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ABSTRACT A preliminary epidemiological study has been carried out to investigate a report that some men working in a factory manufacturing polyvinylchloride (PVC) had abnormally low values of the single breath diffusing capacity for carbon monoxide (T_LCO). All 265 present and past employees of the PVC factory were studied, together with 219 men from the workforce of a nearby foundry. Each man's T_LCO was measured and a smoking history and detailed occupational history obtained. The distribution of standardised T_LCO results from all persons examined was symmetrical and did not indicate an unexpectedly high proportion of men with clinically important impairment of T_LCO . The results of a case-control study showed that, having allowed for age, height, weight, and smoking habit, T_LCO was associated with a history of working in the PVC factory before 1975 (when levels of vinylchloride monomers (VCM) were much higher than subsequently), and slightly associated with working in jobs where exposure to VCM was likely to have been highest. The men with low T_LCO also tended to have smoked more heavily than controls. The relative importance of occupational factors and smoking in relation to low T_LCO is not clear, but the results give some support to the hypothesis that work in the PVC factory before 1975 entailed exposure to a substance that caused impairment of lung function in a small number of men.

The management and occupational physician of a factory making polyvinylchloride (PVC) had become concerned over an apparent excess in their workforce of men with impairment of the single breath transfer factor for carbon monoxide (T_LCO). The present study was planned to determine whether there was such an excess of men with low values of T_LCO in the workforce, and to make a preliminary assessment of whether low T_LCO might be related to occupational factors.

The factory had been in operation since 1969 and produced PVC powder from vinylchloride monomer gas (VCM). All men who had worked at the factory, whether or not they were currently employed there, were invited to participate in the study. A sample of men working in a nearby foundry were also invited to participate; they had been exposed to the same environmental conditions outside the workplace and were included in order to augment the number of men in the study who had not been exposed to possible hazards in the PVC factory.

Methods

SELECTION OF SURVEY POPULATION

All 177 men currently employed at the PVC factory were invited to take part and attempts were made to trace and invite all the 263 former employees. At the foundry, the study was confined to 285 men selected randomly from the 1085 current male employees. The number of men at the foundry aged under 25 was limited to 15 to take account of a disproportionately large number of young men in the foundry population compared with the PVC workers and to provide a group of similar size to the 13 PVC workers of this age. Apart from this, selection did not take account of age.

MEDICAL SURVEY

The medical survey team visited the factories and recorded a full occupational history since leaving school for each man. Trained personnel using a questionnaire which was a modified version of the Medical Research Council questionnaire of respiratory symptoms¹ recorded details of each man's smoking history. Additional questions were related to age of starting smoking and the number of

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cigarettes smoked during a man's maximum smoking period.

Measurements of single breath gas transfer factor for carbon monoxide were carried out on all men using the breathholding method² based on the modified Krogh technique (transfer test B; P K Morgan Ltd, Chatham, Kent). The mean of two measurements was used in the subsequent analysis. All PVC factory employees had forced expiratory volume in one second (FEV₁) and forced vital capacity (FVC) measured using an electronic dry rolling seal spirometer (Ohio 800). The best of three technically satisfactory measurements was used for the analysis. Approval was not obtained for FEV₁ and FVC measurements in the foundry workers.

METHODS OF ANALYSIS

Analysis of data from the total survey population

The data were studied initially by summary descriptive statistics and by multiple linear regression analysis of lung function taking into account age, height, weight, and smoking habit. Men were assigned to one of three smoking categories: lifelong non-smoker, current smoker, and ex-smoker. The two smoking groups included smokers of pipes, cigars, and hand-rolled cigarettes but the majority smoked manufactured cigarettes.

In the regression model used for both T_LCO and FEV₁, different intercepts and age slopes were allowed for the three smoking groups, non-smokers, current smokers, and ex-smokers. This means that the estimated effects of age were not constrained to be the same necessarily in the three smoking habit groups.

The relation between a man's observed and predicted lung function values was expressed as a standardised residual (SR). This is defined by the equation:

$$SR = \frac{(\text{observed value} - \text{value predicted from fitted equation})}{(\text{estimated standard deviation of the prediction})}$$

The distribution of FEV₁ and T_LCO SR values of the whole population was examined.

Case-control study

For each lung function variable, those men with the largest negative SR value were chosen as cases. Two groups of controls were selected randomly, firstly, from those men whose SRs were clustered around zero ("average" controls) and, secondly, from those with largest positive SRs ("healthiest" controls). Two groups were chosen because men with average values may have included some whose lung function had been slightly affected by noxious influences, whereas those with very high values were least likely to have been affected by noxious influences but

Table 1 Classification of all jobs at PVC factory into six broad occupational groups.

Broad occupational group	Jobs included in group
1	All men working in reactors 1 and 2*
2	Dryer room B operators†
3	Dryer room Lead, A and A B operators
4	Warehousemen, maintenance staff, laboratory staff, and drivers‡
5	General staff who visit plant, such as shift supervisors and foremen
6	Management and office staff

*Men most likely to have been exposed to high concentrations of VCM in the past.

†Men engaged in the bagging of PVC and probably exposed to higher concentrations of dust than other workers in the dryer buildings.

‡Men potentially exposed to all raw materials and products

might include men who were highly resistant to these influences.

Cases were initially compared with the rest of the survey population in order to identify any systematic differences in age, smoking habit, and employment status. Then the occupational and smoking histories of cases and controls were examined and compared. Smoking histories were classified as they were for the total population, but additional information about the number of cigarettes smoked and the age of starting smoking was analysed in the case-control study. Broad occupational categories were defined for the PVC factory (table 1) and for the foundry, and the total number of years spent by cases and controls in each occupational category was calculated. Additional information was available for PVC employees in relation to exposure to emulsion polymer (which has a smaller particle size than suspension polymer and which was manufactured at the factory between 1971 and 1974) and employment in the factory before 1975 when levels of VCM were much higher than the currently permitted levels. From the full occupational history the number of years spent in potentially "noxious" industries (such as coal, steel, chemicals, and a miscellaneous group of industries in which exposure to noxious compounds might have occurred) was recorded.

In the analysis Fisher's exact test, the chi-squared test for 2 × 2 contingency tables, and the chi-squared test for linear trend were used where appropriate.

Results

A total of 488 men was seen, consisting of 165 current PVC factory employees (93% of those who were asked to participate), 102 PVC former employees (39% of those invited), and 221 foundry employees (78% of those invited). Four men (two PVC and two foundry) were excluded from the

Table 3 Features of FEV₁ cases, controls, and total survey population. Mean (and standard deviations) of age, height, weight, T_{LCO}, FEV₁, and FVC

No of men	T _{LCO} groups			Total survey population (264)
	Cases (30)	Controls (average) (30)	Controls (healthiest) (30)	
Age (y):				
Mean	43.3	41.3	42.1	42.2
(SD)	(11.0)	(12.5)	(12.0)	(11.8)
Height (cm):				
Mean	176.0	174.5	175.9	174.3
(SD)	(7.4)	(6.6)	(8.0)	(7.1)
Weight (kg):				
Mean	82.2	78.4	80.4	80.4
(SD)	(13.3)	(10.1)	(11.5)	(12.3)
FEV ₁ (l):				
Mean	2.7	3.9	4.5	3.7
(SD)	(0.7)	(0.7)	(0.8)	(0.9)
FVC (l):				
Mean	4.1	5.1	5.9	4.9
(SD)	(0.9)	(0.8)	(0.9)	(1.0)
T _{LCO} (ml/min mm Hg):				
Mean	29.1*	32.3	31.3	30.5†
(SD)	(6.8)*	(6.0)	(6.5)	(6.1)*

*Value based on 29 observations.

†Value based on 262 observations.

had worked in more than one type of job and in more than one broad occupational category during their employment with the companies. More cases than controls had worked in jobs in category 1 (on or near the reactors) at the PVC factory: 11 of 31 cases (35%) had worked in this category compared with 10 of 62 controls (16%) and this disproportion is significant at the 7% level (table 4). No suggestive differences were seen in the pattern of employment of FEV₁ cases and controls.

More cases than controls had worked at the PVC

Table 5 Smoking habits of T_{LCO} cases, controls, and total survey population. Number of men in each smoking category with percentages in parentheses

	Non-smoker	Current smoker	Ex-smoker	Total
Cases	3 (9.7)	20 (64.5)	8 (25.8)	31
Controls (average)	4 (12.9)	15 (48.4)	12 (38.7)	31
Controls (healthiest)	7 (22.6)	15 (48.4)	9 (29.0)	31
Total survey population	109 (22.5)	234 (48.4)	141 (29.1)	484

factory before 1 January 1975, when levels of vinylchloride were much higher than at present. Seventeen of the 19 T_{LCO} cases who had worked at the PVC factory had been employed before 1975 whereas only five of the 15 healthiest controls and 11 of the 13 average controls had been. The difference between cases and healthiest controls was significant ($p < 0.002$), and the increase in the proportion of men with pre-1975 employment in the PVC factory for the three groups over healthiest controls, average controls, and cases was also statistically significant ($p < 0.001$). Analysis of the duration of employment of men within different age groups showed that pre-1975 working was seen in both younger and older men. A similar analysis of FEV₁ cases and controls and foundry T_{LCO} cases failed to show any significant differences in relation to working before 1975. These findings suggest that some factor or factors associated with working at the PVC factory before 1975 had caused impairment of T_{LCO} in some men.

There was no difference in the numbers of T_{LCO} or FEV₁ cases and controls who had been exposed

Table 4 Numbers of men who had spent some time in each occupational group. (Mean time (years) spent in each occupational group)

	No of men	Occupational groups												
		1	2	3	4	5	6	7	8	9	10	11	12	13
Cases:														
PVC workers	19	11 (2.7)	11 (10.6)	4 (7.6)	4 (9.0)	2 (9.7)	—	1 (7.0)	—	—	5 (5.6)	—	1 (1.4)	—
Foundrymen	12	—	—	—	—	—	—	4 (7.3)	2 (3.0)	5 (12.3)	7 (4.0)	2 (3.2)	2 (11.4)	1 (1.0)
Average controls:														
PVC workers	13	4 (7.0)	7 (10.7)	1 (6.8)	5 (6.0)	1 (12.3)	—	—	—	—	—	—	—	—
Foundrymen	18	—	—	—	—	—	—	3 (4.6)	5 (16.1)	1 (30.4)	9 (9.4)	1 (7.4)	5 (10.6)	1 (2.5)
Healthiest controls:														
PVC workers	15	6 (13.0)	11 (11.0)	1 (10.8)	2 (7.3)	2 (13.3)	1 (1.7)	—	—	—	2 (4.0)	1 (0.5)	—	—
Foundrymen	16	—	—	—	—	—	—	5 (13.4)	3 (4.5)	3 (12.7)	8 (12.5)	—	6 (11.8)	—

Note: Occupational groups 1-6 refer to PVC factory (see table 1) and 7-13 jobs at the foundry—that is "work on or near the turntable", sand work and shot-blasting, 9 grinding and welding, 10 general jobs, 11 painting and dipping, 12 casting work, 13 fettling.

that both were important. The men with the lowest T_LCO values selected as cases were not all necessarily suffering from lung disease but among them were 15 men whose T_LCO was less than 70% of the value predicted by published normal values, a level which probably indicates the presence of disease. In eight of the 19 cases who had worked at the PVC factory the low T_LCO was an isolated abnormality, a pattern unlikely to be the result of damage from smoking and which is usually associated with interstitial lung disease or disturbance of pulmonary perfusion.

Reports of both animal and clinical studies give further support to the suggestion that exposure to VCM might have been an important causative factor. Animal studies have shown that exposure to high levels of VCM leads to pulmonary fibrosis, the changes being most severe in the animals which had been exposed for the longest time.⁹ There have been isolated case reports of individuals with interstitial lung disease who had been employed in the manufacture of PVC and who had, therefore, been exposed to VCM.¹⁰ Hunter *et al* described six such workers, three of whom had died from liver disease related to VCM exposure¹¹; none of the six had respiratory symptoms, three had abnormal chest x ray films, and one an abnormal T_LCO , but the lung histology from all six men showed a similar picture with the presence of an inflammatory interstitial infiltrate.

Diligent attempts were made to contact all men who had worked at the PVC factory but response was low (39%). If the men not examined had included either an excess or deficiency of men with impaired gas transfer factor compared with the population examined then the analysis of the distribution of values among the population seen would be unrepresentative to that extent.

We conclude that this preliminary study has shown no evidence that current working conditions in either factory have caused impairment of lung function but it does give some support to the hypothesis that work in the PVC factory before

1975 entailed exposure to a substance that caused impairment of lung function in a small number of men. Further work including clinical studies of affected men would be necessary to characterize this impairment and to explore more fully the relations with occupational and other factors.

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