-486-

BIO-MEDICAL RESEARCH
DOCUMENT DESCRIPTION FORM

R&S 114432

Duplicate in all cards: →

63 – 68	69 – 76	77 – 78
1981	0000~~486~~	VC
year as-1961-	File number [Right justify [Numeric only]	Sub-Index Code

Author(s), as Last Name FS (No Punctuation) and
coden for journal as JAMA preceeded by one blank space

1 – 20	21 – 40	41 – 60	61 62
SCUTAR, CA	COPLAND, LH	THORNLEY, PE	11
HURLEY, JF	OTTERY, J	ADAMS, W.G.F.	12
BENNETT, B			13

Title of Report; end with space-hyphen-hyphen-space. Follow with Index Terms, separated from each other with comma-space. Avoid other punctuation; do not abbreviate.

1 2	61 62
	21
EPIDEMIOLOGICAL STUDY OF RESPIRATORY DISEASE	22
IN WORKERS EXPOSED TO POLYVINYL CHLORIDE DUST	23
-- ICI, EDINBURGH, ENGLISH, BETHESDA, LUNG	24

Source (Journal, Vol., Number, Pages, Date)

1 2	61 62
THORAX 35, 644-652, 1980	31
	32

Brief Summary

1 2 10	61 62
SUMMARY:	61
	62
	63
	64

Torkelson
0000 ~~[illegible]~~
0030 ~~[illegible]~~ 486

EPIDEMIOLOGICAL STUDY OF RESPIRATORY DISEASE IN WORKERS EXPOSED TO POLYVINYLCHLORIDE DUST

BY

C A SOUTAR, L H COPLAND, P E THORNLEY, J F HURLEY, J OTTERY, W G F ADAMS, and B BENNETT

Reprinted from THORAX
September 1980 *Vol* 35 *No* 9 *p* 644

BRITISH MEDICAL ASSOCIATION
TAVISTOCK SQUARE LONDON
WC1H 9JR

Thorax, 1980, 35, 644–652

Epidemiological study of respiratory disease in workers exposed to polyvinylchloride dust

C A SOUTAR, L H COPLAND, P E THORNLEY, J F HURLEY, J OTTERY, W G F ADAMS, AND B BENNETT

From the Institute of Occupational Medicine, Edinburgh, and Imperial Chemical Industries Limited

ABSTRACT The respiratory health of workers exposed to polyvinylchloride (PVC) dust has been investigated in 818 men sampled from the work force of a factory manufacturing PVC. In a cross-sectional survey, the lung function and prevalences of respiratory symptoms and chest radiographic abnormalities were compared with estimates of individual PVC dust exposures based on detailed occupational histories and current measurements of respirable PVC dust. Complaints of slight exertional dyspnoea were associated with PVC dust exposure, though age and smoking effects were much stronger. The forced expired volume in one second (FEV_1) and forced vital capacity (FVC) were inversely related to dust exposure after age, height, and smoking effects had been taken into account. This effect was seen principally in cigarette smokers, and there was suggestive evidence that PVC dust exposure and cigarette smoking interacted in the reduction of FEV_1 and FVC. Gas transfer factor was not related to dust exposure. The chest radiographs were read according to the ILO U/C classification by three experienced readers. One reader recorded a low prevalence of small rounded opacities, and these were not related to age or dust exposure. Another reader recorded a higher prevalence of small rounded opacities category 0/1 or more, and these were related to age but not to dust exposure. The third reader recorded the highest prevalence of small rounded opacities (though none greater than category 1/1), and these were independently related both to age and to PVC dust exposure, indicating an effect of PVC dust on the appearances of the chest radiograph. These appearances were so slight that only the higher sensitivity of this reader in the interpretation of profusion of small rounded opacities on the ILO U/C scale enabled detection of this effect of PVC dust. In conclusion, exposure to PVC dust is associated with some deterioration of lung function, slight abnormalities of the chest radiograph, and complaints of slight dyspnoea. The mean decline in FEV_1 associated with the average dust exposure experienced in the study was small, though some of the men with higher dust exposures may have suffered clinically important loss of lung function as a result of their occupation.

The dust produced during the the manufacture of polyvinylchloride (PVC) includes a large proportion by number of small particles of respirable size.[1,2] Administration of PVC dust to animals has been reported to cause inflammatory changes of the bronchioles and alveoli, including a proliferation of histiocytes and granulomatous lesions,[3,4] and PVC formulations have been found to have cytotoxic effects in vitro.[5-7] These effects were caused in part by the plasticisers, stabilisers, and other additives in the PVC, and there is some evidence that the in vitro toxicity of PVC dust is related to the presence of surfactant in the formulation.[8,9]

Address for reprint requests: Dr CA Soutar, Institute of Occupational Medicine, Roxburgh Place, Edinburgh EH8 9SU.

Case reports[10,11] have described pathological changes in the lungs of workers exposed to PVC dust. In several surveys of PVC workers increase of respiratory symptoms, abnormalities of lung function and of the chest radiograph have been described, although these findings have been difficult to evaluate, principally because of lack of satisfactory control groups, failure to take adequate account of the effects of age, cigarette smoking, or general atmospheric pollution, and lack of clarity in descriptions of radiographic readings.[2,12-15]

Methods

STUDY POPULATION

The sample to be studied was selected in January 1979 from 1501 currently employed men, 339 pensioners (men who received a pension from the manufacturer, most of whom were over 60 years of age) who had retired since 1 January 1967, and 468 men leaving for other reasons since that date.

Men were selected for study according to broad categories of cumulative dust exposure derived from factory records and preliminary estimates of dustiness based on inspection of the plant and measurements of size ranges of typical PVC dusts. The sampling scheme aimed to include all men with heavier dust exposures, and lesser proportions of those with lighter exposures. One hundred and fifty-six men with high or moderate dust exposures did not attend for survey, and were replaced by reserves drawn from moderately exposed groups.

Finally 818 men were studied, comprising 663 currently employed men, 98 pensioners, and 57 men who had left for reasons other than retirement ("leavers"). Single breath gas transfer for carbon monoxide was measured in 332 men sampled proportionally but randomly from each exposure category.

ENVIRONMENTAL SURVEY

Current personal exposures to respirable PVC dust were measured by occupation in each plant in which PVC was manufactured or processed. Preliminary estimates of dustiness were based on subjective observation by the sampling team and on particle size measurements of typical suspension and emulsion PVC dusts, and the major sampling effort was directed towards the apparently more dusty occupations in the drying, packing, and mixing areas.

One hundred and thirty reliable personal samples of respirable PVC dust were obtained from men in 44 different occupations for full shift periods on Sartorius cellulose ester membrane filters (type 11301), diameter 37 mm, pore size 8·0 μm, inserted into a Casella Simpeds 70 cyclone.[16] This device samples a "respirable" fraction of airborne dust in accordance with the Johannesburg Convention,[17] including 100% of all particles with an equivalent aerodynamic diameter of 1 μm, 50% of those of 5 μm, and none greater than 7 μm.

MEDICAL SURVEY

A full occupational history was recorded, and the Medical Research Council Questionnaire of Respiratory Symptoms[18] was administered by a trained clerk.

Forced expiratory volume in one second (FEV_1) and forced vital capacity (FVC) were measured using a modified Gaensler spirometer.[19] The best of three measurements was used for the analysis.

Single breath transfer factor for carbon monoxide (T_{LCO}) was measured by the breathholding method[20] based on the modified Krogh technique (Transfer test B, PK Morgan Ltd., Chatham, Kent). Effective alveolar volume (V_A) was measured by helium dilution in the same single breath, and used in the calculation of T_{LCO} and K_{CO}. The means of two observations were used in the analysis of these measurements. A full-size postero-anterior chest radiograph was taken by a standard technique (95—120 kV).

The chest radiographs were read independently using the ILO U/C International Classification of Radiographs of Pneumoconioses[21] by three readers highly experienced in this work. The readers had all been shown previously t produce readings that correlated with measurements of dust exposure in coalminers and to be highly consistent in their readings when presented with the same films on separate occasions. They did, however, represent a range of interpretation of profusion of small opacities recorded using the ILO U/C scale, and were known to differ consistently from each other in the prevalences of small rounded opacities they recorded.

PVC DUST INDEX

Every occupation within the population under study was allotted a PVC dust concentration on the basis of the measured current dust levels. Sixty-six such job/dust categories were derived from the measurements made and from knowledge of the factory conditions.

A "dust index" was derived from the current dust measurements and the occupational history such that the current dust levels in each of a man's occupations in the plastics factory was multiplied by the years he had spent in that occupation, and this figure added to the figures derived from his other occupations in the factory.

STATISTICAL METHODS

The data were studied initially by cross-tabulations, graphical methods, and summary descriptive statistics. Multiple linear regression analyses of the lung function results were carried out, with subsequent examination of residuals. The radiographic and respiratory symptoms results were studied by maximum likelihood logistic analysis.[22]

Results

ENVIRONMENTAL SURVEY

Respirable dust levels were highest in the older plants and those making polymer by the emulsion method. The highest mean average respirable dust exposure for any occupation over a shift was 2·88 mg/m^3 (SD$\pm$1·84). The distribution of calculated dust indices (years$\times$mg/m^3) for the 818 men studied in the medical survey is shown in fig 1.

MEDICAL SURVEY

Features of the population of 818 men are set out in tables 1 and 2.

It was noted in preliminary analysis that the number of years worked at the PVC works or work in an outside industry in which noxious materials were used were of trivial importance in explaining the prevalence of symptoms, lung function and radiographic abnormality, after index of dust exposure, age, and smoking habit had been taken into account.

Respiratory symptoms

Analysis of respiratory symptoms was based on the answers to the questionnaire.

Two hundred and fifteen men (26%) admitted to dyspnoea on exertion grade 1 ("shortness of breath when hurrying on level ground or walking up a slight hill"). Prevalence was approximately three times higher in the smoking groups (32% in cigarette smokers) than in the non-smokers (10%). A strong age effect was also apparent, prevalence approximately doubling for every 13 years of age in this population. A dust effect was indicated ($p=0{\cdot}054$) after adjustment for age and smoking, and this effect was clear in current cigarette smokers ($p<0{\cdot}02$, 10 dust index units increased the estimated prevalence by a factor of about 20%) after allowing for age and lifetime cigarette consumption. The dust effect was not demonstrated in the other smoking categories, though these differences between smoking categories could have arisen by chance ($p<0{\cdot}5$).

Table 1 *Features of 818 men studied, according to currently employed, pensioner, or other leaver status. Dust index is expressed in years $\times$ mg/m^3, but does not represent actual dust exposure, since only current dust levels are known*

	Current workers	*Pensioners*	*Leavers*
Number	663	98	57
Mean age (yrs)	44·2	63·4	43·2
(SD)	(10·8)	(7·1)	(10·2)
Mean height (cm)	173·0	170·2	171·2
(SD)	(6·5)	(5·4)	(6·2)
Mean weight (Kg)	77·7	75·6	77·4
(SD)	(10·5	(10·8)	(13·5)
Mean dust index	13·39	14·23	4·86
(SD)	(12·84)	(11·86)	(6·69)
Years at the plant	14·34	16·63	5·46
(SD)	(8·48)	(8·06)	(5·48)
Mean FEV$_1$ (l)	3·54	2·43	3·53
(SD)	(0·83)	(0·73)	(0·72)
Mean FVC (l)	4.62	3·41	4·54
(SD)	(0·88)	(0·78)	(0·80)
Mean FEV$_1$/FVC	0·76	0·70	0·78
(SD)	(0·08)	(0·11)	(0·06)

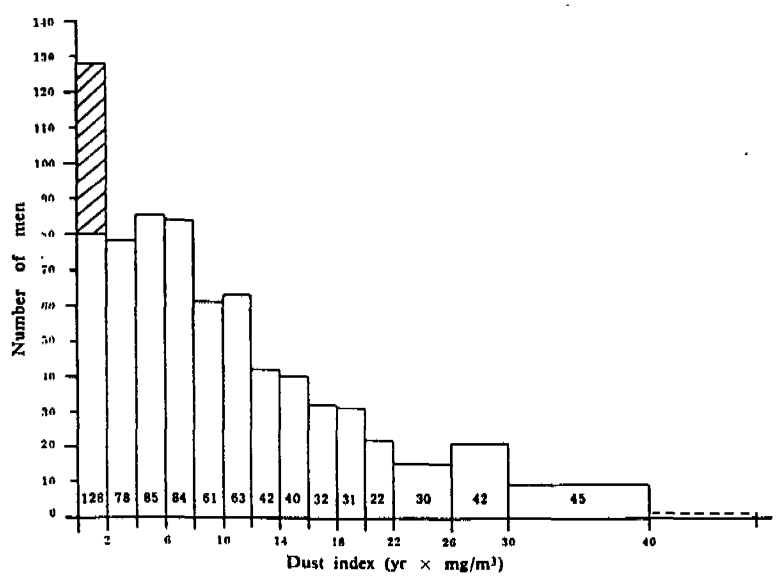

Fig 1 *Frequency of dust indices.* ▨ *= number of men with dust exposure = 0.*

Table 2 *Numbers of men and (mean dust indices) of 818 men grouped by age and smoking category. Units of dust indices are years × mg/m³*

	Age groups (yr)						
	< 35	*35–44*	*45–49*	*50–54*	*55–59*	*60 +*	*All*
Non-smokers	50 (4·1)	41 (6·7)	16 (8·2)	16 (12·3)	5 (15·4)	20 (15·2)	148 (8·0)
Cigarette smokers	65 (5·2)	97 (12·0)	60 (16·4)	60 (16·6)	55 (18·4)	41 (16·9)	378 (13·7)
Other smokers	3 (3·0)	11 (14·7)	12 (13·8)	9 (19·4)	12 (19·1)	11 (11·7)	58 (15·0)
Ex-smokers	37 (6·6)	48 (12·9)	35 (14·5)	41 (16·5)	31 (16·3)	42 (18·1)	234 (14·2)
All	155 (5·2)	197 (11·3)	123 (14·5)	126 (16·2)	103 (17·7)	114 (16·5)	818 (12·9)

No relationships were demonstrated between dust index and history of chronic cough or sputum, asthma or history or acute chest illness.

Forced expired volume in one second

Preliminary analysis indicated different rates of loss of FEV_1 because of age between the smoking categories, and different mean levels of FEV_1 according to current, pensioner, or leaver employment status. These differences were taken into account in the regression model, which also took account of height, weight, and lifetime cigarette consumption.

Within this framework index of dust exposure was significantly inversely related to FEV_1 ($p<0{\cdot}025$) (table 3). Neither the estimated size nor the significance of the regression with dust index was seriously altered when alternative models of age and smoking were examined.

More detailed analysis examined whether the effect of dust index varied according to smoking category and job status groups (current workers, pensioners, or leavers). Though the observed differences in dust effect in these groups could have arisen by chance ($p \simeq 0{\cdot}45$) the numbers of men in some of the subgroups are small, and the pattern of positive and negative effects suggested an interaction between dust effect, current employment at the factory, and cigarette smoking (table 4). The dust effect was seen principally in currently employed cigarette smokers.

After taking into account the effects of age, height, weight, and smoking habits (the model in table 3), the overall loss of FEV_1 associated with one dust index unit (years × mg/m³) was estimated as 0·0041 litres. This would be equivalent to a loss of 53 ml of FEV_1 for the mean dust index, additional to the estimated losses caused by age and smoking (26 ml per year in non-smokers, 39 ml per year for cigarette smokers plus an additional 5·6 ml per year for each packet of cigarettes smoked per day throughout the year).

In currently employed cigarette smokers considered separately (the model in table 4), the loss associated with dust index was estimated as 84 mls of FEV_1 for similar exposure, additional to the loss caused by smoking and age. The mean FEV_1 loss in this group of men in relation to high dust exposure (40 dust index units or more, experienced by only 4·3% of all the men) was estimated at 260 ml.

Table 3 *Regression of FEV_1. Different intercepts for employment and smoking categories allowed but not shown*

Variable		*Regression Coefficient*	*p*
Height (cm)		0·0434	< 0·0001
Weight (kg)		—0·0032	< 0·2
Age (yr)	non-smokers	—0·0260	< 0·0001
	ex-smokers	—0·0350	< 0·0001
	other smokers	—0·0489	< 0·0001
	cigarette smokers	—0·0392	< 0·0001
Lifetime cigarette consumption (1000 packs)		—0·0154	< 0·0001
Dust index (years x mg/m³)		—0·0041	< 0·025

Forced vital capacity

A similar sequence of analysis to that for FEV_1 was followed, with qualitatively similar results. There was a negative effect of dust index on FVC ($p<0{\cdot}1$).

Further analysis of dust effect in the smoking and job category subgroups again showed a significant adverse dust effect in cigarette smokers

Table 4 *Regression coefficients for dust index against FEV_1. Expansion of model of regression for FEV_1 illustrated in table 3. Coefficients and significance of concomitant variables changed little from the model described in table 3. NS = not significant at the 10% level*

	Cigarette smokers	*Other smokers*	*Ex-smokers*	*Non-smokers*
Current workers	—0·0065	—0·0023	—0·0024	—0·0034
(number)	(312)	(47)	(185)	(119)
	(p < 0·02)	NS	NS	NS
Leavers	—0·0278	0·0468	0·0246	0·0118
(number)	(25)	(3)	(13)	(16)
	(p < 0·08)	NS	NS	NS
Pensioners	—0·0018	—0·0154	—0·0004	0·0179
(number)	(41)	(8)	(36)	(13)
	NS	NS	NS	NS

Table 5 *Prevalence of categories of small opacities found by three readers in 818 chest radiographs. Radiographs in which both rounded and irregular opacities were found are also represented here in the rounded and irregular categories*

Reader	*Small rounded opacities*		*Small irregular opacities*		*Both rounded and irregular opacities*
	Category 0/1 or more	*Category 1/0 or more*	*Category 0/1 or more*	*Category 1/0 or more*	*Category 0/1 or more*
3	18 (2·20%)	2 (0·24%)	32 (3·91%)	7 (0·36%)	4 (0·49%)
15	4 (0·49%)	2 (0·24%)	53 (6·48%)	45 (5·62%)	0 (0·00%)
17	50 (6·11%)	10 (1·22%)	29 (3·55%)	8 (0·98%)	4 (0·49%)

currently working at the factory ($p<0.03$). The observed differences in dust effect in these groups could easily have arisen by chance, but an interaction between dust effect, current employment, and cigarette smoking was suggested, broadly similar to that for the FEV_1.

Other measurements of respiratory function
The FEV_1/FVC ratio, TLCO, KCO, and VA were not significantly related to index of PVC dust exposure, nor was any sizeable effect indicated.

Chest radiographs
Small rounded opacities The anticipated differences between readers in interpretation of small opacities were apparent (table 5). Reader 17 recorded the greatest prevalence of small rounded opacities: 50 radiographs (6·1%) with category 0/1 or more, 10 (1·2%) with category 1/0 or more, the latter consisting of six radiographs with category 1/0 and four with category 1/1. Among these 50 radiographs, there was a strong association between classification by reader 17 as category 1/0 or more and classification by either reader 3 or 15 as small rounded opacities category 0/1 or more (chi-square test, $p<0.001$), confirming that inter-reader differences in interpretation of small rounded opacities were differences of degree, rather than classification of unrelated appearances.

The readings for readers 3 and 17 showed clear relationships between prevalence of small rounded opacities and age ($p<0.002$ and $p<0.001$ respectively). The observed data are set out in fig 2. For reader 3, after age had been taken into account, there was no relationship with dust exposure ($p=0.83$). For reader 17 there was a strong dust effect even after age had been taken into account ($p<0.001$, 10 dust index units increased the estimated prevalence by a factor of about 35%). Observed data are set out in fig 3. The dust effect varied according to smoking status ($p<0.02$), and was not observed among current cigarette smokers although the age effect was marked. The reason for these differences was not apparent.

Reader 17 recorded 10 radiographs showing small rounded opacities category 1/0 or greater, and in spite of this small number, a significant relationship with both age ($p<0.005$) and dust

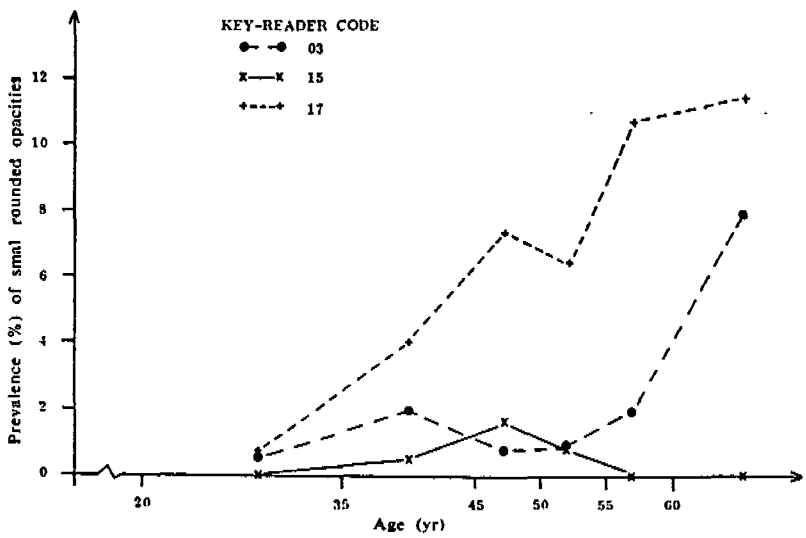

Fig 2 *Prevalence of small rounded opacities category 0/1 or more found by three readers, related to age group.*

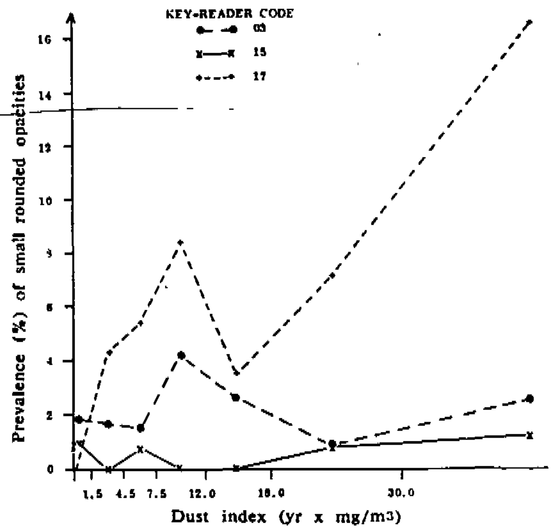

Fig 3 *Prevalence of small rounded opacities category 0/1 or more found by three readers, related to dust index.*

index ($p<0.02$) (after adjusting for the other) was found.

Reader 15 classified only four radiographs as showing small rounded opacities: these classifications were unrelated to age or dust exposure.

Small irregular opacities Analysis showed a clear relationship between prevalence of small irregular opacities category 0/1 or greater and age for all three readers (fig 4) ($p<0.001$ for each reader). There was no relationship of prevalence of small irregular opacities with dust index for any of the three readers.

For reader 15 the relationship of small irregular opacities with age could in small part be explained by a positive history of chronic cough or sputum ($p<0.03$), and by history of chest illness ($p<0.03$). Reader 17 also found a relationship of small irregular opacities with chronic cough or sputum ($p<0.06$), but no relationship with history of chest illness. For both readers, the age effect remained extremely strong even when these symptoms were taken into account.

Reader 3 found differences between smoking categories. Prevalence of small irregular opacities was lowest in non-smokers (0·7%) and highest among other smokers (12·1%). These were not accounted for by the different age distributions of the smoking groups. There was no dust effect. Neither of the other two readers identified smoking differences.

Relationship of lung function to the presence of small rounded opacities Reader 17 recorded small rounded opacities category 0/1 or greater in 50 radiographs. The lung function of these men was significantly reduced. The FEV_1

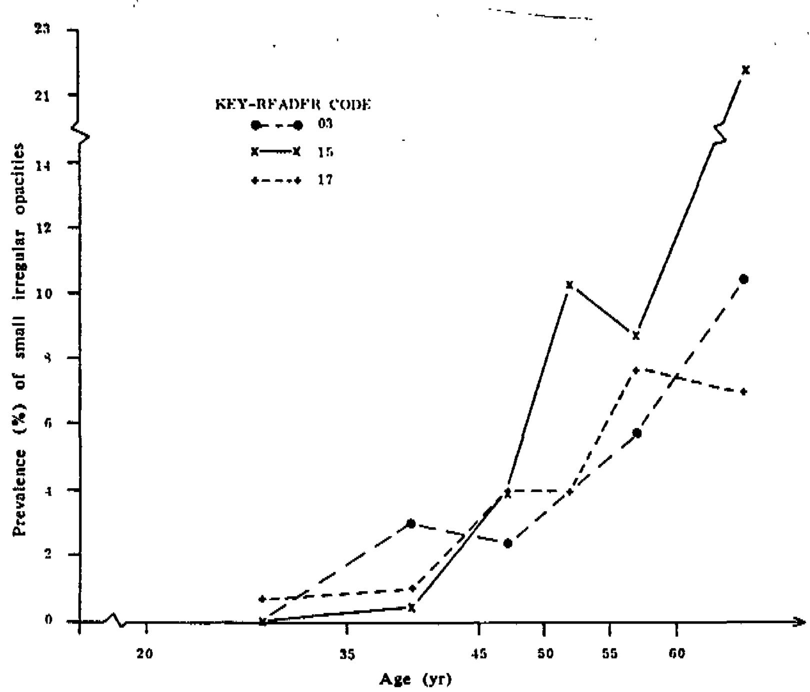

Fig 4 *Prevalence of small irregular opacities category 0/1 or more found by three readers, related to age.*

was reduced by a mean of 206 ml ($p<0.02$ after age, height, weight, smoking, cigarette consumption, and dust index had been taken into account (the less complex model described in table 3). The FVC was reduced by a mean of 253 ml ($p<0.01$), using the same model, and FEV_1/FVC ratio analysed on the log scale was not significantly reduced. TLCO and KCO were measured in 21 of these men, and were not found to be significantly reduced. VA was reduced in these 21 men by a mean of 309 ml ($p<0.05$).

Relationship of lung function to the presence of small irregular opacities

Radiographs of 90 men were thought by one or more readers to show small irregular opacities 0/1 or greater. The lung function of these men was significantly reduced. Their mean FEV_1 was reduced by 205 ml ($p<0.01$) after adjusting for age, height, weight, smoking category, lifetime cigarette consumption, and dust index (the model in table 3). The mean FVC was reduced by 142 ml, using a similar model ($p<0.10$). The ratio FEV_1/FVC was also significantly reduced ($p<0.01$, by a factor of 0.97). TLCO was measured in 45 of these men, and was reduced by a mean of 1.52 ml/min mmHg ($p<0.05$). VA and KCO were not significantly reduced.

Autoclave workers

The effect of a history of work on the autoclaves (where exposure to vinylchloride monomer may have occurred in the past) was examined in the respiratory symptoms, lung function, and chest radiographic abnormality models. A history of having been an autoclave worker had no demonstrable adverse influence on symptoms, lung function, or chest radiographic abnormalities. Thus there was no evidence that apparent PVC dust effects were the result of exposure to vinylchloride monomer during autoclave working.

Clinical readings of chest radiographs

The chest radiograph of one man showed advanced diffuse pulmonary fibrosis. This man had a chest radiograph taken though he was not in the intended study sample. The relevance of his disease to his work is currently being investigated, but has not yet been established. No cases of lung cancer or active tuberculosis were detected in the survey.

Discussion

This study was planned to compare the lung function, chest radiographic appearances, and prevalence of respiratory symptoms in workers in a factory manufacturing PVC with estimates of personal exposure to respirable PVC dust.

The random sample was selected from men who had previously worked in the factory as well as the current work force, and was weighted to include a relatively high proportion of those who had the highest lifetime exposure to PVC dust. These preliminary estimates of exposure were based on factory records and a preliminary inspection of the plants and typical dusts produced. Twenty-five per cent of selected men, thought on this basis to have high or moderate exposures, did not attend for examination. Reserves for these men were included, albeit that these were from medium rather than high dust exposure groups, to ensure that sufficient numbers of men with substantial exposures were studied. It is emphasised that the dust exposure estimates used in the analysis were not based on these preliminary estimates but on a detailed occupational history obtained from each man together with measurements of current personal exposures in the factory. These estimates, though the best available, may nevertheless have been inaccurate to the extent that previous dust exposures may have been higher than those presently experienced. In view of probable overall changes in dust levels conclusions about quantitative relationships between dust and disease should be drawn with caution.

It was not possible in this study to take account of the health effects of the components of the PVC powder other than the PVC itself, nor of changes in the formulation occurring over the years. The "respirable" fraction of airborne dust measured in this survey is suitable for comparisons with both bronchial and alveolar disease, for dust in this size range deposits substantially either in bronchial or alveolar zones. Furthermore, measured exposure to "respirable" coal mine dust has been shown to correlate with mucous hypersecretion and loss of FEV_1 in miners.[23,24] as well as with the radiographic appearances of pneumoconiosis.[25]

The study demonstrated a relationship between estimates of exposure to PVC dust and dyspnoea, lung function, and chest radiological abnormality. A history of moderate exertional dyspnoea was related to dust exposure, though this relationship was apparent only in cigarette smokers. This effect was additional to the effects of smoking and aging which were, however, the predominant explanatory variables for this symptom. It seems unlikely that the effect of PVC dust on symptoms slight abnormalities of the chest radiograph and complaints of slight dyspnoea. While these results are nót unduly alarming, they do indicate that PVC dust exposure should be controlled, and that the men with radiographic abnormalities should be followed clinically to determine future progression or regression of the condition.

This study was carried out with the full cooperation of the management and workforce of Imperial Chemical Industries Limited to whom we are grateful for financial support. We are grateful to Dr JA Dick, Dr JG Bennett, and Dr DJ Thomas for the epidemiological radiographic readings, and to Dr A Seaton, Dr M Jacobsen, and Mr J Dodgson for much advice and help. Further details of the results of this work are recorded in Institute of Occupational Medicine Technical Memorandum TM/79/2.

References

1 Casula D, Cherchi P, Spiga G, Spinazzola A. Environmental dust in a plant for the production of polyvinylchloride. *Ann Inst Super Sanita* 1977; **13**:189–98.

2 Mapp C, Fabbri L, Rossi A, Moro G, Cervi G. Alterazioni funzionali respiratorie da esposizione cronica a cloruro di vinile monomero e polimero. *Med Lav* 1978; **69**:151–62.

3 Frongia N, Spinazzola A, Bucarelli A. Lesioni polmonari sperimentali da inalazione prolungata di PVC in ambiente di lavoro. *Med Lav* 1974; **65**:321–42.

4 Agarwal DK, Kaw JL, Srivastava SP, Seth PK. Some biochemical and histopathological changes induced by polyvinylchloride dust in rat lung. *Environ Res* 1978; **16**:333–41.

5 DeHaan RL. Toxicity of tissue culture media exposed to polyvinylchloride plastic. *Nature New Biol* 1971; **231**:85–6.

6 Salthouse TN, Matlaga BF, O'Leary RK. Microspectrophotometry of macrophage lysosomal enzyme activity: a measure of polymer implant tissue toxicity. *Toxicol Appl Pharmacol* 1973; **25**:201–11.

7 Richards RJ, Desai R, Hext PM, Rose FA. Biological reactivity of PVC dust. *Nature* 1975; **256**: 664–5.

8 Richards RJ, Desai R, Rose FA. A surface-active agent involved in PVC-induced haemolysis. *Nature* 1976; **260**:53–4.

9 Piggott GH, Ishmael J. A comparison between in vitro toxicity of PVC powders and their tissue reaction in vivo. *Ann Occup Hyg* 1979; **22**:111–26.

10 Szende B, Lapis K, Nemes A, Pinter A. Pneumoconiosis caused by the inhalation of polyvinylchloride dust. *Med Lav* 1970; **61**:433–6.

11 Arnaud A, Pommier De Santi P, Garbe L, Payan H, Charpin J. Polyvinylchloride pneumoconiosis. *Thorax* 1978; **33**:19–25.

12 Miller A, Tirstein AS, Chuang M, Selikoff IJ, Warshaw R. Changes in pulmonary function in workers exposed to vinyl chloride and polyvinylchloride. *Ann N Y Acad Sci* 1975; **246**:42–52.

13 Lilis R, Anderson H, Miller A, Selikoff IJ. Pulmonary changes among vinyl chloride polymerization workers. *Chest* 1976; **69**:299–303.

14 Mastrangelo G, Manno M, Marcer G *et al.* Polyvinylchloride pneumoconiosis: epidemiological study of exposed workers. *J Occup Med* 1979; **21**:540–2.

15 Gamble J, Liu S, McMichael AJ, Waxweiler RJ. Effect of occupational and nonoccupational factors on the respiratory system of vinyl chloride and other workers. *J Occup Med* 1976; **18**:659–70.

16 McGuire BA, Barker D, Badel DA. SIMPEDS 70: an improved version of the SIMPEDS personal gravimetric dust sampling instrument. In: Walton WH, ed. *Inhaled Particles III*. Old Woking: Unwin Bros, 1970: 1053–7.

17 Orenstein AJ, ed. *Proceedings of the Pneumoconiosis Conference*. London: JA Chur[illegible] 1960.

18 Medical Research Council. *Report of the Working Party on Research into Chronic Bronchitis.* London: Medical Research Council, 1976.

19 McKerrow CB, McDermott M, Gilson JC. A spirometer for measuring the forced expiratory volume with a simple calibrating device. *Lancet* 1960; **1**:149–51.

20 Meade F, Saunders MJ, Hyett F, Reynolds JA, Pearl N, Cotes JE. Automatic measurement of lung function. *Lancet* 1965; **2**:573–5.

21 International Labour Office. Occupational Safety and Health. *ILO International classification of radiographs of pneumoconioses 1971.* Geneva: ILO, 1972: 22.

22 Cox DR. *The analysis of binary data.* London: Methuen, 1970.

23 Rae S, Walker DD, Attfield MD. Chronic bronchitis and dust exposure in British coalminers. In: Walton WH. ed. *Inhaled Particles III*. Old Woking: Unwin Bros, 1971: 883–94.

24 Rogan JM, Attfield MD, Jacobsen M, Rae S, Walker DD, Walton WH. Role of dust in the working environment in development of chronic bronchitis in British coal miners. *Br J Ind Med* 1973; **30**:217–26.

25 Jacobsen M, Rae S, Walton WH, Rogan JM. The relation between pneumoconiosis and dust-exposure in British coal mines. In: Walton WH, ed. *Inhaled Particles III*. Old Woking: Unwin Bros, 1971: 903–19.

26 Sokol WN, Aelony Y, Beall GN. Meat-wrapper's asthma: a new syndrome. *JAMA* 1973; **226**[illegible] 41.

27 Falk H, Portnoy B. Respiratory illness in meat wrappers. *JAMA* 1976; **235**:915–7.

Published by British Medical Association,
Tavistock Square, London WC1H 9JR, and
printed in England by Bradleys, Reading & London