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AN
EPIDEMIOLOGICAL STUDY
OF THE
LUNG FUNCTION
OF WORKERS
AT A FACTORY
MANUFACTURING
POLYVINYLCHLORIDE

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INSTITUTE OF OCCUPATIONAL MEDICINE

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ABSTRACT

We have conducted an epidemiological study to investigate a report that some men working in a factory manufacturing polyvinylchloride (PVC) had abnormally low values of one lung function test, namely the single breath transfer factor for carbon monoxide (TLco).

We studied 265 present and past employees of the PVC factory, and 219 men from the workforce of a nearby foundry. The foundrymen were included to increase the number of men with little or no exposure to possible respiratory hazards at the PVC factory. Each man's TLco was measured, and smoking history and detailed occupational history obtained. More detailed lung function tests were carried out on the PVC workers only (forced expiratory flow-volume curves).

The study consisted of two parts; measurement of the TLco of current and past employees at the factory and current foundry employees and examination of the distribution of residuals after allowing for age, height, weight and smoking habit, to search for evidence of an excess of men with low values of TLco; and a case-control study. In this, men with the lowest TLco after allowing for age, height, weight and smoking habit were selected as cases, and their occupational history compared with that of two groups of controls; one group selected from those with near average gas transfer values, and another group from those with the highest values.

The TLco results among this combined population conformed to a Normal distribution after allowing for age, height, weight and smoking habit, and did not suggest that a substantial number of men had clinically important impairment of their TLco.

The 31 men selected as 'cases' included 15 men whose TLco was abnormally low (less than 70% of published predicted values), of whom ~~nine~~ twelve were PVC workers and ~~six~~ three were foundrymen. Among the 19 cases working at the PVC factory the pattern of lung function abnormality suggested that the low TLco was

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accompanied by evidence of airflow obstruction in 11 men, suggesting the presence of emphysema, but was an isolated functional abnormality in the other eight, possibly suggesting the presence of pulmonary fibrosis or abnormalities of lung perfusion.

PVC workers were slightly over-represented among the cases, although this difference could easily have arisen by chance. Men who had worked on jobs at the PVC factory which were close to the pressure vessels where exposure to vinyl chloride monomer was most likely to have occurred in the past, were also slightly over-represented among the cases, and this difference approached statistical significance at conventional levels. There was, furthermore, a statistically significant association between low T_{Lco} and a history of having worked at the PVC factory before 1975. This date is important because it was at this time that exposure of the workforce to vinyl chloride monomer was drastically reduced, in the light of information about some of the potential hazards of this gas.

The cases included slightly more smokers than the controls, and those cases who smoked, smoked slightly more heavily than controls.

The relative importance of these and other factors in causing the lung functional abnormalities is not clear, but these findings give some support to the hypothesis that work in the PVC factory before 1975 involved exposure to a substance that caused impairment of lung function in a small number of men.

There was no evidence of a relationship between low T_{Lco} values and current working conditions at the PVC factory or with past or present conditions at the foundry.

The results suggest that more detailed studies of the relationships with vinyl chloride monomer, polyvinylchloride, smoking habit and other causative factors would be desirable, together with a clinical assessment of the lung damage in selected men.

1. INTRODUCTION

The health of workers employed in the manufacture of polyvinylchloride (PVC) has been a cause of concern during recent years. Some adverse effects of exposure to vinyl chloride monomer (VCM) are well recognized, but lung disease in man has not been shown to be related to exposure to VCM. Exposure to airborne PVC dust, however, has been shown to cause slight impairment of lung function and slight chest radiographic abnormalities.

Vinyl chloride is the basic raw material used in the production of PVC. Although the manufacturing process was first developed in 1928 in the USA it was not until 30 years later that evidence of the toxic effects of vinyl chloride exposure began to accumulate. CORDIER (1966) was the first to describe acro-osteolysis in reactor cleaners in Belgium and in the following year SUCIU (1967) described Raynaud's phenomenon among workers in a PVC factory. Changes in the skin and internal organs were subsequently recognized and in 1974 the term 'vinyl chloride disease' was used to describe the syndrome which has many features in common with scleroderma (VELTMAN <u>et al</u>., 1975).

The hepatic effects of exposure to VCM have aroused the most interest and include non-malignant changes. It was the discovery of the association between vinyl chloride exposure and angiosarcoma of the liver (CREECH and JOHNSON, 1974) which caused the greatest concern and affirmed the need for stricter control of exposure levels. In 1975 regulations were introduced which established a ceiling exposure value of 30 parts per million (ppm) and an eight-hour time weighted average (TWA) of 10 ppm. In 1980 the permitted maximum exposure was reduced to an annual average of 3 ppm.

1.1 <u>Respiratory effects of VCM and PVC</u>

The work described in this report was confined to a study of the lung function of workers in a factory producing PVC where men were exposed potentially to VCM, PVC and the other compounds used in the manufacturing process. Previous studies involving the use of animals, observation on patients and epidemiological surveys, have provided information on the potential respiratory effects of these compounds.

1.1.1 Animal studies

The toxicity of both VC and PVC has been investigated in animal experiments. PRODAN et al. (1975) exposed guinea pigs to 10% vinyl chloride concentration for two hours daily for periods of up to three months. At autopsy the lungs of all exposed animals showed the presence of fibrosis which was most severe in the animals which had had the longest exposure time. AGARWAL et al. (1978) studied the effect of intratracheal injections of PVC dust in rats and found that inflammatory changes were induced in the terminal and respiratory alveoli and that granulomatous lesions associated with multinucleated giant cells developed. Similar giant cells and histiocytes were identified in the alveoli of the lungs of small mammals which were kept in the bagging area of a PVC factory (FRONGIA et al., 1974).

1.1.2 Clinical studies

There have been isolated case reports of pulmonary disease in workers employed in factories manufacturing PVC. ARNAUD et al. (1978) studied a 53-year-old man who had worked for 23 years in the bagging plant of a PVC factory. His chest X-ray showed micronodular shadowing and lung biopsy revealed large numbers of macrophages containing particulate material and moderate diffuse fibrosis and a few alveolar granulomata. However, his symptoms were few and apart from a slight reduction in vital capacity, his lung function tests including his transfer factor for carbon monoxide were normal. His disease was probably related to PVC dust rather than VCM.

DARKE (1976) investigated 14 men who had been employed in a PVC manufacturing plant exposed to VCM and all of whom complained of breathlessness. He found that their chest radiographs were normal. In six of these men transfer factor for carbon monoxide is reported as being impaired but no measurements or details of other lung function tests are given. Lung biopsy from one of the men showed focal alveolar wall thickening and macrophages present in alveolar spaces. LANGE et al. (1973) described some cases of VC workers with impairment of transfer factor for carbon monoxide, but the relationship with occupation was not clear.

1.1.3 Epidemiological studies

Studies of pulmonary function of workers employed in PVC manufacturing plants have produced conflicting results, and it has not always been possible to separate the effects of PVC dust from potential effects of VCM. A high prevalence of abnormal lung function, mainly obstructive in type, was found by MILLER et al. (1975) and LILIS et al. (1975; 1976) among workers in two PVC manufacturing plants in the United States of America but smoking was not taken into account in the analysis. Smoking effects were allowed for in the study by GAMBLE et al. (1976) which compared the lung function of workers in a PVC plant with that of rubber workers and chemical workers exposed to VCM: no significant differences were found in the lung function of these three groups but no measured personal exposures were available. VERTKIN et al. (1970) studied 96 PVC workers in the USSR and found a high prevalence of chest radiograph abnormalities but the majority of the workers had normal lung function tests. CHIVERS et al. (1980) similarly found no apparent impairment of lung function among 509 employees in a PVC factory of whom 104 were exposed to PVC dust only, 112 to non-chlorinated solvents only and the remaining 293 were exposed to a mixture of both. No difference between the three groups was identified and the observed impairment of lung function in some men was related entirely to the effects of smoking. However, measured personal exposures were not available for these men.

A study of 818 men currently and previously employed at a PVC manufacturing plant (SOUTAR et al., 1980) in which estimates of personal exposure to PVC dust were based on detailed occupational histories and current measurements of dust levels in the factory showed a statistically significant reduction in tests of lung function among men with the highest PVC dust exposure, and some of these men had small rounded opacities on their chest radiographs. The men with these radiological changes had significantly lower mean lung function test values than men whose films were considered to be normal. No relationship was found between exposure to PVC dust and impaired transfer factor for carbon monoxide.

1.2 The present study

The present study was requested by Vinatex Ltd., and was carried out with the full agreement of management and workforce, and arose from their concern about some employees whose lung function, particularly the transfer factor for carbon monoxide, appeared to be abnormal. The transfer factor for carbon monoxide measures the ability of the lung to exchange gases between the inspired air and the blood. The study was designed to describe the distributions of various measures of lung function, including the transfer factor, in current and former employees at the PVC factory and to identify men with low lung function values. These men would be regarded as 'cases' and would be compared with two groups of controls in order to examine possible associations between abnormally low lung function values and personal, occupational and environmental factors.

The total survey population included the workforce of two factories; one was the PVC factory of interest and the other was a large iron foundry situated a few hundred yards away.

1.2.1 The PVC factory

The plant had been in operation since 1969 and for most of that time had produced suspension polymer. For a period of three years (1971 - 1974) emulsion polymer, which has a smaller particle size than suspension polymer, had been manufactured in one of the two reactor buildings.

During the manufacturing process vinyl chloride is pumped from the tank farm storage area via another storage tank to two reactor buildings. Under conditions of increased temperature and pressure and in the presence of other substances acting as catalysts and surfactants, polymerization of VCM takes place. The resulting PVC is piped as a slurry to blending tanks and is then dried by centrifuging and rotary drying. The dried polymer is sifted and either removed to storage silos or bagged and stored in the warehouse before being dispatched. The manufacturing process is operated in batches throughout the 24 hours and the workforce is divided into four shifts. In the reactor and dryer buildings men usually start as 'B' operators and can then proceed to be 'A' operators and sometimes 'Lead' operators.

Available data suggest that prior to 1975 levels of VCM in the factory were considerably higher than the current low levels. During the period 1969 - 1975 men working in the reactor buildings, and particularly those involved in the manual cleaning of reactors, are likely to have been exposed to the highest levels of VCM.

1.2.2 <u>The foundry</u>

The foundry was situated near the PVC factory in the same industrial valley and manufactured moulded steel products. The manufacturing process involved the production of molten steel which was cast into appropriate moulds to which various finishing techniques were applied.

2. METHODS

2.1 Selection of the survey population

All 177 men currently employed at the PVC factory were invited to take part. The names of another 263 men who had worked at the plant since it started production in 1969 were identified from factory records and attempts were made to trace and invite all these men using information supplied by the management, union representatives and local records.

At the foundry the study was confined to 285 men selected randomly from the 1,085 current male employees.

2.2 The medical survey

The factories were visited by the medical survey team and men were seen by appointment.

Details of each man's smoking history were recorded by a trained clerk using a questionnaire which was a modified version of the smoking section of the Medical Research Council Questionnaire of Respiratory Symptoms (MRC, 1976) (see Appendix 1).

A full occupational history was recorded for each man by a trained clerk who had previously visited both factories and was familiar with their layout and the manufacturing processes. Details of all jobs which a man had done since leaving school were recorded and the time spent in each of them noted.

All PVC factory employees had measurements of forced expiratory volume in one second (FEV_1), forced vital capacity (FVC) and gas transfer factor for carbon monoxide (T_Lco). For foundry workers, approval was obtained for measurement only of T_Lco. Measurements of FEV_1 and FVC were made using an electronic dry rolling-seal spirometer (Ohio 800). After a practice expiration, three forced expirations which were considered to be technically satisfactory from a maximum of six were recorded. The maximum values of FEV_1 and FVC, not necessarily in the same breath, were used for the analysis, and the ratio of FEV_1 to FVC was derived from thes figures.

Single breath gas transfer factor for carbon monoxide ($T_{L}co$) was measured by the breathholding method of MEADE et al. (1965) based on the modified Krogh technique. An automated spirometer/gas sampling system (Transfer Test B, P.K. Morgan Ltd., Chatham, Kent) was used and duplicate estimations were made for each man at least 10 minutes apart. Technically unsatisfactory tests were rejected and repeated (i.e. if the inspired volumes of the two tests differed by more than 10%, if the spirograms of the manoeuvres were of different shape or if the rates of inspiration and expiration were too slow). The mean of the results of the two satisfactory tests was used in the analysis.

Each man was weighed fully clothed and his standing height measured.

2.3 Methods of analysis

The data were studied initially by summary descriptive statistics and multiple linear regression analyses of lung function taking into account age, height, weight and smoking habit. Subsequent examination of the standardised residuals* was carried out and on the basis of this cases and controls were selected.

2.3.1 Classification of smoking histories

Men were assigned to one of three smoking categories; lifelong non-smoker, current smoker and ex-smoker. No distinction was made in the analysis between type of smoking and the two 'smoker' groups included smokers of manufactured cigarettes, hand-rolled cigarettes, pipes and cigars, since the majority of men smoked manufactured cigarettes.

2.3.2 Analysis of data from total survey population

The distributions of lung function and various explanatory variables

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* A standardised residual, SR, is the difference between an observed lung function value and its predicted value from multiple linear regression analysis, divided by the estimated standard deviation of the unexplained variation from this model.

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

were examined for systematic patterns amongst current and former employees of the PVC factory and current employees at the foundry. This was further explored for Tlco and FEV_1 by multiple linear regression analysis taking account of age, height, weight and smoking.

The relationship between a man's observed and predicted values was expressed as a standardised residual (SR). Thus men whose observed values were close to the predicted values would have SR values clustered around zero and correspondingly men with impaired lung function would hav the largest negative SR values.

The distribution of SR values was examined to see if there was evidenc of an unexpectedly large number of men with impaired lung function and if so, to examine if either PVC factory or foundry employees were over-represented amongst these men.

2.3.3 Selection of cases and controls

For each lung function variable those men with the largest negative SR values were chosen as cases. Two groups of controls were selected randomly, firstly from those men whose SRs were clustered around zero and secondly from those with the largest positive SRs.

2.3.4 Case-control study

Cases were initially compared with the rest of the survey population in order to identify systematic differences amongst related factors, e.g. age, smoking habit, employment status.

The occupational and smoking histories of cases and controls were studied for systematic differences. Fisher's exact test, chi-squared test for 2 x 2 contingency tables and chi-squared test for linear trend were used where appropriate.

Classification of smoking and employment histories

Smoking histories were classified as they were for the total population (see Section 2.3.1). Additional information about the number of cigarettes smoked and age of starting smoking was analysed in the case-control study. Broad occupational categories were defined for both PVC factory and the foundry (Tables 1 and 2) and the total number of years spent by all cases and controls in each occupational category was calculated. Additional information was available for PVC employees in relation to exposure to emulsion polymer and employment in the factory prior to 1975.

From the full occupational history, the number of years in 'noxious' industries was recorded. 'Noxious' industries were classified into four groups; the coal and chemical industries have certain well recognized hazards, while the lung function of men in the steel industry has been reported to be lower than men in non-dusty employment (HIGGINS, 1970); the fourth, designated 'other', included industries in which hazards could possibly arise although they would be less likely than those of the other groups (see Appendix 2 for a list of 'other noxious' jobs). Employment of men in the manufacturing of PVC other than at the PVC factory was also noted.

3. RESULTS

3.1 Description of total survey population

A total of 488 men was seen consisting of 165 current PVC factory employees (93% of those who were asked to participate), 102 PVC factory leavers (39% of those who were invited) and 221 foundry employees (78% of those invited). Three men (one from each employment category) did not complete the T_Lco measurement and one foundryman did not have height and weight values recorded; the analysis was based on the remaining 484 men. FEV_1 and FVC measurements were not obtained from three PVC factory leavers and were not carried out on the 221 foundrymen and the analysis was based therefore on 264 men.

3.2 Analysis of lung function data from total survey population

3.2.1 Calculation of predicted values and standardised residuals

The effects of age, height, weight and smoking habit on the T_Lco and FEV_1 were studied in this population by multiple linear regression. The development of the regression model used is described in Appendix 3. Standardised residuals (SR) for T_Lco and FEV_1 were calculated for each man from the final regression model. Thus a man's standardised residual T_Lco represents the amount by which his T_Lco value differs from that predicted by his age, height, weight and smoking habit after standardisation.

3.2.2 Distribution of standardised residual values of T_Lco and FEV_1 for total survey population

After allowing for the above factors, the standardised residual values of T_Lco for the total survey population showed a symmetrical distribution, with no greater number of men in the negative tail of the distribution than would be expected to have occurred by chance. This indicated that there was no evidence that a substantial number of men had suffered a clinically important reduction of their T_Lco. However, for the FEV_1 SR distribution there were slightly more extreme negative values than extreme positive values (Figures 1 and 2).

3.2.3 Selection of cases and controls

It was decided that about 30 cases would form a study group of appropriate size. The threshold SR value for T_Lco below which there was approximately this number of men, was – 1.5, giving 31 men. A control group of 31 men was selected randomly from those men with SR values between - 0.25 and + 0.75 inclusive (T_Lco 'average' controls). A second control group of 31 'extra-healthy' men was selected randomly from those with SR values in excess of + 0.75 (T_Lco 'healthiest' controls).

Similarly 30 men with an FEV_1 SR value of less than - 1.1 were selected as FEV_1 cases and two control groups, each of 30 men, were selected randomly from those with an SR value between - 0.25 and + 0.75 inclusive (FEV_1 'average' controls) and from those with an SR value in excess of + 0.75 (FEV_1 'healthiest' controls).

3.3 General features of cases, controls and the total survey population

3.3.1 Age, height and weight

The mean age, height and weight of T_Lco cases and controls, FEV_1 cases and controls and the total population are given in Tables 3 and 4. T_Lco cases and controls were of similar age but cases tended to be taller than the control groups. Although the mean ages of T_Lco cases and control groups were similar, study of the age distributions (Table 5) showed an excess of current PVC factory employees in the 45 - 54 age group when compared with both groups of controls and the rest of the population. FEV_1 cases were slightly older and taller than the controls and the rest of the population but there was no difference in the age distribution between employment groups or cases and controls.

3.3.2 Employment status and smoking habit

The employment status of cases, controls and the total population is shown in Tables 6 and 7. PVC factory employees were slightly over-represented amongst T_Lco cases but this could easily have occurred by chance.

Differences in smoking habit are discussed in a later section.

3.3.3 Lung function

The mean values of T_Lco for T_Lco cases and controls and the total population are shown in Table 3 and mean values of T_Lco, FEV_1 and FVC for FEV_1 cases and controls are shown in Table 4.

Observed T_Lco and FEV_1 values were expressed as a percentage of values predicted on the basis of Cotes's regression model (COTES, 1979) and the distribution of these values for cases, controls and the total population are shown in Tables 8 and 9.

3.4 Clinical description of T_Lco cases and FEV_1 cases

Fifteen men (nine PVC workers and six foundrymen) of the 31 T_Lco cases had T_Lco values below 70% of their predicted values and four of these were below 60% (Table 8). Nineteen of the 31 cases were from the PVC factory and of those, four men had FEV_1 values of less than 80% of their predicted value and low FEV_1/FVC ratios indicating airflow obstruction. The remaining 15 men had FEV_1 values within the normal range although further examination of their lung function data (forced expiratory flow-volume loops) suggested that seven of these might have mild airflow obstruction. Details of the 10 PVC workers with the lowest T_Lco standardised residual values are given in Table 10.

Of the 30 FEV_1 cases, 13 had observed FEV_1 values below 80% of their predicted values and 10 of these were less than 70% (Table 9). The majority (10) of the 13 men with reduced FEV_1 had FEV_1/FVC ratios below 70% suggesting airflow obstruction. Seven of the FEV_1 cases were also selected as T_Lco cases.

3.5 Case-control study

The occupational histories and smoking habits of cases and controls were compared in order to explore the observed differences in their lung function.

3.5.1 Occupational histories of cases and controls

Analyses of the current employment status of cases and controls showed that PVC factory workers were slightly over-represented amongst the T_Lco cases (Table 6), though this difference could easily have arisen by chance.

The majority of PVC workers had worked in more than one type of job and in more than one broad occupational category during their employment with the company. Analysis of the mean duration of employment in each broad category failed to show any differences between T_Lco cases and their controls (Table 11), though more cases than controls had worked in jobs in category 1, those occupations close to the pressure vessels where exposures to VCM were mostly likely to have occurred in the past. This difference could easily have occurred by chance, if PVC workers alone are considered but if the foundrymen are included, 11 of 31 cases (35%) had worked in category 1 jobs in the PVC factory, whereas only 10 of 62 controls (16%) had done the same. The difference is significant at the 7% level. These occupational differences were not apparent for the FEV_1 cases and controls (Table 13).

There was also movement between jobs at the foundry but there were no differences in the pattern of employment of cases and controls (Table 12).

Pre-1975 employment

Following the recognition of the hazards of VCM exposure in 1973, levels of VCM in the factory were progressively reduced during 1974 and by January 1975 the exposure levels were low. The numbers of cases and controls who had been employed at the PVC factory before 1st January 1975 were compared. Seventeen of the 19 PVC worker T_Lco cases had been employed before 1975 compared with five of the 15 'healthiest' controls and 11 of the 13 average controls (Table 14). Using a X^2 test for trend, there was strong evidence to suggest a significant increase in the proportion of men working before 1975 over 'healthiest' controls, 'average' controls and cases. Looking at comparisons between groups only the difference between cases and 'healthiest' controls was significant. Analysis of the duration of employment of men within different age groups showed that pre-1975 working was seen in younger as well as in older men (Tables 15, 16, 17). No differences were seen in the number of men employed before 1975 between PVC factory FEV_1 cases and controls (Table 18). A similar analysis of foundry T_Lco cases failed to show any relationship with pre-1975 employment (Table 19).

In conclusion there is evidence to suggest that employment at the PVC factory before 1975 was associated with impairment of T_Lco.

Exposure to emulsion polymer

The employment of cases and controls in the manufacturing of emulsion polymer was studied and compared. No man had been exclusively involved in the production of emulsion polymer so men were divided into three groups; those who had worked with suspension polymer only, those who had worked with both suspension and emulsion, and those who had not been exposed to either. Similar proportions of TLco cases and controls (Table 20) and FEV_1 cases and controls (Table 21) are represented in each of these three groups. There is no evidence that exposure to emulsion polymer adversely affected the lung function of those who worked with it.

Previous employment in other industries

There was no evidence that the observed differences between cases and controls could be explained on the basis of previous employment in industries other than the PVC factory or the foundry. No differences were found either in the numbers of cases and controls or in the mean numbers of years spent by them working in other industries which might be considered noxious (i.e. coal, steel, chemicals and 'others') (Tables 22, 23, 24). No men had been employed in the manufacturing of PVC outside this PVC factory.

3.5.2 Smoking habits of cases and controls

A higher proportion of TLco cases (65%) were current cigarette smokers than were either group of controls (43%) or total survey population (48%) (Table 25). This difference was not seen between the FEV_1 cases and controls but there were more ex-smokers among the FEV_1 cases than there were among the controls (Table 26).

The smoking histories were examined in greater detail by analysing the number of cigarettes which current cigarette smokers smoked daily both on weekdays and during the weekend, the number smoked by each man during the maximum smoking period of his life and the age at which each man started smoking.

There was no significant difference in the number of cigarettes smoked on weekdays between both groups of cases and the 'healthiest' controls (see Figures 3 and 4), and similar results were found for 'average' controls.

Analysis of weekend smoking showed that more T_Lco cases smoked 25 or more cigarettes per day than did the T_Lco healthiest controls (Figure 5). No such difference was found to exist with average controls. Comparing the weekend smoking habits of PVC factory and foundry T_Lco cases, it was found that a larger proportion of foundrymen smoked more than 25 cigarettes per day (Figure 5). For the FEV_1 men, more cases than average controls smoked 25 or more cigarettes per day at weekends. This difference was not seen between cases and healthiest controls.

Consideration of the number of cigarettes smoked during a man's maximum smoking period showed that of the men at the PVC factory, five of the 13 T_Lco cases, compared with none of the six T_Lco'healthiest' controls had smoked a maximum of 25 or more cigarettes per day (Figure 6). but this difference in proportions could easily have arisen by chance.

The age at which men started smoking was also examined. There were significant differences between cases and controls. Of the 20 T_Lco cases who were current smokers, eight had started smoking by the age of 15 compared with one out of the 14 'healthiest' controls and 16 had started by the age of 16 compared with five out of the 14 'healthiest' controls (Figure 8a), while the figures for average controls were that six out of 15 had started smoking by the age of 16 (Figure 8b). Of the 13 FEV_1 cases who were current smokers, seven had started smoking by the age of 16 compared with two of the 11 'healthiest' controls (Figure 9a). These differences were not seen between cases and 'average' controls (Figure 9b).

In conclusion T_Lco cases and 'healthiest' controls and FEV_1 cases and 'average' controls differed in the number of men smoking 25 or more cigarettes per day at weekends. A similar difference was found between T_Lco cases at the PVC factory and the foundry. In general, cases started smoking at a younger age than controls.

4. DISCUSSION

The present study had two aims. First, to describe the lung function, particularly the TLco, of current and past employees of a factory manufacturing PVC, and seek evidence of a possible excess of men whose TLco was abnormally low. Second, to examine the relationship between TLco and occupation and other personal and environmental factors by a case-control study, in which the cases were men with lowest gas transfer factor after allowing for age, height, weight and smoking habit.

Men from a nearby foundry were included in the study in order to increase the number of men with low or no exposure to possible respiratory hazards at the PVC factory, but who were exposed to similar environmental conditions outside their workplace. In all 265 men from the PVC factory and 219 men from the foundry were included in the TLco analysis.

The TLco residuals among this combined population conformed approximately to a Normal distribution after allowing for age, height, weight and smoking habit, and did not suggest an undue excess of extremely low values. This indicated that it was unlikely that a substantial number of men in the whole population were suffering from a clinically important reduction of the TLco.

In the case-control study the 31 men with the lowest TLco after allowing for age, height, weight and smoking habit were selected as 'cases'. This does not imply that all 31 were suffering from lung disease, but among them were 15 men whose TLco was less than 70% of the value predicted by published normal values, a level which would generally be regarded as abnormally low. Among the 19 cases at the PVC factory the pattern of lung function accompanying the low TLco was that of definite airflow obstruction in four men, and possible airflow obstruction in another seven men, suggesting the presence of emphysema. The remaining eight men did not have evidence of airflow obstruction or reduction of their lung capacity (vital capacity). This pattern is unusual in clinical practice, and may possibly reflect pulmonary fibrosis or disturbances of the blood flow in the lungs. The degree of reduction of transfer factor of carbon monoxide and associated airflow obstruction might have been sufficient to cause breathlessness on exertion in some of these men.

The possible contribution of occupation in causing these lung function abnormalities was examined by comparing the occupational histories of the cases with those of controls. Two groups of controls were selected; one group from men with values of gas transfer near the mean for this population; the other group from those with values towards the high end of the range ('average' and 'healthiest' controls). The reasons for choosing two such groups were that men with near average values may have included some whose lung function had been slightly affected by noxious influences, while those with very high values were least likely to have been affected by noxious influences, but also could conceivably include men who were highly resistant to these influences, and would therefore not be suitable for the comparisons made in this study.

The PVC workers were slightly over-represented among the cases with low T_Lco, though this difference could easily have arisen by chance. Men who had worked on jobs at the PVC factory which were close to the pressure vessels where exposure to VCM was most likely to have occurred in the past, were also slightly over-represented among the cases, and this difference approached statistical significance at conventional levels.

There was, furthermore, an association between low gas transfer factor and a history of having worked at the PVC factory before 1975. This date is important because it was at this time that, in the light of information about some of the potential hazards of VCM, exposure to this gas was drastically reduced. This association between low gas transfer factor and working before 1975 was demonstrated by comparison with the 'healthiest' controls, the 'average' controls showing an intermediate pattern of association not statistically significantly different from the cases. This association with working before 1975 was not found among foundry workers.

This conjunction of findings suggests that an unknown environmental or personal factor or factors associated with working at the PVC factory before 1975 might have been responsible for some impairment of the gas transfer factor in some of these men. The most obvious candidate for suspicion is VCM, exposures to which are known to have been much higher than post-1975 levels. Some support for this is provided by published case reports of VCM workers with impairment of gas transfer factor, but proof of association has been lacking (LANGE, 1973; DARKE, 1976). [redacted] though it is possible that many workers throughout the factory were exposed to a lesser degree. It is also possible that exposure to respirable PVC dust may have contributed to the low gas transfer factors, for this dust has been shown in other studies to be associated with impairment of other aspects of lung function (though not the gas transfer factor) and slight chest radiographic abnormalities (MASTRANGELO <u>et al</u>., 1979; SOUTAR <u>et al</u>., 1980). There was no evidence to suggest that a current risk to respiratory health exists at either the PVC factory or foundry.

Some differences in smoking habit were found between cases and controls, non-smokers being slightly commoner among controls, and heavier smokers slightly commoner among the cases. The cases tended to start smoking at a slightly younger age. We do not know if these small differences in smoking habit were sufficient to account for the reductions of gas transfer factor in the cases, but they would seem unlikely to account for the whole of the differences between cases and controls.

While the response rate among currently employed workers was excellent, that for those men who had left the PVC factory 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 could be unrepresentative to that extent.

A similar analysis for another lung function test, forced expired volum in one second, was carried out for the PVC workers only. While some men did have impairment of this test result as would be expected in an industrial population of this kind, no associations with occupation could be demonstrated.

5. CONCLUSIONS AND RECOMMENDATIONS

We found no evidence of an unexpectedly large number of men with impairment of their lung gas transfer factor among either PVC factory or foundry employees. There was, however, a small number of men in both factories with impairment of their transfer factor. This could not be shown to be associated with current working conditions at either factory, but the pattern of results among PVC workers suggested that there was an association between impairment of the gas transfer factor and a history of working in the PVC factory before 1975. There was also evidence that heavy smoking was associated with impairment of gas transfer.

These findings give some support to the hypothesis that work in the PVC factory before 1975 involved exposure to a substance that caused impairment of lung function in a small number of men. The results suggest that more detailed studies of the importance of exposure to vinyl chloride monomer, polyvinylchloride, smoking habit and other possible factors in causing impairment of lung function would be desirable, together with a clinical assessment of the extent of lung damage in selected men.

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TABLE 1 Classification of all jobs at Vinatex 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, e.g. shift supervisors and foremen
6	Management and office staff

* These men are most likely to have been exposed to high concentrations of VCM in the past.

** These men are involved in the bagging of PVC and are probably exposed to higher concentrations of dust than other workers in the dryer buildings.

*** These men are potentially exposed to all raw materials and products.

TABLE 2 Classification of foundry jobs into seven broad occupational groups.

Occupational group		Jobs included in group
No.	Description	
1	Furnace and melt:	furnace operator, burner, charger, weigher, skimmer, smelter, slagman, ladle repairer, concrete liner.
2	Sand and blasting:	coremaker, sand tester, sand mixer, shot blaster, core stripper, knock-out, brick maker.
3	Metalwork:	driller, grinder, blacksmith, tinsmith, wagon repairer, rope splicer, cupola repairer, maintenance fitter's mate, maintenance fitter, turner, trainee in the training centre, borer, saw repairer, wagon repairer, milling operator, inspector in machine shop, welder.
4	General and other:	labourer, patternmaker, plater, platelayer, pipe loader, crane driver, driver, cleaner, technician, trainee, pipe roller, slinger, quality control, joiner, greaser, inspector, saddler, bricklayer, core inspector, despatcher, hydraulic attendant, shunter, plumber, pipe recorder, runner operator, sawyer, staff, power house attendant, canteen, tool room attendant, electrician, storeman, ore crusher, ram driver, safety officer.
5	Paint and dipping:	dipper, paint sprayer, painter and decorator.
6	Casting:	caster, manhole maker, socket man, machine moulder.
7	Fettler:	fettler

TABLE 3. Features of $T_{L}co$ cases, controls and total survey population. Mean (and standard deviations) of age, height, weight and $T_{L}co$.

		$T_{L}co$ Groups			
Number of men		Cases 31	Controls (average) 31	Controls (healthiest) 31	Total survey population 484
Age	Mean	41.8	42.3	40.3	42.2
(yrs)	(SD)	(10.2)	(12.5)	(11.3)	(11.9)
Height	Mean	176.1	174.0	173.9	173.8
(cms)	(SD)	(7.1)	(6.6)	(5.6)	(7.0)
Weight	Mean	82.7	84.9	79.2	80.2
(kgs)	(SD)	(13.3)	(18.5)	(9.5)	(12.6)
$T_{L}co$	Mean	22.2	31.8	37.3	30.5
(ml/min. mm Hg)	(SD)	(4.1)	(2.9)	(4.3)	(5.9)

TABLE 4 Features of FEV_1 cases, controls and total survey population. Mean (and standard deviations) of age, height, weight, TLco, FEV_1 and FVC.

		TLco Groups			Total survey population
Number of men		Cases 30	Controls (average) 30	Controls (healthiest) 30	264
Age	Mean	43.3	41.3	42.1	42.2
(yrs)	(SD)	(11.0)	(12.5)	(12.0)	(11.8)
Height	Mean	176.0	174.5	175.9	174.3
(cms)	(SD)	(7.4)	(6.6)	(8.0)	(7.1)
Weight	Mean	82.2	78.4	80.4	80.4
(kgs)	(SD)	(13.3)	(10.1)	(11.5)	(12.3)
FEV_1	Mean	2.7	3.9	4.5	3.7
(litres)	(SD)	(0.7)	(0.7)	(0.8)	(0.9)
FVC	Mean	4.1	5.1	5.9	4.9
(litres)	(SD)	(0.9)	(0.8)	(0.9)	(1.0)
TLco	Mean	29.1*	32.3	31.3	30.5**
(ml/min. mmHg)	(SD)	(6.8)*	(6.0)	(6.5)	(6.1)**

* Value based on 29 observations.

** Value based on 262 observations.

TABLE 5 Age distribution of TLco cases and controls and the total survey population by employment status.

	Age ranges in years						Total
	0 - 24	25 - 34	35 - 44	45 - 54	55 - 64	65+	
CASES							
PVC current men	1		4	6			11
PVC leavers		2	2	2	1	1	8
Foundrymen	1	4	3	4			12
AVERAGE CONTROLS							
PVC current men		1	4	1	3		9
PVC leavers		1	1	2			4
Foundrymen	3	2	5	4	4		18
HEALTHIEST CONTROLS							
PVC current men	2	3	2	4	1		12
PVC leavers	1	2					3
Foundrymen	1	2	6	4	3		16
TOTAL POPULATION							
PVC current men	9	37	57	35	26	0	164
PVC leavers	4	24	33	19	11	10	101
Foundrymen	17	48	50	60	44	0	219

TABLE 6 Employment status of T_Lco cases, controls and total survey population. Number of men in each employment group with percentages in brackets. Four men excluded, see text.

	PVC Current Workers	PVC Leavers	Foundry	Total
Total survey population	164	101	219	484
Cases	11 (34)	8 (53)	12 (26)	31
Controls (average)	9 (28)	4 (27)	18 (39)	31
Controls (healthiest)	12 (38)	3 (20)	16 (35)	31
All	32 (100)	15 (100)	46 (100)	93

TABLE 7 Employment status of FEV_1 cases, controls and total survey population. Number of men in each employment group with percentages in brackets. Three men excluded, see text. Rounding error of percentages not adjusted to justify totals.

	PVC Current Workers	PVC Leavers	Total
Total survey population	165	99	264
Cases	14 (26)	16 (43)	30
Controls (average)	18 (34)	12 (32)	30
Controls (healthiest)	21 (40)	9 (24)	30
All	53 (100)	37 (100)	90

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TABLE 8 Distribution of observed T_{LCO} as a percentage of predicted T_{LCO} using Cotes's regression model for non-smokers. Numbers of men (percentages in brackets) for the cases, two control groups and total survey population.

	T_{LCO} % predicted									Total
	≤ 49	50 - 59	60 - 69	70 - 79	80 - 89	90 - 99	100 - 109	110 - 119	≥ 120	
Cases		4 (12.9)	11 (35.5)	12 (38.7)	4 (12.9)					31
Controls (average)						11 (35.5)	13 (41.9)	7 (22.6)		31
Controls (healthiest)							3 (9.7)	14 (45.2)	14 (45.2)	31
Total survey population		4 (0.8)	14 (2.9)	29 (6.0)	75 (15.5)	114 (23.6)	120 (24.8)	82 (16.9)	46 (9.5)	484

TABLE 9 Distribution of observed FEV_1 as a percentage of predicted FEV_1 using Cotes's regression model for non-smokers. Numbers of men (percentages in brackets) for the cases, two control groups and total survey population.

	FEV_1 % predicted									Total
	≤ 49	50 - 59	60 - 69	70 - 79	80 - 89	90 - 99	100 - 109	110 - 119	≥ 120	
Cases	1 (3.3)	4 (13.3)	5 (16.7)	3 (10.0)	14 (46.7)	3 (10.0)				30
Controls (average)						3 (10.0)	17 (56.7)	9 (30.0)	1 (3.3)	30
Controls (healthiest)							1 (3.3)	6 (20.0)	23 (76.7)	30
Total survey population	1 (0.4)	4 (1.5)	6 (2.3)	9 (3.4)	29 (11.0)	48 (18.2)	74 (28.0)	47 (17.8)	46 (17.4)	264

TABLE 10 Details of the 10 PVC factory TLco cases with the lowest standardized residual values of TLco. Case No. 1 did not complete the spirometry test. Predicted values are for non-smokers (Cotes, 1979).

No.	Age Range	Smoking category	SR	TLco (observed)	TLco (predicted)	TLco % predicted	FEV_1 litres (observed)	FEV_1 litres (predicted)	FEV_1% predicted	FVC litres	$\frac{FEV}{FVC}$ x 100
1	30 - 34	C	- 2.89	20.1	34.6	58.3	-	-	-	-	-
2	65 - 69	E	- 2.75	14.1	27.4	51.3	2.1	3.0	69.8	3.8	55.2
3	35 - 39	C	- 2.22	20.1	31.8	63.5	3.6	3.8	95.2	5.2	68.9
4	40 - 44	E	- 2.15	20.9	30.5	68.4	1.2	3.5	34.3	3.5	35.1
5	35 - 39	C	- 2.11	20.8	32.1	64.6	3.2	3.8	84.9	4.1	77.9
6	55 - 59	C	- 2.02	14.7	23.9	61.4	2.6	2.7	95.5	3.3	77.9
7	50 - 54	C	- 2.01	15.4	25.9	59.5	2.7	3.0	90.6	4.3	62.2
8	35 - 39	C	- 1.99	23.3	35.5	65.6	4.2	4.1	101.7	5.7	74.3
9	45 - 49	N	- 1.92	22.5	29.2	77.0	4.1	3.4	120.1	5.1	80.0
10	50 - 54	C	- 1.84	18.8	29.0	64.8	3.6	3.3	107.9	4.7	75.8

The abbreviations of smoking categories are as follows:

C = current smoker E = Ex-smoker N = life-long non-smoker

TLco units are ml/min. mm Hg.

TABLE 11 PVC factory TLco cases and controls. Mean times (years) spent in each occupational group with number of men in brackets. See Table 1 for key to occupational groups. Amongst these cases and controls, the only man who had spent time in occupational group 6 wasa current employee, selected as one of the 12 'healthiest' controls. He had spent 1.7 years in this group.

	Number of men	Occupational groups				
		1	2	3	4	5
CASES						
Current men	11	3.7 (6)	0.4 (5)	6.1 (3)	9.0 (4)	9.7 (2)
Leavers	8	1.6 (5)	0.8 (6)	11.8 (1)	-	-
AVERAGE CONTROLS						
Current men	9	9.1 (3)	1.1 (3)	6.8 (1)	7.1 (4)	12.3 (1)
Leavers	4	0.7 (1)	0.4 (4)	-	1.8 (1)	-
HEALTHIEST CONTROLS						
Current men	12	3.3 (5)	1.2 (8)	10.8 (1)	7.3 (2)	3.3 (2)
Leavers	3	1.5 (1)	0.5 (3)	-	-	-

TABLE 12 Foundry TLco cases and controls. Mean times (years) spent in each occupational group with number of men in brackets. See Table 2 for key to occupational groups.

	Number of men	Occupational groups						
		1	2	3	4	5	6	7
CASES	12	7.3 (4)	3.0 (2)	12.3 (5)	4.0 (7)	3.2 (2)	11.4 (2)	1.0 (1)
AVERAGE CONTROLS	18	4.6 (3)	16.1 (5)	30.4 (1)	9.4 (9)	7.4 (1)	10.6 (5)	2.5 (1)
HEALTHIEST CONTROLS	16	13.4 (5)	4.5 (3)	12.7 (3)	12.5 (8)	-	11.6 (6)	-

TABLE 13 PVC factory FEV_1 cases and controls. Mean times (years) spent in each occupational group with number of men in brackets. See Table 1 for key to occupational groups.

	Number of men	Occupational groups					
		1	2	3	4	5	6
CASES							
Current men	14	5.5 (7)	1.3 (8)	4.3 (2)	6.1 (6)	6.8 (2)	3.8 (1)
Leavers	16	2.1 (8)	0.8 (9)	4.7 (3)	-	1.0 (2)	-
AVERAGE CONTROLS							
Current men	18	3.2 (10)	1.2 (10)	5.2 (1)	7.6 (5)	7.7 (2)	5.0 (2)
Leavers	12	1.3 (5)	0.9 (7)	4.1 (3)	-	1.2 (3)	3.1 (2)
HEALTHIEST CONTROLS							
Current men	21	6.4 (10)	1.2 (10)	0.7 (2)	7.2 (9)	3.6 (3)	2.6 (2)
Leavers	9	1.2 (2)	0.3 (6)	-	2.1 (2)	-	-

TABLE 14 For TLco analysis, the distribution of numbers of PVC cases and controls who had worked at the PVC factory before 1975 and only after 1975.

	Cases	Average Controls	Healthiest Controls	Total
Pre 1975	17	11	5	33
Post 1975	2	2	10	14
Total	19	13	15	47

TABLE 15 PVC factory TLco cases. Number of men within each age group and duration of pre-1975 employment category.

Time of employment	Duration of employment	Age (yrs)						Total
		0 - 24	25 - 34	35 - 44	45 - 54	55 - 64	65 +	
Pre 1975	< 2 yr		1	3	4	1		9
	2 - 4 yr		1	2				3
	> 4 yr				4		1	5
Post 1975	-	1		1				2
Total		1	2	6	8	1	1	19

TABLE 16 PVC factory TLco average controls. Number of men within each age group and duration of pre-1975 employment category.

Time of employment	Duration of employment	Age (yrs)						Total
		0 - 24	25 - 34	35 - 44	45 - 54	55 - 64	65 +	
Pre 1975	< 2 yr		1	1	2			4
	2 - 4 yr			2		1		3
	> 4 yr			1	1	2		4
Post 1975	-		1	1				2
Total			2	5	3	3		13

TABLE 17 PVC factory TLco healthiest controls. Number of men within each age group and duration of pre-1975 employment category.

Time of employment	Duration of employment	Age (yrs)						Total
		0 - 24	25 - 34	35 - 44	45 - 54	55 - 64	65 +	
Pre 1975	< 2 yr	1	1					2
	2 - 4 yr		1					1
	> 4 yr				1	1		2
Post 1975	-	2	3	2	3			10
Total		3	5	2	4	1		15

TABLE 18 For FEV_1 analysis, the distribution of numbers of PVC cases and controls who had worked at the PVC factory before 1975 and only after 1975.

	Cases	Average Controls	Healthiest Controls	Total
Pre 1975	23	18	19	60
Post 1975	7	12	11	30
Total	30	30	30	90

TABLE 19 For TLco analysis, the distribution of numbers of foundry cases and controls who had worked at the foundry before 1975 and only after 1975.

	Cases	Average Controls	Healthiest Controls	Total
Pre 1975	8	13	12	33
Post 1975	4	5	4	13
Total	12	18	16	46

TABLE 20 For T_{Lco} analysis, the distribution of PVC factory cases and controls who had worked with different polymers.

	Cases	Average Controls	Healthiest Controls	Total
Emulsion and suspension	6	8	4	18
Suspension only	9	3	11	23
Neither suspension nor emulsion	4	2	0	6
Total	19	13	15	47

TABLE 21 For FEV_1 analysis, the distribution of PVC factory cases and controls who had worked with different polymers.

	Cases	Average Controls	Healthiest Controls	Total
Emulsion and suspension	8	7	10	25
Suspension only	18	13	13	44
Neither suspension nor emulsion	4	10	7	21
Total	30	30	30	90

TABLE 22 PVC factory TLco cases and controls. Number of men who have worked in noxious occupations with mean number of years spent by these men in brackets. See Appendix 2 for list of 'other' noxious occupations.

	Number of men	Noxious occupations			
		Steel	Chemicals	Coal	Other
CASES	19	8 (5.5)	1 (1.9)	7 (10.1)	8 (11.5)
AVERAGE CONTROLS	13	0	3 (9.6)	6 (6.9)	7 (10.4)
HEALTHIEST CONTROLS	15	3 (6.1)	0 -	2 (17.4)	8 (7.1)

TABLE 23 PVC factory FEV_1 cases and controls. Number of men who have worked in noxious occupations with mean number of years spent by these men in brackets. See Appendix 2 for list of 'other' noxious occupations.

	Number of men	Noxious occupations			
		Steel	Chemicals	Coal	Other
CASES	30	10 (4.6)	5 (4.0)	16 (15.7)	16 (13.2)
AVERAGE CONTROLS	30	7 (9.8)	6 (14.0)	9 (6.3)	15 (7.5)
HEALTHIEST CONTROLS	30	4 (17.8)	4 (9.1)	11 (13.6)	18 (8.9)

TABLE 24 Foundry Tuco cases and controls. Number of men who hav worked in noxious occupations with mean number of years spent by these men in brackets. See Appendix 2 for list of 'other' noxious occupations.

	Number of men	Noxious occupations			
		Steel	Chemicals	Coal	Other
CASES	12	1 (3.0)	0 (0.0)	3 (5.4)	5 (1.3)
AVERAGE CONTROLS	18	2 (9.6)	0 (0.0)	4 (9.0)	8 (10.9)
HEALTHIEST CONTROLS	16	2 (4.7)	0 (0.0)	5 (2.9)	5 (7.2)

TABLE 25 Smoking habits of $T_{L}co$ cases, controls and total survey population. Number of men in each smoking category with percentages in brackets.

	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

TABLE 26 Smoking habits of FEV_1 cases, controls and total survey population. Number of men in each smoking category with percentages in brackets.

	Non-Smoker	Current Smoker	Ex-Smoker	Total
Cases	5 (16.7)	13 (43.3)	12 (40.0)	30
Controls (average)	7 (23.3)	15 (50.0)	8 (26.7)	30
Controls (healthiest)	9 (30.0)	12 (40.0)	9 (30.0)	30
Total survey population	59 (22.3)	125 (47.4)	80 (30.3)	264

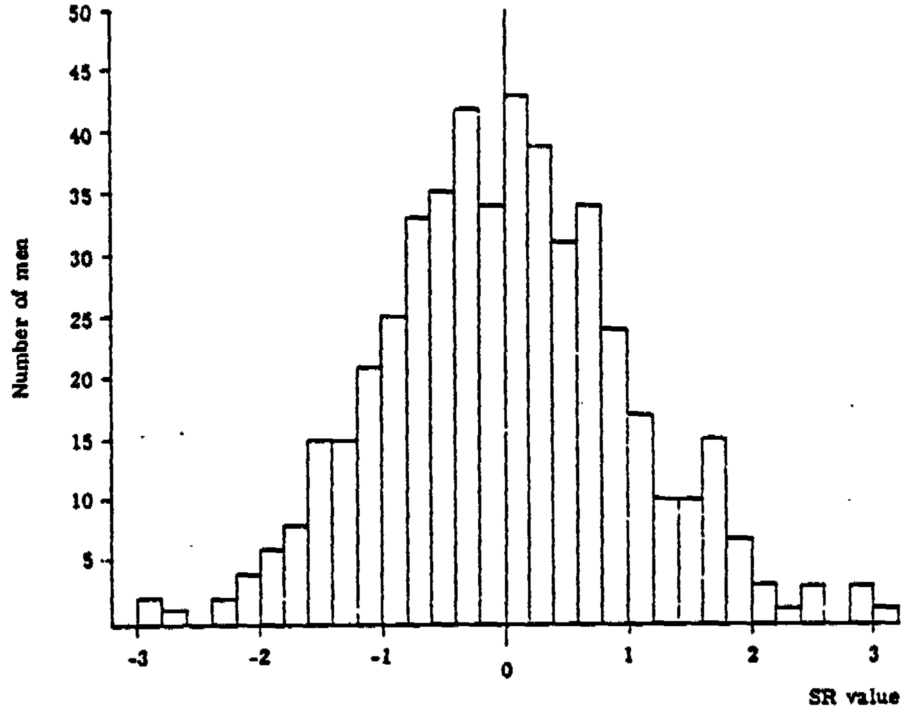

Fig. 1 Numbe- of men by ranges of T. co standardised residuals

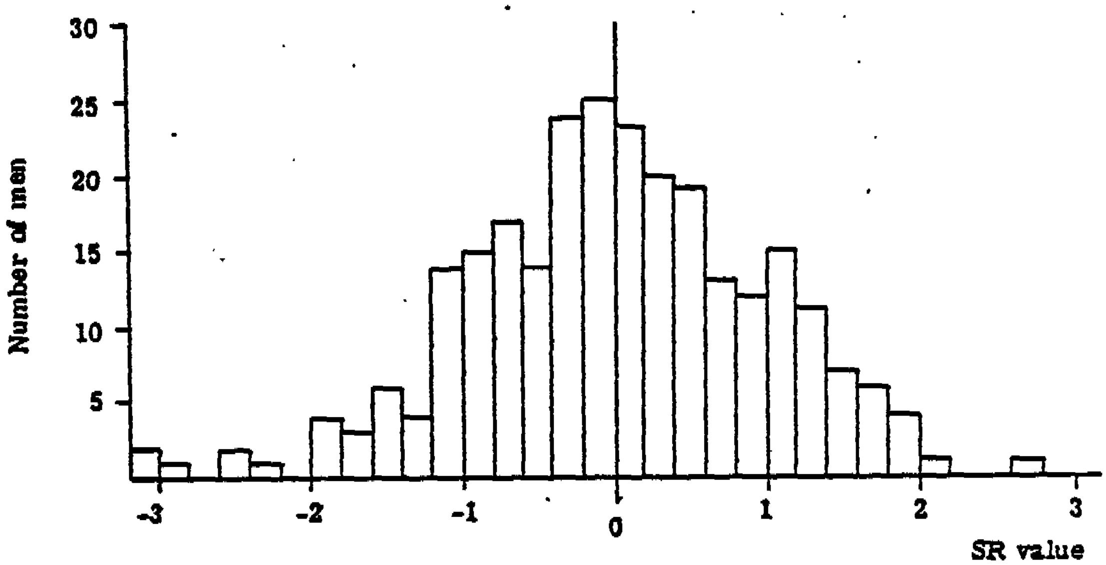

Fig. 2 Number of men by ranges of FEV_1 standardised residuals

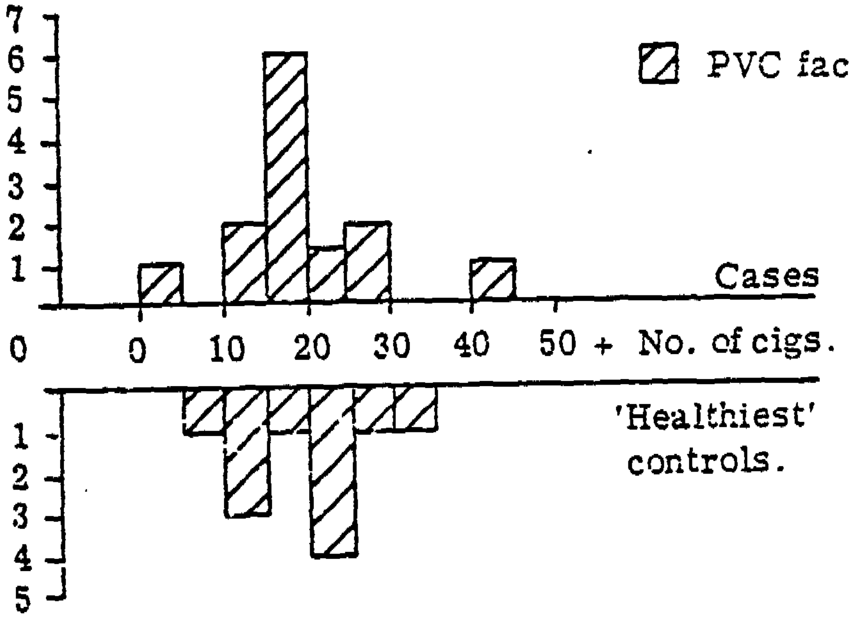

Fig. 3 Number of cigarettes smoked on weekdays by FEV_1 cases and 'healthiest' controls who are current smokers.

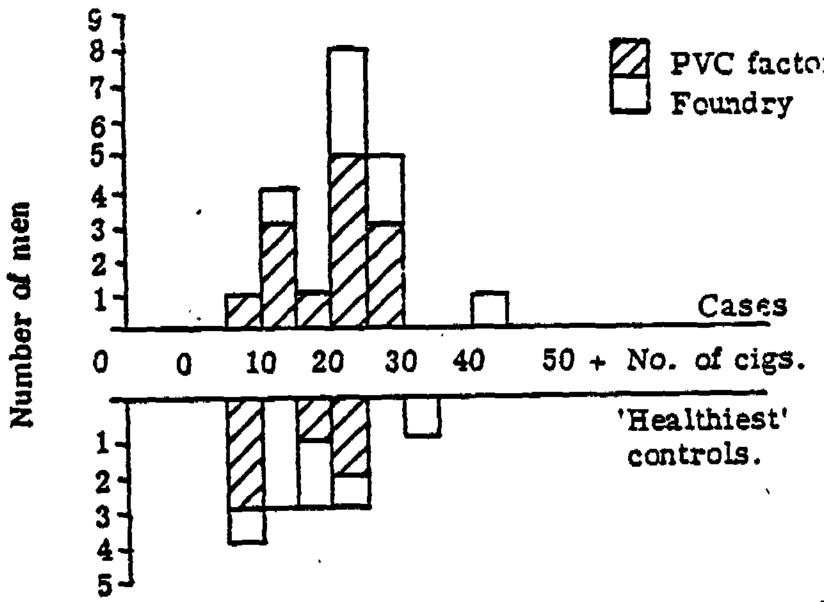

Fig. 4 Number of cigarettes smoked on weekdays by Tʟco cases and 'healthiest' controls, at the PVC factory and the foundry, who are current smokers.

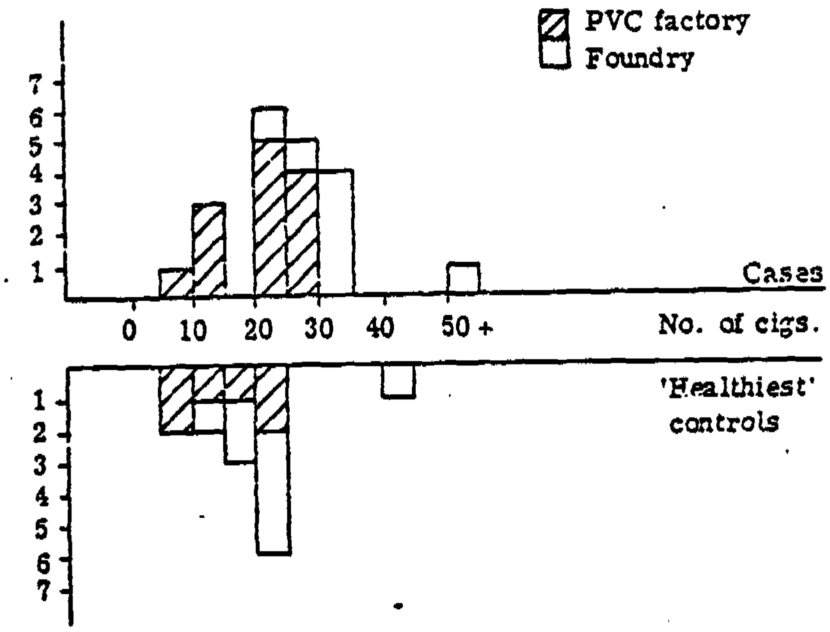

Fig. 5 Number of cigarettes smoked per day at weekends by T.co cases and 'healthiest' controls, at the PVC factory and the foundry, who are current smokers.

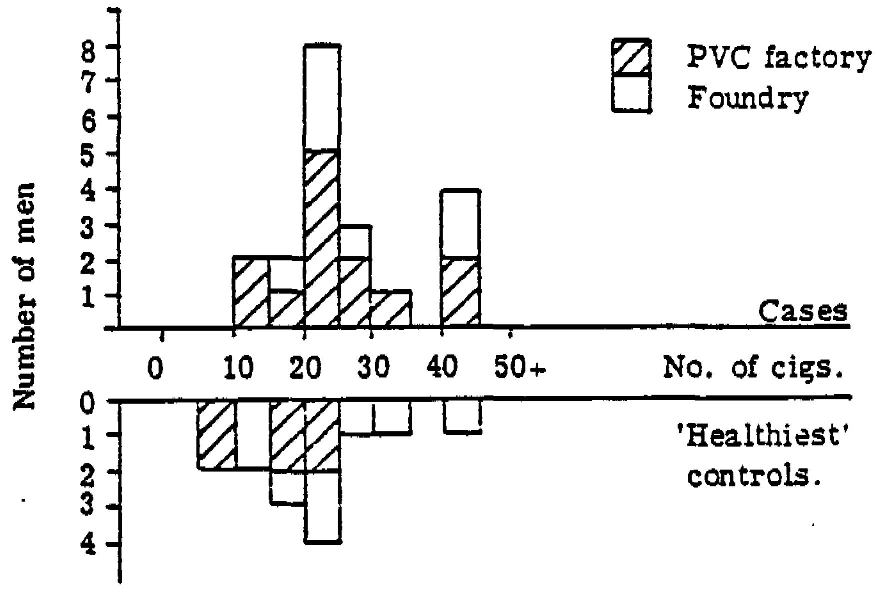

Fig. 6 Maximum number of cigarettes regularly smoked per day by Tʟco cases and 'healthiest' controls, at the PVC factory and the foundry, who are current smokers.

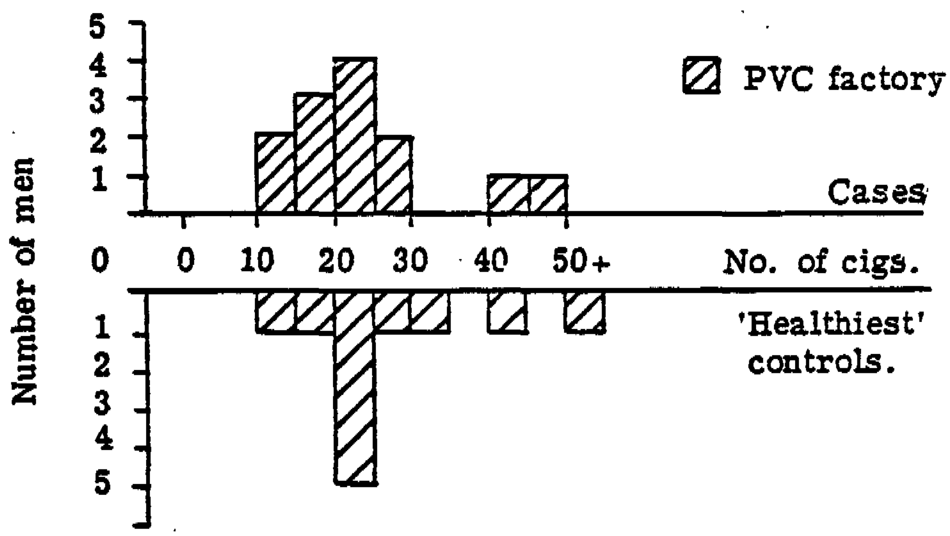

Fig. 7 Maximum number of cigarettes regularly smoked per day by FEV_1 cases and 'healthiest' controls.

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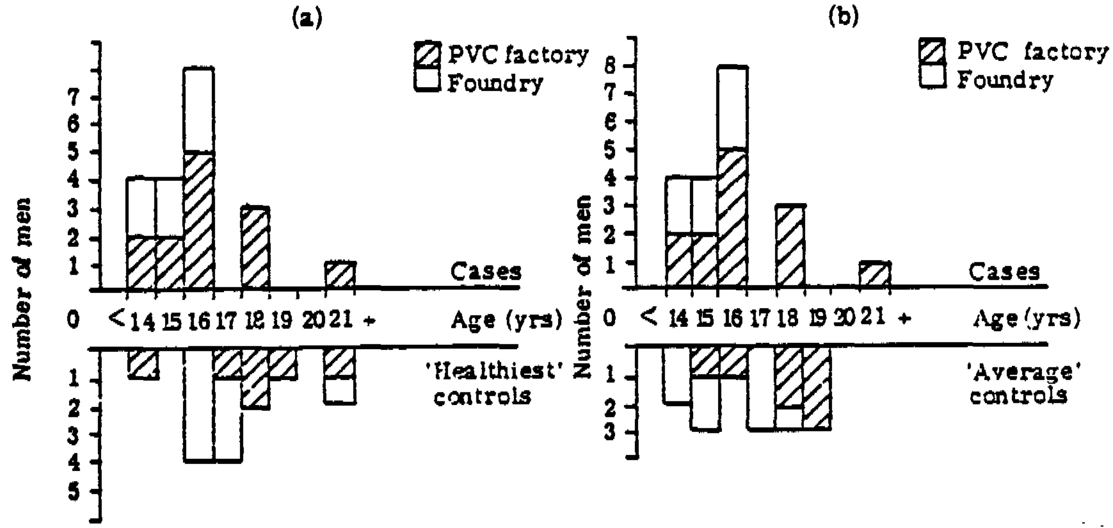

Fig. 8 a) Age when started smoking cigarettes, for $T_L$co cases and 'healthiest' controls at the PVC factory and the foundry, who are current smokers.

b) Age when started smoking cigarettes, for $T_L$co cases and 'average' controls, who are current smokers.

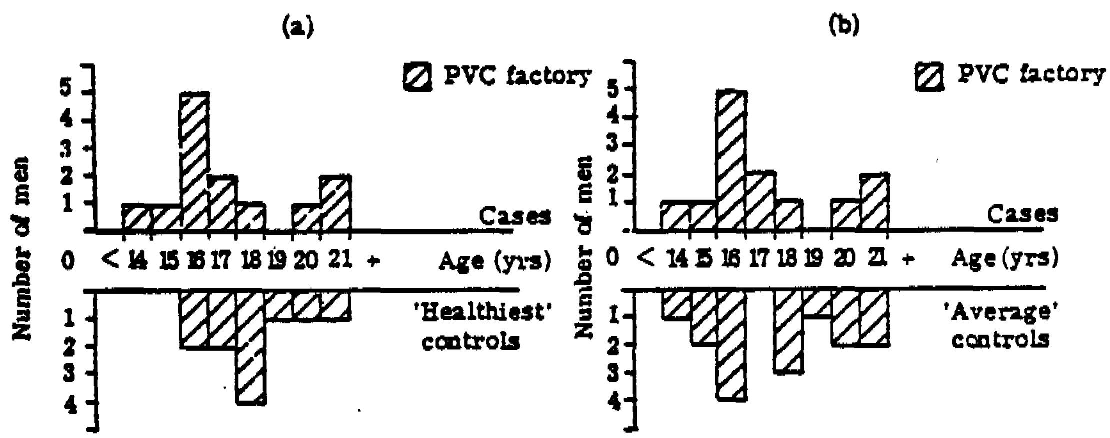

Fig. 9 a) Age when started smoking cigarettes, for FEV_1 cases and 'healthiest' controls, who are current smokers.

b) Age when started smoking cigarettes, for FEV_1 cases and 'average' controls, who are current smokers.

APPENDIX 1

SMOKING QUESTIONNAIRE

1 Do you smoke?

If NO

1a Have you ever smoked as much as one cigarette a day (or one cigar a week or an ounce of tobacco a month) for as long as a year?

If NO to both parts of question 1, omit remaining questions on smoking.

2 How old were you when you started smoking regularly?

3 How old are you now?

4 Do (did) you smoke manufactured cigarettes?

If YES

4a How many do (did) you usually smoke per day on weekdays?

4b How many do (did) you usually smoke per day at weekends?

4c What was the greatest number of cigarettes you ever smoked regularly per day?

4d For how long were you smoking that many?

4e Since starting smoking tobacco have there been periods during which you did not smoke cigarettes?

If YES, for how long altogether were you not smoking cigarettes?

4f (Apart from those times) what was the least number of cigarettes you ever smoked regularly per day?

4g For how long were you smoking that many?

5 Do (did) you smoke hand-rolled cigarettes?

If YES

5a How much tobacco do (did) you usually smoke per week in this way?

6 Do (did) you smoke a pipe?

If YES

6a How much pipe tobacco do (did) you usually smoke per week?

7 Do (did) you smoke small cigars?

If YES

7a How many of these do (did) you usually smoke per week?

8 Do (did) you smoke other cigars?

If YES

8a How many of these do (did) you usually smoke per week?

For ex-smokers:

9 When did you last give up smoking?

APPENDIX 2

NOXIOUS OCCUPATIONS

In the classification of noxious occupations the following jobs were included in the category 'other'. Although it is recognized that some of the jobs included in this category are not widely recognized as 'noxious', it was considered that they may on occasions be associated with health hazards and should therefore be included in the classification of noxious occupations

Brewing
Baker
Flour miller
Farm worker
Wood cutter/sawmill worker
Construction worker
Bricklayer
Plasterer
Quarryman
Paper mill worker
Electrician
Joiner
Glassworker
Welder
Scrap burner
Foreman
Coking plant worker
Furnace operator
Car body repairer
Paint sprayer
Painter/decorator
Tarmacadam exposed workers

APPENDIX 3

Development of the multiple linear regression model used in the analysis of the data from the total survey population

Preliminary multiple linear regression analysis indicated the anticipated relationship between TLco and age, height and weight and between FEV_1 and age and height.

These relationships were looked at again after allowing different intercepts and age slopes for non-smokers and all smokers whether current or ex-smokers. For the TLco analysis, this was a significant improvement in the amount of variation explained. However, this group of smokers did not have a significantly lower mean TLco after age, height and weight had been taken into account than non-smokers and the age slopes were similar. The model used for TLco (but not the FEV_1 model) was further improved by introducing different intercepts and age slopes for three categories of smoking, non-smokers, current smokers and ex-smokers. This analysis showed that for ex-smokers the mean value of TLco was significantly higher than that of current smokers ($P < 0.05$) but that they experienced a greater loss of TLco with age than current and non-smokers although these differences were not statistically significant (Table 1).

Further expansion of this model by allowing different intercepts and age slopes for the different employment categories (current and former employees at the PVC factory and foundry employees) within the three smoking groups did not make a significant improvement to the model. However, this analysis did indicate that the mean TLco level for leavers from the PVC factory who were current smokers was significantly low r ($P < 0.1$) than current PVC factory employees who were non-smokers. However, the age slope of this group did not differ significantly from that of current PVC factory employees who were non-smokers. Hence the model used was the one in which different intercepts and age slop s were allowed for the three smoking groups.

For reasons of consistency the FEV_1 analysis was also based on this same model although there was no significant improvement in the amount of variation explained as there had been for the TLco analysis. The results for FEV_1 analysis show that there was a significant difference ($P < 0.1$) in the rate of loss of FEV_1 with age between non-smokers and current smokers who experienced a greater rate of loss of FEV_1 (Table 2).

TABLE 1 Regression for $T_{L}co$ (ml/min. mm Hg) allowing different intercepts and age slopes for three smoking groups.

Variables	Units	Mean	Regression coefficient	t	P
Age	Years	42.2	-0.2246	-5.74	< 0.001
Height	cm	173.8	0.1552	4.74	< 0.001
Weight	kg	80.2	0.0572	3.23	< 0.002
			Constants (Intercepts)		
Constant for non-smokers			10.3052		
Effect on intercept of:					
Current smokers			-2.5288	-1.34	NS
Ex-smokers			1.4554	0.69	NS
Effect on age slope for:					
Current smokers			-0.0154	-0.33	NS
Ex-smokers			-0.0537	-1.08	NS

TABLE 2 Regression for FEV_1 (ℓ) allowing different intercepts and age slopes for three smoking groups.

Variables	Units	Mean	Regression coefficient	t	P
Age	Years	42.2	-0.0309	-4.55	< 0.001
Height	cm	174.3	0.0420	7.13	< 0.001
Weight	kg	80.4	0.0003	0.09	NS
			Constants (Intercepts)		
Constant for non-smokers			-2.1725		
Effect on intercept of:					
Current smokers			0.4209	1.24	NS
Ex-smokers			0.2675	0.75	NS
Effect on age slope for:					
Current smokers			-0.0149	-1.81	< 0.10
Ex-smokers			-0.0096	-1.13	NS

6

various respiratory symptoms, and gastrointestinal disturbances, such as nausea, vomiting and loss of appetite, are commonly reported by styrene-exposed workers. Other abnormalities reported include headaches, tiredness and sleep disturbance. After a period of exposure, adaptation may occur and there can be a decrease in the various symptoms. Nevertheless, significant alterations still exist among currently employed workers.

Several systematic studies of the various clinical effects from styrene exposure have been conducted in recent years. Many of these focused on possible neurological alterations and clearly demonstrated adverse findings at moderate styrene exposures (less than most national standards). The most extensive of these is that by investigators from the Institute of Occupational Health of Finland (Seppäläinen and Härkönen, 1976; Lindström et al, 1976; Härkönen, 1977; Härkönen et al, 1978). They examined 98 workers employed at 24 plants manufacturing FRP products. Air concentrations were sampled and ranged from 5 to 300 ppm. The means of five post-workday urine mandalic acid (MA) concentrations ranged from 7 to 4,700 mg/l with a linear relationship existing between the log of the MA concentration and the log of the styrene concentration. The mean value of MA in the population was 808 mg/l and corresponded to an exposure of about 40 ppm of styrene. Abnormal EEG's were found in 30% of those with MA in excess of 700 mg/l, compared to about 10% for those with lower MA values and normal controls (Seppäläinen and Härkönen, 1976). Lindström et al (1976) noted increased visuomotor inaccuracy (symmetry drawing and Bourdon-Wiersma tests) and lowered psychomotor performance (Mira test) for various MA concentrations ranging from 800-2,000 mg/l (See also: Härkönen et al, 1978). Fatigue, irritation, difficulty in concentration, nausea, dizziness, and lightheadedness were more frequently reported by the styrene-exposed workers than by unexposed controls (Härkönen, 1977).

A deteriorating EEG among styrene workers has also been described by Klimkova-Deutschova et al (1973). Alterations of nerve conduction have been documented by Rosén et al (1978) who observed an increased duration and decreased amplitude of sensory action potentials. Lilis et al (1978) suggested the possibility of a decrease in peroneal nerve conduction velocity. The decrease, however, was only associated with length of employment and not intensity of exposure. Subjective symptoms of physical and mental tiredness after styrene exposure have been reported by Klimkova-Deutschova et al (1973) and Cherry et al (1980), among others. The reported neurological findings among styrene-exposed workers are less serious than those reported in some other groups occupationally exposed to solvents, such as as painters (Lindström, 1980; Hane et al, 1977). However, the continued exposure to concentrations causing the observed abnormalities may lead to more serious central nervous system impairment.

In addition to neurological disturbances, alterations of pulmonary function have been noted among styrene-exposed workers. Lorimer et al (1977), in an examination of 494 polymerization workers, found a reduction in FEV_1 to be associated with intensity of exposure and with urine MA concentration. Further, the workers in the higher exposed group reported a greater percentage of acute and recurrent lower respiratory symptoms. Härkönen (1977) reported an increase in incidence of chronic bronchitis which correlated with intensity of exposure. On the other hand, Axelson et al (1978) did not find any abnormalities of pulmonary function among 27 FRP boat manufacturing workers.

Laboratory test results have been rather unremarkable. Lorimer et al (1977) suggested the possibility of increased lymphocytosis among polymerization workers and Checkoway (1982) found a correlation between decreased red blood cell count and increased basophil count with styrene/ butadiene exposure. Increased blood enzyme concentrations, characteristic of abnormal liver function, occasionally have been reported. Lorimer et al (1977) found a significant increase in concentrations of GGTP (gamma glutamyl transpeptidase) and Hotz (1980), noted increased concentrations of OCT (orinthine carbamoyl transferase) and ALAT (alanine amino transferase) among polymerization workers.

SUMMARY OF HUMAN MORTALITY AND MORBIDITY

The limited epidemiological studies of mortality associated with styrene exposure do not demonstrate any excess cancer risk that can be attributed to styrene, although elevated risks for leukemia have been noted in exposed groups. However, these excesses may be related to exposures to other chemicals, such as benzene. The studies are severely limited because of the relatively low styrene exposure of the groups studied. They provide no guidance on carcinogenic risk in populations much more heavily exposed as in the FRP industry. The significant clinical findings among styrene-exposed workers are largely limited to abnormalities of the central nervous system, where a variety of objective and subjective symptoms have been reported in the FRP industry. Concern for long-term degnerative neurological disease exists for continued long-term exposure in this industry. The possibility of pulmonary effects from styrene exposure has also been noted.

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