (4.8%)	7/133 (5.3%)	1/33 (3.0%)	43/166 (26%)	32/133 (24%)	11/33 (33.3%)
All	200/348 (58%)	167/272 (61%)	33/76 (43%)	16/348 (4.6%)	13/272 (4.7%)	3/76 (3.9%)	132/348 (38%)	92/272 (33.8%)	40/76 (52.6%)

TABLE 2
MEAN VENTILATORY VALUES RELATED TO AGE AND SMOKING

Age Group	$FEV_1/FVC \times 100$			MMF (Percent Predicted)			$FEF_{25}/FVC \times 100$*		
	Smokers	Nonsmokers	p	Smokers	Nonsomokers	p	Smokers	Nonsmokers	p
<39 yr	76.3 ± 7.0 (139)†	79.4 ± 5.3 (43)	<0.01	78.8 ± 18.6 (100)	85.8 ± 18.6 (32)	<0.2	30.3 ± 11.0 (66)	34.8 ± 14.2 (18)	<0.2
>40 yr	71.9 ± 9.1 (132)	73.3 ± 7.0 (33)	<0.5	65.6 ± 26.4 (90)	77.6 ± 25.9 (25)	<0.05	21.6 ± 10.3 (61)	23.5 ± 10.6 (14)	<0.6
All	74.2 ± 8.4 (271)	76.6 ± 6.8 (77)		72.1 ± 26.7 (190)	82.2 ± 22.3 (57)		25.7 ± 11.7 (127)	30.4 ± 14.4 (32)	

* All subjects tested; 65 of the 159 were tested because they had abnormal FEV_1 or MMF.
† ±1 S.D.; number in parentheses is number of subjects tested.

age and smoking. As expected, values for smokers are lower both in the younger and older age groups, although the differences are not always significant.

Prevalence of reduced values for these three tests is shown in TABLE 3, related to age and smoking. While prevalence of impairment is statistically different for smokers and nonsmokers $\leqslant$39 years of age, smoking is not a significant factor beyond this age.

The relationship of age and smoking to prevalence of air flow impairment, using an abnormality of any of the three tests as the criterion, is summarized in TABLE 4. For all subjects, 57.5 percent were abnormal. For those $\leqslant$39 years of age, 53 percent of smokers and 28 percent of nonsmokers manifested reduced air flow. This difference is significant ($p < 0.01$). For those $\geqslant$40 years of age, the prevalence of impairment in smokers (71 percent) is not significantly different ($p > 0.5$) from the prevalence in nonsmokers (64 percent). In each smoking category, the prevalence of air flow impairment is significantly higher among older workers ($p < 0.01$).

There were 247 workers who performed both FEV_1 and MMF; 141 had impaired flow shown by one or the other test. Of these 141, 40 or 28 percent were severely impaired (27 had MMF $\leqslant$50 percent of predicted; 2 had FEV_1/FVC $\leqslant$60 percent and 11 had both).

Volume impairment was similar in frequency in smokers and nonsmokers.

Duration of Occupational Exposure

The mean age for the 265 current workers was 37.8 years (range, 19–65 years). Mean ventilatory values are shown in TABLE 5 and the prevalence of air flow impairment in TABLE 6, related to duration of exposure and smoking. With MMF or FEF_{25}, prevalence of impairment increased from 48 percent when exposure was less than 10 years, to 56 percent when exposure was 10–20 years, to 84 percent when exposure exceeded 20 years. This increase in prevalence with progressive duration of exposure was true for smokers and nonsmokers. The difference in prevalence between smokers and nonsmokers narrowed from 23 percent ($p < 0.02$) when exposure was less than 10 years to 11 percent ($p < 0.5$) when exposure exceeded 10 years. Any difference between smokers and nonsmokers cannot be attributed to age, since there is no significant difference in age at any duration of exposure.

For a more conventional measurement of air flow, FEV_1/FVC, the frequency of impairment ($\leqslant$74 percent) among all workers was also high although 10 percent lower than for MMF or FEF_{25}. An increase in prevalence for both smokers and nonsmokers is noted when their exposures exceed 20 years.

Severe flow impairment was more frequent with increasing duration of exposure.

Prevalence of volume impairment was not related to duration of exposure.

The mean age for the 83 past workers was 41.8 years (range, 20–68 years). The findings (TABLE 7) were similar, although prevalence rates for nonsmokers exposed less than 10 years are higher than for current workers. Mean values are not shown because of the small numbers in some categories.

Clinical Findings (TABLE 8)

Since the smoking histories and flow rates for those with "suspect" bronchitis or emphysema were no different, they are included with subjects who were considered to have a "definite" clinical abnormality. In all, 106 or 30.5 percent of

TABLE 3
PREVALENCE OF FLOW IMPAIRMENT BY THREE DIFFERENT TESTS RELATED TO AGE AND SMOKING

Age Group	FEV_1/FVC			MMF* (Percent Predicted)			FEF_{25}/FVC*†		
	Smokers and nonsmokers	Smokers	Nonsmokers	Smokers and nonsmokers	Smokers	Nonsmokers	Smokers and nonsmokers	Smokers	Nonsmokers
<39 yr	61/182‡ (34%)	52/139 38%	9/43 21%	61/132 46%	53/100 53%	8/32 25%	20/46 44%	18/36 50%	2/10 20%
		($p < 0.05$)			($p < 0.01$)				
>40 yr	93/165 56%	78/132 59%	15/33 45%	70/115 61%	56/90 62%	14/25 56%	36/48 75%	30/40 75%	6/8 75%
		($p < 0.1$)			($p > 0.5$)				
All	154/347 45%	130/271 48%	24/76 32%	131/247 53%	109/190 57%	22/57 39%	56/94 60%	48/76 63%	8/18 44%

* Random patients.
† p values are not shown for FEF_{25}/FVC because of the large standard deviation.
‡ The denominator indicates the number of subjects tested in each category.

TABLE 4
PREVALENCE OF FLOW IMPAIRMENT* RELATED TO AGE AND SMOKING: SUMMARY

Age Group	Smokers and Nonsmokers	Smokers	Nonsmokers
		($p < 0.01$†)	
⩽39 yr	85/182 (47%)	73/139 (53%)	12/43 (28%)
		($p < 0.01$‡)	($p < 0.01$‡)
⩾40 yr	115/166 (69%)	94/133 (71%)	21/33 (64%)
		($p > 0.5$†)	
All (mean age 38.8 yr)	200/348 (57.5%)	167/272 (61%)	33/76 (43%)

* By any test.
† Comparing smokers with nonsmokers in the same age group.
‡ Comparing workers ⩽39 years of age with those ⩾40 years of age in the same smoking category.

the workers had positive clinical findings. Of these, 93 percent smoked and 79 percent manifested decreased air flow, while only 21 percent had normal flow rates. It is of interest that 47 percent of subjects with negative clinical histories and physical examinations exhibited decreased air flow when their pulmonary function was tested.

DISCUSSION

Surveys of many different populations have shown prevalence rates for chronic cough and expectoration greater than 20 percent,[6–14] similar to the 30.5 percent of the present VC-PVC workers with clinical findings, the great majority of whom had these symptoms. The smoking habits of these workers and the proportion of symptomatic subjects who smoked (93 percent) are also smiliar to those in the literature.

There is less information available concerning prevalence rates for diminished flow rates than for symptoms. Investigators have often reported mean values for ventilatory tests without indicating what percentage of the population was abnormal.[7,8,13–16] The prevalance rates for VC-PVC workers are higher than the rates in the literature for most other occupational groups. An exception is elderly workers with prolonged exposure to plant fibers. Bouhuys *et al.*[10] studied Spanish hemp workers and found that 61 percent of those between 50 and 69 years of age had FEV_1 values below 80 percent of expected, a prevalence similar to the 67 percent of VC-PVC workers of similar age who had FEV_1/FVC ratios <75 percent. Surveys of the American cotton industry have been made on younger workers with exposures more likely to be less than 20 years; prevalence rates have not been as high as in the Spanish hemp industry. However, 54 percent of the carders studied by Zuskin *et al.*[17] had FEV_1 values less than 80 percent of predicted. In a control population of Spanish farm and marble workers, prevalence rates of impaired air flow were significantly lower than in populations exposed to VC-PVC or vegetable fibers: 12 percent of those 20–69 years of age, 15.6 percent of those 40–69 years of age, and 31 percent of those 50–69 years of age.[10] In a different control group, prisoners and guards (mean age about 43 years), 7.4 percent demonstrated a decreased $FEV_{0.75}$[18] while 10 percent of men in rural Denmark, where cigaret smoking is relatively uncommon, had an $FEV_{0.75}$ less than 2 liters.[19]

The survey of Chilliwack, a small Canadian town with low levels of air pollu-

TABLE 5
MEAN VENTILATORY VALUES IN CURRENT WORKERS RELATED TO DURATION OF EXPOSURE AND SMOKING

Duration of Exposure	$FEV_1/FVC \times 100$		MMF (Percent Predicted)		$FEF_{25}/FVC \times 100$*	
	Smokers	Nonsmokers	Smokers	Nonsmokers	Smokers	Nonsmokers
<10 yr	75.8 ± 6.9† (102)	78.1 ± 6.3 (41)	73.8 ± 23.3 (68)	81.3 ± 19.0 (30)	30.5 ± 11.3 (54)	28.5 ± 15.2 (20)
10–20 yr	74.6 ± 7.3 (64)	74.4 ± 8.1 (13)	72.0 ± 22.9 (49)	87.2 ± 30.4 (10)	25.0 ± 9.4 (27)	25.5 ± 10.5 (4)
>20 yr	70.3 ± 9.6 (35)	74.6 ± 4.6 (8)	59.9 ± 21.4 (19)	78.0 ± 34.7 (4)	22.6 ± 12.3 (21)	22.8 ± 6.9 (5)

* All subjects tested; see TABLE 1.
† ±1 S.D.; number in parentheses is number of subjects tested.

TABLE 6
PREVALENCE OF FLOW IMPAIRMENT IN CURRENT WORKERS RELATED TO DURATION OF EXPOSURE AND SMOKING

Smoking Category	Duration of Exposure		
	<10 yr	10–20 yr	>20 yr
Mean age (yr)			
Smokers	32.1 ± 9.4*	42.1 ± 7.4*	51.9 ± 7.4*
Nonsmokers	29.6 ± 9.4*	42.9 ± 10.1*	50.6 ± 7.2*
All subjects	31.4 (range 19–58)	42.2 (range 31–61)	51.7 (range 39–65)
Decrease in MMF or FEF_{25}/FVC			
Smokers	56/103 (54%)	37/64 (58%)	30/35 (86%)
Nonsmokers	13/42 (31%)	6/13 (46%)	6/8 (75%)
All subjects	69/145 (48%)	43/77 (56%)	36/43 (84%)
Decrease in FEV_1/FVC			
Smokers	45/103 (44%)	28/64 (44%)	24/35 (69%)
Nonsmokers	10/32 (31%)	4/13 (31%)	4/8 (50%)
All subjects	55/145 (38%)	32/77 (42%)	28/43 (65%)

* ±1 S.D.

TABLE 7
PREVALANCE OF FLOW IMPAIRMENT IN PAST WORKERS RELATED TO DURATION OF EXPOSURE AND SMOKING

Smoking Category	Duration of Exposure		
	<10 yr	10–20 yr	>20 yr
Mean age (yr)			
Smokers	37.8 ± 11.8*	45.6 ± 9.3*	59.5 ± 4.5*
Nonsmokers	30.8 ± 7.9*	51.4 ± 10.6*	61.5 ± 2.1*
All subjects	37.1 (range 20–68)	46.7 (range 31–67)	60.2 (range 53–63)
Decrease in MMF or FEF_{25}/FVC			
Smokers	27/46 (59%)	13/21 (62%)	4/4 (100%)
Nonsmokers	3/5 (60%)	2/5 (40%)	2/2 (100%)
All subjects	30/51 (61%)	15/26 (58%)	6/6 (100%)
Decrease in FEV_1/FVC			
Smokers	21/46 (46%)	10/21 (48%)	2/4 (50%)
Nonsmokers	2/5 (40%)	2/5 (40%)	2/2 (100%)
All subjects	22/51 (45%)	12/26 (46%)	4/6 (67%)

* ±1 S.D.

TABLE 8
CORRELATION OF CLINICAL FINDINGS WITH SMOKING AND FLOW IMPAIRMENT

Workers with signs and/or symptoms of lung disease	106/348 (30.5%)
Workers with signs and/or symptoms who smoked	99/106 (93%)
Workers with signs and/or symptoms who had reduced flow	84/106 (79%)
Workers with signs and/or symptoms who had reduced flow and smoked	79/84 (94%)
Workers with signs and/or symptoms who had normal flow	22/106 (21%)
Workers with signs and/or symptoms who had normal flow and smoked	20/22 (91%)
Workers with neither signs nor symptoms of lung disease	242/348 (69.5%)
Workers with neither signs nor symptoms who smoked	174/242 (72%)
Workers with neither signs nor symptoms who had reduced flow	114/242 (47%)

tion, showed that 12.6 percent of the men had severe obstructive lung disease. About 70 percent of these had an $FEV_1/FVC \leqslant 60$ percent, for a prevalence of severe impairment of about 9 percent.[13] The most recent survey, of English civil servants $\geqslant 40$ years of age, revealed 26.4 percent to have an $FEV_1/FVC < 75$ percent.[20] While this figure is higher than the others cited, it is considerably lower than the 56 percent of VC-PVC workers of comparable age (TABLE 3).

Previous surveys of occupational groups have generally employed the $FEV_{0.75}$, FEV_1, or peak flow rate. A more sensitive test was desired for the present investigation, one which would reflect early changes in the small airways, at a time when flow impairment is "silent." Only two types of test can be used to survey large numbers of subjects for flow impairment in the small airways: the closing volume and measurements of air flow at low lung volumes. The former requires inhalation of a gas other than ambient air and a specific gas analyzer. The respiratory maneuver is more complicated and time must be allowed for clearance of the gas before the test can be repeated. In addition, uninterpretable tests are obtained in a certain percentage of subjects.[21]

The tests selected for the present study were therefore the MMF and FEF_{25}, which measure flow at lower lung volumes and reflect obstruction in the small airways and/or diminished elastic recoil.[4,22,23] Both processes are involved in chronic obstructive lung disease. These tests are more sensitive than the $FEV_{0.75}$, FEV_1, or peak flow rate, but are as easily performed and repeated.[24–26]

The flow-volume curve has been widely used to detect work-related acute changes in the small airways in workers exposed to such different materials as toluene diisocyanate[25] and cotton dust.[22] Changes in the shape of the curve or in flows at or below 50 percent of FVC were much more marked than changes in FVC or FEV_1 and were most closely related to symptoms of chest tightness ("Monday morning dyspnea"). A smaller percentage of workers who demonstrated only increased airway resistance on body plethysmography were felt to be large airway responders. The symptomatic small airway responders are most likely to develop chronic irreversible airway obstruction.

The greater sensitivity of the tests used in the present study, however, does not account for the high rates of impairment detected. The most commonly employed test, the FEV_1, was reduced in 45 percent of all workers, a higher prevalence than previously reported. In an investigation of male bank employees $\geqslant 40$ years of age, Bower[27] noted that 19 percent had a diminished MMF, compared to 61 percent of VC-PVC workers of the same age. Indeed, the prevalence of air flow impairment in the present population would have exceeded 57.5 percent if all subjects had performed flow-volume curves, since impairment was more likely to be detected by the FEF_{25} than by the MMF, especially in older workers (TABLE 3).

To gain further insight into the significance of the flow impairment detected, we applied the criteria for severe abnormality ($FEV_1/FVC \leqslant 60$ percent; MMF $\leqslant 50$ percent of predicted) utilized at the clinical Pulmonary Function Laboratory of The Mount Sinai Hospital. More than one-quarter of the workers with diminished air flow were severely impaired. The prevalence of severe impairment increased with progressive exposure.

In any investigation of air flow, cigaret smoking must be considered. In most previous studies, the effects of cigaret smoking predominated over any effect attributable to atmospheric pollution or occupational exposure. As stated by Ferris and Anderson[7] in their comprehensive survey of Berlin, New Hampshire, a city selected because its major industry is a pulp mill, "the smoking varia-

ble is so strong it overwhelms the possible effect of atmospheric pollution. Surveys of non-smokers and never-smokers may have to be undertaken to study the effect of atmospheric pollution and occupational exposure as causative factors in chronic nonspecific respiratory disease."

The present investigation demonstrated a high prevalence of air flow impairment which cannot be attributed to smoking. Prevalence in nonsmokers was 36.4 percent when occupational exposure to VC-PVC was less than 10 years, 42 percent when exposure was between 10 and 20 years, and 80 percent when exposure exceeded 20 years. The last is virtually the same rate as for smokers exposed more than 20 years (TABLES 6 and 7). The same trend is shown with increasing age. Unlike younger workers, when smokers and nonsmokers $\geqslant 40$ years of age are compared, prevalence rates of air flow impairment are not statistically different (TABLES 3 and 4).

We did not find a significant prevalence of volume or "restrictive" impairment of the type noted with exposure to mineral dusts like asbestos, talc, or beryllium. It is of interest that isolated cases of restrictive pulmonary impairment have been noted with exposure to VC-PVC. One such case was presented at the discussion of The Working Group on the Toxicity of VC-PVC. Another case was described in the Hungarian literature.[2] Foreign body granulomas, fibrosis, and particles resembling PVC were found on lung biopsy after only 1 year of exposure.

The etiologic significance of our findings remains unclear. Levels of VC and PVC may be higher in the plant whose workers we studied, since drying and bagging are done in an enclosed space. In addition, many of the workers have been occupationally exposed to agents other than VC and PVC and Niagara Falls is a heavily industrialized city which may have inordinate levels of atmospheric pollution. Surveys of other populations in the same city will be necessary to elucidate the latter point. If exposure to VC and/or PVC is causally related to air flow impairment, we do not know which substance is more pathogenic. The fine dust of the polymer might be more likely to concentrate in and damage the small airways.[2] This dust, and other small respirable particles, perhaps from tobacco smoke, may also serve as carriers for molecules of a monomer gas to settle in these airways.

SUMMARY

To determine whether occupational exposure to vinyl chloride gas and polyvinyl chloride dust is associated with changes in pulmonary function, spirometry and maximum expiratory flow-volume curves were obtained in 348 workers in a VC polymerization plant. The major finding was diminution in air flow in 200 workers (57.5 percent). This abnormality correlated with age and duration of exposure. A relationship with smoking was noted only in younger workers with exposures of less than 10 years. When age exceeded 40 years or exposure 20 years, prevalence of this impairment was similar in smokers and nonsmokers, suggesting that occupational or other environmental factors were operative.

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