A STUDY OF PULMONARY FUNCTION IN ASBESTOSIS

by

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ABSTRACT

258 workers in three asbestos factories were examined, by clinical, radiological and pulmonary function tests.

Rales was found in 35 workers (14%), approximately ⅔ of whom had radiological changes, most commonly both pleural and parenchymal, 63% had disturbed lung function and 38%, clubbing.

Those with radiological abnormality 93 (37%) had lower values for $T_{L\ CO}$ and VC than those without. Either pleural or parerchymal abnormality occurred in isolation in 43 (46%). Clubbing occurred in 35% of those with both changes together who often had other abnormalities and the lowest mean values for T_{LCO} and VC.

Airways obstruction was found in some individuals with asbestosis. Pulmonary function and pleural or parenchymal abnormality are probably the earliest signs of asbestosis, rales, clubbing and pleural and parenchymal changes together, appear later.

No evidence for more asbestosis in smokers than non-smokers was found.

Doubt was cast on the methods of certification as some certified workers had minimal grounds for certification, other uncertified workers had good evidence of the disease. An objective method for evaluating the results of any individual was obtained by using principal component analysis. T_{LCO} and VC were the best indicators of general lung disease, FEV/VC%, cough and phlegm of airways obstructive disease and radiological abnormality, rales and finger clubbing of asbestosis.

A correlation between exposure and disease (as measured by component I) in factories B and U but not in factory M suggested that chrysotile, used at M, is less dangerous than amosite (at U) and amosite plus crocidolite (at B). Lack of

comparable past dust figures in the three factories casts doubt on this conclusion.

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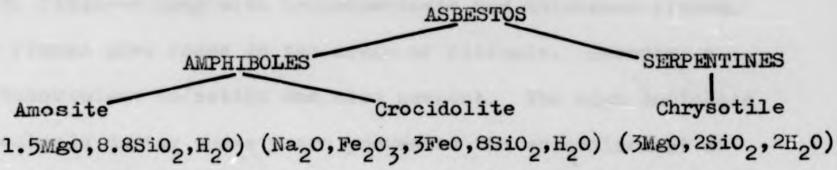
INTRODUCTION

Historical background

The naturally occurring fibrous silicates, known collectively as asbestos, may be divided into two main groups:-



These are the three main types of asbestos, of commercial value, of which chrysotile is the most widely used. These minerals, because of their properties of heat and acid resistance and great tensile strength have been used for at least 2,000 years but have been increasingly used commercially in the last 100 years in the insulation, building and friction material trades. Currently the fibres may also be found in varying proportions in paper, wall board, floor tiles, cements, plastics, putties and many other products.

It was not suggested until the beginning of this century that the inhalation of asbestos dust might cause a specific disease. At this time it was known that inhalation of various dusts caused disease but any dust was considered to be harmful, the nature of the dust being unimportant. In 1906, in a report to the Departmental Committee on Compensation for Industrial Diseases, H. Montague Murray described the case of a 33 year old man in whom the inhalation of asbestos dust was implicated as a possible cause of death. Post mortem the lungs showed a fibrosis which was non-tubercular in origin. On section, asbestos spicules were seen in the lung tissues.

As a result of this report, a study of 40 asbestos workers was carried out between 1910-1911 by the factory department of the Home Office. It was concluded from the results of this study that there was no evidence of a serious health hazard. In 1912 Professor J.M. Beattie showed that inhalation of asbestos dust caused pulmonary

fibrosis in animals.

In 1924 a second case of pulmonary fibrosis in an asbestos worker was reported by W.E. Cooke. This 33 year old female, first exposed to asbestos 20 years previously, showed post mortem a small firm, very fibrosed lung with bronchiectasis and thickened pleura. Asbestos fibres were found in the areas of fibrosis. However, a chronic tuberculous infection was also present. The high incidence of tuberculosis during these years prevented the establishment of an aetiological relationship between the innalation of asbestos dust and pulmonary fibrosis. Cooke stated that his case was the first proven case of pulmonary fibrosis resulting from the innalation of asbestos dust although the harmful nature of this dust had long been suspected, especially after Beattie's animal experiments. In 1927 further evidence was reported incriminating asbestos dust as a cause of lung disease. Sir T. Oliver described the clinical condition of 2 female weavers, thought by him to be cases of pulmonary fibrosis caused by exposure to asbestos. Both complained of shortness of breath and cough, with little expectoration. In one, moist rales were present and in both, dry friction sounds at the lung bases. Chest expansion was less than one inch and neither showed any evidence of tuberculosis.

More cases in which asbestos was implicated as a possible cause of disease were reported during the next few years, both in this country and from abroad, and a picture built up of the signs and symptoms of a pathological condition, asbestosis, resulting from the inhalation of asbestos dust. Dyspnoea and cough with scanty sputum were described as symptoms with reduced chest expansion and signs of fibrosis at the lung bases. The Xray was reported as showing a diffuse, ground glass mottling, quite distinct from the

nodular pattern seen in silicosis. At autopsy the lungs appeared leather like and airless with thickened pleurae. Asbestosis bodies, which are fibres of the mineral coated with an organic deposit, were first described in post mortem lung tissue by S. McDonald in 1927. They were considered to be characteristic of the disease and it was suggested that these could prove to be an important diagnostic feature and even that their presence alone was conclusive evidence of asbestosis.

During 1928 and 1929 an investigation was carried out by the Factory Department of the Home Office, into the asbestos industry. This study was initiated by the report in 1928 by H.E. Seiler of a third case, in addition to those of Montague Murray and Cooke, of pulmonary fibrosis in an asbestos worker. The investigation was carried out by E.R.A. Merewether and C.W. Price to find out if these cases were exceptional or whether there was a grave health risk in the industry. They studied 374 workers from the total of 2,200 believed to be exposed to asbestos in the industry throughout the country. Detailed medical and occupational histories were recorded, each worker was examined clinically and 363 workers were examined by radiology. Of 363 subjects (11 were excluded as they had been exposed to fibrogenic dusts in addition to asbestos), 95 or 26·2% were found to have definite signs of pulmonary fibrosis and a further 21 showed early signs of the disease. As the group studied contained a greater proportion of workers exposed for 5 years or more than the general industrial population, a correction was applied. From the corrected figures asbestosis was estimated to be present in one in eight of the population of the asbestos industry. It was further concluded that there was a direct relationship between the incidence of fibrosis and the length of employment and also the dustiness of the job. From consideration of these two factors, time of exposure and concentration

of dust, it was suggested that by reducing the dust to a minimum the incidence of the disease would also be reduced to a minimum.

This report established a relationship between the inhalation of asbestos dust and pulmonary fibrosis and as a result in 1931 regulations for the industry were drafted. From 1931 a compensation scheme covered all workers in certain scheduled jobs, these workers being required to undergo medical examination at the time of employment and periodically throughout their term of employment.

Since 1930 there have been many reports describing the various aspects of asbestos as a hazard to health. The nature and importance of 'asbestosis' bodies have been studied and it was concluded by Merewether, among others, that, as they may be found in the sputum of workers very soon after first exposure and also in subjects showing no clinical or radiological evidence of asbestosis, these bodies are indicative only of exposure to asbestos. For this reason the name asbestos body was suggested by S. Roodhouse Gloyne (1929), rather than asbestosis body.

Another problem that was investigated was whether asbestos workers, both those with and those without asbestosis, show an increased susceptibility to tuberculosis such as is found in silica workers. Wood and Gloyne (1931) reported the presence of pulmonary tuberculosis in 12 out of 57 cases of asbestosis, a higher incidence than in the general industrial population. Merewether (1933-34) in a review of asbestosis, regarded this figure as unusually high for the industry, but later research into this problem showed that asbestos workers do not show a predisposition to tuberculosis. As evidence against tuberculosis being a complication of asbestosis accumulated, there was growing evidence for a relationship between asbestos exposure and carcinoma of the lung and mesothelial tissues. At the present time the evidence points to a specific relationship between mesotheliomata and asbestos exposure.

Another problem is the length of exposure before signs of the disease appear. Haddow (1929) described 4 female workers with asbestosis in whome the average total length of exposure was 14 years He suggested that the disease was not likelyto appear before the 5th year of exposure. Wood and Page (1930) described the death of a 21 year old girl, 2 years after she began work spinning asbestos. The cause of death was tuberculosis with no clinical or radiological evidence of asbestosis, but according to these authors at post mortem there was evidence of a small amount of pulmonary fibrosis. Merewether concluded from his study that there was no clear evidence of asbestosis occurring in workers with under 5 years of employment. A. Böhme (1942) found evidence of pulmonary fibrosis in 5% of the workers that he examined with less than 3 years exposure, the incidence increasing with years of employment to 79% in workers with over 10 years exposure. However, the bulk of the evidence supports the view that for the majority of workers at least 5 years since first exposure will elapse before signs of the disease appear but the total length of exposure to the dust may be much less than this. Wood and Gloyne (1934) in a study of 100 cases described a few who had worked less than one year in the industry, but it is not clear from their report how many years had elapsed since these very short exposures. Recent studies on small groups of workers showed little correlation between total years of exposure and lung impairment (Kleinfeld et al 1966), but a study of a much larger group (Hunt 1965) showed a relationship between the disease and years since first exposure. However in this study some workers exposed for many years apparently remain unaffected. This contrasts with Merewether's study, from which he concluded that 79% of workers with 10 years or more service in the industry had signs of the disease. This may be considered as evidence that the conditions of work have improved since he studied the industry, but not sufficiently to eliminate the disease entirely.

During the last few years evidence has accumulated (Harries, P.G. 1968, Wallace W.F.M. et al 1971, Sheers G. et al 1968, Selikoff I.J. et al 1965) that workers other than those directly involved in the manufacture of asbestos products are exposed to a health hazard from handling materials containing asbestos for example insulation workers in dockyards. It is believed that 40-50% of new cases of asbestosis now being diagnosed have resulted from this type of work. The asbestos regulations of 1931 did not adequately cover this type of work and as a result of this recent evidence new asbestos regulations were drafted in 1969 which cover any occupation in which employees are exposed to asbestos dust liable to endanger their health.

One of the problems puzzling research workers at the present time is why some workers are more susceptible to the disease than others. It has been suggested by Turner-Warwick et al (1970 and 1971) that immunologic factors may play a role and that screening asbestos workers for circulating rheumatoid and anti-nuclear factors might provide a basis for excluding unusually susceptible persons from exposure.

The Pathology of Asbestosis

Gloyne described the post mortem appearance of the lung in asbestosis as being small, firm and hard, and, like Ellman and Merewether (1933), stressed the frequent occurrence of bronchiectasis. From autopsies of 6 cases, Heard and Williams (1961) found pleural adhesions and fibrosed areas in all 6 and pleural plaques in 3. In 3 out of 4 of these cases studied by pressure fixation the bronchi were dilated and thick walled. Hourihane (1966) mentions bronchiectasis as a feature of asbestosis and also describes the occurrence of cystic changes in the air spaces between fibrotic areas

giving rise to so-called honeycomb lung, but considered this change as rarely extensive. The fine nodular fibrosis apparent on sectioning the lung is generally described as most severe in the lower parts of the lung and sub pleurally but solid areas of fibrosis do occasionally occur in other parts of the lung (Hourihane, Heard and Williams).

The abnormality starts as a peribronchiolar fibrosis and gradually extends outwards from the bronchiole to the surrounding alveoli. Gross (1967) in a recent paper on the mechanism of some structural alterations in the lung, describes the proliferation of alveolar epithelial cells. When this occurs at a greater rate than the desquamation of the cells the alveolar membrane becomes thickened and may ultimately obliterate the air space, therefore reducing the surface area of the alveolar capillary membrane. Much of the fibrosis is intra-alveolar as many areas with obliterated alveoli have an intact elastic network (Webster, 1970). The alveolar blood vessels are often sclerosed and narrowed by fibroelastic, intimal thickening and in areas of marked cellular proliferation may disappear altogether. Eventually in areas of solid fibrosis collagen may entirely replace the lung parenchyma.

The overall picture is of a lung limited in its movement both by pleural thickening and adhesions and also by the increase in relatively inelastic collagen. In areas of fibrosis the alveoli may be partially and completely obliterated and therefore if the tissue is normally perfused the blood in these capillaries will be underventilated. Where the blood vessels have disappeared there will be patches of non-functioning lung tissue. The functioning

of the lung and its radiological appearance will be affected by these changes, the degree of disturbance depending upon the distribution and severity of the changes.

Theories of mechanism of fibrosis

It is still uncertain how asbestos causes fibrosis although much research has been carried out into this problem. At the present time there are several theories. One of the earliest theories postulated that needle like fibres of the mineral wedge in the airways and air spaces of the lung, causing physical irritation and damage to the tissues. In a prolonged series of experiments Gardner and Cummings (1938) exposed animals to chrysotile dust of varying fibre lengths and found that the very finely ground asbestos dust appeared inert. This finding supported the theory of the physical irritation as by finely grinding chrysotile the fibres were destroyed and this apparently rendered it non-toxic. Vorwald et al (1951) confirmed this result and found in addition that amosite and crocidolite also cause fibrosis. The authors explained this rather odd result by suggesting that it was due to the greater rigidity of fibres of glass wool. Schepers (1959) from the results of a similar series of experiments concluded that the fibrogenic action of asbestos is not purely mechanical. Knox (1954) pointed out that as the length of time between initial exposure and development of the disease may be many years in humans, the stimulus to fibrogenesis is more likely to be chemical than physical. As early as 1932 it was suggested by Gerbis and Ucko that silicic acid dissolved out from the asbestos caused the fibrosis by chemical irritation. Knox supported this solubility theory but suggested that the development of fibrosis resulted from the breakdown products of asbestos bodies.

With the introduction of high power microscopes the cellular reaction to mineral particles has been seen, these particles being phagocytosed by cells of the alveoli. After ingesting silica or asbestos particles the macrophage has been seen to undergo lysis and it has been suggested that the substances released initiate fibrosis either by an auto immune reaction or by the sclerosing nature of the released substances. Another autoimmune concept (Pernis et al 1965) is the reaction of the asbestos within the phagocyte to produce or localise abnormal globulin which act as auto antigens in producing auto antibodies recognised as rheumatoid factor in the serum. Greater knowledge of the toxicity of dust particles of different size and different chemical constitution would help to solve this problem. Recent work by Davis (1965) in contradiction to the work of Gardner et al (1938) has shown that very small dust particles are capable of causing fibrosis in animals. Wagner (1963) has shown that chrysotile will cause fibrosis in guinea pigs but causes only a very slight reaction in monkeys and rabbits, whereas marked fibrosis will follow exposure to amosite in these two animals.

Type of Asbestos Exposure

Wagner et al 1963 produced asbestosis in experimental animals by exposing them to mill dusts. He found that amosite was more toxic than chrysotile. Unfortunately he was unable to draw any conclusions as to the relative toxicity of crocidolite as the dust sample was found to be impure. In more recent work (1972) with rats he found that chrysotile in inhalation experiments seldom caused mesothelioma and fibrosis unlike amphibole asbestos and suggested that this was due to the aerodynamic properties of chrysotile which prevent it penetrating deeply into the lung. To prove this point he

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demonstrated that if chrysotile is inoculated directly into the pleura it does cause mesothelioma. Amphibole asbestos has short straight fibres which travel readily in the air stream (Speil et al 1969) to reach the peripheral airways and there cause fibrosis and mesothelioma. Wagner said that the position of amosite was not clear and concluded that its toxicity depends upon the source of the mineral. Timbrell 1970 said that the behaviour of inhaled particles depends less on their size than on their shape, the soft curly, chrysotile fibres are more likely to be intercepted higher up the small airways. Vigliani et al McDonald et al found chrysotile to be less likely to produce tumours than crocidolite. Parezzi et al from "in vitro" studies concluded that crocidolite is more markedly cyto toxic than chrysotile. Kogan et al (1966) from studies of the effect of serpentine and amphibole asbestos on human lung tissue cultures concluded that chrysotile is much less active than anphibole asbestos. Wyers (1946) in his thesis suggested that amosite was the most dangerous, followed by crocidolite, chrysotile being least dangerous. This comment does not appear to have been based on any experimental or epidemiological evidence. Weill stated that his study (1975) was the first to show that crocidolite produces more pulmonary fibrosis than chrysotile. He found chrysotile workers had more normal values for transfer factor and lung volumes than crocidolite workers.

In a recent article (C. Wagner, 1974) quoting from a summary of the Proceedings and Report of the Advisory Committee to the International Agency for Research in Cancer, it is said that all types of asbestos produce pulmonary scarring if there has been excessive exposure to the dust. The author of this article then goes on to say that he has evidence that the physical form of the fibre is a factor in producing mesotheliomas in animals.

The Diagnosis of Asbestosis

By using pulmonary function tests, radiology and clinical examination asbestosis can now be diagnosed at a much earlier stage of the disease than in the past. In the first recorded case of asbestosis in this country (Murray 1906) diagnosis of non-tubercular pulmonary fibrosis was only made with certainty at post mortem. The second case, reported by W.E. Cooke in 1924 complained of cough, dyspnoea and lassitude. The Xray showed extensive fibrosis in both lungs with some calcification of the left lower lobe. The diagnosis of asbestosis was confirmed by autopsy. Seiler's case, in addition to the symptoms of cough with scanty sputum dyspnoea, was described as being slightly cyanosed with well marked finger clubbing and poor chest expansion (less than 1 inch). Pleural friction sounds could be heard at both bases and the Xray showed fine mottling. Wood and Gloyne in a description of the disease in 1930 confirmed these findings and emphasised that cough and dyspnoea with breathlessness on exertion are early signs and also that the Xray appearance is quite distinct from that of silicosis, appearing as a fine 'ground glass' haze over the lower lung fields with, in advanced cases, a shaggy outline to the heart. In a review of 100 cases in 1934, these same authors considered that diagnosis in life rested on radiological appearance, symptoms and physical signs and asbestosis bodies as evidence of exposure, in this order of importance. They emphasised that, by these means, diagnosis was made at a relatively advanced stage of the disease, no adequate methods being available at this date for earlier diagnosis. (An interesting point in connection with this is that in their 1930 paper these authors reported a vital capacity of only 1.6 1. in one of their patients, but apparently did not realise the

possible use of this observation). In an extensive study of asbestosis in the American asbestos textile industry Dreessen et al (1938) also stressed the importance of the Xray in establishing a diagnosis of asbestosis. They classified the Xrays into 4 grades, 1st and 2nd degree linear and 1st and 2nd degree ground glass markings and considered that although early asbestosis might be diagnosed in a case with a 2nd degree linear film if symptoms and signs of fibrosis were present in a sufficiently advanced degree, in general the diagnosis was not made unless ground glass markings were present. These workers also measured chest expansion, which they found was reduced in a significant proportion of workers with Xray evidence of asbestosis. This finding confirmed that limitation of movement of the chest, probably due to pleural adhesions and the inelasticity of fibrotic lung tissue, was a symptom of the underlying disease. These workers also found a raised respiratory frequency at rest in cases of asbestosis.

Roemheld et al (1940) studied the changes in pulmonary function in more detail. In the 19 subjects studied they confirmed the finding of Dreessen et al (1938) of an increased respiratory rate, and also found arterial O_2 desaturation on exercise, restriction of maximum ventilation and reduced vital capacity. Baldwin et al (1949) found in addition one case with a low arterial O_2 saturation at rest. Gernez-Rieux et al (1954), in contrast to Roemheld et al (1940) and Baldwin et al (1949) found a well preserved maximum breathing capacity. They also found an increased residual volume but Gregoire, in a paper presented before the 7th Saranac Conference in 1952, reported that unlike silicotics, asbestotics rarely showed pulmonary function evidence of emphysema. Bastenier et al (1952-55) described further cases which showed low arterial O_2 saturation

at rest and concluded that there was no correlation between the radiological appearance and degree of pulmonary dysfunction, in contrast to Roemheld et al who reported a rough relationship between the reduction in vital capacity and radiological abnormality. Wright (1955) agreed with Bastenier that there was little correlation between the degree of clinical and pulmonary function abnormality and the radiological picture. He described the asbestotic lung as stiff, uncompliant, with restricted expansion resulting in a reduced TLC and VC, the RV remaining normal, indicating little impairment to emptying of the lung. He found the maximum breathing capacity well maintained except in advanced cases, which probably explains the contradictory findings of other workers. He and other workers (Williams et al 1960, Bjure et al 1964, Wallace et al 1971) reported a reduced arterial oxygen tension and a raised alveolar-arterial oxygen difference. He concluded, like some previous workers, that the finding of a raised A- a gradient for O_2 was indicative of a defect of pulmonary diffusion. Austrian et al 1951 suggested that thickening of the alveolar blood gas barrier in certain diseases would limit diffusion across the membrane and introduced the term alveolar-capillary block syndrome to describe this condition. Asbestosis was grouped with other diseases under this heading (Bader et al 1961). Measurement of the diffusing capacity of the lung in asbestosis was first reported in 1957 by Marks et al who found reduced values for D_{O_2} and D_{CO} in a case of questionable asbestosis. In the same year Bader et al found a significant reduction in D_{O_2} in 3 out of 5 cases studied. For a while it was believed that the defective pulmonary diffusion and oxygenation of the blood was entirely due to the increased thickness of the alveolar capillary membrane. However, Finley et al (1962) pointed out that changes in the

blood-gas barrier would have to be very gross to cause any significant degree of impairment in diffusion. Such an increase in thickening would probably be uneven and almost certainly inequality of ventilation would be present and the pulmonary capillary blood would be affected. Several studies Donald et al 1952, Holland et al 1962, Read et al 1959, and Finley et al 1962 have since shown that the ventilation-perfusion relationship is upset in generalised lung disease. Therefore, it seems far more likely that the defective gas transfer in asbestosis is caused by the upset in this relationship rather than by the increased thickness of the alveolar-capillary membrane.

Since 1957 when the first measurements were made of transfer factor of the lung for CO and O_2, there have been many other studies of lung function in asbestosis. These studies confirmed the earlier findings and established the value of lung function tests for the diagnosis of early asbestosis, especially the measurement of diffusing capacity, now called transfer factor, vital capacity and lung compliance. They also showed that changes in lung function may occur before abnormalities appear on the radiograph. Functional deterioration is often not accompanied by radiological deterioration and therefore measurement of lung function may give a better idea of progressive disability than the appearance of the Xray. Many of the subjects of these studies have had the disease in its early stages. Unlike the earliest cases examined, they were often still employed and only mildly affected by the disease. In the diagnosis of a disease it is important to recognise the earliest signs, and several of these studies have considered the problem of the earliest signs of asbestosis. Busser et al 1971, from a study of one hundred asbestos workers, concluded that reductions in vital capacity and compliance are early signs of the disease which may precede radiological abnormality. Jodoin et al

examined twenty-four workers with normal Xrays who had been exposed to asbestos for up to twenty-four years. He found that those with the longest exposure had a higher static lung recoil pressure and smaller vital capacity than those with less exposure to asbestos. Ghezzi et al (1972) from a study of two hundred and seventy asbestos miners concluded that the presence of rales and a reduced transfer factor are early signs of the disease and may precede radiological abnormality. Sartorelli et al (1972) from a study of seven hundred and twenty-four workers came to the same conclusion. Beverly et al (1973) from a study of seventy one certified cases of the disease, listed these factors in early detection in order of importance, Xray, clinical signs, reduced transfer factor. However, he allowed that there are exceptions where Xray changes may not appear until later. Murphy et al (1972) found evidence to suggest that the transfer factor declines more rapidly than the vital capacity. In a recent paper Britton et al (1977) carried out serial pulmonary function tests and concluded that there is an initial marked fall in transfer factor preceding any significant fall in vital capacity which is later followed by a steady decline in both which is greater than that due to ageing alone. Parkes (1973) said that crepitations are the earliest physical sign and often precede abnormality of lung function and Xray.

From earlier studies it was thought that exposure to asbestos dust did not significantly affect the pulmonary air ways. Airways obstruction is not generally a feature of asbestosis, although it does occur (Thomson et al 1964, Williams et al 1960, Scheaning et al. 1965, Leathart 1960, Sartorelli et al 1964, Muldoon et al 1972). It has been suggested that there may be small airways obstruction due to fibrosis of the respiratory and terminal bronchioles, Macklem et al 1969,

Jodoin et al 1971, Muldoon et al 1972, but Woitowitz 1970 could find no clear evidence that asbestos contributes to obstructive respiratory disorders as measured by FEV. Weill 1975 suggested that early adverse effects of asbestosis may be on the airways, particularly the smaller ones. Recently, Seaton (1977) has shown evidence of impaired ventilation of the lower zones of the lung in subjects with asbestosis, using a radioactive method. As few workers have used methods which detect narrowing in the small airways this may be the reason that many workers have concluded that asbestos does not generally affect the airways. Muldoon et al (1972) suggested that the possibility that asbestos dust can induce bronchial wall damage needs further critical study.

At the present time evidence from these studies suggests that there is no definite pattern in the development of asbestosis. Xray changes may or may not precede pulmonary function changes or the first signs of the disease may be found on clinical examination. There is still no general agreement as to which pulmonary function parameter is first affected. Jodoin et al considered static elastic recoil pressure as the most useful measurement, but other workers (Britton et al, Ghezzi et al) favoured transfer factor and Busser et al, Thomson et al, Bader et al and Becklake et al, vital capacity as the best test for distinguishing between subjects with and without the disease. However, in well developed cases, the picture is of a lung restricted in its movement resulting in low values for pulmonary compliance and lung volumes. Fibrotic changes result in disturbance of ventilation perfusion relationships leading to reduced gas transfer and arterial oxygen tension and increased alveolar-arterial oxygen difference. There may also be increased airways obstruction in the small airways but

further work is needed to clarify this point.

Parkes in 1973 gave this list of mandatory criteria for the diagnosis of asbestosis:-

(1) Definite asbestos exposure

(2) Bilateral basal crepitations

(3) Radiological changes of diffuse inter-stitial fibrosis in the lower halves of the lung fields

(4) Impairment of lung function

He added clubbing, pleural plaques, dyspnoea on effort and asbestos bodies in the sputum to this list as providing corroborative evidence.

Pulmonary function in asbestosis

The pathological changes in the lung already described will affect pulmonary function. In asbestosis, fibrosis occurs in the inter-alveolar and peribronchiolar tissue. This increase in interstitial tissue prevents full expansion of the lung, reduces its compliance and increases the elastic recoil pressure. These changes, together with a loss of alveoli due to obliteration by fibrosis, result in a reduction of vital capacity. The residual volume at an early stage of the disease may be reduced to a greater extent than TLC due to increased elastic traction on the walls of the small airways preventing their collapse until a later stage of expiration. At a later stage of the disease, RV/TLC% may rise because lung movement is restricted by the fibrosis.

Ventilatory capacity as measured by FEV/VC% is unchanged, as both volumes are reduced proportionately, or a higher than normal value may be recorded due to the increased elastic traction on the walls maintaining their patency (Pilzer et al 1965).

Another effect of the fibrosis is in limiting expansion of some alveoli. This leads to an increase in the range of ventilation-perfusion ratios, an increase in the physiological dead space and a rise in the alveolar-arterial O_2 tension difference, particularly on exercise. This hypoxaemia results from a low transfer factor which is due partly to a loss of capillaries, partly to the increased distances necessary for gaseous diffusion in the respiratory bronchiles. The hypoxaemia may be said to be due to the imperfect distribution of the surface available for the exchange of gas with respect to lung volume (T_L/Va inequality) the blood flow (T_L/Qc inequality) and the capillary blood volume (T_L/Vc inequality) - (Cotes J.E. 1975).

AIMS OF THIS STUDY

At the time when this study was planned (1962-63) various questions relating to asbestos exposure remained unanswered. Although it was thought that amphibole asbestos was possibly more cytotoxic than serpentine asbestos, there had not been any comparative studies of workers exposed to these different forms of the mineral. One of the main aims of this study was to determine the relative toxicities of three types of asbestos amosite, crocidolite and chrysotile. It was also hoped that answers might emerge to such questions as:-

(1) Is there a pattern of lung function disturbance relatable to patterns of Xray abnormality, and is this disturbance more severe in subjects with parenchymal changes than in those with only pleural thickening?

(2) Are basal rales present in the absence of Xray abnormality and what evidence is there of disturbance of lung function in those with rales?

(3) Does clubbing relate to any particular test of lung function?

(4) Do smoking habits affect the development of asbestosis?

A further aim was to assess the relative importance of various clinical signs and symptoms, radiological appearance and pulmonary function tests in identifying asbestosis. Around this date (1963) diagnosis by the Medical Panels of the Pneumoconiosis Boards for the purpose of notification was based on the following: adequate exposure to asbestos dust which may be either as little as 3-4 years of recent exposure or a shorter exposure some years in the past, plus two positive findings from the following: 1. Basal rales 2. Finger clubbing 3. Radiological abnormality 4. Abnormal pulmonary function (McVittie 1965).

PLAN OF THE STUDY

At this point I would like to say that I, personally, was not involved with the designing or planning of this study, the factories to be studied and the tests and examinations to be used were already decided upon before I was engaged to help with the study which was carried out between 1964 and 1967.

As one of the aims of this study was to compare the effects of exposure to different kinds of asbestos, it was planned to examine workers in three factories using different kinds of asbestos.

Permission was obtained to examine workers in three factories, Factory B using all three types of asbestos, Factory M chrysotile only, and Factory U, amosite plus a small amount of chrysotile. Unfortunately, it was not possible to examine workers exposed solely to amosite or crocidolite. However, it was hoped that some indication of the relative fibrogenicities of these three forms of the mineral might emerge.

Table (1) gives details of the departments within the factories involved in the manufacture of products using asbestos. It shows the percentage of asbestos and other materials used in the different products.

Population to be examined

Although everyone on the factory site is exposed to some extent to asbestos, because of the large numbers involved, the size of the population to be examined had to be reduced. It was, therefore, decided to examine only those caucasian male workers directly involved with the manufacturing process - this included ancillary processes such as unpacking and preparing the materials to be used and packing the finished product. To reduce the numbers still further, only those workers who had been first employed to work with asbestos, three or more years before the

PLAN OF THE STUDY

At this point I would like to say that I, personally, was not involved with the designing or planning of this study, the factories to be studied and the tests and examinations to be used were already decided upon before I was engaged to help with the study which was carried out between 1964 and 1967.

As one of the aims of this study was to compare the effects of exposure to different kinds of asbestos, it was planned to examine workers in three factories using different kinds of asbestos.

Permission was obtained to examine workers in three factories, Factory B using all three types of asbestos, Factory M chrysotile only, and Factory U, amosite plus a small amount of chrysotile. Unfortunately, it was not possible to examine workers exposed solely to amosite or crocidolite. However, it was hoped that some indication of the relative fibrogenicities of these three forms of the mineral might emerge.

Table (1) gives details of the departments within the factories involved in the manufacture of products using asbestos. It shows the percentage of asbestos and other materials used in the different products.

Population to be examined

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date of commencement of the survey, were included in the population. In giving us permission to examine workers in the three factories, the factory management made it quite clear that these workers were under no compulsion to attend for the tests. It was entirely up to the individual whether he agreed to undergo the examination.

Techniques employed in the survey

As I have already said, I was not involved at the planning stage of this survey and so took no part in deciding upon the methods to be used.

In allowing their workers to be examined, one of the stipulations laid down by the factory management was that the tests must be acceptable to the workers. This immediately excluded certain tests, among them any involving blood sampling and also compliance. As attendance for examination was not compulsive, any unpleasant tests would most certainly have affected the response rate.

The techniques finally chosen were as follows:-

I Clinical examination to include:

(a) Chest examination for rales and rhonchi

(b) Blood pressure

(c) E.C.G. recording

(d) Collection of sputum

(e) Clubbing measurement

(f) Cardiac questionnaire

(g) Respiratory questionnaire

II Radiological examination

III Pulmonary function examination to include measurements of the following parameters:-

(a) Total lung capacity and its subdivisions

(b) Transfer factor and Dm and V_c

(c) Peak flow rate

(d) Forced expiratory flow rate (1 sec) and forced vital capacity

(e) Specific conductance by the whole body plethysmograph

(f) Arterial O_2 saturation by the ear oximeter (Waters-Conley)

METHODS

I Clinical examination

Rales

It has been known for many years that crackling sounds at the lung bases are a sign of asbestosis and the presence of these sounds is one of the criteria used in the diagnosis of the disease (McVittie 1965).

In an article in the Lancet Forgacs (1967) discussed the clinical interpretation of rales and concluded that these sounds are due to the equalisation of gas pressure as airways, closed in territories of the lung deflated to residual volume, open suddenly during inspiration. He further suggests that persistent rales are often a sign of regional deflation in lungs stiffened by diffuse fibrosis. These sounds are confined to the lung bases where the force of gravity and increased elastic recoil combine to deflate the lung.

In this survey, the subjects were examined for the presence of rales by M.L. Thomson. They were sought at both lung bases in the midaxillary line and at the posterior lung bases. For the analysis, their presence was coded as 1 and absence as 0.

Rhonchi

These sounds, generally described as wheezing, are believed to be caused by air passing at high velocity through airways, narrowed to the point of closure. Forgacs (1967).

M.L. Thomson examined each worker for their presence at the same time as the examination for rales. The absence of rhonchi was coded as 0 and the presence as 1.

Finger clubbing

Finger clubbing was noted as a feature of asbestosis as early as 1928 (H.E. Seiler). McVittie (1965) recorded the presence of finger clubbing in 35% of workers, certified throughout the country, between 1933-1963 but commented that this finding was subject to inter and intra observer error. For this reason it was felt that precise measurement of finger clubbing would reduce this error and increase the value of finger clubbing as a diagnostic indicator of asbestosis.

Cudkowitz and Wraith (1957) and Stavem (1959) suggested various methods for measuring finger clubbing and it was decided to test these methods.

As a result of a study carried out on fifty finger casts (Appendix 1) it was concluded that the hyponychial angle provided the best measurement of finger clubbing and therefore this was the method used in the study.

Blood pressure

This was measured on all subjects by the usual sphygmomanometric method.

E.C.G.

A thirteen lead E.C.G. was recorded using a Cambridge minigraph. The tracings were read clinically by A.J. Thomas. They were also measured and coded by the modified Minnesota code (Silvester et al 1967). It was thought that right heart strain might show on the E.C.G. at an early stage of the disease and could be useful in diagnosis.

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Cardiac questionnaire

A cardiac questionnaire (G. Rose 1962) was completed for each subject. It was hoped that heart disease resulting from pulmonary dysfunction might be detected.

Respiratory questionnaire (MRC 1960)

This was completed (long form) for each subject. From this the degree of dyspnoea was graded by the method of Fletcher C.M. (1959). Cough and phlegm were coded according to the recommendations outlined in "Suggestions for the coding and presentation of results of surveys using the questionnaire on Respiratory symptoms (MRC 1961). Details of smoking habits were recorded on this form and coded according to past habits, (non smokers 0, smokers 1) present habits, (non smokers 0, smokers 1) and present amount, (1-14 g/day = 1, 15-24 g/day = 2, 25 or more g/day = 3).

Thus, non smokers were coded	0,	0,	0	
ex smokers " "	1,	0,	0	
smokers " "	1,	1,	1 or 2 or 3	

A detailed occupational history recorded on this form included all jobs from leaving school to the date of examination. The total number of years of work in the asbestos factory was noted and also the time since first exposure for cases of broken service.

Sputum analysis

An early morning specimen of sputum, collected on the day after the physiological examination, was analysed by C. Wagner for the presence of asbestos bodies and fibres.

II Radiological examination

The X-rays, A-P films taken by the Pneumoconiosis Research Units' (Penarth) mobile unit, were read twice by J. Gilson, the repeat being made several months after the first reading, and once by P. Elmes. Where any discrepancy existed a final reading was agreed upon. The results were entered on a modified I.L.O. form.

Abnormality of pattern, whether linear, reticular or blotchy and whether in one or both lungs was coded 1, 2, 3 for the lower, mid, and upper zones respectively. Pleural thickening was coded 1 if present only in the wall or diaphragm and 2 if present also in the mediastinum or fissure, whether in one or both lungs. This coding was decided upon after this and various alternative methods were compared with the results of the clinical and pulmonary function tests. None of these more complex methods appeared to be superior.

III Physiological examination

The physiological examination of each worker consisted of a wide range of pulmonary function tests. As I was mainly concerned with this part of the study details of the methods used will be described much more fully than the methods used in the clinical and radiological examination.

Lung function

Introduction

The function of the lung is to supply O_2 to the tissues of the body and to remove CO_2. This process may be considered to occur in several stages, ventilation by which stale air leaves and fresh air enters the alveoli, transfer of O_2 and CO_2 across the alveolar capillary membrane to the red cell where it combines with haemoglobin and circulation of the blood between the lungs and the rest of the body. To obtain some idea of the total functioning of the lung it is necessary to assess these various aspects.

Ventilation

The maximal capacity to ventilate the lungs will vary directly with the maximal volume of gas that is moved per breath and the maximal rate at which gas can be moved in and out of the lungs. Therefore the ventilatory capacity will be reduced by any processes that reduce the vital capacity, increase the resistance of the airways to gas flow, or restrict movement of the lungs or thoracic cage.

Other important aspects of ventilation are the distribution of inspired gas and the percentage of the total lung capacity that can be renewed with fresh air at each breath.

With the methods at present available it is relatively simple to measure most of these properties of the lung.

1. Lung Volumes

Borelli (1679) is believed to be the first person to have attempted measurement of the amount of air in the lungs. Jurin (1718) commenting upon Borelli's figures noted that not only did these values vary between different people but also at different times in the same person. Goodwyn (1788) pointed out that a temperature correction was necessary and also that the lungs still contain quite a lot of air even after full expiration, the amount left depending upon the capacity of the thorax. In 1846 Hutchinson invented the spirometer for the measurement of vital capacity which he defined as the 'greatest voluntary expiration following the deepest inspiration'. He measured the VC in 1012 subjects and demonstrated a relationship with age, height, weight and sex. He also showed that the VC is reduced in tuberculosis.

For the next 50 years the VC, because of its ease of measurement, was used as the index of lung function until Bohr (1906) objected to its sole use, the total lung volume and residual air being ignored completely. He investigated and stressed the importance of the relationships between TLV, RA and VC.

Davy (1800) was the first person to measure the RA which he defined as the air left in the lungs after the fullest possible expiration. He used a gas dilution method, the subject taking 5-7 deep breaths from a bag containing a known volume of hydrogen. From analysis of the hydrogen dilution the RA was calculated.

In 1882 Pflüger described a pneumatometric method for the measurement of lung volumes which was based on Boyles law /vol. of gas $\frac{1}{\alpha}$ pressure/. However, it was not widely used because it needed a complex apparatus, much cooperation from the subject and was easily upset by leaks which were difficult to detect. Intestinal

gases were included in the volume measured by this method.

In the early part of this century Lundsgaard and Van Slyke (1918) modified Davy's method by measuring the dilution of the nitrogen in the lungs when breathing oxygen. The main draw back of this method, like that of Davy, was the need for maximal forced ventilation which did not necessarily ensure complete mixing in diseased lungs in the time available. Other sources of error in this method were due to hyperventilation affecting the respiratory quotient and also variability of the N_2 concentration in the lungs.

In 1923 Van Slyke and Binger described a gas dilution method which did not involve forced breathing. They included a carbondioxide absorbent in the circuit and used a known mixture of hydrogen and oxygen in the spirometer. This method was a great improvement on the earlier methods but the errors due to secretion of N_2 and absorption of H_2 were still not avoided. Also, as the gas mixture was explosive, great care had to be taken. In 1932 Christie modified this method by using O_2 as the test gas. He also pointed out that it is more reliable to measure FRA not RA as measured by previous workers. The two methods of Van Slyke et al and Christie remained in general use until 1937 when Lassen, Cournand and Richards emphasised the errors in these methods, due to the nitrogen lag effect, and to the limited time available for mixing which might be insufficient in disease. In 1939 Herrald and McMichael modified Christie's method by introducing O_2 into the circuit at the rate at which it was absorbed. This enabled quiet breathing to continue until mixing, measured by a Katherometer was complete.

Since 1940 the Christie closed circuit method modified by Herrald and McMichael has been further modified by the introduction of He as the test gas, and the inclusion of a pump for mixing the gases in the circuit. He has an extremely low solubility in the tissues and is easily analysed using a Katherometer.

In 1940 Darling, Cournand and Richards described an open circuit, N_2 washout method which had the advantage of providing information on the distribution of gas in the lung.

At present therefore the choice of method lies between the open circuit method or the modified closed circuit method of Christie and McMichael but as the open circuit method is very sensitive to errors in the analysis of N_2 concentration, the closed circuit method using He is generally preferred.

Details of the closed circuit method

In the closed circuit method which was used in this study, He and air are mixed by a pump in a closed spirometer. When the concentration of He in the mixture has been noted, the subject is connected to the apparatus and rebreathes from it until mixing of the gases is complete throughout the circuit which now includes the lungs. CO_2 is removed by a canister containing soda lime included in the circuit and O_2 is fed into the circuit at the rate at which it is removed by the lungs. The point of equilibration may be considered to have been reached when the He concentration, read from the Katherometer, does not change for about two minutes. This second He concentration is noted and the subject is then asked to expire completely to record the expiratory reserve volume. The inspiratory capacity is obtained similarly by a maximal inspiration and the vital capacity by addition of the IC and ERV. From the dilution of He

by the air in the lungs this volume of gas, the FRC may be calculated as long as the initial volume of gas in the apparatus is known. The ERV measured from the tracing is subtracted from the calculated FRC to give the RV which is often expressed as a percentage of the TLC (calculated by addition of the IC to the FRC).

2. Ventilatory capacity

From the measurement of lung volumes as previously described the maximal stroke volume, the VC has been obtained and also an index of the dilution of fresh air by the residual air at each breath (RV/TLC %). However, to obtain a more complete picture of ventilation it is necessary to assess the resistance of the airways to gas flow. One method is to measure the maximal amount of air that the subject can move over a timed interval. This is called the maximum breathing capacity, MBC and was first suggested by Hermannsen in 1933. It is often measured over 15 seconds of voluntary hyperventilation in which case it is called the maximum voluntary ventilation MVV. This test calls for cooperation from the subject and is difficult to measure in an ill person. The VC is measured to ascertain whether a reduction in MVV is due to the volume or speed of gas movement.

Bruce (1950) in a personal communication to Gaensler, reported that he had measured the minimum time required to expel the VC and divided the VC by this time to give what he called 'the vital rate'. He found that this correlated well with pulmonary disability. Gaensler (1951) similarly measured fast vital capacities and found that the volume of gas expired after three seconds correlated well with the MBC in health and disease. He found, on expressing this timed vital capacity, TVC, as a percentage of the VC, that no normal volunteer expired less than 72% of the VC in one second. In patients with asthma and emphysema this percentage was much reduced but in restrictive diseases he showed that although both TLC and VC may be reduced, the TVC/VC percentage remains normal.

Gaensler then devised an instrument that automatically measured the volume expired in a pre-set time interval and after many experiments he eventually concluded that the volume expired

over one second correlated better with the MBC than shorter or longer time intervals. In this study we have used a modified Gaensler spirometer for assessing ventilatory capacity by the measurement of $TVC_{(1)}$ now called $FEV_{(1)}$ (forced expiratory volume in one second). The subject is asked to inspire fully and after placing the mouthpiece in his mouth, to expire as fast and as far as possible thus recording $FEV_{(1)}$ and $FVC_{(1)}$. This is repeated five times and the mean taken of the last three readings. The mean value is taken rather than the maximum to allow for the random error of measurement. Also it is believed that the vital capacity changes with circulatory changes in the lung and therefore the mean is more representative of the VC at any time. (This is assuming that the subject is fully cooperative).

Another instrument for assessing ventilatory capacity was invented by Wright and McKerrow (1959). The method for measuring FEV became popular as it is simpler and less tiring than the measurement of MBC but the spirometer needed for its measurement is rather cumbersome and so these authors suggested the modification of a flow meter and produced a small portable instrument, the Wright Peak Flow Meter, which measures the highest flow rate obtained over ten millisecs, the Peak Flow rate, PFR. The first attempt to measure the PFR, apart from the crude assessment of air velocity obtained by physicians of the last century who asked their patients to blow out a candle, was made by Hadorn 1942 using an aneroid manometer connected across a simple orifice. This did not become popular as the maximum value had to be judged by eye, the resistance of the water system was high, and the apparatus was no more portable than a spirometer. The flow meter used by Wright is based on a completely different principle - the variable area orifice meter, and overcomes the drawbacks of the earlier instruments. However, compared with the FEV, the PFR is more variable and improves to a greater extent

with practice. Also the instrument may vary with time and therefore should be calibrated frequently by a somewhat tedious process. The PFR was measured in this study and the mean of the last 3 of 5 readings taken.

Gas transfer

The importance of the role of the lungs in introducing fresh air into the body was known as early as the 14th century when Vesalius resuscitated an apnoeic dog by artificially ventilating the lungs. In the 18th century Lavoisier, among others, postulated that the lung was the site of combustion but this idea was finally disproved by Magnus in 1837 and it was realised that the function of the lung is to exchange gases between the atmosphere and the body. There was a great deal of contention during the latter half of the 19th century as to the mechanism for this gas exchange. One school of thought believed that O_2 was actively secreted by the alveolar cells. Böhr supported this view on the basis of finding that alveolar O_2 tension was sometimes lower than arterial O_2. Haldane, among others also supported the secretion theory. Opponents of the secretion theory were A. Krogh and J. Barcroft who believed that gas exchange in the lungs occurred solely by diffusion. At this time the study of gas exchange was hindered by the lack of adequate techniques for gas analysis in blood and air. As a result of further experiments Böhr modified his original theory and concluded that at rest, diffusion was sufficient to explain gas transfer in the lungs. Then in 1910, A. and M. Krogh published the results of experiments using improved gas analysis techniques, which failed to show evidence of any mechanism apart from diffusion, to be involved in CO_2 elimination or O_2 absorption. These results were generally accepted with regard to CO_2 elimination but Haldane and others still continued to support and to search for evidence in favour of the O_2 secretion theory. As late as 1927 Haldane was in favour of O_2 secretion occurring under stress even if not at rest but experiments since then have failed to show evidence to support this.

With the advent of more efficient methods for blood gas analysis it has been shown that Pa_{O_2} is invariably less than $P_{A_{O_2}}$ and by 1944 it was clear that most of the evidence favoured diffusion as the mechanism for gas exchange.

Methods for measuring alveolar capillary gas transfer

Böhr defined the diffusion constant of the lungs for O_2 as the quantity of gas in ml STPD passing from the alveoli to the blood in unit time, when the partial pressure of gas on either side of the membrane differs by one mm Hg. Since then this quantity has also been called the diffusion factor, diffusion coefficient, and diffusion capacity. When this last term was introduced by Comroe et al 1950, the reaction rate for the combination of O_2 with haemoglobin was believed to be extremely fast and therefore the diffusing capacity of the lung was believed to be limited only by the diffusing capacity of the alveolar capillary membrane. However, it has since been shown that this assumption is false. The reaction of O_2 with Hb proceeds at a finite rate and therefore Cotes 1964 suggested transfer factor as an alternative term for this composite index. The earliest measurements of the transfer factor for O_2 TI_{O_2} made by Hüfner (1897) and Loewy and Zuntz (1904) were based on the principle that $TI_{O_2} = \dot{V}_{O_2} / A-\bar{c}$ gradient. They used the average of Pv_{O_2} and Pa_{O_2} to obtain the mean $P\bar{c}_{O_2}$ and made no allowance for O_2 gradients within the blood. Böhr 1909 showed that the rate of O_2 uptake falls off towards the arterial end of the capillary as the $A-\bar{c}$ gradient decreases and blood O_2 saturation increases. He developed a method of integration whereby $P\bar{c}_{O_2}$ could be calculated using PA_{O_2}, Pv_{O_2} and Pc_{O_2}

which he took to be equal to last Pa_{O_2}, in conjunction with the Hb dissociation curve for O_2. He assumed that gaseous diffusion within the blood and combination with Hb were instantaneous. This is now known to be untrue but in spite of the difficulty of obtaining accurate data his value of 16 ml/min X mm Hg agrees with those of later workers. Improvements have since been made in the techniques for measuring TI_{O_2} but at present many difficulties still remain and therefore it is rarely measured. J.S. Haldane 1895 was the first person to measure the uptake of CO in the lungs but it was Böhr who recognised the advantages of CO in measuring gas transfer in the lungs. He suggested that, as the affinity of Hb for CO was 200 times greater than that for O_2, and as there was an apparently negligible back tension of CO in the blood, TI_{CO} could easily be measured without using the integration procedure necessary in measuring TI_{O_2}. TI_{CO} could therefore be obtained by measuring the total rate of absorption per unit pressure of alveolar CO.

There are two main types of method for measuring TI_{CO}, the single breath method and the multiple breath method.

Multiple breath method

The re-breathing method developed by Kruhøffer (1954) resembles the single breath method theoretically. CO is rebreathed from a bag over a period of about 40 seconds at a rate approximating 25 breaths per minute. During this procedure the gas in the bag is sampled and analysed several times and so the rate of CO disappearance and therefore the constant k can be calculated using a similar equation to the Kroghs.

The steady state method measures the rate of uptake when the CO entering the lungs is equal to the CO absorbed by the blood and can be measured either by measuring the rate of disappearance of

CO from the lungs or the rate of appearance in the blood, Böhr measured the appearance of CO in the blood but as methods improved for sampling gas from the lung, the disappearance of CO from the lung came to be more widely measured. The advantages of this method over the single breath technique are the ease of performance for the subject, little cooperation being required and the fact that the measurement is made during normal respiration.

For the equilibration technique, Gilson J.C. et al 1955 the subject breathes a mixture of CO, He and air, during which samples of expirate are analysed until a steady state is reached. The equilibration process in a homogeneous lung will be exponential and the constant will be the difference between that due to ventilation and that due to diffusion. By including He in the mixture, the exponential constant of ventilation is obtained and thus that for diffusion can be calculated. Theoretically this method is very good as deviations from the exponential form would give estimates of non-uniformity of both ventilation and diffusion throughout the lung. At first the accuracy of this technique was limited by the slow response of the gas analysers but Harper and Burrows (1958) using N_2 instead of He and faster analysers were able to sample and analyse each breath up to a rate of 25 breaths per minute.

Single breath method

This method was developed by A. and M. Krogh at the beginning of this century.

The subject took a maximum inspiration of a gas mixture containing CO, immediately expired sufficient gas to obtain an alveolar sample, breath held for about six seconds and then expired maximally, a second alveolar sample being collected from this expiration. The concentration of CO in the first sample

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was assumed to be representative of the lungs at the beginning of breathholding and the CO concentration in the second sample representative of the lungs at the end of breathholding. Assuming that the lung was homogeneous and the rate of fall of CO concentration proportional to the CO concentration at any instant, the constant of proportionality, k, was calculated.

$k = \log_e \frac{F_{CO_A}}{F_{CO_E}} / t$

F_{CO_A} is /CO/ at the beginning of breathholding.
F_{CO_E} is /CO/ at the end of breathholding.
t is the time of breathholding.

This constant was said to give a measure of the permeability per unit lung volume. TI_{CO} was then calculated from k:-

$TI_{CO} = \frac{k \times Va}{B.P. - 47}$

Va is the total lung volume obtained by a separate experiment.

The Kroghs assumed that the diffusing surface and the distribution of inspired gas were homogeneous throughout the lungs. Haldane criticised the method, claiming that these assumptions were untrue and that the first sample would have a greater proportion of atrial air due to uneven distribution of ventilation, than the second sample and this would therefore give an over estimate of TI_{CO}. To overcome this problem, Forster (1954) suggested the addition of an inert gas such as He to the inspired mixture. The He being virtually insoluble in blood and lung tissue, would provide an estimate of the dilution of the inspired mixture by the residual air.

$$F_{CO_A} = F_{CO\ I} \times \frac{F_{He\ E}}{F_{He\ I}}$$

The method was modified to exclude the first sample collection, the breath was held at full vital capacity, and a single alveolar sample collected for analysis at the end of breathholding.

Later workers, Forster et al 1954 and Ogilvie et al 1957 noticed that k was inversely proportional to the time of breathholding. They suggested that this indicated non-uniformity of diffusion throughout the lung and to avoid variation due to this factor, Ogilvie et al suggested standardizing breathholding time to ten seconds. Jones et al later suggested an improved formula for calculating breathholding time to allow for changing rates of CO uptake during inspiration and expiration (Fig. 1).

This still however did not solve the problem of obtaining a true estimate of TI_{CO}, representative of the whole lung. Ogilvie et al 1957 and other workers found differences of up to 10% between the TI_{CO} calculated from collection of the sample at the beginning and collection at the end of expiration. Jones R. and Meade F. suggested that the collection of an 85 ml sample directly after discarding 1 litre of the dead space gas, would give a value for TI_{CO} representative of the TI_{CO} of the whole lung. However, this assumes that the sample is from an equivalent region in all subjects and ignores variations in lung size and pattern of ventilatory distribution between individuals.

The estimate of Va for the calculation of TI_{CO} may be obtained by adding the RV measured by a multiple breath method to the volume of test gas inspired. McGrath and Thomson claimed that by doing this, TI_{CO} was overestimated especially in patients with ventilatory defects as the Va, thus calculated, included parts of the lung which were not ventilated during a single breath and which therefore did not contribute to the

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The estimate of Va for the calculation of TI_{CO} may be obtained by adding the RV measured by a multiple breath method to the volume of test gas inspired. McGrath and Thomson claimed that by doing this, TI_{CO} was overestimated especially in patients with ventilatory defects as the Va, thus calculated, included parts of the lung which were not ventilated during a single breath and which therefore did not contribute to the

overall TI_{CO}. The actual volume of lung reached by the test gas during breathholding, after a single breath of the mixture, can be calculated by the dilution of the He in the test gas by the residual air, multiplied by the volume of gas inspired. This also avoids errors due to incomplete expiration before inspiration of the gas mixture.

Ideally all these methods should give similar results. However, as each is subject to different sources of error, different results are obtained. The equilibration and steady state techniques are superior to rebreathing and breathholding methods as the measurement is made during normal respiration. It is not completely known how the manoeuvres of breathholding and hyperventilation affect the pulmonary circulation. The steady state technique also requires less apparatus and is relatively simple to calculate. The main source of error lies in the measurement of CO_2 tension (Marks et al) and for this reason this method is less widely used than the single breath method, which requires more cooperation from the subject but is very quick to perform and therefore ideally suited to studying large numbers of subjects in the field.

All these methods are affected to a varying degree by irregularity of ventilation. In normal subjects there is reasonable correlation between the different methods but this is not the case in patients with lung disease. However, despite its disadvantages it has been said (Forster 1959) that the single breath technique probably gives the nearest estimate to the true TI_{CO}. For this reason and also for the speed with which the test can be carried out, the single breath method was used in this study.

Membrane Dm and intracapillary Vc component of Transfer Factor

Early workers studying the problem of gas transfer in the lungs assumed that the intracapillary phase of the reaction did not limit diffusion. They concluded that the resistance of the alveolar capillary membrane alone limits gas transfer Roughton 1945 and Roughton et al, Forster et al 1957 who studied the kinetics of the reaction of CO with Hb in vitro discovered that this assumption

is false. By 1957, they were able to show that the resistance to diffusion in the lungs consists of two parts, $1/Dm$, the resistance of the alveolar capillary membrane and $1/\theta Vc$ which is the intra-capillary resistance.

$$1/TI = 1/Dm + 1/\theta Vc$$

θ is the rate of reaction of the gas with Hb and Vc is the instantaneous pulmonary capillary blood volume.

The variation in the rate of uptake of CO by the lungs, first demonstrated by Haldane 1895 could now be explained. The effect on TI of varying $P_{A_{O_2}}$ assuming that this does not also affect Dm and Vc (Cander et al 1955) will be entirely due to variations in θ. Roughton and his co-workers demonstrated a method by which if TI_{CO} and θ are known at varying O_2 tensions, Dm and Vc can be calculated. Since its introduction, this method has been widely used and it has been used in this study.

Calculation of θ

Roughton et al 1957 investigated the various factors involved in the reaction of CO with Hb in the lungs using in vitro preparation. They found that the red cell membrane acts as a barrier to gaseous transfer. Recent work Yahr et al suggests that in vivo the permeability of the red cell membrane is much greater and the membrane may be considered to be infinitely permeable, when the following relationship applies.

$$1/\theta = (0.33 + 0.0057\, P_{CO_2}) \div \text{Hb \% of normal} / 100$$

The reaction rate θ is proportional to the amount of the Hb present and therefore this should be measured. In this study however, estimation of Hb was not possible and so in all cases it was assumed to be 100%. This may introduce a small error into the determination of Vc but will not affect Dm.

$P_{\bar{c}O_2}$, the mean capillary O_2 tension may be calculated by the Bohr integration technique but as this is very tedious, the method of McNeill et al (1958) is generally used where $P_{\bar{c}O_2}$ is calculated by subtracting the $A\text{-}\bar{c}O_2$ gradient from the average $P_{A_{O_2}}$ during breathholding which is approximately equal to $P_{\bar{A}O_2}$ + 5 mm Hg

The average $A\text{-}\bar{c}$ gradient $= \dot{V}_{O_2}/D_{\bar{A}O_2}$

$= \dot{V}_{O_2}/(D_{\bar{A}CO} \times 1.23)$ $\dot{V}O_2$ taken as 0.35 l/min

Back tension of CO

The back tension of CO in the blood was considered by the Kroghs to be negligible in measuring TI_{CO} by the single breath test. Roughton et al 1957 concluded that, even in heavy smokers, at a $P_{A_{O_2}}$ of 20%, the error introduced by ignoring the back pressure is very small. However, the higher the $P_{A_{O_2}}$ the greater the error and so in the estimation of Dm and Va where the alveolar O_2 approaches 100%, the back pressure is considerable and must be estimated and included in the calculation. Various methods have been used for measuring the back pressure. In this study, the indirect rebreathing method developed by Sjöstrand 1948 has been used. 100% O_2 is rebreathed via a CO_2 absorbent, after first washing out N_2 from the lungs by breathing 100% for several minutes until the CO in the bag is in equilibrium with that in the blood. The gas in the bag at the end of the rebreathing procedure is analysed for CO.

Back pressure of CO during breathholding

$$= \text{equilibrium CO\%} \times \frac{\text{breathholding } O_2\%}{\text{equilibrium } O_2\%}$$

RESULTS

258 workers in three asbestos factories were studied. Table 1b gives a summary of the results obtained. Mean age was 45.5 years and height 169.6cm. The mean value for exposure to asbestos was 11.8 years since first exposure. The majority of the subjects smoked (77%) only 8% being non-smokers and 15% ex-smokers.

There was evidence from the clinical results of some disease as rales were present in 14.2% of the population, and rhonchi in 10.6%. Approximately half of the study group complained of cough, 42.3% of phlegm, and 34.6% of dyspnoea. Asbestos bodies were present in 62.8% of the samples (approximately 100 workers said that they were unable to produce a sample of sputum on the morning of the examination) and asbestos fibres in 29.5% 18% of the population had an abnormal ECG. Radiological abnormality was present in 37% of the study group. 35% had pleural thickening alone, 28% had abnormal parenchymal pattern alone, and 37% had both changes together. The mean value for clubbing (hyponychial angle) was 188°.

The mean values for the pulmonary function results are set out in Table 1(b). The value for $T_{L_{CO}}$ of 24.2ml/min per mm Hg was somewhat reduced, 85% of the value predicted from the equation in "Lung Function" J.E. Cotes, 1965.
To check whether the results obtained during the survey were comparable with results used in deriving this prediction equation, $T_{L_{CO}}$ was measured in a group of thirty subjects from the London School of Hygiene and Tropical Medicine who had not been exposed to dusts likely to cause pneumoconiosis and were not, to their knowledge, suffering from any disease likely to affect pulmonary function). The mean percentage predicted value

was 105% (reproducibility of duplicates S.D. 1.37, S.E. .166). This rather low value for T_{LCO} together with the evidence of clinical and radiological abnormality suggested that there was some disease - presumably asbestosis, in this study population. 26 of the 258 workers were in fact certified cases of asbestosis. Presumably, there were other cases of the disease at various stages in its progression within this group.

In the following sections, the results of the three factories will be considered separately. Also the results of the whole population will be examined to try to answer some of the questions outlined in the description of the aims of this study.

Is there a pattern of lung function disturbance relatable to patterns of radiological abnormality and, if so, is it more severe in subjects with parenchymal changes than in those with only pleural thickening?

Tables (41 a, b) give details of some lung function tests in subjects with abnormal radiographs. The mean values of these tests were expressed as a percentage of the predicted value (using the predictions in Table 31) as there were differences in age and height in the sub-groups.

Those with normal radiographs had higher mean percentage predicted values than those with abnormal Xrays for both VC and T_L.

Radiological abnormality has been split up into three grades for abnormal parenchymal pattern and two grades for pleural thickening, as described earlier, and the mean values for the pulmonary function tests calculated for these subgroups. For changes in the lung parenchyma and in the pleura, a higher grade indicates more extensive changes on the radiograph. It might be expected, therefore, that those with a higher grade of pleural thickening or abnormal pattern would have poorer lung function, and lower values for T_L and VC. However, there was very little difference in mean T_L and VC between the different grades of abnormality for those with either pleural thickening or abnormal parenchymal pattern alone. In those with pleural thickening, together with abnormal pattern, there were differences in the mean values of VC and T_L in the different grades. For VC the mean percentage predicted values for different grades of abnormal pattern were very close but there was a considerable difference between the values for those with grade 1 and grade 2 pleural thickening. This difference was also shown for T_L but to a lesser degree. There was a slight tendency for T_L to be lower in those with grades 2 and 3 abnormal pattern compared with grade 1.

When the results of all subjects with abnormal radiological pattern were combined, there seemed to be a slight trend for a lower T_L with a higher grade of abnormality, but no similar trend for VC. For all those with pleural thickening, there was a lower VC and T_L in grade 2 compared with grade 1.

When the values for T_L and VC were compared for subjects with all grades of abnormal pattern and thickening combined, the lowest mean values were seen in those with both abnormalities together, 72% of the predicted value for T_L and 94% for VC. For those with either parenchymal changes or pleural thickening, the mean T_L and VC were slightly lower in those with pleural thickening.

Discussion

T_L and VC were both reduced in those with radiological abnormality compared to those without. Mean values for other lung function tests were very similar in the two groups:- For those with radiological abnormality, mean FEV/VC% was 70% and RV/TLC% was 37%, for those without Xray abnormality, mean FEV/VC% was 72% and RV/TLC% was 36%.

The grading of abnormal radiological pattern showed only a very slight degree of correlation with pulmonary dysfunction as measured by T_L and not at all to that measured by VC. The grading of pleural thickening showed some correlation with both T_L and VC, that is, in those with grade 2 pleural thickening, pulmonary function disturbance was more severe than in those with grade 1 pleural thickening. These differences between pleural thickening and abnormal pattern may reflect a less efficient method for grading parenchymal changes than that used in grading pleural thickening.

There was no evidence to support the suggestion that changes of lung function in those with only parenchymal abnormality were greater than in those with only pleural thickening.

The lowest mean values for T_L and VC were found in those with both abnormal parenchymal pattern and pleural thickening together which suggests that possibly the disease is more severe or more advanced in those with both changes.

The mean percentage predicted VC for those people with pleural thickening and abnormal pattern together was 94% compared with 100% for the population with no radiological abnormality, i.e. 6% difference. The mean percentage predicted T_L for the same two groups was 72% compared with 91%, that is a difference of 19% which was significant $P < .001$. This greater difference for T_L suggests:-

1. in those with radiological abnormality, T_L is reduced to a greater extent than VC, or,
2. it is reduced in a greater proportion of those with radiological abnormality than VC, or,
3. it is reduced at an earlier stage of the disease than VC

From several previous studies, Ghezzi et al, Sartorelli et al, Murphy et al, Britton et al, it was concluded that there is a marked fall in transfer factor preceding any significant fall in VC. The results obtained here would fit in with this suggestion.

Are rales present in the absence of radiological changes?

Table (42) gives figures for the incidence of rales in the presence and absence of radiological abnormality. Of the 246 workers examined, rales were present in 35, 14.2%. Of these 35, 11 (31%) had no radiological abnormality, and 24 (69%) had concomitant changes on the Xray. These figures were in close agreement with those of Langlands et al 1971 who found rales in the absence of radiological abnormality in 28% of their group.

Of those 24 subjects with rales plus radiological changes, 3 (12.5%) had changes only in the lung parenchyma, 5 (20.8%) had only pleural thickening, and the rest 16 (66.7%) had changes in both parenchyma and pleura. There is little difference in those with pleural or parenchymal changes alone between those with or without rales, the greatest differences being in the group with no radiological abnormality, more than twice as many workers without rales having normal Xrays ($P < .001$) and in the group with pleural and parenchymal changes together. In this last group 46% of those with rales had abnormal radiological pattern and pleural thickening together compared with only 7% in those without rales ($P < .001$). The finding of lung field $\pm$ pleural abnormality in 54% of those with rales compares with the results of Langlands et al 1971 who found lung field $\pm$ pleural thickening in 61% of those insulators with rales. However, they found rales less commonly in those with normal Xrays (9% compared with 31% in this survey).

Conclusions

Those subjects with rales were significantly more likely to have concomitant radiological abnormality than those without rales. However, rales did occur without Xray changes.

In considering pulmonary function changes related to radiological findings, the most abnormal pulmonary function values were in those with changes in both pleura and parenchyma which suggested that the disease is more severe or advanced in those with both radiological abnormalities. Two-thirds of those with rales and radiological abnormality had pleural thickening together with abnormal parenchymal pattern. This suggests that rales may be a feature of more advanced disease. In another section (page 4.9) it was concluded that crepitations are not an early sign of asbestosis generally occurring with at least one other abnormality.

<u>In what proportion of cases with rales is there also evidence of disturbance of lung function?</u>

Table (43) gives the mean values for T_L, and VC, FEV/VC%, RV/TLC% and hyponychial angle in all subjects with rales. As the mean age and height were different in the sub-groups, the mean value was expressed as a percentage of the predicted value. For those subjects with rales, both the mean T_L (17.8, 76% of predicted value) and mean VC (3.68, 76% of predicted value) were significantly, $P < .001$, lower than the mean values for the rest of the population (mean VC 4.25, 99% of predicted value, mean T_L 24.8, 91% of predicted value).

Of those with rales, 50% had values for T_L and VC which were less than 75% of the predicted value, and 69% had values less than 85%. Fig. 6.

The mean values for T_L and VC in those workers with rales and Xray abnormality together, were lower than for those with rales and a normal Xray (Table 44).

If an abnormal value for T_L and VC was taken as equal to or less than 85% and 80% of the predicted value, then 63% of those with rales had evidence of disturbance of lung function.

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If an abnormal value for T_L and VC was taken as 85% and equal to or less than 80% of the predicted value, then 63% of those with rales had evidence of disturbance of lung function.

There were no large differences in the mean values for FEV/VC% and RV/TLC% in those with and without rales. This was not surprising as although airways obstruction may be present in some cases of asbestosis, it is not generally accepted as a feature of the disease.

Is finger clubbing related to radiological abnormality?

In those with Xray evidence of abnormality of the pleura and parenchyma together, the mean hyponychial angle was higher, 194°, when compared to that of those with no Xray abnormality or abnormality either of the pleura or parenchyma, 186° (Table 45). 10% of workers without radiological abnormality have a hyponychial angle $\geq$ 198° compared with 22% of those with radiological abnormality. 4% of those workers with a normal radiograph have a hyponychial angle $\geq$ 205°, and 4% of those with changes in the parenchyma alone and 16% with changes in both pleura and parenchyma have values for clubbing $\geq$ 205°.

In those with rales, the highest value for the hyponychial angle was in those with rales plus radiological abnormality (Table 45) but the value for all those with rales was higher than that for the rest of the study population. If an abnormal value for clubbing was taken as $\geq$ 198°, then clubbing was present in 38% of those with rales.

Conclusion

24% of those with Xray abnormality had some evidence of clubbing. In those with pleural and parenchymal changes together, the incidence rose to 35%, which was close to the incidence in subjects with rales where 38% had a hyponychial angle $\geq$ 198°. The most abnormal mean value for finger clubbing was in those with rales plus pleural and parenchymal abnormality. This suggests that clubbing may correlate with the severity of the disease as pulmonary function was most abnormal in this group with rales plus both Xray changes.

What are the earliest signs of asbestosis?

Parkes 1973, Ghezzi et al 1972 and Sartorelli et al 1972 suggested that crepitations are among the earliest signs of the disease and often precede radiological abnormality. Parkes also commented that rales are invariably present at a later stage of the disease. Other workers concluded that reduction in pulmonary function parameters are the earliest signs of the disease (see page 1.15).

To examine this problem, the incidence of the occurrence of the various types of abnormalities was considered. Table (46, 47).

Of those workers with rales, 2 (6%) had it in isolation, 11 (31%) had it with one other abnormality, 22 (63%) had it with either two or three other abnormalities. That is, the majority of those with rales had other abnormalities. If rales were an early sign of the disease one would expect to find a greater incidence of rales without other abnormalities. Therefore, these results suggest that crepitations are probably not among the earliest signs. Radiological abnormality occurred without any other abnormalities in 43 (46.2%) of those with changes on the Xray and in 22 (23.7%), 21 (22.6%) and 7 (7.5%) of those with one, two, and three other abnormalities respectively. Of those with just an abnormal radiograph, approximately half had pleural thickening alone, 37% had abnormal parenchymal pattern and only 14% had pleural thickening and abnormal pattern together. Pleural thickening, together with abnormal pattern, occurred in 50% of those with one other abnormality, 57% of those with two other abnormalities and in 71% of those with three other abnormalities. Of those with one or two additional abnormalities, the radiographic change was either pleural thickening or abnormal parenchymal pattern in approximately equal numbers. In conclusion, in those with an abnormal Xray without any other changes, pleural thickening together with abnormal pattern is

much less common than either of these two changes alone. In contrast, when several other abnormalities are present, both Xray changes together are more likely. It looks, therefore, as though radiological abnormality appears early in the disease as either a change in the pleura or parenchyma and then as the disease progresses, the Xray change progresses also to include both the pleura and parenchyma. Therefore, although radiological abnormality appears early in the disease (- in 46% without any other abnormality) changes extending to both pleura and parenchyma together appear later, early changes being confined either to the pleura or parenchyma.

If a hyponychial angle equal to or greater than 198% is taken as evidence of early or definite finger clubbing, from these results, finger clubbing does not appear to be as early a sign of asbestosis as radiological changes as it occurs in isolation without other abnormality in only 18% (of those with finger clubbing). As 40% of those with clubbing have only one other abnormality, it may appear relatively early on compared with rales.

If an abnormal value for VC is taken as less than or equal to 80% of the predicted value and for T_L as less than or equal to 85% of the predicted value, abnormal values for pulmonary function occur in isolation in 54%, with one other abnormality in 19% and in 27% of those with two or three other abnormalities. Therefore, this suggests that a decline in pulmonary function occurs early on in the disease. (85% was taken as the cut off point for T_L as from my study of 20 normal workers in LSHTM, my results seem to be about 5% above those used for calculating the prediction formula). When the mean percentage predicted value for T_L was calculated for a group of normal workers within the survey - (see page 4.26) a similar result was found, the mean percentage predicted value for T_L

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was 104.7% and for VC 100.2%).

From looking at the frequency of occurrence of these abnormalities, Xray changes and reduced lung function occur very much more commonly than rales or finger clubbing which might be expected if they are early signs of the disease.

Therefore, from this study, these results suggest that Xray changes either in the parenchyma or in the pleura and pulmonary function changes occur earlier than rales and finger clubbing in the development of the disease.

As a fall in VC and T_L can occur in airway obstructive disease, the results of those with an FEV/FVC% less than 60% were excluded. The incidence of reduced pulmonary function then dropped by 7%. This crude attempt to correct the effects of airway obstructive disease did not alter the conclusion that a reduction in VC and T_L probably appears early on in the development of asbestosis.

Whether a reduction in VC precedes a fall in T_L or vice-versa, or whether they both decline simultaneously is debatable. In this study 33 (32%) subjects had a reduced T_L, 30 (30%) had a reduced VC, and 39 (38%) had a reduction in both. From these findings, there is no evidence to suggest that a fall in T_L precedes a fall in VC or vice-versa.

Conclusions

The earliest signs of asbestosis appear to be radiological changes generally confined to the pleura or to the parenchyma and reduction in pulmonary function. Rales and finger clubbing do not generally appear so early. These conclusions are supported by the finding (page 4.6) that mean values for T_L and VC are lowest in those with rales and pleural and parenchymal changes together. Although changes in the lung probably do not follow a set pattern, it looks as though most

commonly the disease first appears in the pleura or parenchyma (as seen on the Xray) and causes some reduction in lung function. With progression of the disease, both pleura and parenchyma become involved, clubbing and rales may appear (but are not invariable) and pulmonary function deteriorates still further. From the mean values for VC and T_L in those with radiological changes, it looks as though T_L is possibly affected earlier and to a greater extent than VC. When rales is present, in addition to pleural thickening and abnormal pattern, the values for T_L and VC are still lower - Table 44 which suggests that when rales are present the disease is probably no longer at an early stage.

Asbestosis and smoking

Parkes 1973 pointed out that as smoking is known to affect pulmonary function, Gause et al 1972, when diagnosing asbestosis, its effects must be allowed for when standardising the results against those of normal workers. There is also some evidence to suggest that development of pulmonary fibrosis is affected by smoking. In a study of 100 asbestos textile workers, Weiss (1971) found radiological evidence of fibrosis in 40% of the smokers contrasted with 24% of the non-smokers. This fibrosis was also positively related to the amount and duration of smoking. Langlands et al 1971 showed that smoking and exposure to asbestos have an additive effect in causing impairment of lung function as measured by VC and TL. They found the mean values of these parameters to be lower in smokers with normal Xrays than in non smokers with lung field abnormality. Weill (1975) however found little evidence of interaction between smoking and the diffuse fibrogenic effects of asbestos dust exposure.

To consider whether there is any evidence from this survey of a link between smoking and the development of asbestosis, those variables, such as abnormal Xrays, rales, and finger clubbing, which are commonly found in asbestosis but not obstructive airways disease, will be considered.
Table (48) gives details of age and exposure for smokers and non smokers in the three factories. This shows that although there are differences between the factories, any differences between the smokers and non smokers are small. This means that any differences found in comparing, radiology, rales and finger clubbing are not due to differences in exposure to asbestos or age.

Radiological results in smokers and non smokers

Table (49) gives the incidence of radiological abnormality in smokers and non smokers, for the three factories separately and also for the whole population. When considering the whole population together, any differences between the smokers and non smokers are very small. Therefore there is no evidence that smoking influences asbestosis. In factory B, there is a somewhat higher incidence of pleural thickening together with abnormal radiological pattern in the smokers which suggests that smoking might have affected the development of asbestosis in this factory. However, the evidence is not very convincing. The difference between the two groups is not as great as that found by Weiss.

Rales in smokers and non smokers

Table (45b) gives details of the incidence of rales in smokers and non smokers. Any differences between the three factories considered separately and also combined are small and provide no evidence for any relationship between smoking habits and the development of rales which are characteristic of pulmonary fibrosis.

Finger clubbing in smokers and non smokers

Table (44b) gives the mean hyponychial angle for non smokers and smokers in the three factories separately and also for the whole population. Although there are differences in the values for clubbing between the factories, within each factory the smokers have a higher value than the non smokers. This difference is approximately 5° and is significant ($P < 0.002$ for three factories combined). This result suggests that as there is higher hyponychial angle in the smokers there may be more asbestosis in the smokers than in the non smokers.

However, possibly smoking may affect the hyponychial angle independently of exposure to asbestos. From the literature

there is no evidence available on this point. Ideally the hyponychial angle should be measured in smokers and non smokers to solve this problem. I have measured it in a small number (20 non smokers and 18 smokers) and found a mean value in the smokers 4° greater than that of the non smokers. These results suggest that the hyponychial angle may be affected by smoking. Further evidence to support this conclusion was obtained by comparing the hyponychial angle in a group of 'normal' smokers and non smokers within the study population. Those workers with no clinical or radiological abnormalities and with percentage predicted values for VC above 80%, for TL above 8 5%, values for FEV/VC% above 80% and for RV/TLC% below 45% were classified as normal. Their results are shown in Table (44b) and support the suggestion that smoking affects the hyponychial angle as the mean value for the smokers was 4.5° higher than that of the non smokers.

Airways obstructive disease in asbestosis?

It has been suggested that asbestosis and airway obstructive disease do not occur together. Britton *et al* 1976 found FEV/FVC% to be above 70% in all their cases of asbestosis. However, there is evidence from a number of other research reports to dispute this. Thomson *et al* 1964, Williams *et al* 1960 and Muldoon *et al* 1972 are among those reporting evidence of the co-existence of asbestosis and airways obstruction.

In this survey population, of the 26 certified workers, 7 (27%) had an FEV/FVC% less than 70%, and, of these, 5 (19%) had an FEV/FVC% of less than 65%.

On page 4.26 a group of uncertified workers with some evidence of asbestosis will be identified. Of these 18 (49%) had an FEV/FVC% less than 70%, and of these 14 (38%) had a value less than 65%.

If all those workers with radiological abnormality are considered, 13 (38%) of those with parenchymal and pleural changes together had an FEV/FVC% less than 70%, and 10 (38%) of those with parenchymal changes alone, and 16 (47%) of those with pleural thickening alone also had evidence of some airways obstruction. Therefore, the findings from this survey support the suggestion that asbestosis and airways obstruction are not mutually exclusive.

Comparison of the results in the three factories

Table 2 shows the number and percentage of workers that were examined in the three factories.

The percentage studied in B (83%) was less than in the other two factories as a small group of workers were adamant in their refusal to undergo the tests, possibly as a result of earlier surveys in this factory. Of the 22 workers that refused to be examined two were certified cases of asbestosis. At M, 92% of the population at risk was examined and at U, 96% were examined. Of the six refusals at U one was a certified case of asbestosis.

A complete set of results was not obtained for the total group. Tables 4 and 5 give details of the missing results and reasons for their omission.

1. Physical characteristics

Height

Workers in factory U were the tallest, mean height 170.5 cm, those in factory M the shortest mean height 168.2 cm and those in factory B intermediate, mean height 169.6 cm. (Table 6, Fig 12)

Age

Mean age was highest in B, 46.9 years, lowest in U, 43.7 years, and intermediate in M, 46.0 years. (Table 6, Fig 12)

Exposure to asbestos

The longest average exposure to asbestos was found in Factory M, the mean date of commencement of employ being 1948, compared to 1950 at factory B and 1957 at Factory U. (Table 6, Fig 12) Table 7 shows the population of each factory, grouped by years since first employed and mean ages within these groups. At factory B nearly half the population, 43.7%, were first employed 16-20 years ago, and 29.1% were first employed 11-15 years ago. This is rather similar to factory M where approximately one third of the workers were first employed over 20 years before this study was carried out, and over three quarters of the workers were first employed over 10 years ago. At factory U the situation is very different as 70% of the workers commenced their employ in the last 10 years.

2. Smoking habits

Table 8 gives details of smoking habits in the three factories. Factory B had the highest percentage of smokers and ex-smokers and the lowest percentage of non-smokers. In U this situation was reversed with the lowest incidence of smokers and ex-smokers and the highest incidence of non-smokers. The smoking habits in M were intermediate between the other two factories. However, these differences were very small.

When the tobacco consumption of the smokers was examined, quite big differences were found between the three factories. At B 71.9% of the smokers were in grade I, compared to only 28.3% at M and 54.3% at U. The differences between the factories were significant (Table 9). The remaining smokers at B were fairly equally divided between grade II and grade III, the lowest percentage being in grade III. Similarly, only 14.3% of the smokers at U were in grade III. However at M a third of the smokers were in grade III and 39.1% were moderate, grade II, smokers. Therefore although there was very little difference between the factories in smoking habits, among the smokers there were significant differences in tobacco consumption Table 9. In M, the mean was 20.3 gm/day in U 16.9 gm/day and in B 14.2 gm/day.

3. Clinical findings

Symptoms and signs of chest disease

Rales

The prevalence of rales was highest in B (24%) (Table 10) and the difference between this and the other two factories (M 3%, U 11%) was significant, $P < 0.05$. The incidence was lowest in factory M.

Rhonchi

Differences between the factories in the prevalence of rhonchi were small and insignificant.

Cough and Phlegm

The prevalence of cough was somewhat higher than of phlegm in all three factories but the ranking was the same for both indices with M > B > U. However, the differences between factories were small and not significant for phlegm. For cough, the incidence was significantly higher in M than in B and U. (B vs M, $P < 0.05$, M vs U, $P < 0.01$). The differences between cough and phlegm of different grades Table 11, were small.

As there were differences in age, smoking habits and exposure to asbestos between the factories, the incidence of cough and phlegm were re-examined after allowing for these variables (Cochrans' method Cochran W.G. 1954). Tables 12a, b, c. (It was not possible to do this for different grades of cough and phlegm because of the small size of the sub groups.) After this correction, the only significant difference was a higher incidence of cough in M compared to B ($P < 0.05$) and U ($P < 0.01$).

Dyspnoea

Tables (10, 11) show the prevalence of dyspnoea in each factory. There were no large differences between the factories when different grades of dyspnoea were compared separately but when all grades were combined, factory B had the highest incidence, the difference between B and U being significant at the 5% level. After correcting for age, exposure and smoking habits (Cochran W.G., 1954) (Table 12c) there were no longer any significant differences.

Clubbing

Although the mean hyponychial angle was highest for B, 189.1° and lowest for M 186.1° there were no significant differences between the three factories after standardizing the mean values for height.

Sputum analysis

The percentage of workers who produced specimens of sputum was higher than the percentage who complained of phlegm in reply to the questionnaire. However the ranking of the factories was the same M > B > U. 78% of the population at M produced sputum compared with 64% at B and 46% at U. Table 14.

Asbestos bodies

37.9% of the sputum samples from B, 29.5% from U and 17.4% from M contained asbestos bodies. The difference between B and M was significant $P < 0.05$.

Asbestos fibres

Factory U had the highest percentage of samples positive for asbestos fibres 79.5% compared to 72.7% at B and 32.6% at M. The percentage positive in M was significantly lower than in B, $P < 0.001$ and U, $P < 0.001$.

ECG results

Table 15 gives the percentage of workers in each factory with abnormal ECG readings as coded by the modified Minnesota code (Silvester, Rubin Prineas, 1967);the differences between the results for each factory were small and not significant (M 29.4%, B and U 17.8% abnormal recordings).

4. Radiological findings

These are summarised in Tables 16 and 17. Factory B had the highest percentage of abnormal radiographs and factory M the lowest (difference overall $P < 0.01$). However after correcting for differences in exposure to asbestos (Cochran, W.G. 1954) the only significant difference was that between B and M ($P < 0.01$).

The highest incidence of workers with abnormal pulmonary radiology (X patt. in tables) alone was in M and the lowest in U. After correcting for differences in exposure to asbestos (Cochran, W.G. 1954) the incidence in M was significantly higher than in U ($P < 0.02$) None of the other differences were significant.

The greatest prevalence of workers with pleural thickening (x thick) alone was in B but after allowing for exposure to asbestos the differences between this and the other two factories were not significant.

There were significant differences between the three factories in the percentage of workers with both pleural and pulmonary abnormality. B had the highest incidence 18.4%, M the lowest, 1.9% with U almost as great as B 14.9%. After correcting for exposure to asbestos (Cochran, W.G. 1954) M was found to have a significantly lower percentage of workers with both pulmonary and pleural abnormality than B, $P < 0.001$ and U, $P < 0.02$.

When the severity of the radiological abnormality was examined, the results were found to be very similar for the three factories except for pleural thickening grade I which was higher in B than in M, $P < 0.005$ and U, $P < 0.025$.

5. Pulmonary function

Tables 19-20 give the mean pulmonary function values before and after correcting for age and height by analysis of covariance (weight and exposure were excluded after a preliminary analysis as they were not found to affect the results greatly).

Lung volumes

The mean VC was lowest in factory B but the difference between this factory and the other two was not significant. The mean IC was also lowest in factory B and the differences between it and the other two factories were both significant ($P < 0.001$). Similarly the TLC was lowest in B, significantly lower than in both M ($P < 0.001$) and U ($P < 0.01$).

Therefore apart from the mean IC which was identical in M and U, M had the highest mean values for the other lung volumes.

Ventilatory capacity

M had the lowest mean values for FEV/FVC % and PF but the differences between the factories were small and not significant.

The mean RV/TLC % was significantly higher, however, in M than in both B ($P < 0.001$) and U ($P < 0.001$). B also had a significantly higher mean RV/TLC % than U ($P < 0.001$).

Transfer factor and its subdivisions

All the indices of gas transfer were lowest in B. The mean TI was significantly lower than that of both other factories ($P < 0.001$) and the mean Dm was significantly lower than in M ($P < 0.001$). Although mean K_{CO} and Vc were also lowest in B the differences between the factories were small and not significant.

Summary of results

The mean TI, Dm and IC were significantly reduced at B. This factory also had the highest incidence of radiological abnormality, rales and dyspnoea suggesting the presence of more pulmonary fibrosis in B than in M and U. Factory M had the highest incidence of cough and phlegm and evidence from the pulmonary function tests of more airway obstructive disease than the other two factories. The workers at U appeared to be the most healthy.

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Discussion of results so far

One way of comparing the incidence of asbestosis in the three factories would be to use the Pneumoconiosis Medical Panels (PMP) method of evaluation on the results of each factory as a whole. These Panels diagnose asbestosis where there is evidence of adequate exposure to asbestos dust plus two positive findings from the following:- presence of basal rales, finger clubbing, abnormal radiology of the lung and abnormal pulmonary function. (McVittie J.C. 1965). These clinical and radiological signs and symptoms and changes in pulmonary function have been found by many other workers in asbestosis and are well documented. The changes in pulmonary function are generally agreed to be:- reduced TI and Dm and a reduction in lung volumes without any significant airway obstruction.

First, considering B, the incidence of rales was significantly higher than in M and there was a significantly higher incidence of radiological abnormality in this factory when compared with M. The mean TI and Dm in B were significantly lower than in M and there was also evidence of significantly lower lung volumes in B. (Tables 10, 12, 17, 18, 19, 20). Therefore of the four criteria considered by the PMP, three were fulfilled by B when compared with M. (Although the mean hyponychial angle was higher in B than in M, the difference was not significant). This therefore suggests the presence of more pulmonary fibrosis, presumably asbestosis in B than in M.

The only significant difference between U and M was the higher incidence of abnormal radiographs in U. There were no significant differences in the incidence of rales and in the mean values for gas transfer, lung volumes (except for RV) and hyponychial angle. Therefore of the four points considered in diagnosing asbestosis, only one suggested the presence of more fibrosis in U than in M.

As there was a higher incidence of rales and abnormal pulmonary function results in B than in U, it might be concluded that there was more fibrosis in B.

Therefore, using the Pneumoconiosis Medical Panel's method of evaluation the suggested ranking for prevalence of asbestosis in the factories is B > U > M. This is in agreement with the certification figures Table 21. After correcting for differences in exposure (Cochran W.G. 1954) both B and U had a greater number of certified cases of asbestosis than M, for B $P < 0.002$ and for U $P < 0.1$.

If the total number of certified cases in each factory is compared (Table 3 - includes refusals and those certified cases moved to departments not included in our study) these tentative conclusions are not affected.

Results of the certified workers

In using the certification figures and methods for certification (McVittie 1965) to compare the incidence of asbestosis in the three factories, it has been assumed that the methods used by the Pneumoconiosis Medical Panels are correct. To examine this assumption, the results of the certified workers will now be considered in detail.

The information obtained from the questionnaires and from the clinical and radiological examinations of the certified workers was compared with the same information obtained from the non-certified workers. The results of the pulmonary function and clubbing tests for the certified workers were compared with those of a group of 'normal' workers. As a control group had not been examined 41 men were allocated to the 'normal' group as their results fulfilled the following criteria:- Absence of rales, rhonchi, cough, phlegm, dyspnoea, clubbing (hyponychial angle greater than 195°) any abnormality on the Xray and abnormal pulmonary function. Pulmonary function was considered abnormal if the percentage of the predicted value (Table 31) was less than 85% for TI and less than 80% for VC and FEV/VC%. For RV/TLC%, if the percentage was greater than 45% this result was considered to be abnormal.

Students 'T' was calculated when comparing the mean values of the pulmonary function tests (after standardising the means by analysis of covariance) and X^2 was calculated when comparing the incidence of clinical abnormalities in the two groups.

1. Clinical findings

Rales

69% of the certified workers were found to have rales compared with only 8% of the uncertified workers (Table 22). This difference was highly significant ($P < 0.001$). Therefore it was decided to include rales as a variable in the principal component analysis.

Rhonchi

There was no difference in the percentage of workers in the two groups with rhonchi (Table 22). However, the presence of rhonchi are generally believed to indicate airway obstruction. Therefore to find out if this was the case in our subjects, all those uncertified workers with an FEV/VC% of 55% or less were put into a separate group the bronchitic group. The incidence of rhonchi in the certified, uncertified and bronchitic groups was then compared as before (Table 23). As expected the highest incidence of rhonchi was found to be in the bronchitic group. Although the differences between this group and the other two groups were not very great, it was decided to include rhonchi as a variable in the analysis as it was hoped that it would help to differentiate workers with airway obstruction from rest of the group.

Cough and Phlegm

Table 22 gives the results of a comparison of the incidence of cough and phlegm in the certified and uncertified workers. This table shows that any differences between the two groups were insignificant. The workers with the different grades of cough and phlegm were also compared but again there were no large differences between certified and uncertified workers.

However, when the incidence of cough and phlegm in the group of workers with airway obstruction was examined (Table 23) it was found to be higher than in the other two groups. The difference

between this group and the certified group was not significant for cough or phlegm but when this group was compared with the group of remaining uncertified workers, a significantly higher percentage complained of cough and phlegm. The percentage of certified workers complaining of phlegm was extremely close to the percentage of the remaining uncertified workers who complained of phlegm. The incidence of cough in the certified group was intermediate between that of the other two groups but the differences were not significant.

From these results, cough and phlegm were included as variables in the analysis as it looked as though they might prove useful indicators of airway obstruction.

Dyspnoea

The incidence of dyspnoea (all grades), in the certified group was significantly higher than in the uncertified group $P < 0.005$ (Table 22). When the different grades of dyspnoea were compared for these two groups, the only significant difference was for dyspnoea grade 3, $P < 0.05$.

Table 23 shows the prevalence of dyspnoea to be higher in the certified group than in the group with airway obstruction. The remaining workers had the lowest incidence. These differences were not significant except for the certified workers when compared with the remaining workers $P < 0.005$. It looked therefore as though dyspnoea might be helpful in identifying asbestosis.

Sputum analysis

There was only a small difference between the percentage of certified and uncertified workers with asbestos bodies in the sputum. This difference was not significant (Table 22). Similarly there was no significant difference between the two groups for the presence of asbestos fibres in the sputum. There was also no evidence of higher or lower incidences of bodies or fibres in the sputum of the workers with airway obstruction.

ECG results

There was a small difference between the percentage of uncertified workers and certified workers with abnormal ECG recordings, with more uncertified workers showing abnormalities than certified workers. However, this difference was not significant. Table 22.

The ECG results of the workers with airway obstruction were then examined (Table 23). 51.7% of them were found to have an abnormal recording compared with only 15.4% of the certified workers and 25.7% of the remaining workers. This high proportion of abnormal recordings in the group with airway obstruction was significantly different from the proportions in the other two groups. The ECG was therefore included as a variable in the analysis as it was hoped that it might prove useful in separating workers with airway obstruction from the rest.

2. Radiological findings

The radiological results for the certified and uncertified workers, are shown in Table 2 . As the numbers within some of the subdivisions of this table were too small for accurate statistical comparisons to be carried out, the results were summarised as shown in Table 25. When those workers with pleural thickening alone were compared, there was no significant difference between the certified and uncertified groups. Similarly there was no significant difference between certified and uncertified workers with abnormal pattern by itself. However, the proportion of certified workers with pleural thickening plus abnormal pattern was significantly higher $P < 0.001$. Also there were significantly fewer certified workers with no radiological change at all $P < 0.001$.

3. Pulmonary function and clubbing results

Analysis of covariance

Table 26 gives the mean values of the lung function and clubbing results, before and after standardization for age and height, for three sub groups, normal, certified and remaining workers. As the normal group was chosen so that none of the results were below a certain standard, differences between this group and the certified group might be exaggerated. Therefore the remaining workers were included. The results of this group, which probably includes cases of early asbestosis and obstructive airway disease as well as reasonably healthy men, might be expected to be intermediate between those of the other two groups.

Lung volumes

(The mean values referred to are after standardization for age and height.)

There was an overall difference between the groups for the mean lung volumes (Table 26) significant at the 0.1% level. The mean VC, IC and TLC of the certified group were smaller than those of the normal group $P < 0.001$ but the mean RV was not significantly different. The mean values for the remaining group were, as expected, intermediate between those of the other two groups. The IC was smaller, $P < 0.01$, and the RV greater $P < 0.05$ than those of the normal group. The mean TLC was slightly larger and the VC somewhat smaller than those of the normal group but these differences were not significant. The VC, IC and TLC were significantly greater than those of the certified group $P < 0.001$.

Ventilatory capacity

There was a significant overall difference between the three groups for the FEV/VC % (< 0.01) which was due to a low mean FEV/VC% in the remaining group. The mean FEV/VC% of the

certified group was not significantly reduced below that of the normal group.

Although the mean PF was lower in the certified group than in the normal group this difference was not significant. The mean PF was lowest in the remaining group, the difference between this group and the normal group being significant ($P < 0.05$). This finding, together with the reduced mean FEV/VC%, suggested that there was more airway obstruction in the remaining group than in the other two groups. This would fit with the evidence of pulmonary hyperinflation provided by the higher mean RV and RV/TLC% in this group compared to the normal group $P < 0.05$.

Gas Transfer

There was an overall difference between the three groups for TI, K_{CO} and Dm which was significant at the 0.1% level. The mean TI, K_{CO} and Dm of the certified group were significantly smaller than that of both normal and remaining groups ($P<0.001$). The mean Vc was lowest in the certified group but the difference between the three groups was not significant.

The results of the remaining group were somewhat smaller than those of the normal group, the most significant reduction being the mean TI ($P < 0.05$).

This supports the suggestion that the men in the remaining group are less healthy than those in the normal group. The reduction in gas transfer could be due to early cases of asbestosis in the workers in this group but it might also occur in some of the men with airway obstruction and pulmonary hyperinflation (Cadigan J.B. et al 1961, and Palmer K.N.V. et al 1969).

TI/TI%

It was thought that TI/TI% might be a useful variable

This was therefore calculated for the certified group 75.7% and the group with obstructive airway disease 71.7%. However these mean values were not significantly different t 1.77 and so it was concluded that this would not help to separate the two types of disease in the PCA.

Clubbing

There was an overall significant difference between the groups for clubbing measured by the hyponychial angle $P < 0.001$. The highest mean angle was in the certified group and this was significantly different from the angle in the normal group and the remaining group ($P < 0.001$). There was very little difference in the mean angle in the normal and remaining groups.

From comparing the results of the certified workers with a group of 'normal' workers it was found that they had lower values for lung volumes and indices of gas transfer, and a higher incidence of rales, Xray abnormality and finger clubbing. It has been said (McVittie 1965) that in certification of asbestosis, adequate exposure to asbestos is necessary plus two of the following abnormalities:-

(1) abnormality of Xray

(2) rales

(3) finger clubbing

(4) abnormal lung function

Parkes (1973) listed the criteria for diagnosis by the Pneumoconiosis Medical Panel as:-

(1) Definite asbestos exposure

(2) Bilateral basal crepitations

(3) Radiological changes characteristic of diffuse fibrosis

(4) Impairment of lung function

In their paper, Britton and Hughes (1976) comment that these four items are as a rule mandatory but in a few cases rales may be absent in the presence of early radiological evidence of asbestosis. They also pointed out that claims for indudstrial benefit fail if the radiological changes are confined to the pleura as the statutory definition of pneumoconiosis refers only to fibrosis of the lung and does not include the pleura.

If the results of the 26 certified workers in this study population are examined a number do not appear to fulfil these criteria. If arbitrary levels for abnormal values are taken as $\leq$ 80% of the predicted value for VC and $\leq$ 85% for T_L and $\geq$ 198° for blubbing, then of the 26 certified workers, 7 had all four of the abnormalities listed by McVittie, 10 had 3, 7 had 2,

and 2 had only one abnormality (pleural thickening grade 1 in one individual, and parenchymal and pleural changes grades 2 and 1 in the other) - Table (50) gives details of the results of this group. Therefore, from the results obtained during this survey, it can be seen that the changes necessary for certification are minimal in some individuals and in two cases do not fulfil the criteria suggested by McVittie 1965.

The results of the uncertified workers were considered in the same way. Ninety-seven were found to have a single abnormality, commonly a reduced value for TL or VC or radiological abnormality (Tables 44,45). (If those with a reduced TL and VC and a value for FEV/FVC% of less than 60% are excluded, the numbers are reduced - see figures in parenthesis.) Only 2 of the ninety-seven had rales alone and 7 a hyponychial angle $\geq$ 198°. The results of those with two or more of the listed abnormalities (McVittie 1965) are shown in Table (60) for comparison with the results of the certified workers as they fulfil the criteria for certification of definite exposure to asbestos plus two abnormalities. Of these 37, 1 had all four abnormalities, 8 had 3, and 28 had 2.

Allowance should be made for variation between the results of this survey and those obtained by the Pneumoconiosis Medical Panels. However, the results of this comparison are surprising as a number of uncertified workers have changes which would appear to be sufficient to satisfy the criteria of the Pneumoconiosis Medical Panel. Conversely it is puzzling to know how some of those certified, fulfilled those criteria, case number 19 for instance. The methods used by the Pneumoconiosis Medical Panels do not appear to be foolproof. Their results must be assessed subjectively and errors are inevitable. Some objective method for evaluating the results as a whole would appear to be preferable.

Consideration of further methods of analysis

From examination of the results in an earlier section (see page 4.6), conclusions were drawn as to the occurrence, both separately and together, of rales, Xray abnormality, clubbing and abnormal pulmonary function in this study population of workers who have been exposed to asbestos dust for varying periods of time. The conditions necessary for certifying asbestosis in any individual have already been considered (page 1.17)

However, although advanced asbestosis is relatively easily recognised, the disease in its early stages is more difficult to diagnose as there is no general agreement on the order of appearance and relative importance of the initial manifestations. To take evidence of exposure to asbestos plus two abnormalities from the lists given by McVittie & Parkes. seems a crude method for diagnosis. From consideration of the results of the certified workers and comparing them with the results of other workers in the study population, it was concluded that an objective method of ascertaining the relative importance of the clinical radiological and pulmonary function variables and integrating them to provide a more reliable diagnosis and assessment of the disease is needed. One method suggested was the use of discriminant analysis to find the linear function of the original variables which discriminated best between a group of normal workers and a group of certified workers. However, apart from the lack of a control group the certified workers might not adequately represent the disease. Therefore, the basic condition for the use of discriminant analysis - two well defined groups with similar variances and covariances of the variables - were not fulfilled by our data and, as a result, this method could not be used.

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It was therefore decided to try using the technique of Principal component analysis (Hotelling 1933; Kendall 1961) as for this method no preliminary subdivision of the group is necessary. The aim of this analytical technique is to condense the data by finding those factors that represent independent attributes of lung disease. A linear transformation is applied to the original set of correlated variables to produce a new set of uncorrelated variables or components. Each component is extracted in the order of the magnitude of its contribution to the total variance of the original variables. The first few components usually account for most of the total variance and reveal the underlying nature of the variability in which case the remainder can be ignored. A component score for each individual is calculated as a weighted sum of the values of the original variables after they have been standardised by subtracting the mean and dividing by the standard deviation. The individual scores plotted against the axes of the components may then show meaningful trends. The meaning of such trends must be determined by means external to the analysis. Generally a valid interpretation may be expected for those components which account for a significant part of the total variation but this is not always the case.

Gilson J.C. et al 1955 used factor analysis to examine disturbances of lung function related to radiological changes in coal mines. They used the complete centroid method which is not strictly comparable to principal component analysis. They pointed out that in the interpretation of results, any two tests may overlap and, therefore, partially measure the same thing. Factor analysis enables the results of all the tests to be viewed concurrently, interrelationships to be seen, and independent aspects of lung function to be identified.

In their analysis, the first three factors extracted 65% of the covariance, including a fourth factor only added 3%. They identified four basic independent attributes of the lung:-

1. Size
2. Ventilation power
3. Gas distribution
4. Gas transfer

They concluded that tests measuring the "bellow" action of the lung were the best in assessing disability in coal mines pneumoconiosis.

Hopefully, some means of assessing disability in asbestos workers will emerge from the principal component analysis.

Principal Component Analysis

Table 27 lists the variables used in the analysis. First the programme No. BMDO1M, Health Sciences computing facility UCLA was run with the population of each factory separately. As the three sets of results were very similar, the analysis was continued using the combined results of 201 workers (those subjects with missing results Table 4, were not included in the analysis).

Results of PCA

Theoretically most of the variance should have been taken out by the first few components for the analysis to produce meaningful results. The results were therefore disappointing as components I and II accounted for less than 40% of the total variance. In an attempt to improve this proportion, each variable was examined and those with eigen vectors near to zero for both of the first two components were discarded (ECG, rhonchi and sputum analysis). Other variables with one value near to zero were retained if the value for the other component was appreciably greater than zero (TI, phlegm). The correlation coefficient matrix after these alterations is given in Table 28. Table 29 lists the eigen vectors for the first two components in descending order of magnitude. The further the distance from zero, either positive or negative, the greater the contribution to that component. Thus TI is the greatest contributor to component I followed by VC, age, Dm etc. For component II FEV/VC% is the greatest contributor, followed by phlegm, pleural thickening and cough.

Usually those components accounting for a considerable proportion of the total varience would be expected to be capable of some meaningful interpretation. The percentage of the total

varience taken out by the sixteen components was:-

Component	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
%	26	13	10	7	7	5	5	5	4	4	3	4	2	2	2	1

As components I and II only accounted for 39% of the total, components III, IV and V were carefully examined by plotting co-ordinate points against pairs of component axes for all combinations of components I-V. Apart from component I plotted against component II, (fig. 2) there appeared to be no consistent trends nor was the distribution of the variables about the axes meaningful. Therefore further analysis was confined to the first two components.

From the plot of component I against component II, Fig. 2 it was noticed that FEV/VC, phlegm and cough were at the positive end of the scale for component II and Xray, rales and clubbing were at the negative end of the scale. This suggested that component II might be distinguishing between asbestosis and obstructive airways disease. For component I, no meaningful interpretation was apparent on first examination. However this is not unusual as the first component in PCA is often a general component. Fig. 3 is a plot of the 201 individuals using the scores of component I on the horizontal axis and component II on the vertical axis. The individual scores were calculated as follows:

$$Z_{AI} = \frac{W_1(x_1-\bar{x}_1)}{SD(x_1)} + \frac{W_2(x_2-\bar{x}_2)}{SD(x_2)} \ldots\ldots + \frac{W_{16}(x_{16}-\bar{x}_{16})}{SD(x_{16})}$$

where Z_{AI} is the score for subject A for component I, W_{1-16} are the weightings (eigen vectors) of the variables (Table 29) and x_{1-16} and $\bar{x}_{1-16}$ are respectively their observed values and means. The unstandardized weightings are also listed in Table 29; they enable any further subjects for whom the sixteen variables are known to be plotted on the diagram in Fig. 3. The certified workers and those

with presumptive obstructive airway disease were identified on the plot (Fig. 3). These presumably unhealthy workers, with few exceptions, were found to be distributed towards the left hand side of the plot which suggested that component I, normally of a general nature in PCA, was separating the healthy individuals from those with lung disease. Component II appeared to separate those with lung disease into asbestosis at the top and obstructive airway disease at the bottom of the plot.

To check the validity of this interpretation the mean values of the sixteen variables (unadjusted for age and height) were calculated for individuals lying in each quadrant Tables 33, a, b. In addition, the results of the certified workers were calculated separately from the rest in the upper left quadrant and similarly those with obstructive airway disease were calculated separately from the rest in the lower left quadrant. Also, combined means for all the workers on the right hand side of the plot were calculated (excluding two certified subjects and two with obstructive airway disease on this side).

Without exception, there are consistent trends in the means of all variables indicating decreasing health from right to left. There is a fall in mean age, amount smoked and length of exposure (hardly surprising as one might expect to find the healthiest workers among the youngest, non-smokers, with shortest exposure to asbestos.) There is a rise in mean FEV/VC%, VC, TI and Dm and a fall in mean RV/TLC%, hyponychial angle and prevalence of abnormal clinical and radiological findings going from left to right. After allowing for differences in age and height, using the regressions in Table 31 (Cotes J.E. 1965) these trends remain, supporting the interpretation that component I separates the healthy from those with lung disease.

Considering component II, there are consistent changes from upper to lower quadrants on both sides. The mean VC is lower and the mean hyponychial angle and prevalence of rales and abnormal Xrays are higher in the upper left hand quadrant. The mean FEV/VC% is lower and the mean RV/TLC% and incidence of cough and phlegm are higher in the lower left hand quadrant. These changes from upper to lower quadrants, on both sides, conform with the known abnormalities in asbestosis and chronic obstructive airway disease.

To check whether these trends were present within the quadrants, the means of TI, VC, rales and Xray abnormality were calculated after further subdividing the PCA plot (Fig. 3) into the following sub groups:-

subjects in the intervals -4 to -3, -3 to -2 .... +3 to +4.

Figs. 4 a, b show these means. For component I, Fig. 4a, there is a steady rise in VC and TI going from left to right of the plot and a fall in rales and Xray abnormality. These changes are consistent with individuals on the right having better health than those on the left. For component II (Fig. 4b) rales and Xray abnormality fall from a maximum on the right side of the plot (asbestosis) to near zero at the mid range and remain low on the left hand side (obstructive airway disease). In contrast VC and TI show maxima at the mid-range and fall symmetrically on both sides. These results fit with the finding that VC and TI are reduced in both asbestosis and obstructive disease but rales and an abnormal Xray are features of asbestosis alone.

These trends were consistent with the interpretation that component I separates healthy individuals from those with disease and component II separates those with asbestosis from those with obstructive airway disease. For component I if a particular variable has a positive weighting eg. TI, a high value will indicate health and a low value disease. For a negative weighting,

a high value is indicative of disease and vice versa, e.g. age. For component II a positive weighting indicates that the variable will have high values in asbestosis e.g. Xray and a negative weighting, a high value for the variable indicates obstructive airway disease e.g. phlegm.

For each component, those variables with the highest weightings (Table 29a, b) either positive or negative are the best differentiators.

This interpretation of the meaning of the components is in keeping with the position of the certified workers and those with obstructive airway disease on the plot (Fig. 3). Only two of the certified workers were not in the upper left hand quadrant (the one in the upper right quadrant deteriorated rapidly in the two years following the survey) and all but two of those with obstructive airway disease were in the lower left quadrant.

Conclusions

From the PCA, the most important variables for determining lung disease were TI, VC, age and Dm in that order. The FEV/VC, phlegm, Xray (pleural thickening) cough and clubbing in that order were the best variables for differentiating between asbestosis and obstructive airway disease.

In an attempt to improve the proportion of the total variance extracted by the first three components which was:-

Component	1	2	3
Percentage	27	40	51

some of the variables included in the PCA were changed. RV was used instead of $^{RV}/_{TLC\%}$ as by using it and VC instead of $^{RV}/_{TLC\%}$ duplication of information was reduced. Although the eigen vector value for RV was very near to zero for component I it had a high value for component II. It had very little effect on the proportion of the total variance extracted by the first three components:

Component	1	2	3
Percentage	26	40	50

Dm was expressed as $\frac{1}{Dm}$ because the distribution of the reciprocal is less skew, (Hamer N. 1962). This slightly raised the proportion of the total variance extracted:-

Component	1	2	3
Percentage	28	41	52

IC was tried instead of VC as it has been suggested (Thomson et al 1965) that a reduction in IC might occur earlier than a reduction in VC. However the eigen vector for CI and CII was nearer to zero for IC than for VC. The proportion of the total variance extracted was not improved appreciably:

Component	1	2	3
Percentage	28	41	51

Therefore it did not replace VC in the final analysis, but $\frac{1}{Dm}$ was used instead of Dm and RV instead of $^{RV}/_{TLC\%}$.

Consideration of further variables

In an earlier section (page 4.44) IC was considered as a variable for use in the PCA but rejected as it did not improve the results. As a further check on this conclusion, the IC expressed as a percentage of the VC has been considered to see if the reduction in VC in asbestosis is due to a reduction in IC, and also to see if this differs from the reduction of VC from other causes. IC/VC% was calculated for individuals in different areas of the principal component analysis plot (Table 51) Although the IC/VC% was reduced from 70% to 66.9% going from positive to negative for component I (i.e.'health' to 'disease') there was no difference going from positive to negative (i.e. asbestosis to airway obstructive disease) for component II. Therefore this provides no evidence to suggest that the reduction in VC in asbestosis is any different to the reduction of VC in airway obstructive disease. In both cases the IC as a percentage of the VC dropped.

Similarly TL'/TL % was considered to see if it would be a useful variable to include in the principal component analysis but was rejected. As a further check on this conclusion, TL'/TL % has been calculated for individuals subdivided by their values for components I and II (Table 51). For component I there was very little difference in the values for TL'/TL % going from positive to negative values for the component. That is, this variable would not prove useful in separating healthy workers from those with disease. There was a fall in TL'/TL % going from positive to negative values for component II - that is this variable might be useful in separating workers with asbestosis from those with airway obstructive disease. To check on this point, TL'/TL % was included as a variable in a further run of the PCA. As expected, for component I, the eigen vector was very near to zero. For component II,

although the eigen vector was somewhat greater, it was not among the best at differentiating between those with asbestosis and those with airway obstructive disease. Also, it did not improve the proportion of the total variance extracted and as it was important to keep the number of variables in the analysis to a minimum, it was not included in further runs of the PCA.

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Discussion - Lung function in asbestosis

The basic lesion in asbestosis is reported (D. O'B. Hourihane et al) to be peribronchiolar fibrosis which obliterates the surrounding alveoli. Zones of solid fibrosis may occur in which laminated collagen replaces the entire parenchyma and in these zones of severe fibrosis, alveolar cell hyperplasia may be prominent and blood vessels are frequently sclerotic. The pleura are nearly always abnormal.

From this pathological picture of the lung in asbestosis, certain changes in pulmonary function might be predicted. With loss of elastic tissue and fibrotic change in the pleura, a fall in lung volumes would be expected. This was noticed by the earliest workers (see historical section) and has been confirmed by later studies. In this study the VC, IC and TLC were all reduced in the certified group (Table 26). The possibility that the IC might be more useful than the VC in separating workers with asbestosis from those with obstructive airway disease because of a proportionately greater reduction, was considered. The mean IC was reduced in both the certified group and the group with obstructive airway disease. However the IC expressed as a percentage of the VC was nearly identical in both groups (58% in certified and 59% in obstructive airway group) compared with 74% in the normal group.

The TLC tends to be decreased in asbestosis and increased in obstructive airway disease and so might be useful in distinguishing between the two groups. However, when it was included as a variable in the PCA, the percentage of the total variance extracted was not improved and the position of the individuals in the plot (Fig. 3) was practically identical. In measuring TLC in the survey the time necessary for complete gaseous mixing in cases of uneven

ventilation was probably insufficient and so this variable might have been underestimated in these cases which could explain why it was not particularly helpful in the PCA.

The increased 'stiffness' of the lung tends to widen and support the airways with the result that the FEV/VC% is normal or increased (Pelzer, A.M. et al 1965). In this study the FEV/VC % was not found to be reduced in the certified cases and was the most useful discriminator in the PCA between asbestosis and obstructive airway disease where FEV/VC%is decreased.

The RV is reduced proportionately in asbestosis and not until a late stage in the disease does the RV/TLC% rise above 45%. Therefore in this group of working men an increased value would not be expected. From the PCA it was found to be a useful indicator of obstructive airway disease.

From examination of the pathology of the fibrotic lung, the reduced surface area and thickened membrane might be expected to interfere with gas transfer from the alveoli into the blood. A reduced TI in asbestosis was first reported (1 case studied) in 1957 (Marks et al) and since then this reduction has been confirmed by many workers, (Williams, R. et al 1960, Leathart G.L. 1960, McGrath, M. et al 1959, Bader M.E. et al 1961, Bjure J. et al 1964, Bader M.E. et al 1965, Hunt, R 1965). The results of this study provide further confirmation of this reduction. TI measured by the single breath method is difficult to interpret when there is appreciable airways obstruction because of uneven ventilation (Cadigan J.B. et al 1961). When hyperinflation is present, TI is usually found to be decreased (Palmer K.N.V. et al 1969). In this study TI was found to be decreased in both asbestosis and chronic obstructive airway disease.

The membrane component of TI, Dm, would be expected to be reduced. McNeill R.S. et al 1958 found a reduced Dm in five patients with pulmonary fibrosis and Bates D.V. et al 1960 thought that this index might prove to be the most sensitive indicator of diffuse interstitial fibrosis. In the study of Thomson et al 1965, Dm was found to be less sensitive than TI in discriminating between certified and uncertified workers. The U/U max%(Mann-Whitney U statistic, Siegel, S. 1956) was used to calculate the power of the pulmonary function tests in discriminating between the two groups. Table 32 shows these values and also U/U max % calculated from the results of the group of normal and certified workers in the present study. This shows Dm to be extremely close to TI in discriminating between the two groups.

From the results of the PCA, Dm was found to be a good indicator of lung disease. It was not so good at differentiating between asbestosis and bronchitis but it had a higher weighting than TI. Measurement of Dm is subject to error and airway obstruction causes greater artifact in Dm than in TI. This may explain why although theoretically it should be very good at identifying pulmonary fibrosis, in practice it does not seem to be superior to TI.

The mean blood component Vc of the transfer factor, although somewhat lower in the certified group was not significantly reduced below the mean of the normal group (Table 26) and for this reason was not included in the PCA.

Hamer N.A.J. 1963 examined the effects of increasing lung volume on Dm and Vc and found that Dm increases as the lung expands from FRC to TLC proportionately to the estimated increase in surface area. Vc was little affected and they suggested that as the lung expands, the blood vessels behave like rubber tubes getting

longer and thinner without any increase in volume. As the main defect in asbestosis is a reduction in lung volume this reduction would not be expected to affect Vc. So unless fibrosis is very severe with destruction of lung tissue and pulmonary hypertension, Vc remains unchanged.

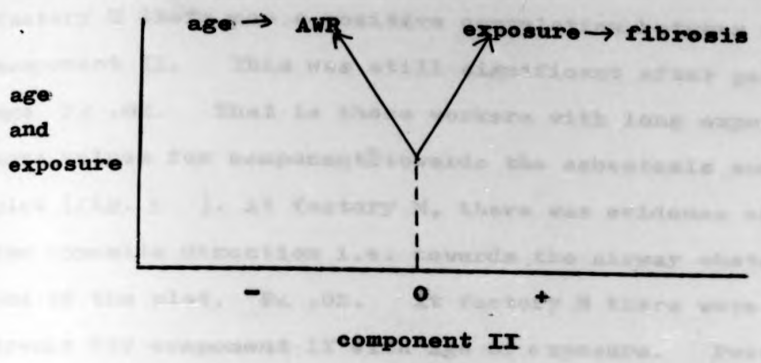
Comparison of factories b y P.C.A. (after excluding exposure)

As a result of the PCA, a group was identified in one quadrant as those having asbestosis on the basis of the occurrence of many of the certified cases in this quadrant. However, by using the distribution of certified cases in arriving at these conclusions, the correctness was tacitly acknowledged of the methods used by the Pneumoconiosis Medical Panels in evaluation of the disease and some doubt has already been cast on these methods (page 4.34).

If exposure could be shown to correlate with the results obtained from the PCA this would provide a firmer basis for any conclusions drawn from the results. Therefore, the PCA was repeated excluding exposure as a variable. (Table 33).

Figs (10 a,b,c) show CI plotted against exposure for the three factories separately. For Factory B there is evidence of a negative trend with exposure for CI - that is with increasing length of exposure there is increased evidence of disease. Factory U also shows the same tendency but Factory M does not. As age and exposure may be linked, these two were plotted against each other for each factory and also age against CI. Figs.(10d-j) All three factories showed a correlation between age and CI which was very slight for Factory M, moderately good for Factory B, and good for Factory U. Factory B showed a positive correlation between age and exposure but there appeared very little evidence of a similar trend in the other two factories. Scatter diagrams were also plotted for Components II versus age and exposure. (Figs.10j-o) If the interpretation of the results of the Principal Component Analysis in an earlier section (page 4.41) is correct - i.e. those workers with airway obstructive disease have values for component II towards the negative end of the scale and those with asbestosis have values towards the positive end of the scale - then a bipolar type of relationship

might be expected.



The scatter diagrams were very difficult to interpret. There was little evidence of any correlation between exposure and component II or age and component II except for factory U where there appeared to be some evidence of a negative correlation between component II and age and a slight positive trend of component II with exposure.

To examine these results in more detail multiple regression analysis was used. Table (52) gives details of the results. At factory B there was a significant negative correlation between exposure and C I, $P < .001$. As age and exposure were linked in this factory, the effects of age were partialled out, Table(52) After this the correlation was still significant $P < .01$. At factory U there was also a significant correlation between exposure and CI and as age and exposure were only slightly linked the correlation coefficient for exposure, with age held constant, was only reduced very slightly and still significant, $P < .001$. At factory M, the correlation coefficient was not significant and after partialling out age it was extremely small ($r = 0.067$).

Therefore factories B and U both show a significant correlation between exposure and CI - that is, in those with longer exposure to asbestos there is evidence of more disease. At factory M, there is no evidence of a correlation between exposure to asbestos and disease.

The results for CII were difficult to interpret. At factory U there was a positive correlation between exposure and component II. This was still significant after partialling out age $P < .02$. That is those workers with long exposure to asbestos have values for component II towards the asbestosis end of the plot (fig. 3). At factory M, there was evidence of a trend in the opposite direction i.e. towards the airway obstructive disease end of the plot. $P < .02$. At factory B there were no significant trends for component II with age or exposure. Possibly in this factory the pattern of disease is of a mixed type which would be very difficult to analyse because of the bipolar type of relationship of component II with age and exposure

Discussion

From this analysis, there is evidence at factories B and U of a significant link between exposure to asbestos and disease. At factory M there is no evidence of such a link. Unfortunately from this survey it is impossible to be sure of the reasons for this difference. It is possible that chrysotile is less dangerous than the other two forms of the mineral. There is evidence from animal experiments, Wager et al (1963) and Wagner 1972, and also from "in vitro" studies, Parazzi et al 1968, that chrysotile is less cytotoxic than amphibole asbestos. Weill 1975 found less normal values for pulmonary function tests in workers handling crocidolite compared with those working with chrysotile. However, because there are no comparable records of dust measurements in the three factories over the past twenty years it cannot be definitely concluded from this study that chrysotile is less dangerous. The methods for dust control might have been much more efficient in factory M so that the workers were exposed to lower concentration of asbestos. Dust levels, measured at the time of the survey were very close in the three factories (Table 36) but it cannot be assumed that they were so similar in the past.

There is some evidence at factory M of a higher incidence of airway obstructive disease. This could be due to higher atmospheric pollution in this area, the greater tobacco consumption in this factory or to the use of cotton with asbestos in the mixture. Cotton dust produces a lung disease byssinosis of which airway obstruction is a feature Lammers et al 1964, Berry et al 1973. If a control population of workers with similar smoking habits, and exposure to cotton dust could have been examined it might have been possible to solve this problem.

Conclusions

From this study it seems that chrysotile may be less dangerous than amosite and crocidolite. However the lack of comparable past dust measurements casts doubt on this conclusion. No evidence was obtained as to the relative toxicities of amosite and crocidolite.

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Conclusions

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Certified workers reviewed subsequent to the PCA

In an earlier section when the results of the certified workers were examined, a few appeared to have minimal grounds for certification. Conversely, it was difficult to see why some workers were not certified (Table 50) as they had two or more of the abnormalities listed by McVittie 1965 and Parkes 1973 as necessary for certification by the pneumoconiosis medical panels. As the methods for their selection were very crude and the degree of abnormality minimal in many cases, I do not think all of this group should have been certified. In some cases severe airways obstruction could have been the cause of reduced values for T_L and VC. However, a number had good evidence of asbestosis.

In figs. 3 and 11 the values for the certified workers are shown as crosses on a plot of component I against component II and the values for the selected group of uncertified workers are shown within a triangle. Some of this group are towards the bottom left hand corner of the plot - that is the obstructive airway disease quadrant which was not unexpected as I have already pointed out that values of T_L and VC could have been reduced by airway obstruction in some cases. As noted from fig. 3 one of the certified cases was in this quadrant too. Quite a considerable number of points within triangles (those selected as possible cases of asbestosis) were in the top left hand quadrant (that is, in the asbestosis quadrant) and have comparable values for the two components to the certified cases. A few individuals who were not selected as possible cases of asbestosis were mixed in with the certified and possible cases of asbestosis. On looking at those subjects with values for component I equal to or less than -1.0, and a positive value for component II, many had a single abnormality (see page 4.9) and, in addition, five had low values for Dm, four had abnormal

Xrays, and several had values for clubbing T_L and VC very near to the cut off point for abnormality (see page 4.6 for definition of abnormal values). That is, their position on the plot was compatible with early asbestosis and their results illustrate how difficult it is to assess results subjectively ....

In conclusion, although well developed cases of asbestosis are readily recognised and diagnosed, early cases are much more difficult to assess. In the population under study, a number of individuals appeared to have been wrongly diagnosed as cases of asbestosis and others who had good evidence of the disease were not certified. From examination of the position of these workers on the plot figs. 3, 11, these mistakes were apparent. Therefore, an objective method for assessment of asbestosis such as the principal component analysis described in this study, would be more accurate than the subjective assessment of the pneumoconiosis medical panels.

Smoking and Components I and II

In an earlier section (page 4.13) the results were considered to see if there was evidence of more asbestosis in smokers compared with non-smokers. No evidence was found to support this suggestion from examination of the crude results. Mean values of Components I and II have been calculated for non-smokers and for smokers of different grades. Table (53) gives the results. For Component I at factory B there is no difference between the mean value for smokers and non-smokers unlike the other two factories which both have less "healthy" values for the smokers compared to the non smokers. When the results of the three factories were combined there was a fall from .245 in the non smokers to -.550 in smokers grade 3 with smokers grade 1 and 2 between There appears to be a correlation between smoking and disease as measured by component I when the results of the three factories are combined. Table (48) gives the mean values for age and exposure to asbestos in the smokers and non smokers. This shows that the mean age and exposure are quite close in all grades and therefore fall in component I with an increase in tobacco consumption is not due to either age or exposure.

For component II all three factories have values for smokers (all grades combined) towards the negative end of the scale (airway obstructive disease) when compared with the non smokers. This finding of a link between airway obstructive disease and smoking is not surprising. Factory M shows the trend most clearly throughout the grades of smoking whereas the other two factories although there is a difference between smokers and non smokers do not show a steady fall of CII going from non smokers to smokers grade 3. This is possibly because of the presence of more fibrosis in these two factories which would affect CII in the opposite direction and so confuse the results.

Possible sources of error

A. Subjects excluded from PCA

As 30% of the study population were not included in the PCA for various reasons their results were examined to check whether their inclusion in the PCA would have materially affected the analysis. Table (54) gives mean values of some variables for the two groups, those included in the PCA and those not included. As the two groups differed slightly in age and height some of the lung function variables were expressed as a percentage of the predicted values.
The mean values for the two groups were very close in all cases and also the incidence of clinical and radiological abnormalities was very similar in the two groups. Therefore this suggests that exclusion of these subjects from the PCA probably did not affect the results of the analysis.

B. Subjects missing and excluded from study population

From comparison of the factories it was concluded that B had most asbestosis and M had least. As the percentage of workers at risk who were studied, differed in the three factories, Table 2, the refusals were considered to find out if their omission affected the conclusions.

Of the seven missing at M and six at U, none were certified cases of asbestosis. However, two of the twenty-two refusals at B were certified. The mean length of exposure to asbestos of these twenty-two refusals at B was seventeen years compared with fourteen years for the population studied. If these refusals are included in the population the percentage certified (Tables 3 and 21) changes from 20.4% to 18.4%.
This doesn't affect the conclusions drawn from consideration of certification details.

The Xrays of the missing subjects at B were examined

(Table 37). Exclusion of these workers from the population at risk probably did not affect the results.

On enquiry it was found at B, that workers who became disabled by asbestosis, were moved to other departments within the factory where the work was less demanding. For example, printing, office work or general service. These departments were not included in our survey as asbestos was not used by the workers. Thirteen men were working in these departments at the time of the survey. In M and U there were not any certified workers except in the departments studied. This feature of B therefore supports the conclusion that the highest incidence of asbestosis is at B.

LIMITATIONS OF THIS STUDY

1. Lack of a control group

One of the biggest limitations in this survey was the failure to examine a control group. Ideally a control group of workers not exposed to asbestos should have been examined in each area. By comparing the results of the control groups any differences due to atmospheric pollution would have been found. Analysis of the results would have been simplified as discriminant analysis could have been used to find out which variables discriminated best between the asbestos workers and the controls. One of the problems to be investigated - assessment of the relative importance of those variables used in the survey in identifying asbestos - could have been solved by this method.

2. Lack of comparable dust measurements in the three factories

Although examination of a control group would have been useful, it would not have solved one of the main difficulties in analysis of the results - that of differences between the factories in dust levels to which workers were exposed in the past. If comparable measurements, both of type of exposure and quality of dust, had been made in the past in all three factories, comparison of the results of the three factories might have been simplified.

3. In factory M, a further problem was imposed by the use of cotton in addition to asbestos. A control group of workers in a cotton factory in addition to a control group from a non-dusty environment should ideally have been included in the study.

4. Method of defining the population

The workers included in this study were, by definition, those in which at least three years had elapsed since the date of first employment in the factory. In addition, at the date of

commencement of the survey, they had to be directly involved in one of the manufacturing processes (i.e. office workers, electricians, engineers were excluded). The problem arising from this definition is that those examined were a "survivor" group. At factory B, in particular, workers either certified or suspected of having the disease were moved to occupations not directly involved in the manufacture of asbestos products and therefore did not come within our group as defined. Ideally the study group should have been re-defined to include such individuals.

5. Differences in Volunteer rate

For this survey we had to depend on volunteers. At factory B, in particular, there was a reluctance to volunteer due to earlier surveys in this factory including such non-acceptable tests as compliance. Additionally, those volunteering often differ from those who fail to come forward. Ideally one would hope to examine at least 90% of the population and also have the reasons for exclusion of the remainder and any information about them.

6. Limitations in the tests used

Ideally those tests known to be efficient in assessing the disease under study should be used. Additionally, other tests that might prove to be useful in diagnosis should be included.

Compliance was excluded because it was found not to be acceptable to the workers in an earlier survey and would certainly have affected the response rate of volunteers. This test has long been known to be reduced in asbestosis and is one of the most sensitive in identifying the disease - Thomson et al 1965. These workers found a normal VC and IC in the presence of a reduced T_L and compliance in some individuals although Bader

et al 1965 found a linear relationship between VC and compliance. However, the most useful point about compliance is its specificity to asbestosis when compared with obstructive airways disease. From the principal component analysis although T_L was very good at identifying individuals with poor health, it was poor at discriminating between asbestosis and bronchitis. Compliance would probably have proved to be a useful discriminator between these two groups.

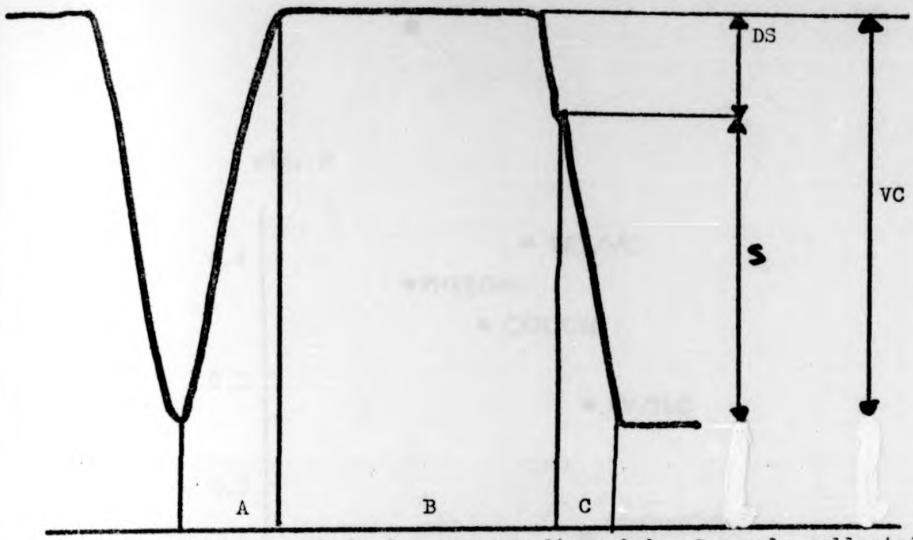
Oxygen saturation of arterial blood was first reported to be reduced at rest by Baldwin et al as early as 1949. Since then this finding has been confirmed both at rest and more commonly on exercise - Wright 1955, Williams et al 1960, Bjure et al 1964, Bader et al 1965, Wallace et al 1971. In asbestosis the fibrotic changes in the lung affect the ventilation perfusion relationships resulting in an increase of the alveolar-arterial O_2 tension difference which causes hypoxaemia, particularly on exercise in many cases of the disease. Bader et al 1965 considered that O_2 desaturation on exercise might prove to be one of the most sensitive indicators of the disease. In this survey when early signs of the disease were being looked for, measurement of arterial O_2 saturation at rest and on exercise might have provided valuable information. As the factory management had prohibited the drawing of blood an indirect method was suggested. The Waters-Conley ear oximeter was used to measure O_2 saturation at the beginning of the survey. Unfortunately, both examples of the instruments that were used were found to be unreliable and this test was discarded after a short while.

However, unlike compliance a fall of which is specific to restrictive diseases of the lung contrasted with obstructive airways disease, hypoxaemia at rest often occurs in patients

with obstructive airways disease. On exercise desaturation may occur also but it is not invariable. So, although measurement of arterial O_2 saturation at rest and on exercise would probably have provided valuable information it would not necessarily have helped in distinguishing between asbestosis and airways obstruction.

Bader et al 1965 found hyperventilation commonly in their group, but Wallace et al 1971 did not confirm this finding or that of a reduced arterial carbon dioxide tension. Probably hyperventilation and a reduced CO_2 tension do not occur early in the disease. From this survey it was hoped to find those tests most useful in identifying early asbestosis and therefore measurement of minute volume and blood CO_2 tensions would probably not have helped further this aim.

Fig. 1a



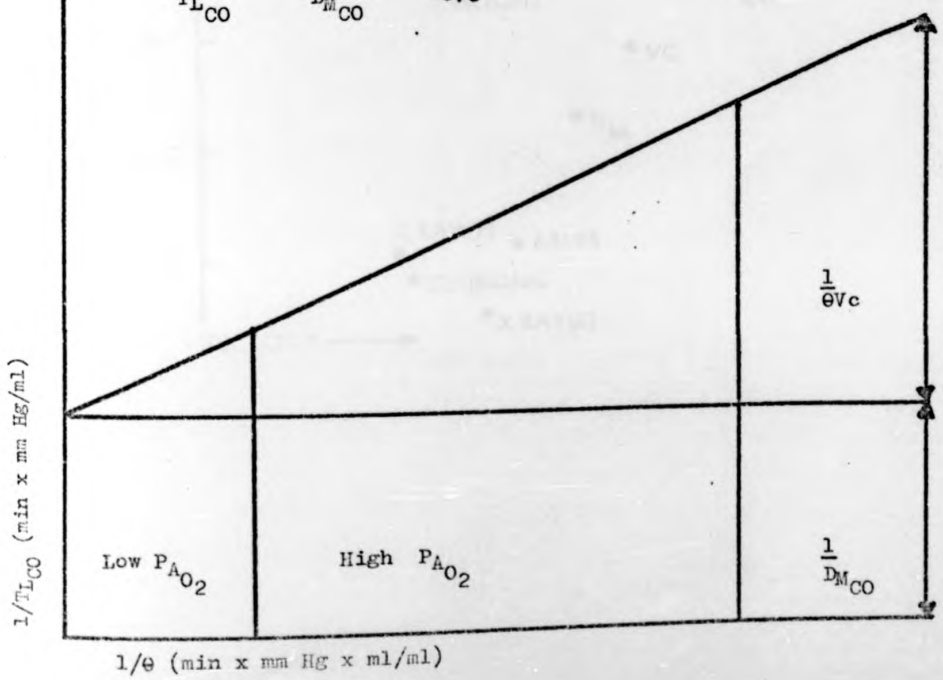
VC vital capacity, DS dead space gas discarded, S sample collected

$$\frac{1}{t} = \frac{68.2}{0.7A + B + 0.5C}$$

Spirogram with timing formula used in measurement of T_L

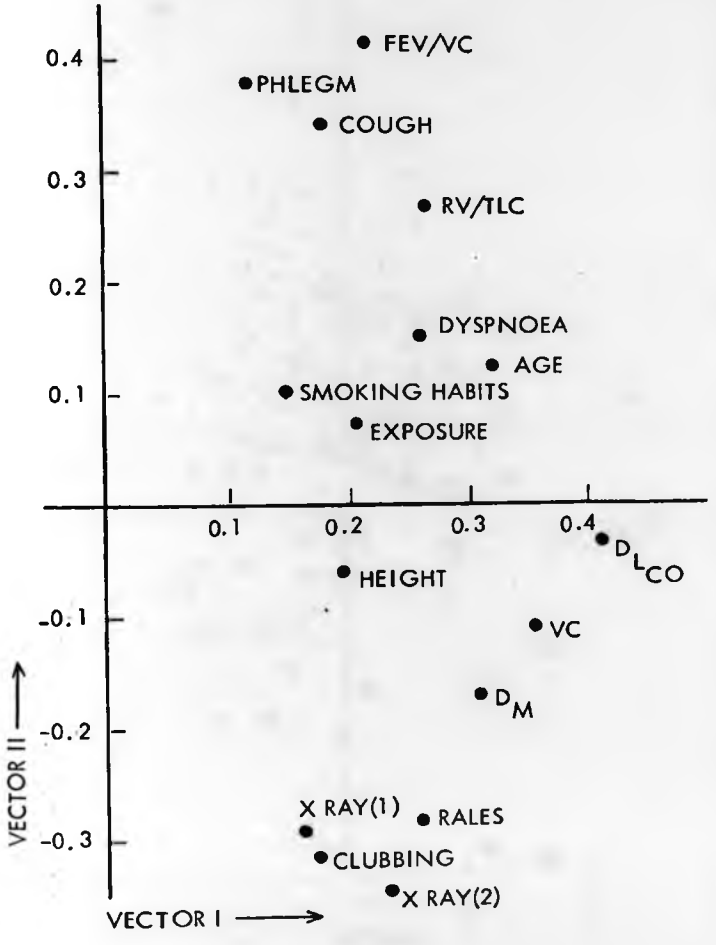
Fig. 1b

$$\frac{1}{T_{L_{CO}}} = \frac{1}{D_{M_{CO}}} + \frac{1}{\theta Vc}$$



Relationship between $T_{L_{CO}}$, θVc, $D_{M_{CO}}$

Fig. 2


FEV/VC
PHLEGM
COUGH
RV/TLC
DYSPNOEA
AGE
SMOKING HABITS
EXPOSURE
HEIGHT
D_{LCO}
VC
D_M
X RAY(1)
RALES
CLUBBING
X RAY(2)
0.4
0.3
0.2
0.1
-0.1
-0.2
-0.3
0.1
0.2
0.3
0.4
VECTOR II
VECTOR I

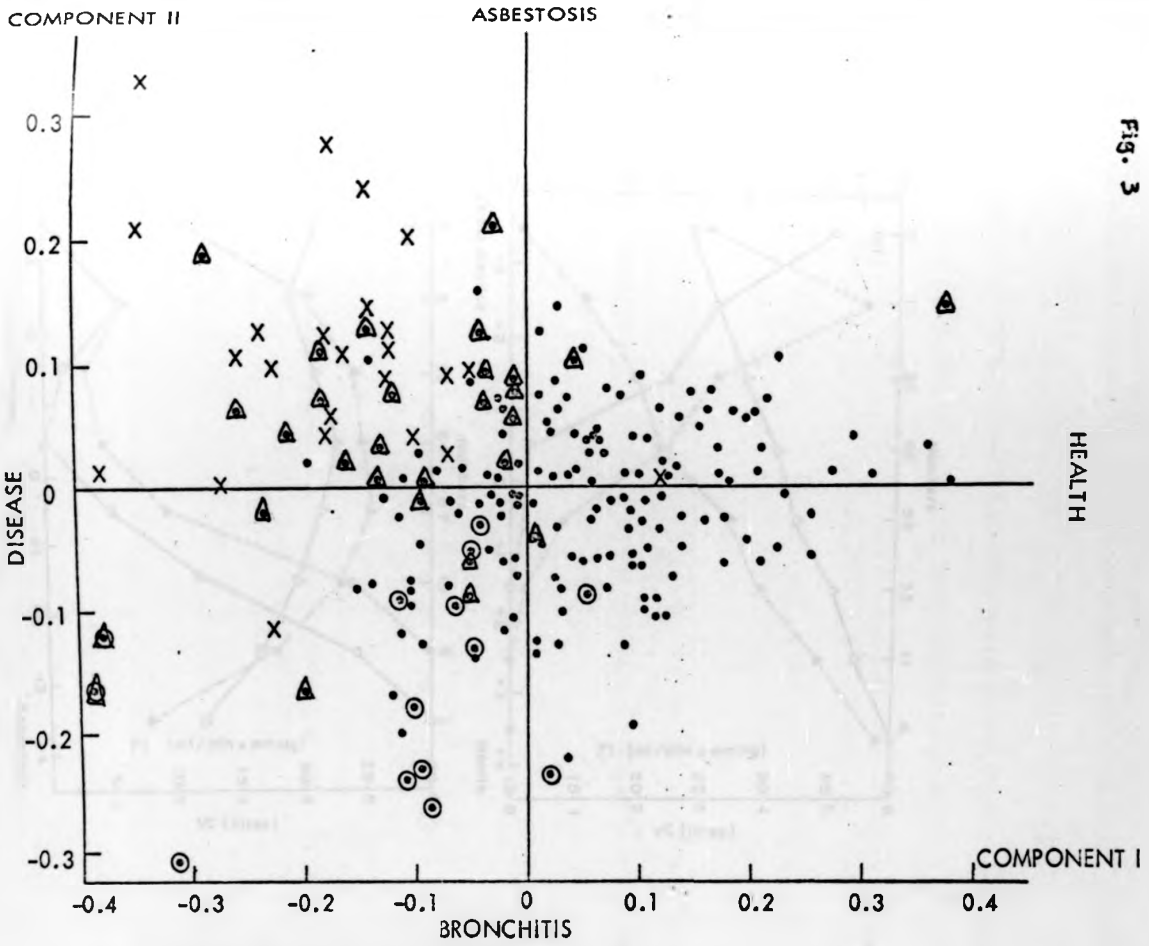


Fig. 3

x - certified cases of asbestosis
△ - possible " " "
⊙ - cases with airways obs. dis.

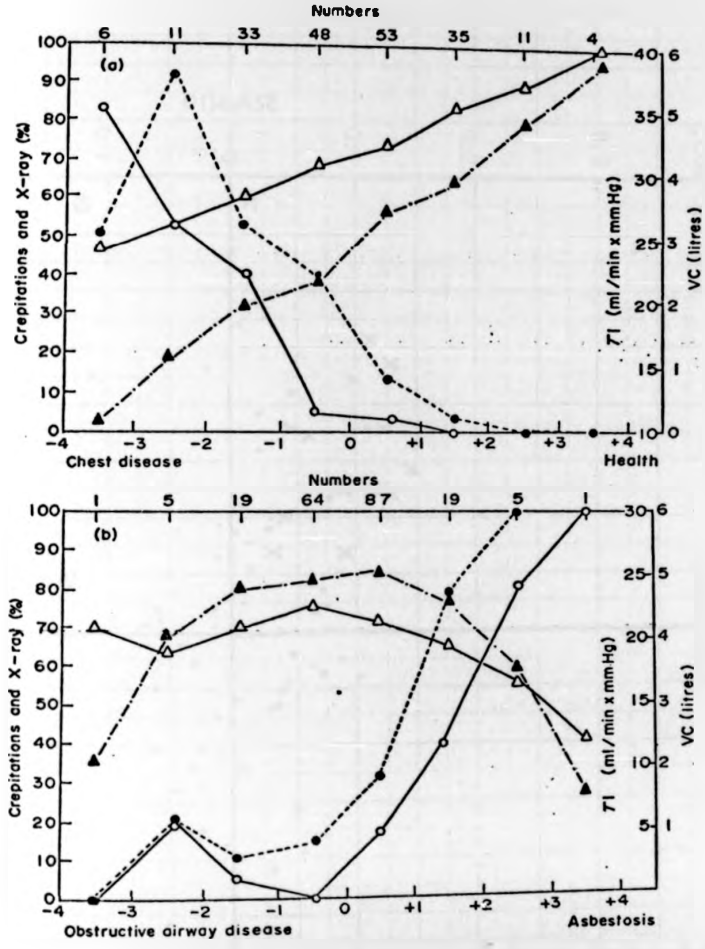


FIG. 4 Unadjusted means of the transfer factor (*TI*) (▲), vital capacity (VC) (△), and the prevalence of X-ray abnormality (●) and crepitations (○) for subjects lying within (a) the horizontal intervals (component I) of the PCA (Fig. 1), and (b) the vertical intervals (component II) of the PCA (Fig. 1).

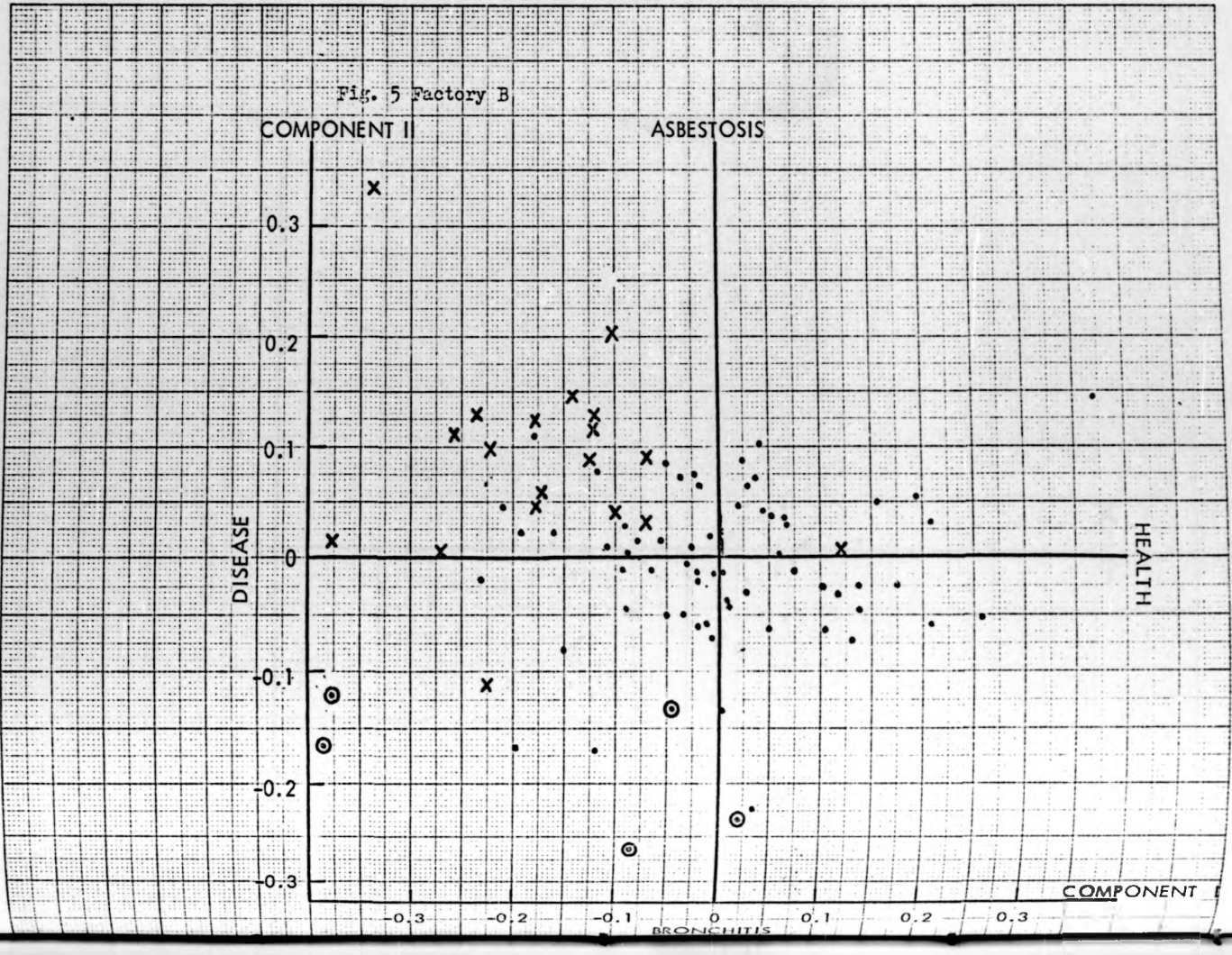


Fig. 5 Factory B

Fig. 5 Factory M

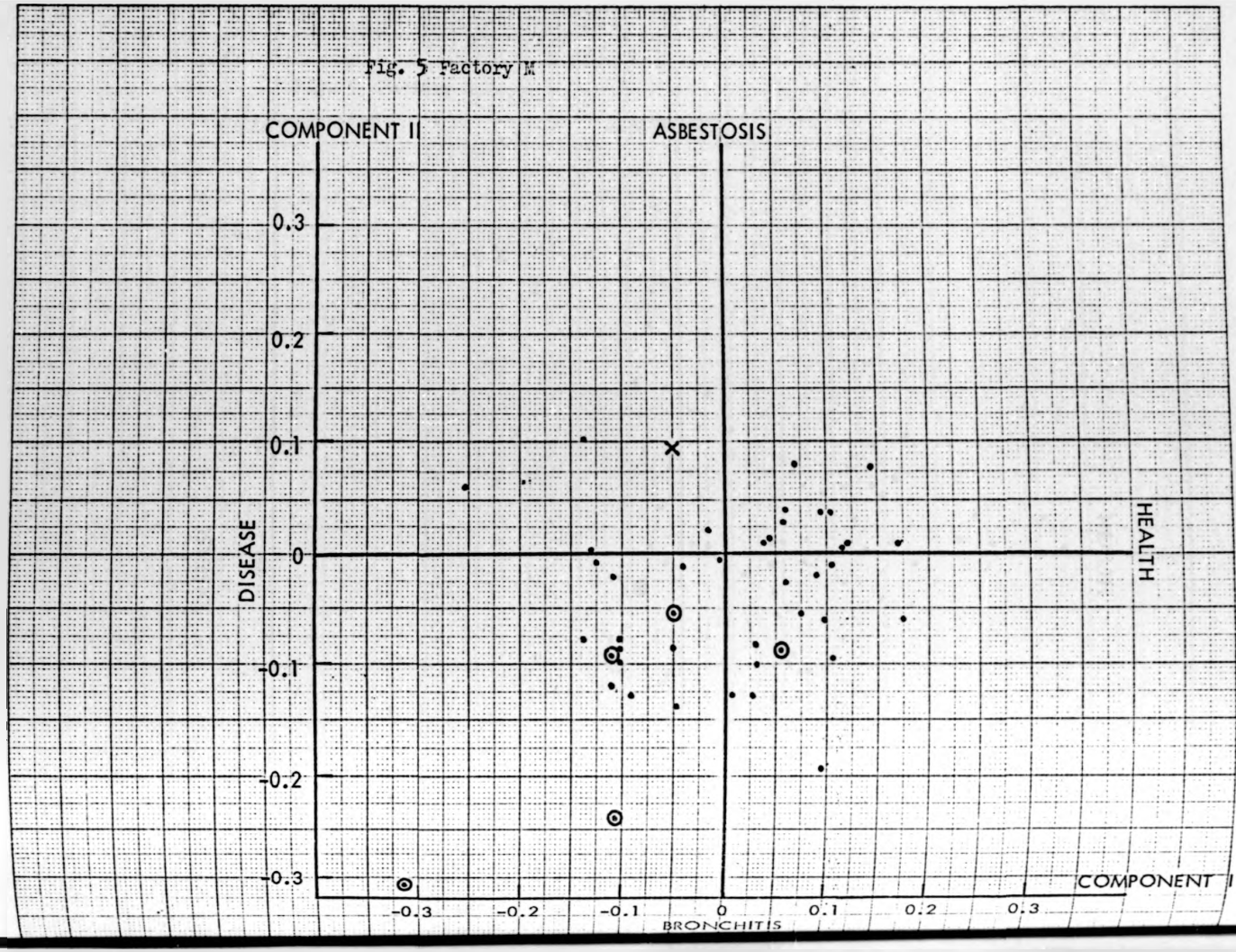


Fig. 5 Factory U

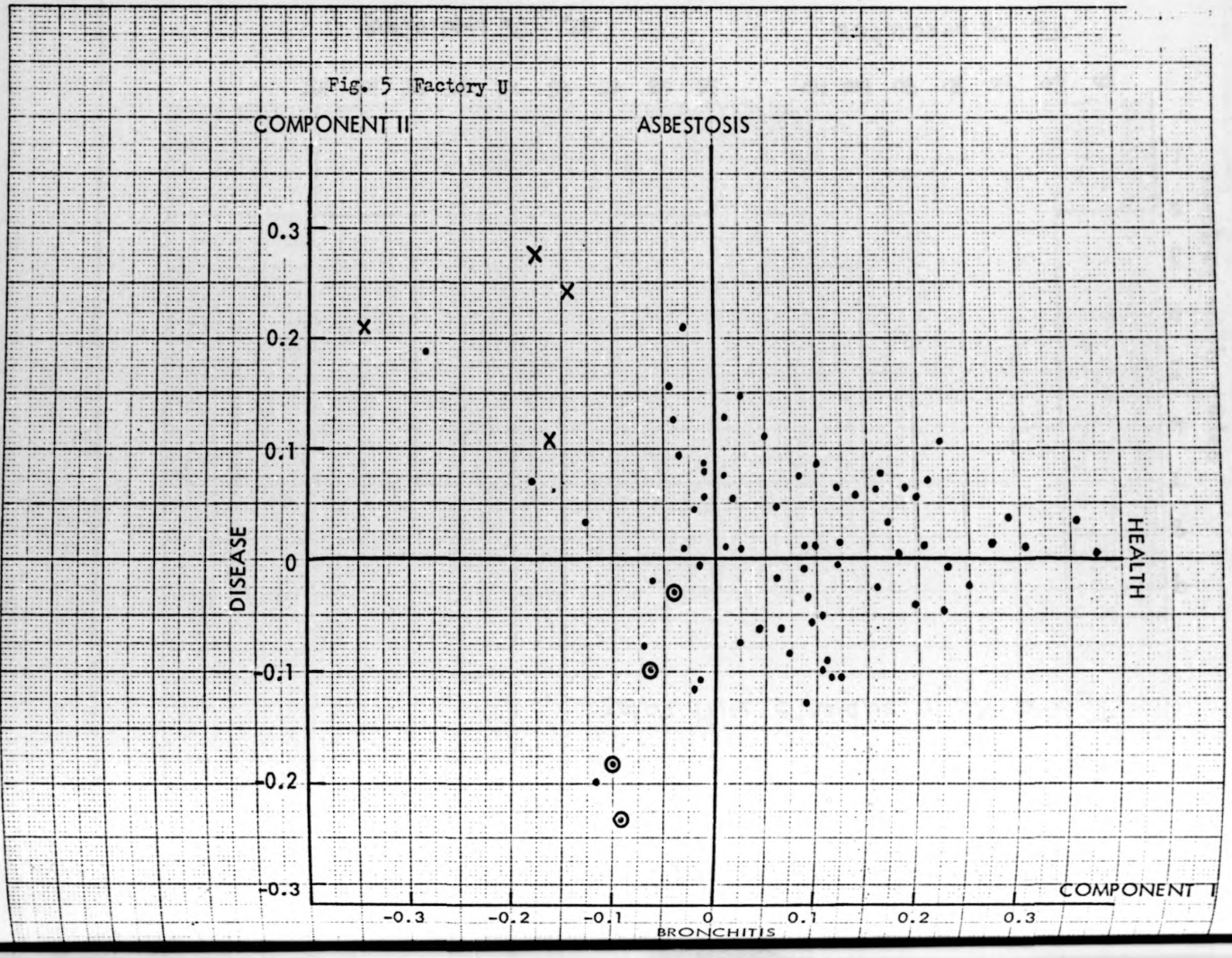
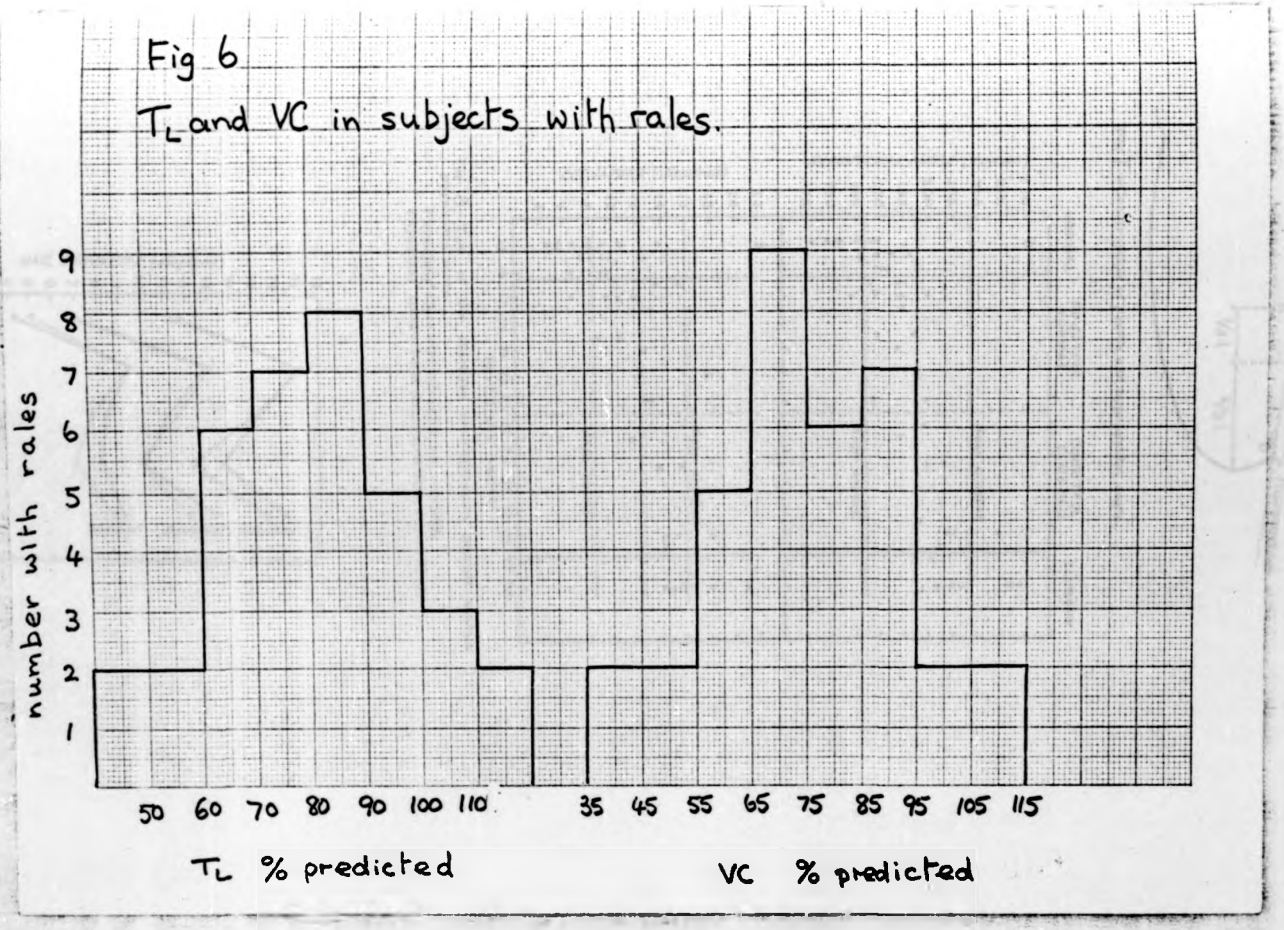


Fig 6

T_L and VC in subjects with rales.



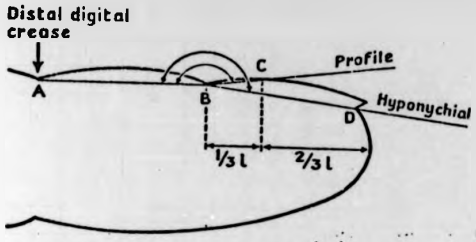


Fig. 7—Construction of profile and hyponychial angle.

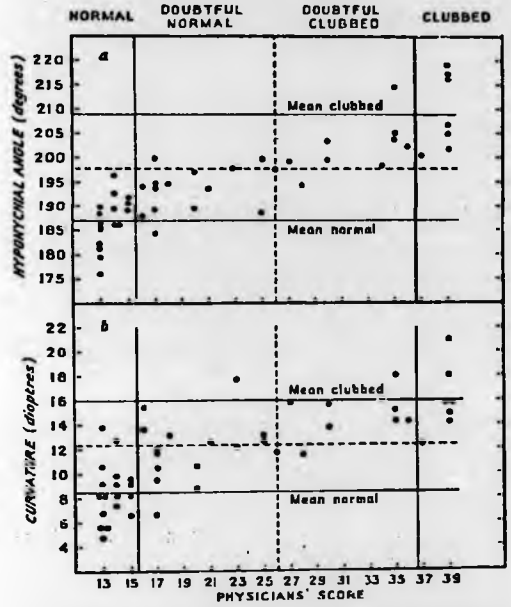


Fig. 8—Two of the objective measurements plotted against physicians' score.

Physicians' score = 0·846²−142·5; S.E. = 0·0752.
Physicians' score = 1·918 dioptres−0·786; S.E. = 0·7512.

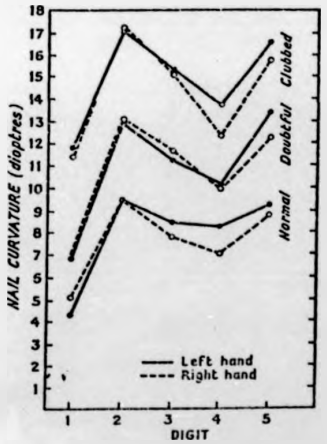


Fig. 9—Mean longitudinal curvature of normal, doubtful, and clubbed fingers.

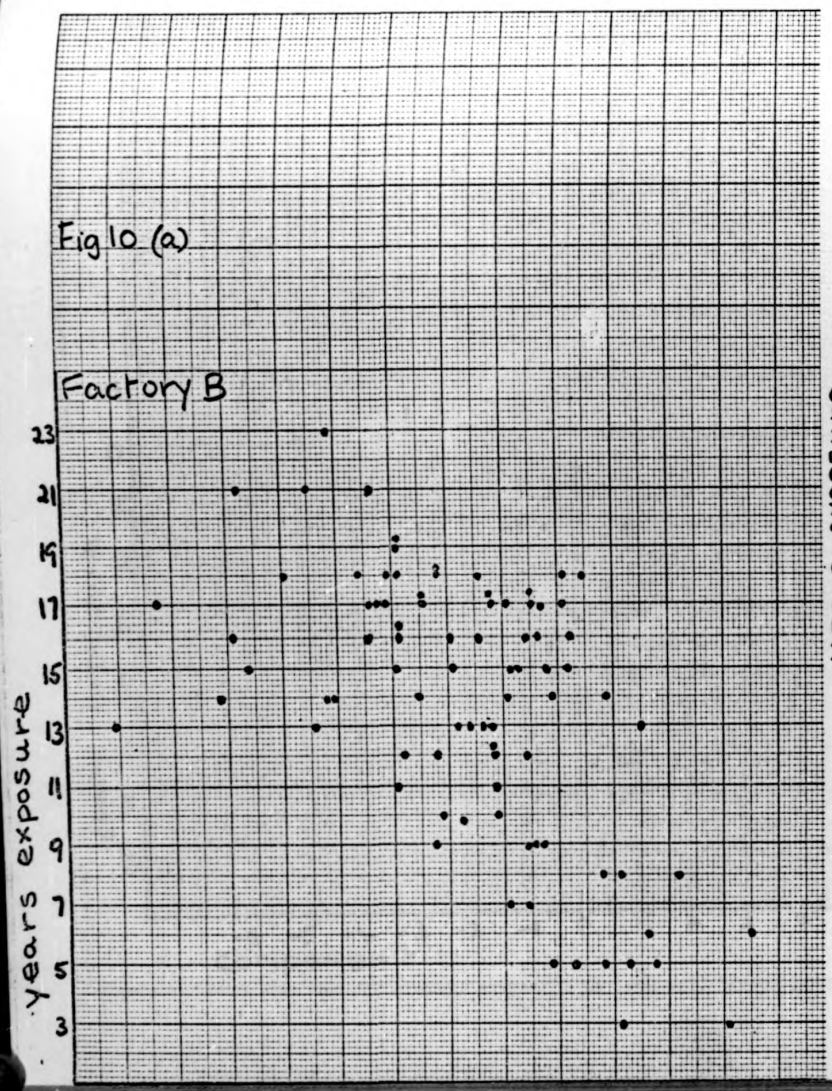


Fig 10 (a)
Factory B
years exposure
23
21
19
17
15
13
11
9
7
5
3

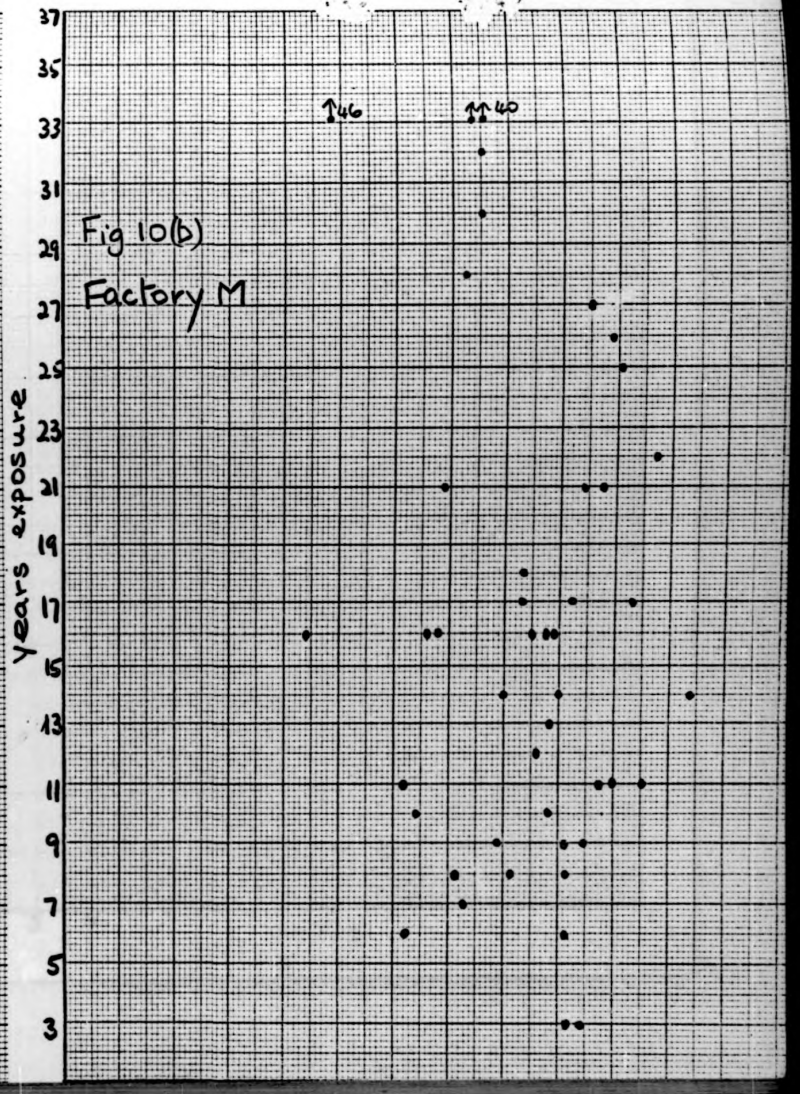


Fig 10(b)
Factory M
years exposure
37
35
33
31
29
27
25
23
21
19
17
15
13
11
9
7
5
3
M46
M40

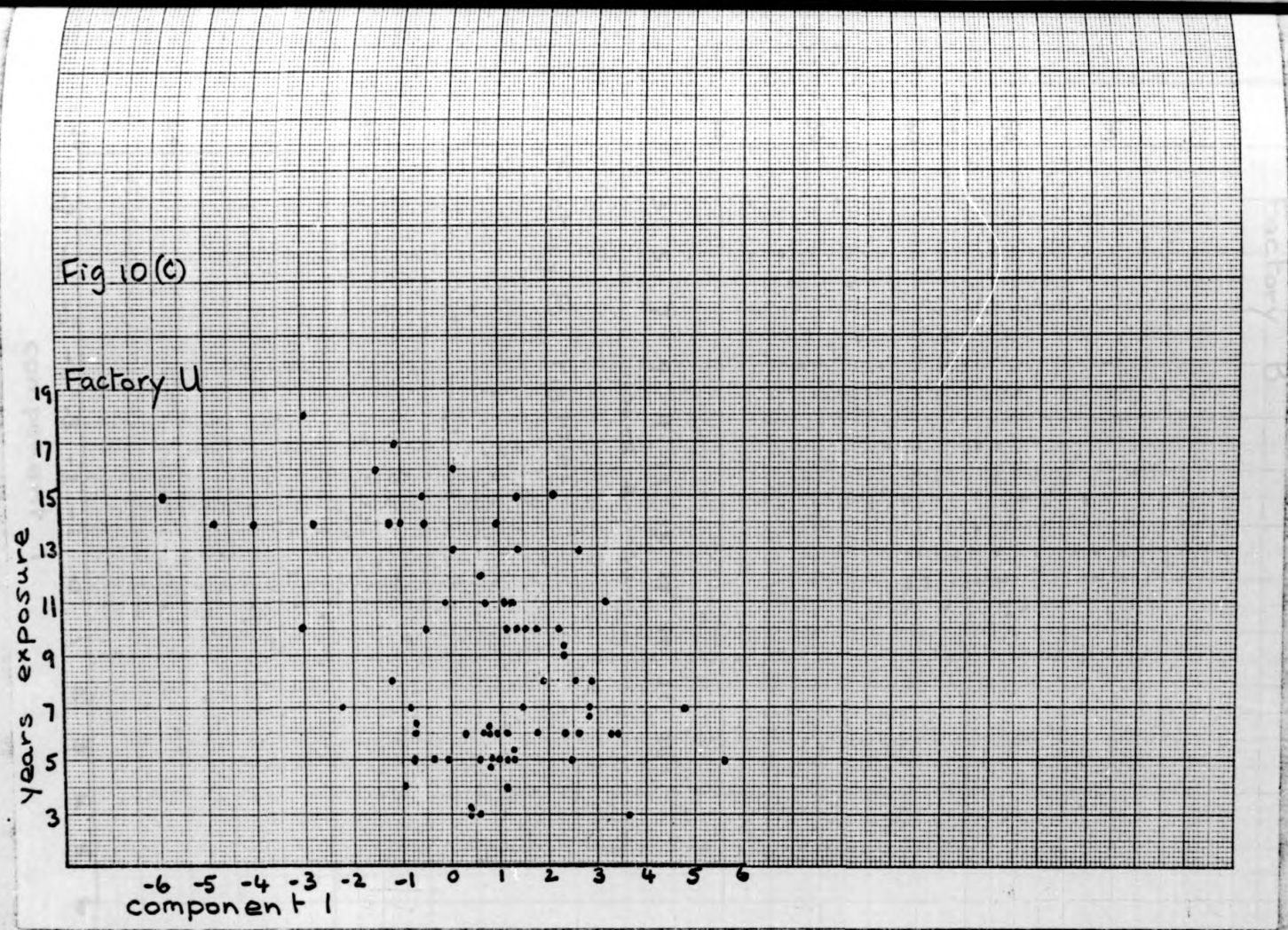
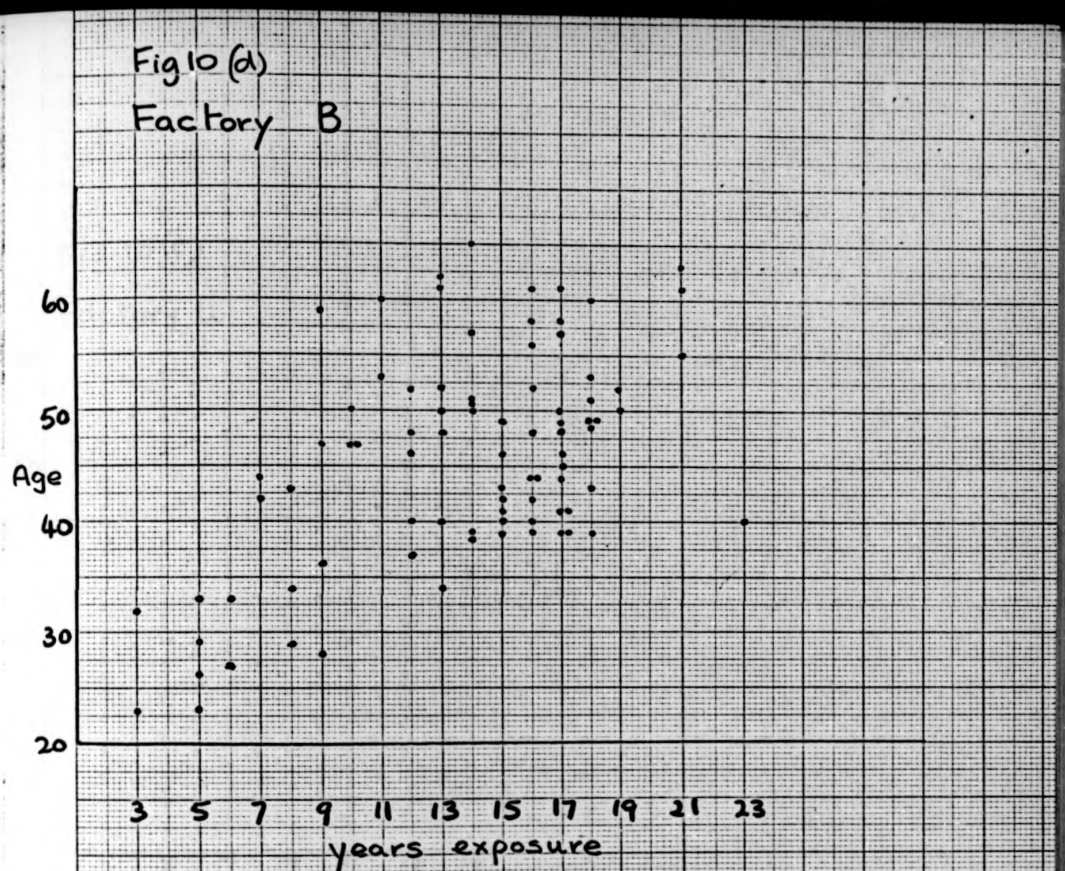


Fig 10(c)
Factory U
years exposure
19
17
15
13
11
9
7
5
3
-6 -5 -4 -3 -2 -1 0 1 2 3 4 5 6
component 1

Fig 10 (d)

Factory B



Factory B Fig 10(e)

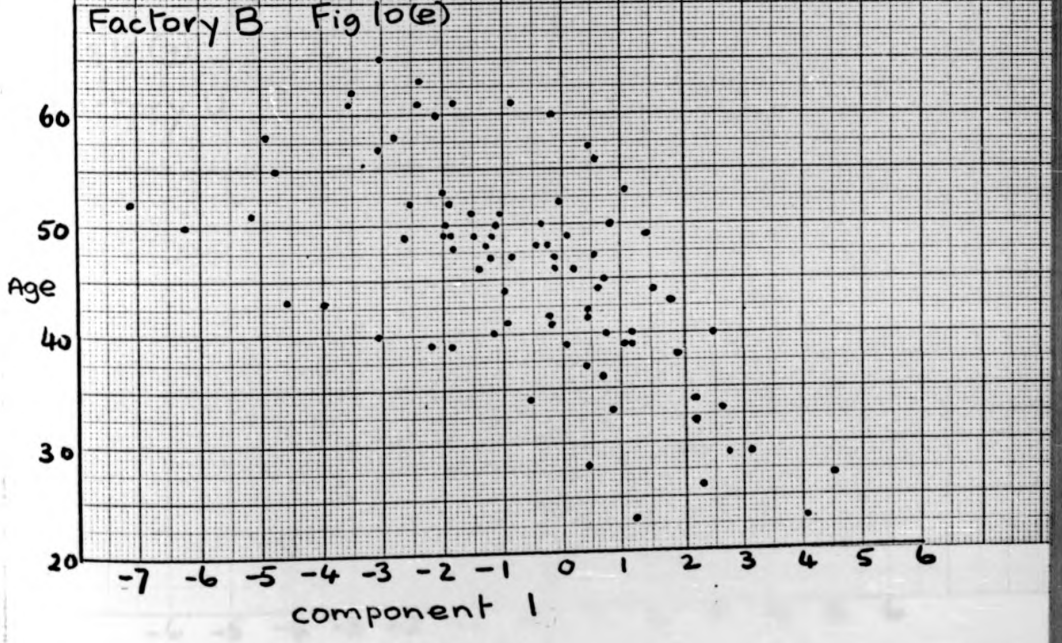


Fig. 10 (f)

Factory U

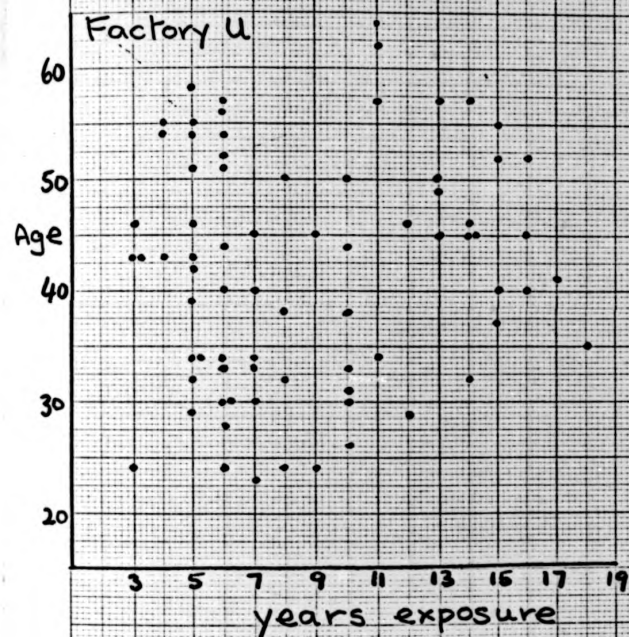
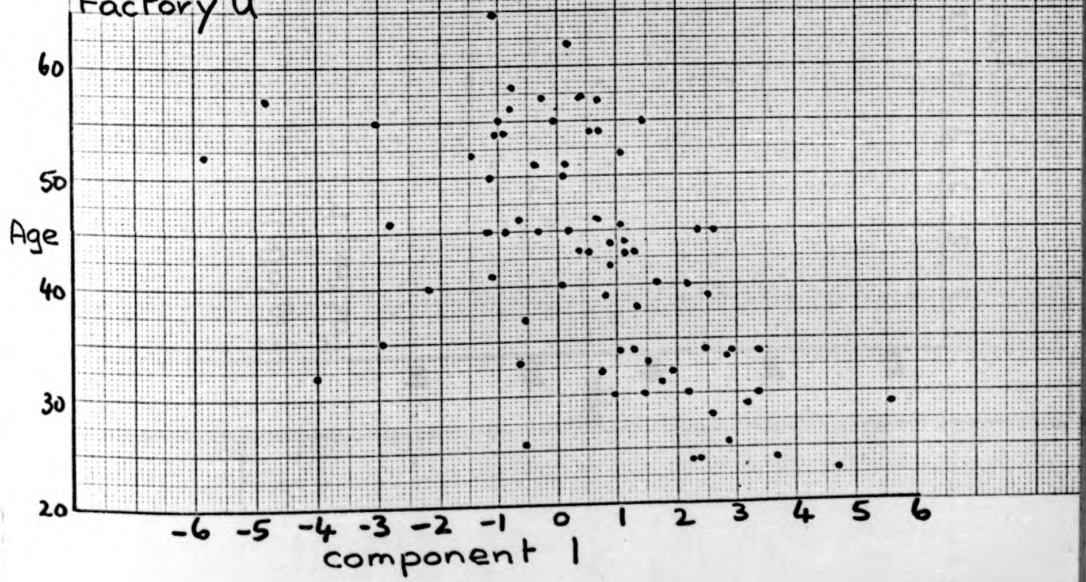


Fig 10 (g)

Factory U



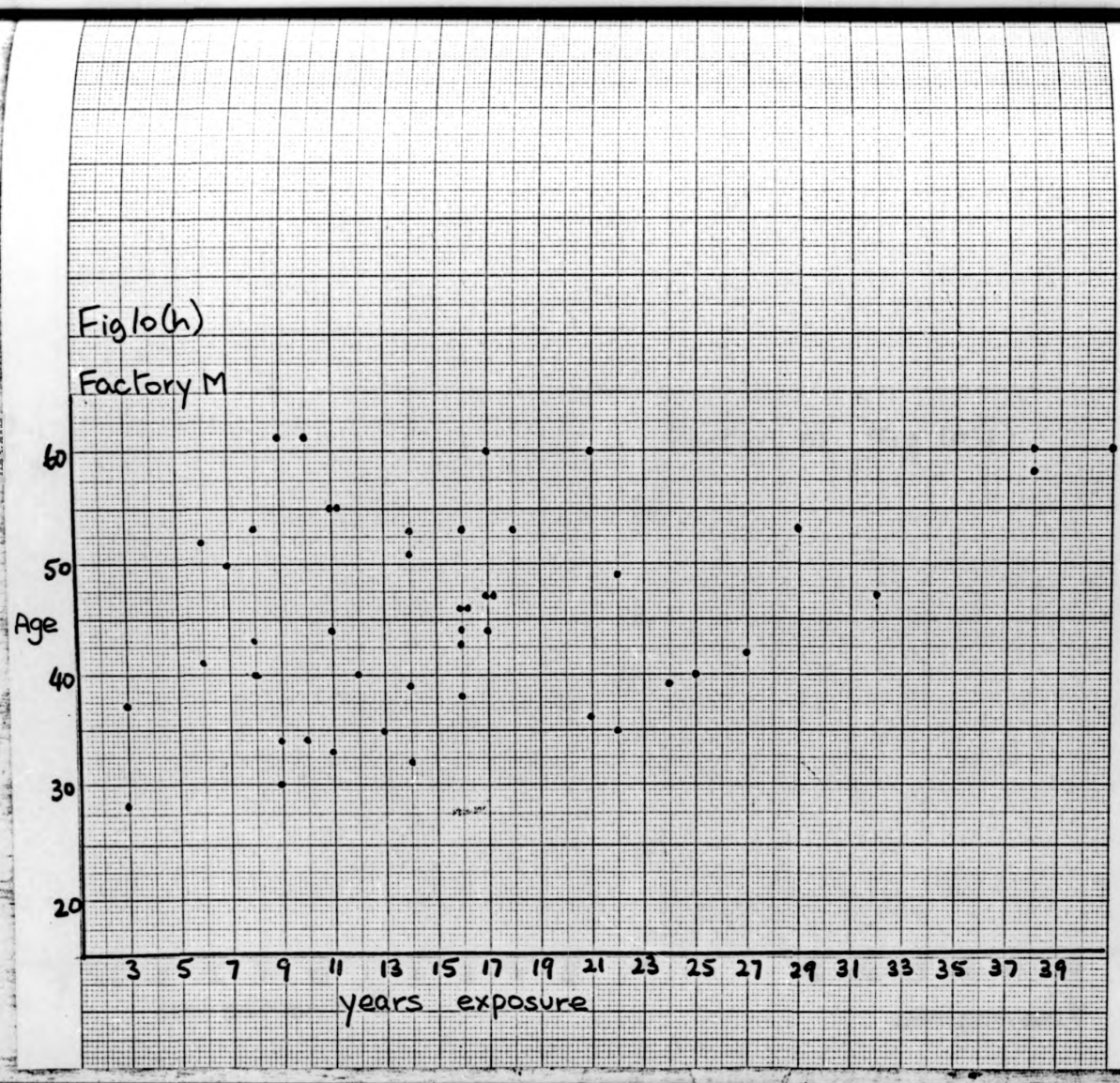


Fig 10(h)
Factory M
Age
60
50
40
30
20
3 5 7 9 11 13 15 17 19 21 23 25 27 29 31 33 35 37 39
years exposure

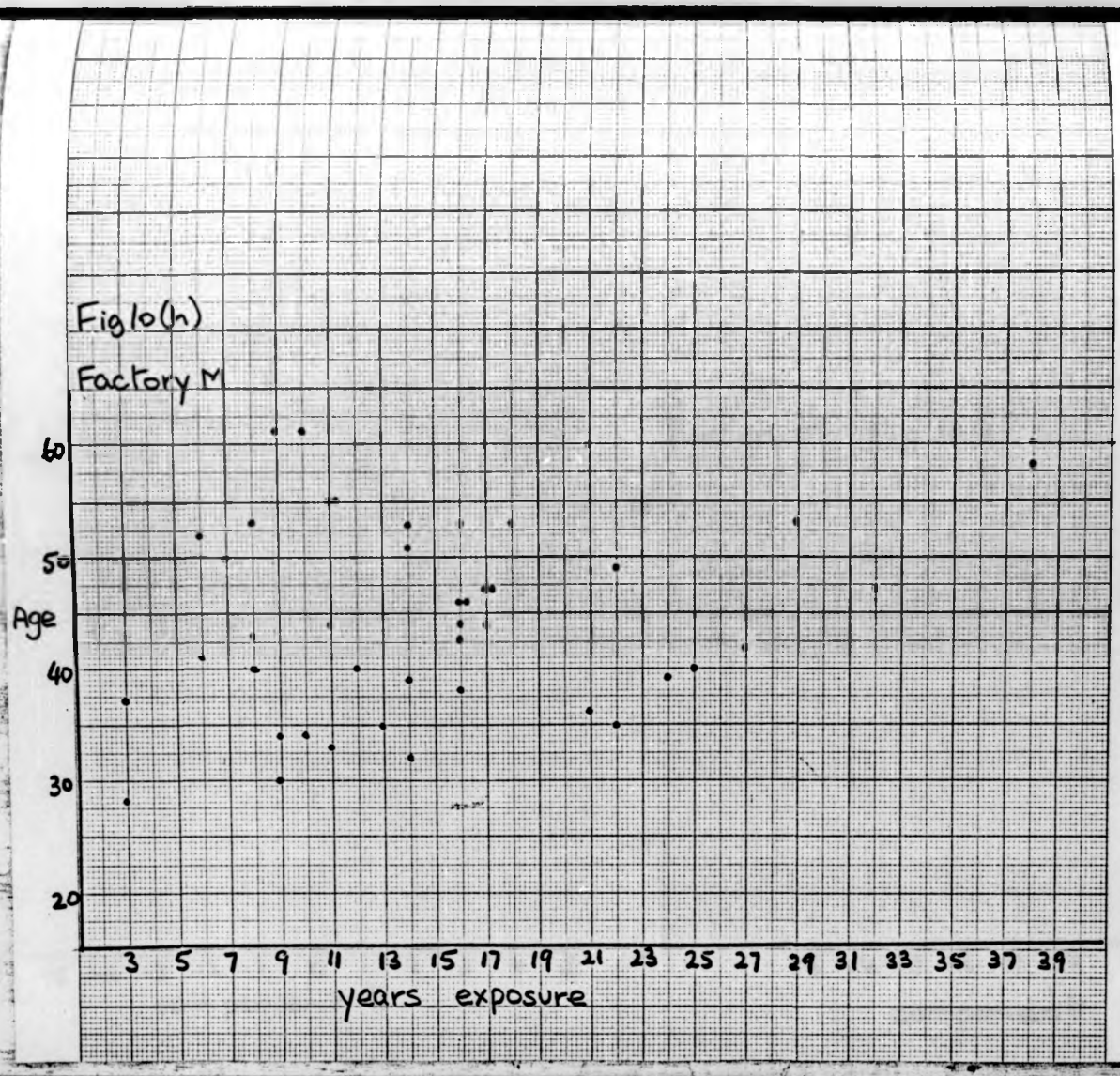
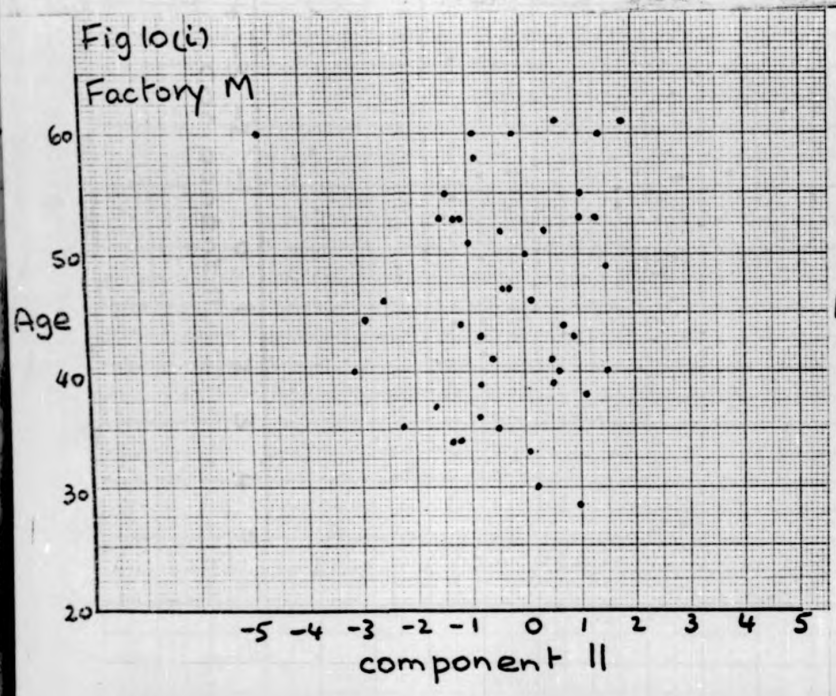
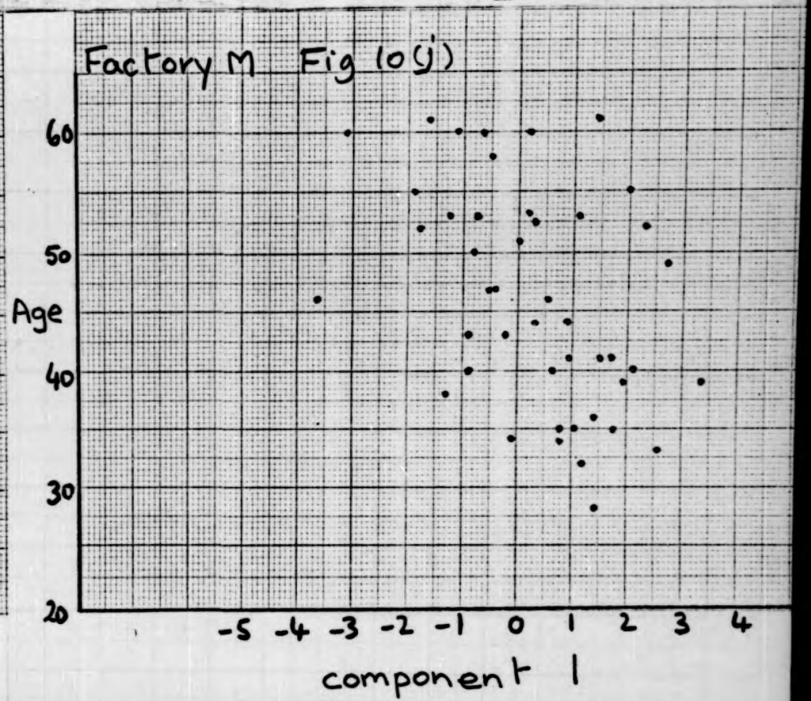


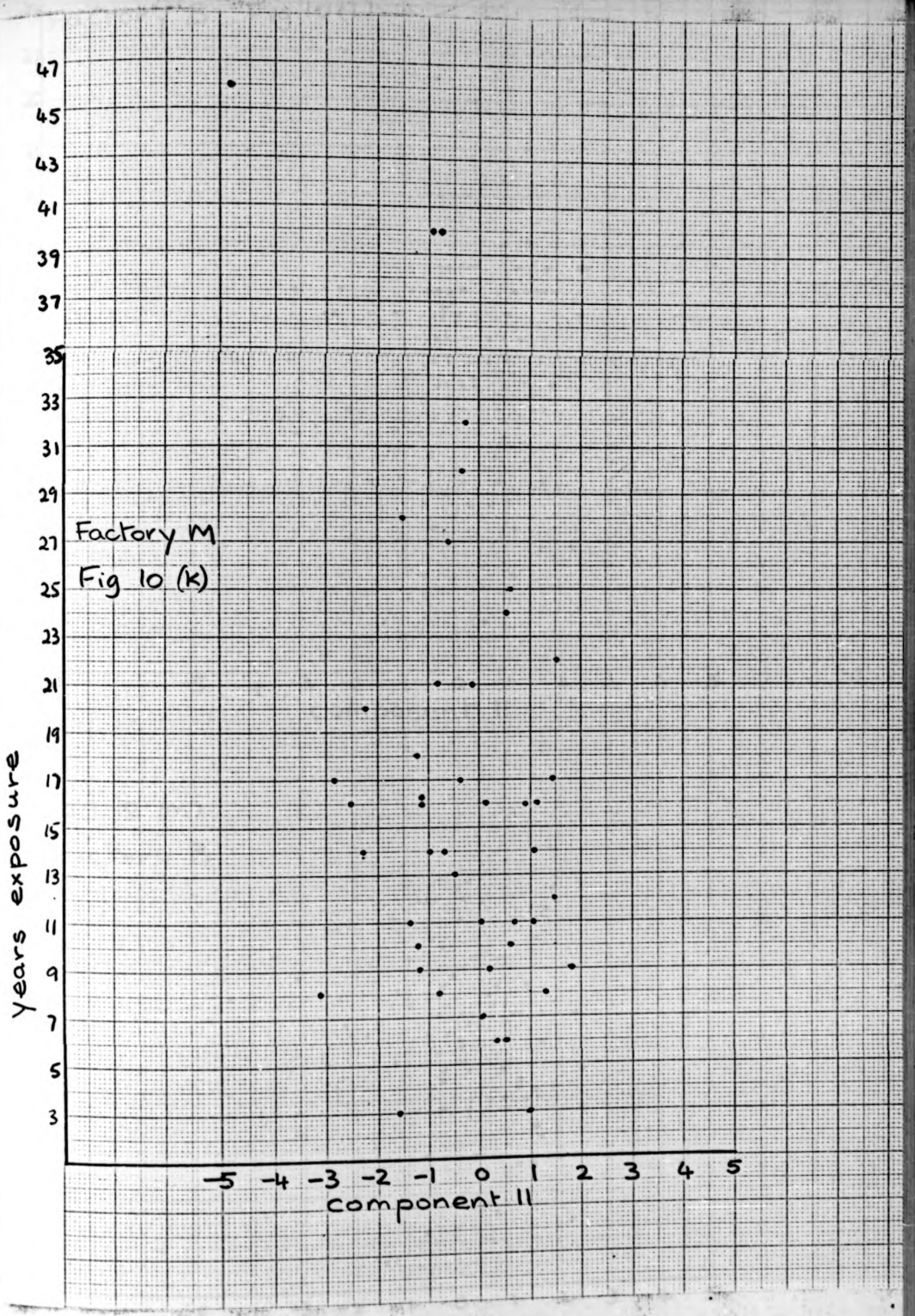
Fig 10(h)
Factory M
60
50
Age
40
30
20
3 5 7 9 11 13 15 17 19 21 23 25 27 29 31 33 35 37 39
years exposure

Fig 10(i)



Factory M Fig 10(j)




Factory M
Fig 10 (K)
years exposure
47
45
43
41
39
37
35
33
31
29
27
25
23
21
19
17
15
13
11
9
7
5
3
-5 -4 -3 -2 -1 0 1 2 3 4 5
component II

Factory B Fig 10(L)

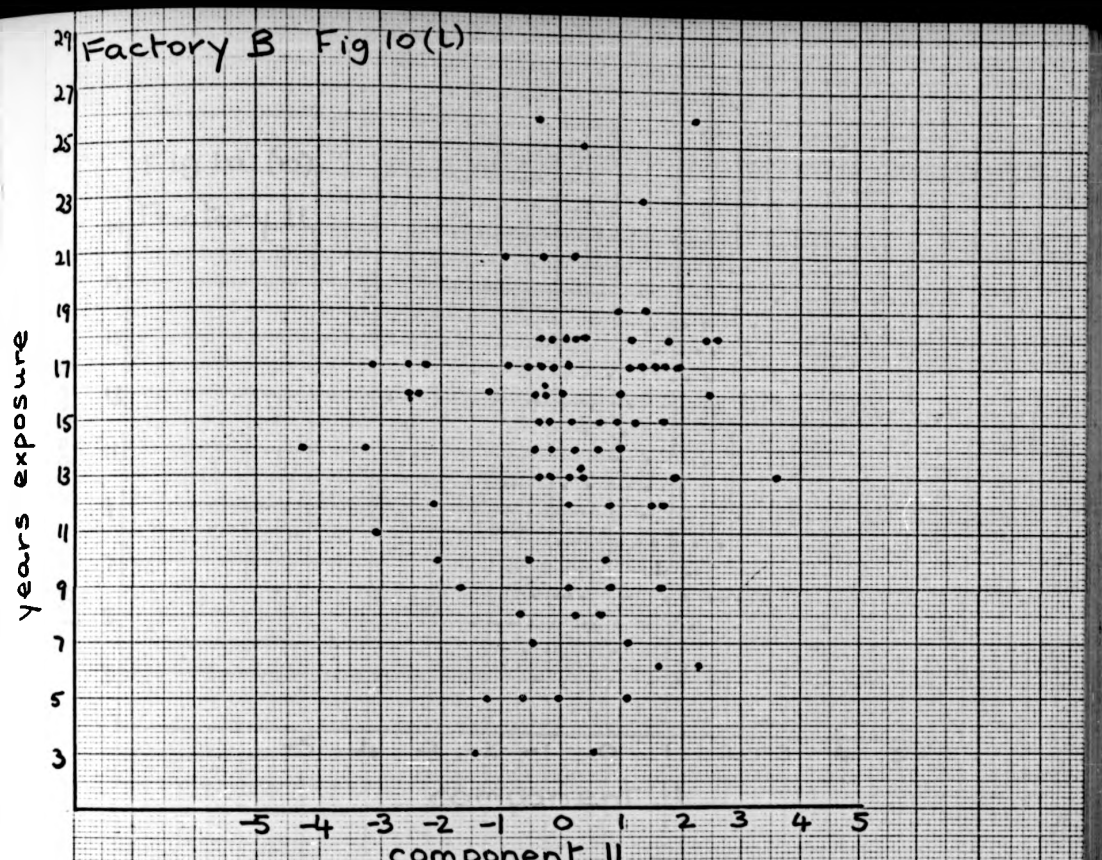


Fig 10 (m)

Factory B

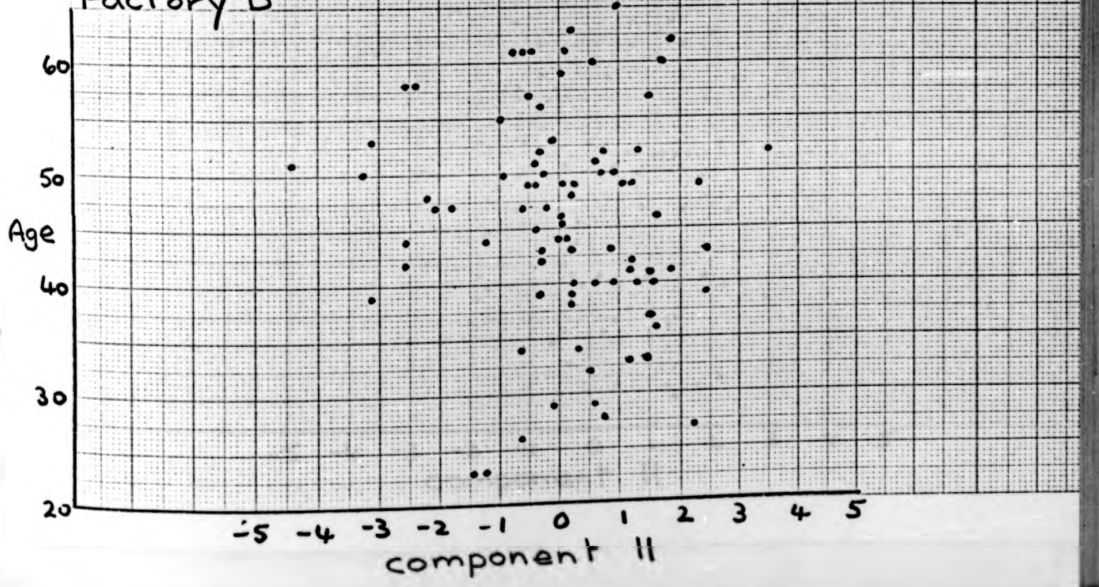


Fig 10 (n)
Factory U

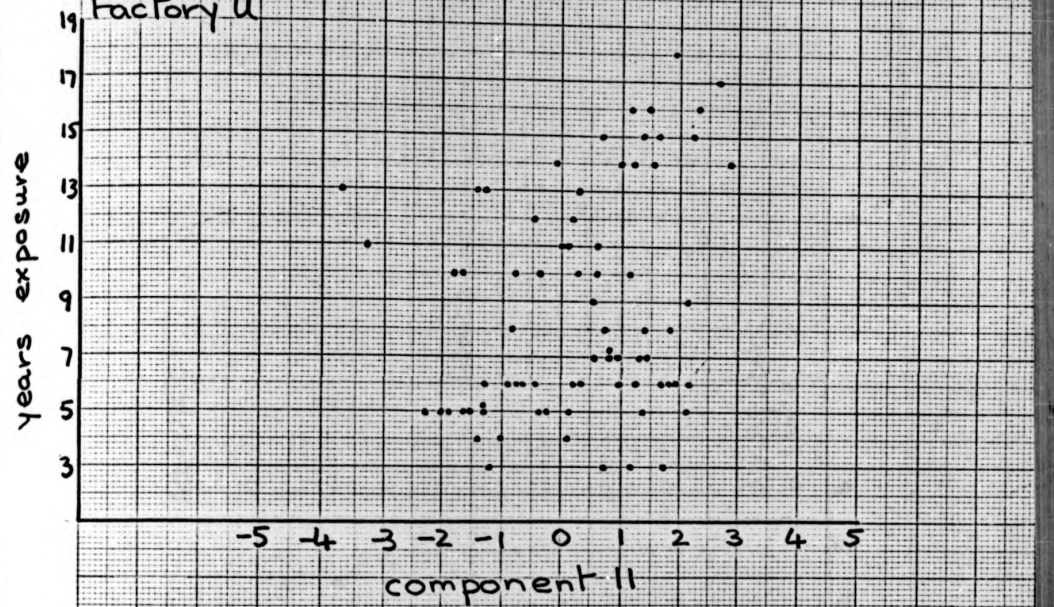


Fig 10 (o)
Factory U

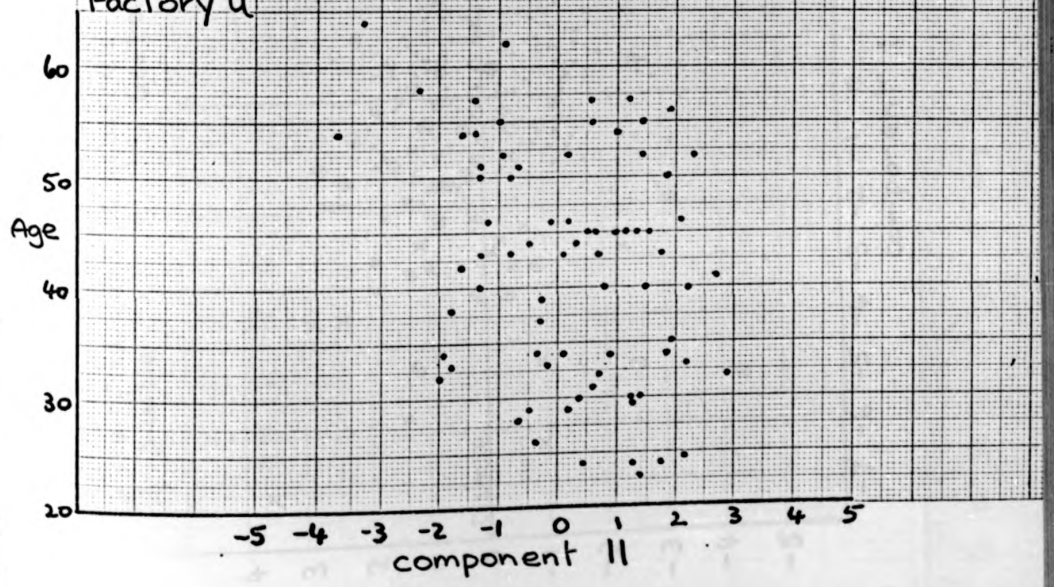


Fig. 11 (exposure excluded)

x = certified cases of asbestosis
⊙ = possible " " " (see text)

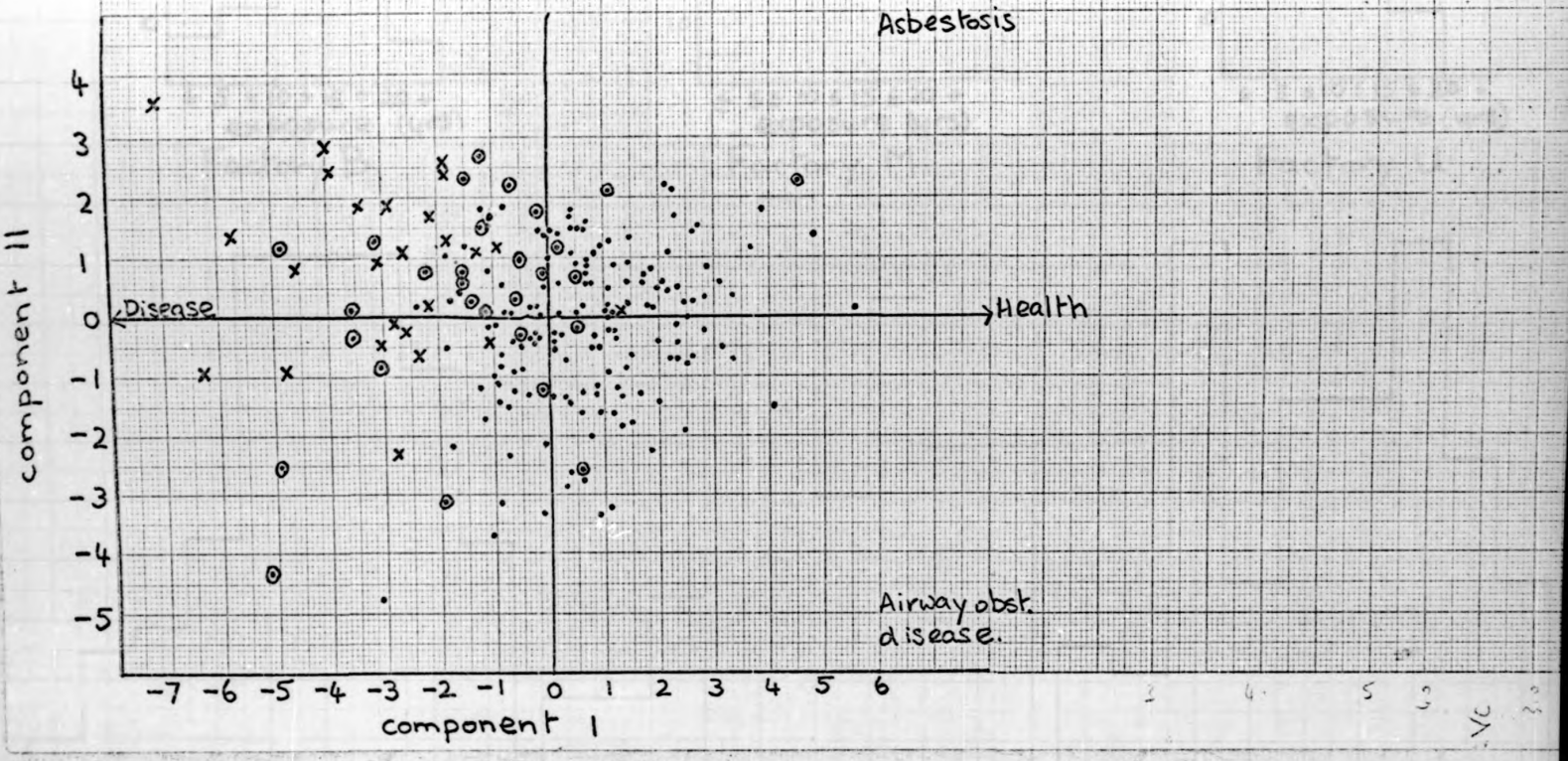
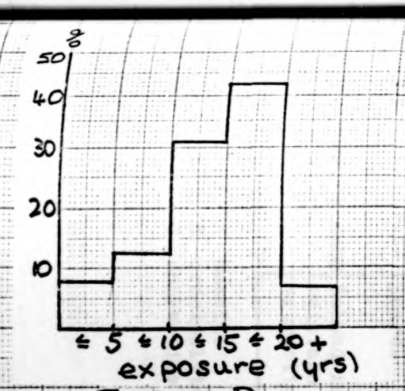
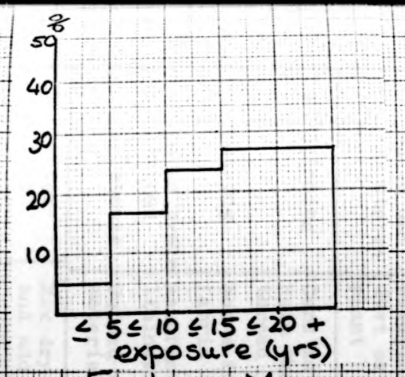


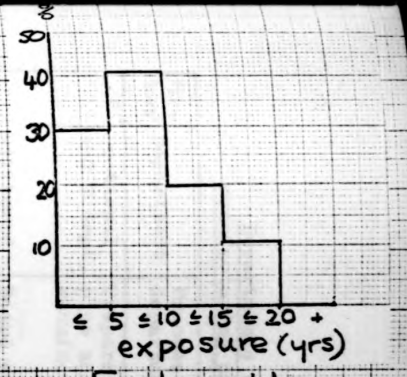
Fig 12



Factory B



Factory M



Factory U

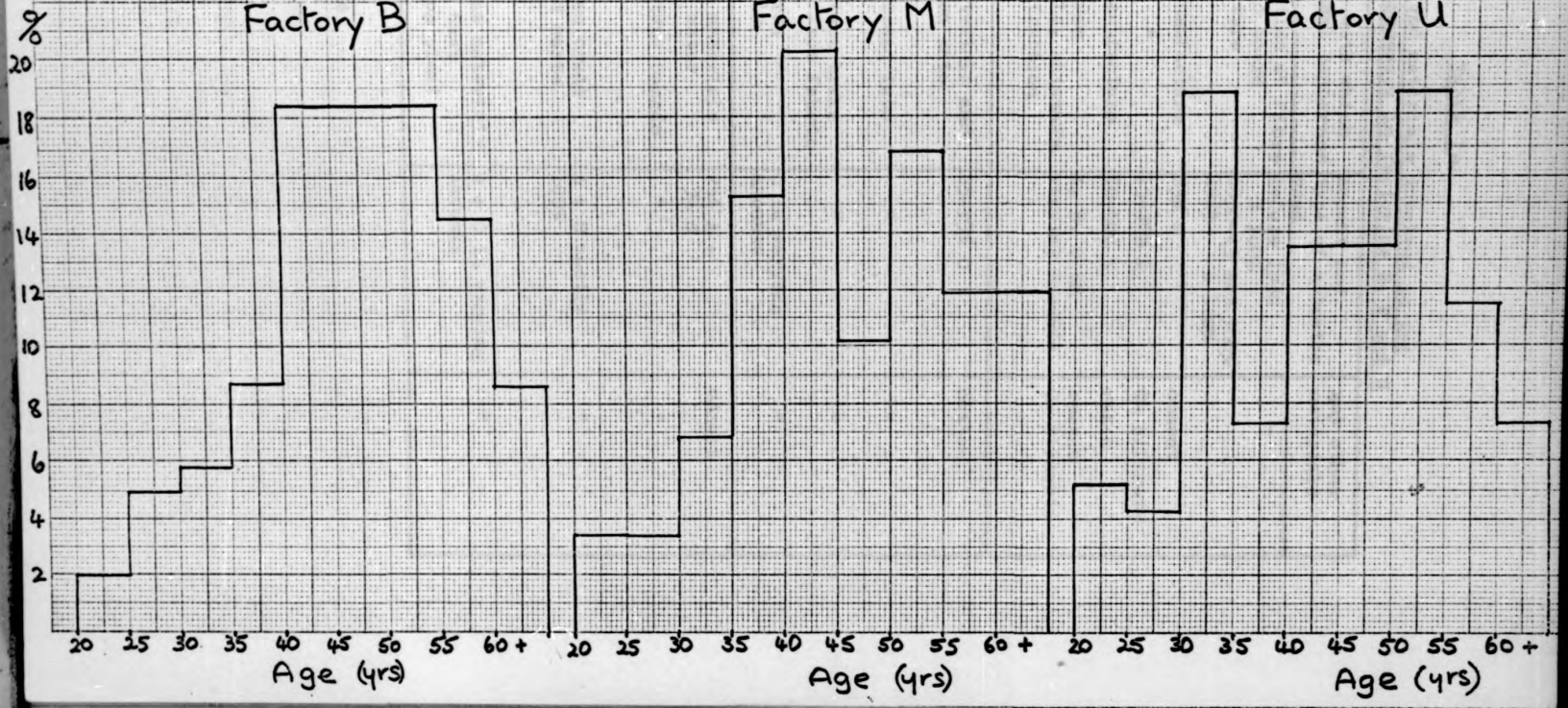
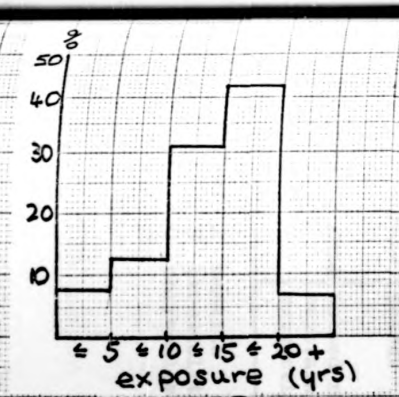
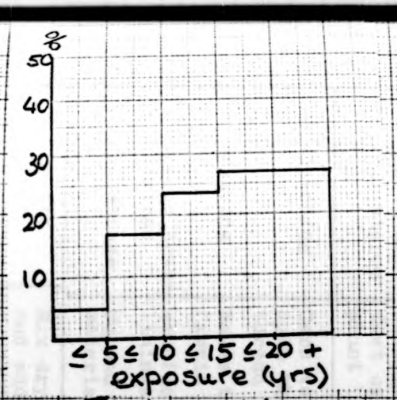


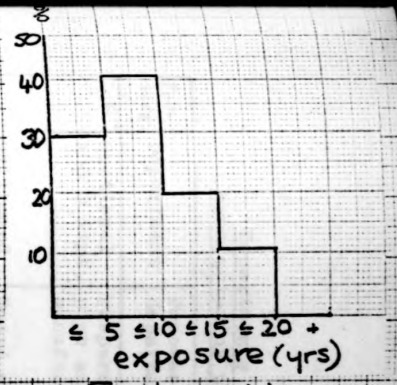
Fig 12



Factory B



Factory M



Factory U

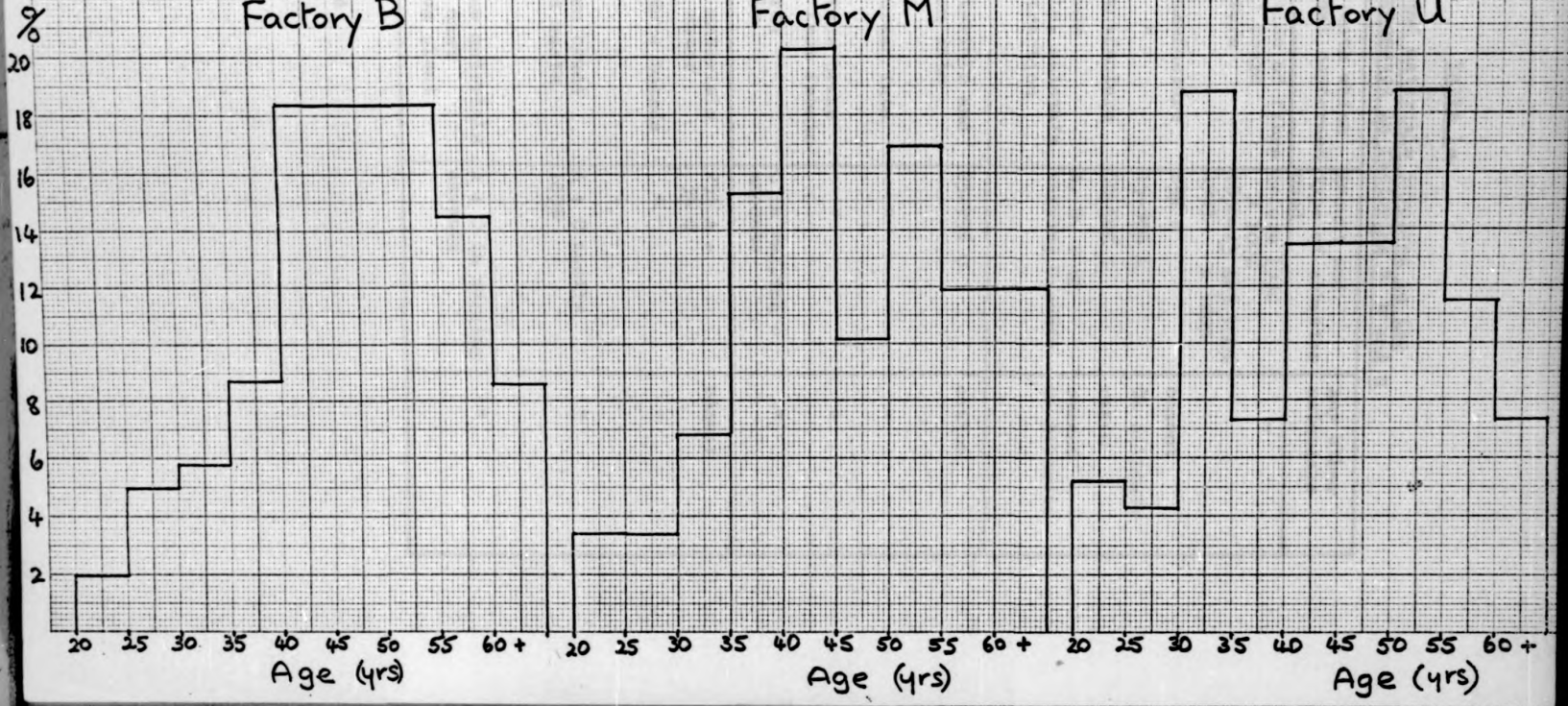


Table 1a

Departments and materials involved in the manufacturing processes in factories B, M and U

Factory	Department	Process with which department concerned	Amount and type of asbestos used	Any other materials
B	Sectional and D dept.	Preparation of fibre pipe and board manufacture	Before 1930 B 100% 1930–45 A+B 100% 1945– A 100%	-
	Millboard	Board manufacture	65% C	cement
	Ca Silicate	" "	15–30% A	Ca Silicate
	Jointing	Joint manufacture	50–60% C	resin
	Dust and waste and 'E' stores	Unload raw materials, maintain dust extraction plant	A, B, C in varying amounts	cement Ca Silicate
M	Spinning	Card materials and spin them into thread	85–95% C	cotton
	Weaving	Weave thread into fabric	"	"
	Woven brake linings	Manufacture brake linings from fabric	"	"
	Warehouse	Unload raw materials	C in varying amounts	"
U	Beaten floor	Mix dry materials and add water	25% A + 3% C	cement
	Board making and finishing	Manufacture boards	"	"
	Fiberizing and disintegrating	Break down crude fibre and waste boards	A + C mostly 100%	"
	Heavy gang	Unload raw materials maintain dust extraction plant	A + C in varying amounts	"

Key: A amosite
B crocidolite
C chrysotile

Table 1 (b)

Results of 258 workers summarised

Age (years)	45.5		
Height (cm)	169.6		
Years since first exposure	11.8		
Non-smokers	21/258	8%	
Ex-Smokers	39/258	15%	
Smokers	198/258	77%	
Rales +	35/246	14.2%	
Rhonchi +	26/246	10.6%	
Cough +	130/246	52.8%	
Phlegm+	104/246	42.3%	
Dypsnoea +	85/246	34.6%	
Clubbing	188.0°		
Asbestos bodies+	98/156	62.8%	(of those who produced sputum)
Asbestos fibres+	46/156	29.5%	"
Abnormal ECG+	47/ 254	18%	
Pleural thickening (XT)	33/251	13.2%	
Parenchymal abnormality (XT)	26/251	10.4%	
Both together (XPT)	34/251	13.6%	

Pulmonary function

VC	4.16
IC	2.75
RV	2.39
TLC	6.4
RV/TLC%	36.9
$FEV_1/FVC\%$	70.2
PF	46 3
TL_{CO} ml/min per mm Hg	24.2
K_{CO} min^{-1}	3.5
Dm ml/min per mm Hg	53.7
Vc ml	53.2

Table 2

Population studied

Factory	B	M	U	Total
Number studied	103	59	96	258
Number at risk	125	64	102	291
% studied	83	92	94	89

Table 3

Certified cases of asbestosis in factories B, M and U

Factory	B	M	U
Number studied	21	1	4
Number refused	2	0	1
Total in defined pop.	23	1	5
% of defined pop.	18.4	1.5	4.9
Total within factory	36	1	5

Table 4

Number of workers in each factory with missing information

(The figures in brackets in the final column are the number of workers in each factory with one or more tests missing)

Factory	Rales and Rhonchi	ECG	Clubbing	Xray	Resp. Quest.	FEV	RV	DM and Vc	Total No. of missing tests
B	6	2	3	0	0	2	0	9	21 (16)
M	1	1	2	6	3	2	2	5	22 (13)
U	5	1	2	2	0	1	0	14	25 (21)
Total No. of missing tests	12	4	7	8	3	5	2	28	68 (50)

Table 5

Reasons for Missing Information

Rales and Rhonchi and Xray	Workers absent from the factory at the time of the examination which was carried out at a later date to the other tests
ECG	4 Workers refused this examination
Clubbing	Nails bitten too low to permit measurement
Respiratory Questionnaire	1 Questionnaire lost and 2 not completed
FEV	Apparatus failed and workers unable to return at a later date
RV	1 Worker refused this test and 1 too nervous to co-operate
Dm-Vc	1 Worker too nervous to co-operate, 2 deaf and dumb workers also unable to co-operate successfully. 1 Worker not tested as ran out of gas mixture and he was unable to return at a later date. Results of tests on 23 workers discarded because of unreliability. 18 of these workers had severe obstruction but in remaining 5 no reason was found for poor results.

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Table 6

Physical characteristics and length of exposure to asbestos in factories B, M and U

Mean	Factory		
	B	M	U
Age (years)	46.9	46.0	43.7
Height (cm)	169.6	167.8	170.6
Exposure (years)	14	16	7

Table 7

Mean age within exposure groups in factories B, M and U

Exposure	Factory B			Factory M			Factory U		
Years since first exposed	No. in sub group	%	Mean age	No. in sub group	%	Mean age	No. in sub group	%	Mean age
0-5	8	7.8	34.2	3	5.1	26	28	29.2	46.7
6-10	13	12.6	40.5	10	16.9	44.2	39	40.6	41.1
11-15	30	29.1	48	14	23.8	44.7	19	19.8	45.2
16-20	45	43.7	48.8	16	27.1	47.8	10	10.4	43.8
20+	7	6.8	54	16	27.1	48.6			

Table 8

Comparison of the smoking habits in factories B, M and U

	Factory B		Factory M		Factory U		χ^2
	No.	%	No.	%	No.	%	
Non smokers	5	4.9	4	6.8	12	12.5	4.07
Ex smokers	16	15.5	9	15.3	14	14.7	0.04
Smokers	82	79.6	46	77.9	70	72.9	1.31

Table 9

Comparison of the degree of smoking in factories B, M and U

		Smokers Grade I	Smokers Grade II	Smokers Grade III
Factory B	No.	59	13	10
	%	71.9	15.9	12.2
Factory M	No.	13	18	15
	%	28.3	39.1	32.6
Factory U	No.	38	22	10
	%	54.3	31.4	14.3
Overall	χ^2	22.85	9.35	9.49
	P	<0.001	<0.01	<0.01
B v M	χ^2	20.46	9.94	5.47
	P	<0.001	<0.005	<0.05
B v U	χ^2	6.85	5.48	0.05
	P	<0.01	<0.025	
M v U	χ^2	4.86	0.74	4.59
	P	<0.05		<0.05

Table 10

Symptoms and signs of chest disease comparison between B. M and U

Test	Factory	No.	%	Overall comparison χ^2	Comparison between factories B v M χ^2	B v U χ^2	M v U χ^2
Rales	B	23/97	24				
	M	2/58	3	13.35	9.57	4.41	1.79
	U	10/91	11	<0.005	<0.005	<0.05	NS
Rhonchi	B	10/97	10				
	M	7/58	12	0.19			
	U	9/91	10	NS			
Cough	B	52/103	50				
	M	36/57	63	5.39			
	U	42/96	44	NS			
Phlegm	B	42/103	41				
	M	28/57	49	2.79			
	U	34/96	35	NS			
Dyspnoea	B	42/103	41				
	M	16/57	28	5.56			
	U	27/96	28	NS			

Table 11

Comparison of different grades of cough, phlegm and dyspnoea in B, M and U

Test	Factory	Incidence of abnormality No.	%	Overall comparison χ^2	Comparison between factories B v M χ^2	B v U χ^2	M v U χ^2
Cough Grade I	B	31	59.6	6.694	4.918	0.001	4.124
	M	28	77.8	<0.05	<0.05		<0.05
	U	30	71.4				
Grade 2	B	21	40.4				
	M	8	22.2	2.512			
	U	12	28.6				
Phlegm Grade I	B	23	54.8				
	M	17	60.6	1.212			
	U	26	76.5				
Grade 2	B	19	45.2				
	M	11	39.4	5.171			
	U	8	23.5				
Dyspnoea Grade 2	B	30	71.5				
	M	12	75.0	1.907			
	U	21	77.8				
Grade 3	B	8	19.0				
	M	2	12.5	2.592			
	U	3	11.1				
Grade 4	B	3	7.1				
	M	1	6.25	0.916			
	U	1	3.7				
Grade 5	B	1	2.4				
	M	1	6.25	0.410			
	U	2	7.4				

Table 12a

Workers with cough subdivided by age, exposure and smoking habits

	Factory B		Factory M		Factory U	
	No. with cough	Total in sub. gp.	No. with cough	Total in sub. gp.	No. with cough	Total in sub. gp.
Age 21-40 yrs						
Exposure 3-10 years						
Smoking +	5	10	5	7	10	22
Smoking -	0	2	0	0	0	6
Exposure 10+ years						
Smoking +	5	15	9	13	3	8
Smoking -	0	0	0	0	0	2
Age 40+ yrs						
Exposure 3-10 years						
Smoking +	4	8	2	3	24	36
Smoking -	0	1	0	2	2	4
Exposure 10+ years						
Smoking+	38	65	20	28	6	19
Smoking -	0	2	0	2	0	0

Comparison of factories		
	N.D.	P
B v M	-2.239	<0.05
B v U	0.890	
M v U	2.718	<0.01

Table 12b

Workers with phlegm subdivided by age, exposure and smoking habits

	Factory B		Factory M		Factory U	
	No. with phlegm	Total in sub.gp.	No. with phlegm	Total in sub. gp.	No. with phlegm	Total in sub. gp.
Age 21-40 yrs						
Exposure 3-10 yrs						
Smoking +	4	10	4	7	8	22
Smoking -	0	2	0	0	2	6
Exposure 10 + yrs						
Smoking +	5	15	6	13	4	8
Smoking -	0	0	0	0	0	2
Age 40+ yrs						
Exposure 3-10 yrs						
Smoking +	3	8	1	3	15	36
Smoking -	0	1	0	2	1	4
Exposure 10 + yrs						
Smoking +	30	65	17	28	5	19
Smoking -	0	2	0	2	0	0

Comparison of factories		
	N.D.	P
B v M	-1.53	NS
B v U	0.456	NS
M v U	1.704	NS

Table 12c

Workers with dyspnoea subdivided by age, exposure and smoking habits

	Factory B		Factory M		Factory U	
	No. with dyspnoea	Total in sub. gp.	No. with dyspnoea	Total in sub. gp.	No. with dyspnoea	Total in sub. gp.
Age 21-40 yrs. Exposure 3-10 yrs						
Smoking +	2	10	2	7	5	22
Smoking -	0	2	0	0	0	6
Exposure 10 + yrs						
Smoking +	5	15	2	13	2	8
Smoking -	0	0	0	0	0	2
Age 40 + yrs Exposure 3-10 yrs						
Smoking +	4	8	1	3	9	36
Smoking -	0	1	0	2	2	4
Exposure 10 + yrs						
Smoking +	31	65	11	28	7	19
Smoking -	0	2	0	2	0	0

Comparison of factories	N.D.	P
B v M	1.066	NS
B v U	1.125	NS
M v U	-0.142	NS

Table 13

Comparison of the hyponychial angle in factories B, M and U

(adjusted for height)

Factory	Mean ∠	Adjusted mean ∠	S.E. of adjusted mean ∠	F	Probability
B	189.1	189.1	0.8061	2.37	NS
M	186.3	186.1	1.1310		
U	188.0	188.1	0.8755		

Table 12c

Workers with dyspnoea subdivided by age, exposure and smoking habits

	Factory B		Factory M		Factory U	
	No. with dyspnoea	Total in sub. gp.	No. with dyspnoea	Total in sub. gp.	No. with dyspnoea	Total in sub. gp.
Age 21-40 yrs. Exposure 3-10 yrs						
Smoking +	2	10	2	7	5	22
Smoking -	0	2	0	0	0	6
Exposure 10 + yrs						
Smoking +	5	15	2	13	2	8
Smoking -	0	0	0	0	0	2
Age 40 + yrs Exposure 3-10 yrs						
Smoking +	4	8	1	3	9	36
Smoking -	0	1	0	2	2	4
Exposure 10 + yrs						
Smoking +	31	65	11	28	7	19
Smoking -	0	2	0	2	0	0

Comparison of factories	N.D.	P
B v M	1.066	NS
B v U	1.125	NS
M v U	-0.142	NS

Table 13

Comparison of the hyponychial angle in factories B, M and U

(adjusted for height)

Factory	Mean ∠	Adjusted mean ∠	S.E. of adjusted mean ∠	F	Probability
B	189.1	189.1	0.8061	2.37	NS
M	186.3	186.1	1.1310		
U	188.0	188.1	0.8755		

Table 14

Prevalence of sputum and asbestos bodies and fibres in factories B, M and U

Factory	No. in group	Specimens produced No.	%	Specimens +ve for asbestos fibres No.	%	Specimens +ve for asbestos bodies No.	%
B	103	66	64.2	48	72.7	25	37.9
M	59	46	78	15	32.6	8	17.4
U	96	44	45.8	35	79.5	13	29.5

Comparison of the incidence of asbestos bodies and fibres

	Overall comparison		B v M χ^2	B v M P	B v U χ^2	B v U P	U v M χ^2	U v M P
Asbestos bodies	5.47	<0.01	4.53	<0.05	0.48		1.24	
Asbestos fibres	26.02	0.001	16.14	0.001	0.35		18.21	0.001

Table 15

Incidence of abnormal ECG recordings in the three factories

Factory	No.	%
B	18	17
M	11	19
U	18	19

Table 16

Radiological findings

(population grouped by length of exposure)

Exposure in years	Xray findings	Factory B			Factory M			Factory U		
		X	Y	Z	X	Y	Z	X	Y	Z
0-5	XP	0	8	0	0	2	0	2	28	7.1
	XT	0		0	0		0	1		3.6
	XPT	0		0	0		0	3		10.7
6-10	XP	2	13	15.4	3	10	30	2	37	5.4
	XT	1		7.7	2		20	4		10.8
	XPT	0		0	0		0	2		5.4
11-15	XP	2	31	6.5	2	12	16.7	1	19	5.3
	XT	8		25.4	0		0	2		10.5
	XPT	6		19.3	1		8.4	5		26.2
16-20	XP	7	44	15.9	2	15	13.3	0	10	0
	XT	9		20.4	1		6.7	1		10
	XPT	9		20.4	0		0	4		40
20 +	XP	0	7	0	3	15	20	-	-	
	XT	2		28.6	2		13.3	-	-	
	XPT	4		57.2	0	15	0	-	-	
Total Population										
	XP	11	103	9.7	10	54	18.5	5	94	5.3
	XT	20		19.4	5		9.4	8		8.5
	XPT	19		18.4	1		1.9	14		14.9
Total Abnormality		50	103	48.6	16	54	29.6	27	94	28.7

Key to Factory

X - Number with abnormality

Y - Number in sub group

Z - % with abnormality

Table 16

Radiological findings

(population grouped by length of exposure)

Exposure in years	Xray findings	Factory B			Factory M			Factory U		
		X	Y	Z	X	Y	Z	X	Y	Z
0-5	XP	0	8	0	0	2	0	2	28	7.1
	XT	0		0	0		0	1		3.6
	XPT	0		0	0		0	3		10.7
6-10	XP	2	13	15.4	3	10	30	2	37	5.4
	XT	1		7.7	2		20	4		10.8
	XPT	0		0	0		0	2		5.4
11-15	XP	2	31	6.5	2	12	16.7	1	19	5.3
	XT	8		25.4	0		0	2		10.5
	XPT	6		19.3	1		8.4	5		26.2
16-20	XP	7	44	15.9	2	15	13.3	0	10	0
	XT	9		20.4	1		6.7	1		10
	XPT	9		20.4	0		0	4		40
20 +	XP	0	7	0	3	15	20	-	-	
	XT	2		28.6	2		13.3	-	-	
	XPT	4		57.2	0	15	0	-	-	
Total Population										
	XP	11	103	9.7	10	54	18.5	5	94	5.3
	XT	20		19.4	5		9.4	8		8.5
	XPT	19		18.4	1		1.9	14		14.9
Total Abnormality		50	103	48.6	16	54	29.6	27	94	28.7

Key to Factory

X - Number with abnormality

Y - Number in sub group

Z - % with abnormality

Table 17

Statistical comparison of radiology of B, M and U

Xray		B v M	B v U	M v U
XP	ND	-1.24	-1.21	2.45
	P			<0.02
XT	ND	1.85	0.63	-0.24
	P			
XPT	ND	3.35	-1.37	-2.56
	P	<0.001		<0.02

Table 18

Comparison of the grades of radiological abnormality

Factory		XP1	XP2	XP3	XT1	XT2
B	No.	9	14	7	27	12
	%	30.0	46.7	22.3	69.3	30.7
M	No.	3	8	0	3	3
	%	27.3	72.7	0	50	50
U	No.	6	8	5	12	10
	%	31.6	42.1	26.3	54.6	45.4
Overall comparison	χ^2	0.27	1.15	3.68	14.88	1.54
	P				<0.001	

Comparison of incidence of XT1

	B v M	B v U	M v U
χ^2	9.80	6.16	1.25
P	<0.005	<0.025	

XP (1, 2, 3) grades of abnormal radiological pattern

XT (1, 2, 3) grades of pleural thickening

Table 19

Lung function in B. M and U
compared by analysis of covariance

Test	Factory	Mean	Adjusted Mean	SE of adjusted mean	F	Probability
VC	B	4.00	4.05	0.0690	1.924	
	M	4.14	4.25	0.0931		
	U	4.33	4.20	0.0715		
IC	B	2.50	2.54	0.0573	11.565	<0.001
	M	2.83	2.90	0.0773		
	U	2.97	2.90	0.0594		
RV	B	2.36	2.31	0.0763	10.104	<0.001
	M	2.73	2.78	0.1029		
	U	2.20	2.22	0.0791		
TLC	B	6.10	6.10	0.1044	7.616	<0.001
	M	6.59	6.75	0.1413		
	U	6.60	6.51	0.1081		
FEV/VC	B	70.6	71.2	0.9863	2.003	
	M	67.7	68.0	1.3201		
	U	71.2	70.4	1.0190		
PF	B	464	471	9.64	0.507	
	M	448	456	13.00		
	U	472	460	9.99		
RV/TLC	B	38.5	37.7	0.7676	18.876	<0.001
	M	41.5	41.2	1.0273		
	U	32.5	33.4	0.7930		
DL_{CO}	B	22.0	22.4	0.5461	9.100	<0.001
	M	25.3	25.8	0.7365		
	U	25.8	25.1	0.5659		
K_{CO}	B	3.31	3.36	0.0743	2.686	
	M	3.63	3.64	0.0994		
	U	3.56	3.49	0.0767		
D_M	B	46	47	1.988	9.734	<0.001
	M	60	61	2.784		
	U	58	57	2.169		
V_C	B	51	52	1.767	0.680	
	M	51	53	2.474		
	U	57	55	1.927		

Table 20

Comparison of adjusted means

Test	B v M 't'	P	B v U 't'	P	M v U 't'	P
IC	3.742	<0.001	4.362	<0.001	-	
RV	3.669	<0.001	0.8189		4.315	<0.001
TLC	3.6995	<0.001	2.728	<0.01	1.349	
RV/TLC	3.3974	<0.001	3.896	<0.001	6.0102	<0.001
DL_{CO}	3.708	<0.001	3.433	<0.001	0.7537	
DM	4.09	<0.001	3.399	<0.001	1.1335	

Table 21

Certified cases of asbestosis in B, M and U grouped by exposure to asbestosis

Exp. in yrs	Factory B No. cert.	No. in sub gp	%	Factory M No. cert.	No. in sub gp	%	Factory U No. cert.	No. in sub gp	%
0-5	0	8	0	0	3	0	0	28	0
6-10	0	13	0	0	10	0	0	39	0
11-15	7	31	22.5	0	14	0	2	19	10.5
15 +	14	51	27.4	1	32	3.1	2	9	22.2

B v M $P < 0.002$

M v U $P < 0.1$

Table 22

Comparison of the incidence of abnormal clinical findings in certified and uncertified workers

Test	Certified No. +ve	%	Not certified No. +ve	%	χ^2	P
Rales	18	69	17	8	67.12	<0.001
Rhonchi	4	15	22	10	0.25	
Cough						
Total	15	58	115	50	0.28	
Gd. I	8	53	81	70	0.05	
Gd. II	7	47	34	30	1.73	
Phlegm						
Total	10	38	94	41	0.001	
Gd. I	7	70	59	63	0.009	
Gd. II	3	30	35	37	0.04	
Dyspnoea						
Total	16	62	67	29	9.76	<0.005
Gd. 2	9	56	53	79	1.13	
Gd. 3	4	25	9	14	4.21	<0.05
Gd. 4	2	13	3	4	2.20	
Gd. 5	1	6	2	3	0.14	
Asbestos bodies	5	28	43	25	0.012	
Asbestos fibres	13	72	90	53	0.382	
Abnormal ECG	4	15	42	31	1.98	

Table 23

Comparison of the incidence of abnormal clinical findings in the certified, bronchitic and remaining workers

	No. +ve	%	Comparison overall χ^2	1 v 2 χ^2	1 v 3 χ^2	2 v 3 χ^2
Rhonchi						
Certified 1	4	15.4	5.576	0.081	0.666	3.678
Bronchitic 2	6	22.2	<0.1			<0.1
Remaining workers 3	16	8.3				
Cough						
Certified 1	15	58	9.996	1.617	0.785	8.225
Bronchitic 2	21	75	<0.01			<0.005
Remaining workers 3	94	46.5				
Phlegm						
Certified 1	10	38	6.189	1.899	0.001	5.186
Bronchitic 2	17	60.8	<0.05			<0.025
Remaining workers 3	77	38.1				
Dyspnoea						
Certified 1	16	62	13.079	1.536	10.801	1.411
Bronchitic 2	11	39.3	<0.005		<0.005	
Remaining workers 3	56	27.7				
Abnormal ECG						
Certified 1	4	15.4	10.21	6.48	0.73	5.99
Bronchitic 2	15	51.7	<0.01	<0.025		<0.025
Remaining workers 3	27	25.7				

Table 24

Sputum Analysis

Group	No. of specimens analysed	No. of specimens +ve for Asbestos bodies		No. of specimens +ve for Asbestos fibres	
Certified	18	5	27.8%	13	72.2%
Uncertified	138	41	29.6%	85	61.6%

Table 24

Sputum Analysis

Group	No. of specimens analysed	No. of specimens +ve for Asbestos bodies		No. of specimens +ve for Asbestos fibres	
Certified	18	5	27.8%	13	72.2%
Uncertified	138	41	29.6%	85	61.6%

Table 25a

Radiological results of normal and certified workers

Radiological abnormality	Certified workers		Uncertified workers		χ^2	P
None	No.	%	No.	%		
None	4	15.4	155	68.8	26.47	<0.001
XP	2	7.7	23	9.0	0.0038	
XT	5	19.2	28	12.4	0.4396	
XP +XT	15	57.7	19	8.4	44.16	<0.001

Table 25b

Radiological results of normal and certified workers in more detail

		XT absent No.	%	XT grade 1 No.	%	XT grade 2 No.	%	χ^2	P
XP absent	C	4	15.4	5	19.2	0	0		
	N	155	68.8	21	9.4	7	3.1		
XP grade 1	C	1	3.9	1	3.9	3	11.5	4.43	<0.05
	N	7	3.1	3	1.3	3	1.3		
XP grade 2	C	1	3.9	1	3.9	6	23	7.79	<0.01
	N	13	5.8	6	2.7	3	1.3		
XP grade 3	C	0	0	2	7.7	2	7.7	5.66	<0.025
	N	3	1.3	3	1.3	1	0.5		
χ^2				5.25		29.76			
P				<0.025		<0.001			

Key

XP abnormal radiological pattern
XT pleural thickening
C certified workers
N uncertain workers

Table 26

Comparison of pulmonary function and clubbing results in normal, certified and remaining workers

Test	Group	Mean	Adj.M.	SE	F	P	1 v 2 t	1 v 2 P	1 v 3 t	1 v 3 P	2 v 3 t	2 v 3 P
DL_{CO}	1	17.0	18.1	0.9854	25.634	<0.001	6.87	<0.001	6.381	<0.001	2.188	<0.05
	2	28.4	26.9	0.8190								
	3	24.7	24.9	0.4056								
K_{CO}	1	2.92	3.02	0.1399	8.276	<0.001	4.013	<0.001	3.437	<0.001	1.618	
	2	3.89	3.75	0.1163								
	3	3.52	3.54	0.0576								
Dm	1	32.8	34.4	3.6287	16.782	<0.001	5.532	<0.001	5.199	<0.001	1.694	
	2	62.5	60.5	3.0159								
	3	54.6	54.8	1.4937								
Vc	1	43.0	45.8	3.2918	2.730	NS						
	2	58.5	54.6	2.7360								
	3	53.3	53.8	1.3551								
SVC	1	3.55	3.71	0.1370	7.841	<0.001	3.775	<0.001	3.577	<0.001	1.102	
	2	4.58	4.38	0.1139								
	3	4.22	4.24	0.0564								
IC	1	2.15	2.26	0.1096	17.342	<0.001	5.952	<0.001	4.556	<0.001	3.050	<0.01
	2	3.24	3.11	0.0911								
	3	2.78	2.80	0.0451								
RV	1	1.93	1.87	0.1344	7.929	<0.001	1.489		3.647	<0.001	2.166	<0.05
	2	2.04	2.13	0.1147								
	3	2.41	2.40	0.0553								
TLC	1	5.36	5.48	0.1884	12.256	<0.001	4.022	<0.001	4.918	<0.001	0.347	
	2	6.54	6.42	0.1551								
	3	6.47	6.48	0.0765								
FEV/VC	1	72.6	73.7	1.8061	6.344	<0.01	0.5109		2.099	<0.05	3.164	<0.002
	2	76.5	74.9	1.5008								
	3	69.4	69.6	1.7440								
PF	1	480	496	18.18	3.369	<0.05	0.381		1.526		2.313	<0.05
	2	525	505	15.11								
	3	463	466	7.48								
RV/TLC	1	35.8	34.2	1.5419	3.345	<0.05	0.3990		1.499		2.308	<0.05
	2	31.2	33.4	1.2813								
	3	37.0	36.7	0.6352								
Clubbing	1	195.6	195.65	1.4597	5.178	<0.001	5.459	<0.001	1.844		15.534	<0.001
	2	185.86	185.86	1.2015								
	3	187.4	187.39	0.5928								

1 = normal
2 = certified } workers.
3 = remaining

Table 27

The sixteen variables used in the analysis with their means and standard deviations for 201 asbestos workers

No.		Mean	SD
1.	Age (years)	44.3781	10.0909
2.	Height (cm)	169.3781	6.4200
3.	FEV/VC (%)	71.3632	9.9771
4.	VC (litres)	4.2066	0.9016
5.	RV/TLC (%)	35.6219	9.3897
6.	Tl (ml/mm Hg x min)	24.5383	6.7207
7.	Exposure	51.9950	7.0735
8.	Crepitations	0.1542	0.3621
9.	Clubbing (degrees)	188.1294	7.7996
10.	Cough	0.6965	0.7632
11.	Phlegm	0.5572	0.7402
12.	Dyspnoea	1.4229	0.7248
13.	Smoking	9.8716	33.1656
14.	Dm (ml/mm Hg x min)	53.3682	20.4264
15.	Xray pattern	0.4950	0.9022
16.	Xray thickening	0.4000	0.6799

Table 27

The sixteen variables used in the analysis with their means and standard deviations for 201 asbestos workers

No.		Mean	SD
1.	Age (years)	44.3781	10.0909
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6.	Tl (ml/mm Hg x min)	24.5383	6.7207
7.	Exposure	51.9950	7.0735
8.	Crepitations	0.1542	0.3621
9.	Clubbing (degrees)	188.1294	7.7996
10.	Cough	0.6965	0.7632
11.	Phlegm	0.5572	0.7402
12.	Dyspnoea	1.4229	0.7248
13.	Smoking	9.8716	33.1656
14.	Dm (ml/mm Hg x min)	53.3682	20.4264
15.	Xray pattern	0.4950	0.9022
16.	Xray thickening	0.4000	0.6799

Table 28

CORRELATION COEFFICIENT MATRIX

	AGE	HEIGHT	FEV/VC	VC	RV/TLC	D_{LCO}	YEAR	RALES	CLUBBING	COUGH	PHLEGM	DYPSNOEA	SMOKING	D_M	X-RAY (PATT)	X-RAY (THICK)
AGE	1.0000	-0.1793	-0.4163	-0.4945	0.5558	-0.5400	-0.3272	0.2239	0.0427	0.0600	0.0547	0.2615	0.0626	-0.2789	0.1460	0.1525
HEIGHT		1.0000	0.1295	0.4689	-0.0959	0.3109	0.0408	-0.1352	-0.1598	-0.0836	-0.1069	-0.0673	-0.0740	0.2139	-0.0120	-0.0920
FEV/VC			1.0000	0.1567	-0.4578	0.3429	0.1720	-0.0287	0.0886	-0.3123	-0.2903	-0.2642	-0.1780	0.0549	0.0633	0.0154
VC				1.0000	-0.4484	0.5643	0.2244	-0.3817	-0.1830	-0.0872	-0.0042	-0.3317	-0.0580	0.3873	-0.1903	-0.3458
RV/TLC					1.0000	-0.3736	-0.2721	0.1125	0.0178	0.1267	0.1324	0.1984	0.0695	-0.1297	-0.0231	0.0644
D_{LCO}						1.0000	0.2737	-0.4166	-0.2903	-0.2297	-0.1017	-0.3491	-0.2677	0.7050	-0.1688	-0.3626
YEAR							1.0000	-0.1035	-0.0466	-0.1023	-0.0845	-0.2117	-0.1705	0.1330	-0.1295	-0.2135
RALES								1.0000	0.3190	0.1377	0.0355	0.1994	-0.0015	-0.3832	0.2631	0.3216
CLUBBING									1.0000	0.0024	-0.0150	0.1397	0.1827	-0.2448	0.2388	0.3126
COUGH										1.0000	0.5564	0.3436	0.2496	-0.1346	0.0586	0.0618
PHLEGM											1.0000	0.2300	0.1765	-0.0260	0.0624	-0.0831
DYPSNOEA												1.0000	0.1483	-0.2351	0.1352	0.1602
SMOKING													1.0000	-0.1772	0.0454	0.1155
D_M														1.0000	-0.1918	-0.3329
X-RAY (PATT)															1.0000	0.4166
X-RAY (THICK)																1.0000

Table 29

Relative power of sixteen clinical, radiological and pulmonary function variables to assess lung disease (component I) and to separate asbestosis from chronic obstructive airway disease (component II) in 201 asbestos workers

Component I			Component II		
Variables	Standardized weightings	Raw weightings	Variables	Standardized weightings	Raw weightings
Tl	+0.416	+0.0613	FEV/VC	+0.416	+0.0416
VC	+0.356	+0.3948	Phlegm	-0.380	-0.5133
Age	-0.320	-0.0317	Xray (thickening)	+0.350	+0.5147
Dm	+0.309	+0.0151	Cough	-0.345	-0.4520
RV/TLC	-0.263	-0.0283	Finger clubbing	+0.315	+0.0403
Crepitations	-0.258	-0.7125	Xray (pattern)	+0.293	+0.3247
Dyspnoea	-0.257	-0.3545	Rales	+0.288	+0.7954
Xray (thickening)	-0.234	-0.3441	RV/TLC	-0.272	-0.0289
FEV/VC	+0.214	+0.0214	Dm	-0.170	-0.0083
Exposure	-0.207	-0.0381	Dyspnoea	-0.152	-0.2097
Height	+0.193	+0.0300	Age	-0.124	-0.0122
Cough	-0.178	-0.2332	VC	-0.111	-0.1231
Finger clubbing	-0.172	-0.0220	Smoking	-0.101	-0.0030
Xray (pattern)	-0.161	-0.1784	Exposure	-0.074	-0.0104
Smoking	-0.149	-0.0044	Height	-0.059	-0.0091
Phlegm	-0.117	-0.1580	Tl	-0.035	-0.0052
Constant term		+2.1197			+5.1032

Increasing power to separate lung disease and health

Increasing power to separate asbestosis and obstructive airway disease

Table 30

Means of the sixteen variables for 201 subjects in the four quadrants of the principal component analysis plot (Fig. 3) with further subdivision of the left upper quadrant into certified asbestosis and others and of the left lower quadrant into obstructive airway disease and others

	Left upper quadrant	Certified asbestosis	Other	Left lower quadrant	Obstructive	Other	Right Upper quadrant	Right lower quadrant	Mean RUQ and RLQ
No.	53	24[7]	31	44	13[7]	33	54	50	104
Age	49	48	50	51	50	51	38	41	40
Height	167	168	167	168	167	167	170	172	171
FEV/VC	72.7	73.3	72.3	62.9	46.7	68.3	77.6	70.0	73.8
VC	3.53	3.55	3.57	3.90	3.95	3.96	4.60	4.81	4.71
RV/TLC	37.1	35.5	38.3	43.4	47.8	41.6	30.2	33.3	31.7
Tl	19.3	17.2	20.9	20.1	18.4	21.4	29.0	29.4	29.2
Exposure	50.2	48.2	51.4	48.6	49.5	48.3	54.7	54.0	54.4
Rales	0.49	0.67	0.32	0.07	0.23	0.00	0.03	0.00	0.02
Clubbing	193	196	191	187	186	187	187	184	186
Cough	0.64	0.79	0.55	1.20	1.46	1.06	0.17	0.95	0.56
Phlegm	0.40	0.50	0.35	1.16	1.31	1.06	0.12	0.73	0.43
Dyspnoea	1.60	1.96	1.39	1.70	1.69	1.73	1.12	1.23	1.18
Smoking	10.3	10.5	10.3	10.7	11.1	10.6	7.9	11.1	9.5
Dm	39.7	33.7	44.3	47.3	49.1	49.4	59.1	68.4	63.8
Xray (pattern)	1.11	1.29	0.90	0.33	0.08	0.42	0.33	0.14	0.24
Xray (thickening)	1.09	1.25	0.94	0.27	0.23	0.27	0.14	0.05	0.10

[7] Includes two certified asbestosis cases from other quadrants

[7] Includes two cases with obstructive airway disease from other quadrants

Table 31

Predictions (J.E. Cotes) (Male)

Index	Ht.	Wt.	Age	Constant
VC	5.20		-0.022	-3.60
RV/TLC			0.343	16.7
FEV/VC			-0.373	91.8
Tl	32.5		-0.20	-17.6
Dm	66.0		-0.19	-46.9

Table 32

U/U max % values for normals vs certified in this study compared with values from study of Thomson et al 1965

(Variables listed in descending order of discriminant power from this study)

Test	U/U max %	U/U max % results of ML Thomson 1965
TI	97	92
Dm	96	69
IC	89	97
K_{CO}	87	
Clubbing	19	
UC	80	92
TLC	79.5	
V_C	78	74
RV/TLC%	32	38
FEV/VC%	64	38
PF	57.5	55
RV	57	

If U/U max% = 100% complete separation
50% complete overlap

	AGE	HEIGHT	FEV/VC	SVC
AGE	1.0000	-.1752	-.4143	-.4944
HEIGHT	-.1752	1.0000	.1054	.4658
FEV/VC	-.4143	.1054	1.0000	.1462
SVC	-.4944	.4658	.1462	1.0000
RV	.3259	.1413	-.4578	.0321
DLCO	-.5376	.3125	.3476	.5679
RALES	.2249	-.1398	-.0369	-.3848
CLUBBG	.0481	-.1635	.0835	-.1850
COUGH	.0484	-.0725	-.2927	-.0812
PHLEGM	.0225	-.0942	-.2658	.0038
DYSP	.2527	-.0340	-.1962	-.3310
SMOKE	.0632	-.0717	-.1788	-.0566
DM	.2763	-.1849	-.1642	-.4363
XPATT	.1466	-.0168	.0564	-.1935
XTHICK	.1293	-.0938	.0054	-.3377

	COUGH	PHLEGM	DYSP	SMOKE
AGE	.0484	.0225	.2527	.0632
HEIGHT	-.0725	-.0942	-.0340	-.0717
FEV/VC	-.2927	-.2658	-.1962	-.1788
SVC	-.0812	.0038	-.3310	-.0566
RV	.1131	.1533	.0475	.0365
DLCO	-.2221	-.0934	-.3571	-.2711
RALES	.1408	.0364	.2201	.0002
CLUBBG	.0085	-.0090	.1596	.1827
COUGH	1.0000	.5477	.3228	.2507
PHLEGM	.5477	1.0000	.1965	.1766
DYSP	.3228	.1965	1.0000	.1503
SMOKE	.2507	.1766	.1503	1.0000
DM	.1971	.3389	.3248	.1521
XPATT	.0614	.0664	.1546	.0472
XTHICK	.0779	-.0761	.1612	.1131

RV	DLCO	RALES	CLUBBG
.3259	-.5376	.2249	.0481
.1413	.3125	-.1398	-.1635
-.4578	.3476	-.0369	.0835
.0321	.5679	-.3848	-.1850
1.0000	-.0549	-.1182	-.0843
-.0549	1.0000	-.4158	-.2989
-.1182	-.4158	1.0000	.3202
-.0843	-.2989	.3202	1.0000
.1131	-.2221	.1408	.0085
.1533	-.0934	.0384	-.0090
.0475	-.3571	.2201	.1596
.0365	-.2711	-.0002	.1827
-.0647	-.7121	.4721	.3155
-.1177	-.1662	.2615	.2400
-.0916	-.3466	.3268	.2880

DM	XPATT	XTHICK
.2763	.1466	.1293
-.1849	-.0168	-.0938
-.1642	.0564	.0054
-.4363	-.1935	-.3377
-.0647	-.1177	-.0916
-.7121	-.1662	-.3466
.4721	.2615	.3268
.3155	.2400	.2880
.1921	.0614	.0779
.0389	.0664	-.0701
.3248	.1546	.1812
.1521	.0472	.1131
1.0000	.2097	.3509
.2097	1.0000	.4236
.3509	.4236	1.0000

Table 33
correlation coefficient matrix (exposure left out of PCA.)

Table 34a

Mean values of component I
(factories subdivided by exposure to asbestos)

Exposure group years	B_1	B_2	$(B_1 + B_2)$	M	U
0–10	0.0818 (16)	0.1793 (3)	0.0966 (19)	0.0226 (10)	0.0785 (49)
11–15	-0.0761 (16)	-0.1160 (10)	-0.0914 (26)	0.0349 (8)	0.0204 (16)
Over 15	-0.0574 (24)	-0.1103 (18)	-0.0802 (42)	-0.0265 (27)	-0.007 (8)

(Numbers within subgroups in parentheses)

Analysis variance

Horizontal axis

0–10 years F = 1.265
11–15 " F = 3.279 P <0.05
Over 15 " F = 2.301

Vertical axis

B_1 F = 9.025 P < 0.001
B_2 F = 6.729 P < 0.01
M F = 1.359
U F = 3.960 P <0.025

Comparison of factories - within exposure group 11–15 years

B_1 v U 't' = 2.02 P < 0.05
B_2 v M 't' = 2.34 P < 0.05
B v M 't' = 2.13 P < 0.05
B v U 't' = 2.21 P < 0.05
(Other comparisons not significant)

Table 34b

Mean values of component II
(factories subdivided by exposure to asbestos)

Exposure group years	B_1	B_2	$(B_1 + B_2)$	M	U
0-10	0.0014	0.0683	0.0119	-0.0246	-0.0009
11-15	0.0031	0.0691	0.0285	0.0218	0.0352
Over 15	-0.0167	0.0466	0.0105	-0.0706	0.0975

(Numbers within subgroups as for 34a)

Analysis of variance

Horizontal axis

0-10 years F = 1.031
11-15 " F = 0.749
Over 15 " F =10.125 P <0.001

Vertical axis

B_1 F = 0.300
B_2 F = 0.170
M F = 4.394 P <0.025
U F = 4.09 P <0.025

Comparison of factories - within exposure group over 15 years

B_1 v B_2 't' = 2.24 P <0.05
B_1 v M 't' = 2.12 P <0.05
B_1 v U 't' = 3.10 P <0.02
B_2 v M 't' = 5.22 P <0.001
M v U 't' = 4.62 P <0.001
B v U 't' = 2.32 P <0.05

(Other comparisons not significant)

Table 35

Mean age within exposure subgroups of workers included in PCA for B, M and U

Factory	B_1	B_2	$B_1+B_2=B$	M	U
Exposure					
0-10 yrs.	38.3	32.7	37.4	39.2	43.1
No. in subgroup	16	3	19	10	50
11-15 yrs.	46.0	50.4	47.6	44.5	45.4
No. in subgroup	16	10	26	8	16
15 + yrs.	48.0	51.2	49.4	47.9	44.0
No. in subgroup	24	18	42	27	8

Table 36

Mean Dust Levels

Factory	Mean dust concentration mg/m^3
B	0.61
M	1.29
U	0.57

Table 37

Xray results of workers examined at B compared with the xray results for the total study population at B

(this includes those who refused the examination)

	Number		Percentage	
	Population studied	Total Population	Population studied	Total population
Any radiological abnormality	50	61	48.6	48.7
XP	50	12	9.4	9.6
XT	20	28	19.4	22.4
XPT	19	21	18.4	16.8

Table 38

Usefulness of four objective measurements in distinguishing between normal and clubbed fingers

Measurement	Mean normal (18)	Mean clubbed (7)	Pooled S.E.M.	t	P
Profile angle (^{o})	173.5	181.1	1.879	4.044	<0.001
Hyponychial angle (^{o})	187.0	209.4	2.698	8.302	<0.001
Curvature (diptres)	8.42	16.0	1.416	5.353	<0.001
Plethysmography (%)	55.8	68.0	5.388	2.260	<0.050

Table 37

Xray results of workers examined at B compared with the xray results for the total study population at B

(this includes those who refused the examination)

	Number		Percentage	
	Population studied	Total Population	Population studied	Total population
Any radiological abnormality	50	61	48.6	48.7
XP	50	12	9.4	9.6
XT	20	28	19.4	22.4
XPT	19	21	18.4	16.8

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Curvature (diptres)	8.42	16.0	1.416	5.353	<0.001
Plethysmography (%)	55.8	68.0	5.388	2.260	<0.050

Table 39

Misclassifications by four objective measurements

Measurements	Errors in subgroup			
	Normal (18)	Doubtful normal (16)	Doubtful clubbed (9)	Clubbed (7)
Profile angle	28%	63%	22%	0%
Hyponychial angle	0%	13%	11%	0%
Curvature	11%	44%	11%	0%
Plethysmography	28%	31%	56%	14%

Table 40

Xray and pulmonary-function abnormality indicative of chest disease

Subgroup	No.	Abnormal Xrays (%)	Abnormal pulmonary function (%)
Clubbed	7	100	71
Doubtful clubbed	9	44	33
Doubtful normal	16	37	0
Normal	18	28	6

Table 41a

Mean VC and percentage of the predicted value in subjects with different grades of Xray abnormality (three factories combined)

		Abnormal radiological pattern (XP)				Pleural thickening (XT)				
		Grades			All grades combined	Grades		Both grades combined		
		1	2	3		1	2			
XP alone or XT alone	Mean VC	4.17	4.71	4.08	4.44	3.99	4.11	4.01		
	% predicted	95	108	95	102	96	96	96		
XP and XT together	Mean VC	3.93	3.81	3.96	3.84	4.10	3.55	3.84	Total workers with Xray abnormality	Total workers without Xray abnormality
	% predicted	95	89	96	94	100	84	94		
Total with XP and/or XT	Mean VC	4.00	4.2	4.00	4.1	4.04	3.69	3.91	4.06	4.3
	% predicted	95	97	95	96	97	87	95	96	100

Table 41b

T_L -mean values and percentage predicted values for subjects with different grades of Xray abnormality (three factories combined)

		Abnormal radiological pattern(XP)				Pleural thickening (XT)				
		Grades			All grades combined	Grades		Both grades combined		
		1	2	3		1	2			
XP alone or XT alone	Mean T_L	23.5	26.7	23.8	25.2	21.9	22.1	21.9		
	% predicted	81	90	85	86	81	78	80		
XP and XT together	Mean T_L	21.7	19.0	19.1	19.8	20.0	19.1	19.8	Total workers with Xray abnormality	Total workers without Xray abnormality
	% predicted	80	67	70	72	74	69	72		
Total with XP and/or XT	Mean T_L	22.4	22.5	20.9	22.2	21.3	19.9	20.8	21.4	24.9
	% predicted	80	78	76	78	78	71	75	79%	91%

Table 42

Comparison of Xray findings in those with and without rales

	Workers with Rales		Workers without Rales	
	No.	%	No.	%
No Xray abnormality	11/35	31	147/216	68
XP alone	3/35	9	25/216	12
XT alone	5/35	14	28/216	13
XPT	16/35	46	16/216	7

Table 44

VC and T_L in those with pleural thickening and abnormal pattern (XPT) with and without rales

	Mean VC	% predicted	Mean T_L	% predicted
Rales + XPT (16)	3.38	82.4	17.2	63.2
XPT without rales (18)	4.19	99.0	22.0	81.4

Table 44b

Mean hyponychial angle in smokers and non smokers

(Results from study population)

	Non Smokers	Smokers
Factory	hyponychial angle	hyponychial angle
B	185.6	190.0
M	182.8	187.1
U	185.5	191.5
Three factories together	185.0	189.8
"normal" workers	182.4	186.9

(Results from group of subjects not exposed to asbestos)

Non Smokers	Smokers
hyponychial angle	hyponychial angle
181.2	184.3

Table 43

Incidence of abnormal lung function and radiology in workers with rales

	No.	%	T_L Mean Value	T_L %predicted Value (mean)	VC Mean Value (mean)	VC %predicted Value (mean)	Clubbing (hyponychial angle) (mean)	FEV/VC% (mean)	RV/TLC (mean)
Rales + normal Xray	11/35	31.4%	19.64	85%	4.09	85%	190.9	73%	35
Rales + Xray abnormality	24/35	68.6%	17.0	70%	3.53	72%	194.5	71%	36
Total with Rales	35/246	14.2%	17.8	76%	3.68	76%	193.3	72%	35
Rest of pop. without rales	211/246	85.8%	24.8	91%	4.25	99%	187.3	70%	37

't'=5.26 P<.001

't'=3.39 P<.001

Table 45

Incidence of rales and clubbing and mean hyponychial angle related to radiological results

	Normal Xray No.	%	XP No.	%	XT No.	%	XPT No.	%	Any Radio-logical Abnormality No.	%
Rales Present	11/158	7	3/28	11	5/33	15	16/32	50	24/93	26
Mean Hyponychial <	185.1		185.8		187.1		194.3			
Percentage with hyponychial angle ≥ 198° but < 205	10/158	6	3/28	11	6/33	18	6/32	19	15/93	16
Percentage with hyponychial angle ≥ 205	6/158	4	1/28	4	0		5/32	16	6/93	6

Table 45b

Incidence of rales in non-smokers and smokers

Factory	Non-Smokers No.	%	Smokers No.	%
B	6/20	30	17/82	21
M	0/13	0	2/45	5
U	3/26	12	7/65	11
Three factories combined	9/59	15	26/192	14

Table 46

Incidence of rales, Xray abnormality, finger clubbing and pulmonary function occurring alone and together

	Single Abnormality		Two Abnormalities		Three Abnormalities		Four Abnormalities		Total incidence of abnormality	
	Number	%	Number	%	Number	%	Number	%		
Rales	2	6	11	31	15	43	7	20	35/246	14
Radiological abnormality	43	46	22	24	21	23	7	8	93/250	37
Hypony-chial angle $\gg 198^{o}$	7	18	13	40	9	24	7	18	38/251	15
VC < 80 + $T_L < 85$ } of predicted value	55	54	20	19	19	19	8	8	102/258	39

Table 47

Incidence of Xray abnormality occurring alone and with other abnormalities

	Xray Changes Alone		Xray + 1 other Abnormality		Xray + 2 other Abnormalities		Xray + 3 other Abnormalities	
	No.	%	No.	%	No.	%	No.	%
XP	16	37	6	27	4	19	0	0
XT	21	48	5	23	5	24	2	29
XPT	6	14	11	50	12	57	5	71

Table 48

Age and Length of exposure to asbestos in smokers and non smokers

	Non Smokers Grade 0	Grade 1	Smokers Grade 2	Grade 3
Age				
Factory B	46.7	44.6	43.6	48.8
Factory M	47.2	42.8	46.0	43.1
Factory U	42.9	42.7	42.7	42.5
3 Factories Combined	45.5	43.9	43.8	44.9
Years Exposure				
Factory B	14.1	13.8	13.2	14.1
Factory M	15.6	17.3	17.4	15.3
Factory U	10.2	7.7	9.1	8.5
3 Factories Combined	12.9	12.8	12.4	13.4

Table 48

Age and Length of exposure to asbestos in smokers and non smokers

	Non Smokers Grade 0	Smokers Grade 1	Smokers Grade 2	Smokers Grade 3
Age				
Factory B	46.7	44.6	43.6	48.8
Factory M	47.2	42.8	46.0	43.1
Factory U	42.9	42.7	42.7	42.5
3 Factories Combined	45.5	43.9	43.8	44.9
Years Exposure				
Factory B	14.1	13.8	13.2	14.1
Factory M	15.6	17.3	17.4	15.3
Factory U	10.2	7.7	9.1	8.5
3 Factories Combined	12.9	12.8	12.4	13.4

Table 49

Incidence of radiological abnormality in smokers and non smokers

	Factory B				Factory M				Factory U				Three factories combined			
	Non Smokers		Smokers		Non Smokers		Smokers		Non Smokers		Smokers		Non Smokers		Smokers	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
XP	2/21	10	10/82	12	5/13	38	5/42	12	1/26	4	4/68	6	8/60	13	9/192	10
XT	4/21	19	12/82	15	0/13	0	5/42	12	2/26	8	5/68	7	6/60	10	2/192	11
XP + XT	3/21	14	19/82	23	0/13	0	1/42	2	5/26	19	10/68	15	8/60	13	30/192	16
Any radiological abnormality	9/21	43	41/82	50	5/13	38	11/42	26	8/26	31	19/68	28	22/60	37	71/192	37

Table 50

Xray results, hyponychial angle, rales and some lung function results, in certified and some uncertified workers

Uncertified Workers								Certified Workers							
Code Number	Rales	XP	XT	Clubbing	Abnormal TL	Abnormal VC	FEC/FVC	Code Number	Rales	XP	XT	Clubbing	Abnormal TL	Abnormal VC	FEV/VC
22	+	2	1	–	–	–	71	16	+	1	2	–	–	+	71
26	+	2	–	–	–	+	73	18	+	2	2	+	+	+	85
30	+	2	1	–	+	+	67	19	–	–	1	–	–	–	80
37	–	–	–	+	+	–	61	23	+	1	1	–	–	–	71
40	–	2	2	–	+	+	58	27	+	3	2	–	+	+	84
47	+	2	1	–	–	–	44								
58	+	–	–	–	+	–	35	29	+	3	1	+	–	–	73
79	–	2	1	–	–	+	78	34	+	–	–	–	+	+	73
80	–	1	–	+	–	–	76								
84	–	2	–	+	–	–	92	48	+	2	–	–	–	+	69
89	+	1	–	–	+	+	50	51	+	3	2	+	+	+	82
105	–	–	–	+	–	+	74								
110	–	–	–	+	–	+	58								
116	+	2	2	–	+	+	81	62	–	1	2	–	–	+	62
149	+	–	–	–	+	+	55	73	+	3	1	+	–	–	69
153	–	–	1	+	–	–	72	86	+	–	–	+	–	–	63
163	–	–	1	–	–	+	54	117	–	2	1	–	–	–	64
169	+	1	–	–	–	–	64	109	+	–	1	+	+	+	84
212	+	–	2	+	+	+	63	121	–	2	2	–	+	–	72
215	–	2	–	+	+	–	70	128	–	2	2	+	+	+	80
218	–	–	1	+	–	–	51	136	+	–	1	–	+	+	54
225	+	1	–	–	–	–	62	142	–	–	1	–	+	+	74
255	–	–	–	+	–	+	68								
289	–	–	2	–	–	+	71	143	+	2	1	–	+	+	62
304	–	2	–	+	–	+	71	157	+	–	1	+	–	–	74
401	+	3	1	+	–	–	75	165	–	–	1	+	+	+	71
408	–	1	1	+	–	–	76	247	+	–	–	–	+	–	78
411	–	2	1	–	+	–	49	417	+	1	2	+	–	–	77
425	–	–	1	+	+	+	72	430	+	2	2	–	+	–	76
448	–	2	2	–	–	+	85	445	+	2	2	+	+	–	75
450	–	3	1	–	+	–	75	475	+	2	2	+	+	+	75
451	–	–	–	+	+	–	53								
468	–	3	1	+	–	–	65								
488	–	3	2	+	–	+	72								
497	–	1	–	–	–	+	77								
498	+	–	–	+	–	+	83								
501	+	–	1	–	–	+	65								

Table 51a

$\frac{IC}{VC}$ % for subdivision of Component I and Component II

	←+1.0	+1.0←0	0→-1.0	-1.0→
Component I	70.0	67.8	65.8	66.9
Component II	68.3	68.2	66.6	68.4

$\frac{TL'}{TL}$ % for subdivision of Component I and Component II

	←+1.0	+1.0→0	0→-1.0	-1.0→
Component I	90.1	91.3	89.5	90.2
Component II	96.8	89.0	93.9	80.1

Table 51b

Numbers in the subgroups of the principal component analysis plot of Component I versus Component II

CI	CII: asbestosis ← 0 → Obstructive airway disease			
	< - 1.0	- 1.0 - 0	0 - 1.0	>1.0
disease ↑ >1.0	21	13	12	9
0—1.0	7	9	13	10
1.0—0	13	9	9	14
↓ health <1.0	14	23	13	12

Table 52

Correlation matrices for the three factories - age, exposure, and components I and II

		Component I		Component II		Exposure	
		r	Significance level	r	Significance level	r	Significance level
Factory B	Exposure	-.552	P<.001	.035	NS		
		(-.322	P<.01	(.103)	NS		
	Age	.621	P<.001	-.093	NS	.549	P <.001
Factory M	Exposure	-.211	NS	-.334	NS		
		(.067)	NS	(-.371)	P <.02		
	Age	-.422	P<.02	.031	NS	.366	P <.05
Factory U	Exposure	-.386	P<.001	.242	P <.01		
		(-.377)	P<.001	(.288)	P <.02		
	Age	-.522	P<.001	.264	P< .01	.128	NS

Figures in parenthesis are correlation coefficients for exposure versus components I and II with age held constant.

Table 52

Correlation matrices for the three factories - age, exposure, and components I and II

		Component I		Component II		Exposure	
		r	Significance level	r	Significance level	r	Significance level
Factory B	Exposure	-.552	P<.001	.035	NS		
		(-.322	P<.01	(.103)	NS		
	Age	.621	P<.001	-.093	NS	.549	P <.001
Factory M	Exposure	-.211	NS	-.334	NS		
		(.067)	NS	(-.371)	P <.02		
	Age	-.422	P<.02	.031	NS	.366	P <.05
Factory U	Exposure	-.386	P<.001	.242	P <.01		
		(-.377)	P<.001	(.288)	P <.02		
	Age	-.522	P<.001	.264	P< .01	.128	NS

Figures in parenthesis are correlation coefficients for exposure versus components I and II with age held constant.

Table 53

Component I in smokers and non smokers

Factory	Non Smokers	Smokers			All three grades of Smoker Combined
	Grade 0	Grade 1	Grade 2	Grade 3	
B	-.610	-.500	-.808	-.333	- .677
M	.552	1.049	.007	-.208	.237
U	.707	.354	.421	-1.525	.151
three factories combined	.245	-.023	-.207	- .550	- .219

Component II in smokers and non smokers

Factory	Non Smokers	Smokers			All three grades of Smoker Combined
	Grade 0	Grade 1	Grade 2	Grade 3	
B	.375	-.046	.743	- .931	.014
M	.377	-.108	-.839	-1.06	-.720
U	.927	-.390	-.138	- .062	-.265
three factories combined	.641	-.167	-.054	- .800	-.241

Table 54a

Mean values of some tests for those subjects excluded from the P.C.A. compared with those subjects included in the P.C.A.

(Predicted values calculated from regression equations given in "Lung Function" - J.E. Cotes, Table 14.5)

	Values for subjects included in P.C.A.		Values for subjects not included in P.C.A.	
	Mean value	% predicted	Mean value	% predicted
Age	44.4		49.5	
Height	169.4		169.5	
FEV/VC%	71.4	95	72.4	98
VC	4.21	98	4.08	97
RV/TLC%	35.6	112	37.9	113
TL_{CO}	24.5	86	23.4	85
Dm	53.4		53.8	
Clubbing	188.1		187.7	
Years exposure	12.0		11.3	

Table 54b

Incidence of abnormal clinical and radiological findings in two groups, subjects included in the P.C.A. and subjects not included in the P.C.A.

	Subjects excluded from P.C.A.		Subjects included in P.C.A.	
Test	No.	%	No.	%
Rales	4/41	10	31/201	15
Rhonchi	6/41	15	20/201	10
Cough	23/49	47	107/201	53
Phlegm	21/49	43	83/201	41
Dyspnoea	14/49	29	71/201	35
Abnormal radiological pattern	8/44	18	52/201	26
Pleural thickening	10/44	23	57/201	28

Table 54b

Incidence of abnormal clinical and radiological findings in two groups, subjects included in the P.C.A. and subjects not included in the P.C.A.

	Subjects excluded from P.C.A.		Subjects included in P.C.A.	
Test	No.	%	No.	%
Rales	4/41	10	31/201	15
Rhonchi	6/41	15	20/201	10
Cough	23/49	47	107/201	53
Phlegm	21/49	43	83/201	41
Dyspnoea	14/49	29	71/201	35
Abnormal radiological pattern	8/44	18	52/201	26
Pleural thickening	10/44	23	57/201	28

Table 54b

Incidence of abnormal clinical and radiological findings in two groups, subjects included in the P.C.A. and subjects not included in the P.C.A.

	Subjects excluded from P.C.A.		Subjects included in P.C.A.	
Test	No.	%	No.	%
Rales	4/41	10	31/201	15
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Phlegm	21/49	43	83/201	41
Dyspnoea	14/49	29	71/201	35
Abnormal radiological pattern	8/44	18	52/201	26
Pleural thickening	10/44	23	57/201	28

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APPENDIX

Finger clubbing

As finger clubbing is quite a common feature of asbestosis, it was decided that it would be useful to be able to measure it for correlating with the clinical, radiological and physiological results obtained from the survey. On referring to the literature very few people were found to have attempted a precise measurement (Cudkowitz, L. and Wraith, D.G. 1957, Stavem, P. 1959).

A copy of the brass disc described by Stavem was made and found to be difficult to use to measure longitudinal nail curvature. M.L. Thomson then suggested modifying a spherometer and this modified instrument was found on experiment to be easier to use and much more accurate in measuring this parameter.

For further research into this problem it was decided that a finger cast of all the asbestos workers in the study population should be made and Mrs. O.L. Wade devised the following method. A negative impression of the right index finger (or the left if the right had been damaged) was obtained by pushing the finger into a perforated cylindrical mould containing dental impression material (Tissutex). After the Tissutex had hardened, (2-5 minutes) the finger was removed and a positive cast made with plaster of paris (kaffir, D.).

Four different measurements were then made on these casts:-

a) The nail curvature was measured using the modified spherometer.

b) After making the casts non-porous by coating them with latex, the volumes of the terminal two phalenges were measured by plethysmography using water displacement. These volumes were divided by length to give the mean cross-sectional areas and that of the terminal phalanx was expressed as a percentage of that of the middle phalanx, to give an index of swelling. This method was believed to be less crude than that described by Cudkowitz et al (1957) who measured the volume

of a set length of finger tip. This volume would vary not only with swelling of the finger tip but also between individuals with fat and thin fingers.

c) The casts were outlined with a planimeter and an angle similar to the profile angle of Lovibond J.L. (1938) measured on this outline (Fig. 8).

d) A further angle was constructed on the outline drawing of the finger cast (Fig. 8) which we called the hyponychial angle.

A study was then carried out on fifty of these finger casts chosen at random to find out which was the best method of measurement.

To obtain a criterion of clubbing, these fifty finger casts were sent to 13 chest physicians and others with experience in occupational medicine. They were asked to grade the casts as normal doubtful or clubbed and a combined score was then arrived at for each cast, awarding 1 for normal, 2 for doubtful and 3 for clubbed. The maximum score was 39 and the minimum score 13. Those casts scoring 37 or more were graded as clubbed and those scoring 15 or less as normal and the rest as doubtful. 14% of the fingers were classified as clubbed, 38% as normal and the rest as doubtful. All four measurements gave significant differences between the means of clubbed and normal groups Table 37. Fig. 9 shows two of the four measurements, nail curvature and hyponychial angle, plotted against the physicians combined score. There was good correlation between the measurement and the score throughout the doubtful range. For the hyponychial angle there was no overlap between the normal and clubbed groups, unlike the other three methods. Plethysmography was the poorest discriminator.

The doubtful group was divided into 'doubtful normal' and 'doubtful clubbed' groups (Fig. 9) horizontal and vertical dotted lines, and those observations lying in the upper left and lower right quadrents were considered to be misclassified. The

hyponychial angle correctly classified 94% of the 50 finger casts followed by nail curvature 80%, plethysmography 68% and profile angle 66%. Table 38.

The incidence of radiological and pulmonary function abnormality was examined for the fifty individuals. The highest incidence of chest disease (as indicated by the Xrays and lung function) was found in the clubbed group and the lowest in the normal group. Table 39.

To exclude the possibility of methodological bias measurement of the hyponychial angle was carried out by two non medical observers unfamiliar with clubbing. Both found a similar degree of separation between normal and clubbed groups (5^{o} and 2^{o}) and similar misclassification rates.

As the normal group had been exposed to asbestos, finger casts of ten healthy normal workers in the LSHTM were made. The mean hyponychial angle in this group 186.1^{o}, range 178.5^{o} - 192.0^{o} was very close to that of the normals in the test group 187.0^{o} , range 176.5^{o} - 192.0^{o} (pooled SE 1.967^{o}).

It has often been claimed (Lovibond 1938, Just-Viera 1964) that clubbing starts in the first two digits and spreads later to the other digits. As this seems rather unlikely finger clubbing, measured by spherometer on all digits, was examined in the group of fifty workers. Fig. 10 shows the mean values for the five digits in normal doubtful and clubbed groups, for both hands separately. This shows that there are differences in curvature, between the digits, the thumb being least and the index finger most curved. It also shows that the abnormality occurs in both hands and in all digits. Therefore clubbing may be measured on any digit of either hand but comparison between individuals must be made on the same digit.

ACKNOWLEDGMENTS

I am very grateful to Dr. M.L. Thomson for all his help and encouragement while I was working at the LSHTM and I would like to thank the staff for their assistance. Also I am indebted to the management of the three factories as without their co-operation this study would not have been possible.

I would like to thank Beryl Tagg for her help in carrying out the tests, in particular, the electrocardiograph, measurement of peak flow, airway resistance by body plethysmograph, PAO_2 by ear oximeter and also preparation of finger casts.

Also, I would like to thank Professor P. Armitage for his helpful suggestions of suitable techniques for the statistical analysis and Miss J. Walford for her advice and help in the interpretation of these analyses.

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SUBJECTIVE ASSESSMENT AND OBJECTIVE MEASUREMENT OF FINGER CLUBBING

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Summary A criterion of finger clubbing was obtained, by a questionary, from 13 chest physicians to whom casts of the index fingers of 50 asbestos workers were circulated. The physicians were in good agreement that 7 of the fingers were definitely clubbed, 18 were normal, and the remainder were doubtful. This classification was used to evaluate four objective measurements. Of these, the best discriminator was the hyponychial angle, which distinguished normal and clubbed fingers without overlap. The validity of using this angle as a continuous variable for correlation with other indices of abnormality was indicated by the close rectilinear correlation with the physicians' assessment over the doubtful range. All 7 workers with definitely clubbed fingers had radiological abnormality; 5 had pulmonary-function defect and 2 had basal rales. As measured by longitudinal curvature, clubbing commences simultaneously, and progresses uniformly in all digits.

Introduction

SINCE Hippocrates first noted the association between finger clubbing and empyema (cited by Adams [1849])

many workers have described the morphological features (Lovibond 1938, Bigler 1958), pathology (Lovell 1950, Bigler 1958), and causation (Lovibond 1938, Mendlowitz 1938, Semple and McCluskie 1955, Ginsberg 1958) of this deformity but few have attempted to measure it precisely (Cudkowitz and Wraith 1957, Stavem 1959). An objective estimate of the degree of abnormality was required for correlation with clinical, radiological, and physiological data, obtained in a survey of asbestosis.

We have established a criterion of clubbing from the answers of experienced physicians to a questionary and used this to evaluate four objective measurements on the fingers.

Materials and Methods

Material

A negative impression of the right index finger, or the left if the right had been damaged, was obtained by pushing the finger into a cylindrical mould (3·5 × 1·3 in. diameter) containing dental impression material ('Tissutex'). After allowing approximately 2 minutes for the tissutex to harden, the finger was withdrawn and a positive cast made with plaster of paris (Kaffir D).

To obtain a criterion of clubbing, finger casts of 50 asbestos workers were sent in turn to 13 consultant chest physicians and others with experience in occupational medicine. They were asked to grade the casts as normal, doubtful, or clubbed. The degree of clubbing for each cast was scored by awarding 3 points where the physician's grading was "clubbed", 2 for "doubtful", and 1 for "normal"—i.e., maximum and minimum scores 39 and 13, respectively. Those fingers with a score of 37 or more were then classified as clubbed, those with a score of 15 or under as normal and the rest as doubtful.

Measurements

The lateral profile of each finger cast was outlined with a planimeter. Two angles were measured on this outline of the nail (fig. 1). One arm of both angles was constructed by a line AB drawn from the distal digital skin crease to the cuticle. A standardised profile angle (ABC) (similar to that of Lovibond [1938]) was constructed by a line BC from the cuticle through a point C on the nail a third of the axial distance from the cuticle to the finger tip. A second angle (ABD), which we have called the hyponychial angle, was completed by a line BD from the cuticle to the hyponychium (thickened stratum corneum of epidermis lying under the free edge of the nail).

The longitudinal curvature of the nail was measured in dioptres by a modified spherometer. This instrument is normally used to measure the power of lens. The curvature was recorded from the cuticle to a point 1 cm. along the centre

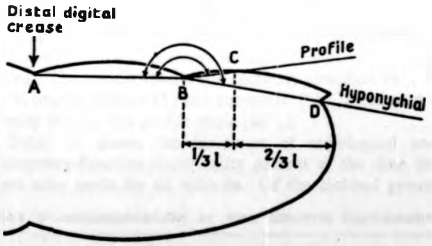

Fig. 1—Construction of profile and hyponychial angle.

of the nail and was routinely measured for all fingers on both hands of the 50 workers as well as on the casts.

The casts were made non-porous by coating them with latex, and the volumes of the terminal two phalanges were measured by plethysmography using water displacement. These volumes were divided by length to give the mean cross-sectional areas and that of the terminal phalanx was expressed as a percentage of that of the middle phalanx.

Results

The physicians were unanimous in grading six of the fifty casts as clubbed and nine as normal. When those fingers with no more than one "dissentient" or two "doubtful" votes were included in the normal and clubbed groups, 14% of the fingers were classified as clubbed, 36% as normal, and the rest as doubtful.

All four objective measurements gave significant differences between the means of clubbed and normal groups; all but the plethysmography were highly significant (table I). Fig. 2 shows two of the measurements plotted against the physicians' score. The hyponychial angle was the only measurement which showed no overlap between

TABLE I—USEFULNESS OF FOUR OBJECTIVE MEASUREMENTS IN DISTINGUISHING BETWEEN NORMAL AND CLUBBED FINGERS

Measurement	Mean normal (18)	Mean clubbed (7)	Pooled S.E.M.	t	P
Profile angle (°) ..	173·5	181·1	1·879	4·044	<0·001
Hyponychial angle (°)	187·0	209·4	2·690	8·302	<0·001
Curvature (dioptres) ..	8·42	16·0	1·416	5·353	<0·001
Plethysmography (%)	55·8	68·0	5·388	2·260	<0·050

the normal and clubbed groups; there was a separation of 3° between these groups. The hyponychial angle and the curvature seem to correlate well with the score throughout the doubtful range. Plethysmography was the poorest discriminator.

The doubtful group was then further subdivided into "doubtful normal", and "doubtful clubbed" groups at the midpoint of the physicians' score and at the midpoint of the mean normal and mean clubbed groups (vertical and horizontal dotted lines respectively in fig. 2).

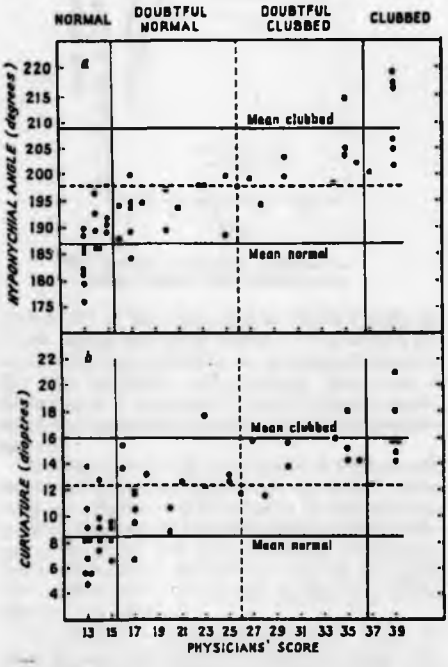

Fig. 2—Two of the objective measurements plotted against physicians' scores.

Physicians' score = 0·846°–142·5; s.e. = 0·0752.
Physicians' score = 1·948 dioptres–0·786; s.e. = 0·7512.

Observations lying in the upper left and lower right quadrants defined by these dotted lines indicate misclassification. Table II shows the misclassification in more detail. The hyponychial angle correctly classified 94% of all 50 fingers, followed by nail curvature (80%), plethysmography (68%), and profile angle (66%).

Table III shows the incidence of radiological and pulmonary-function abnormality present at the time the casts were made for all subjects. Of the clubbed group,

TABLE II—MISCLASSIFICATIONS BY FOUR OBJECTIVE MEASUREMENTS

Measurements	Errors in subgroup:			
	Normal (18)	Doubtful normal (16)	Doubtful clubbed (9)	Clubbed (7)
Profile angle	28%	63%	22%	0%
Hyponychial angle ..	0%	13%	11%	0%
Curvature	11%	44%	11%	0%
Plethysmography ..	28%	31%	56%	14%

TABLE III—X-RAY AND PULMONARY-FUNCTION ABNORMALITY INDICATIVE OF CHEST DISEASE

Subgroup	No.	Abnormal X-rays (%)	Abnormal pulmonary function (%)
Clubbed	7	100	71
Doubtful clubbed	9	44	33
Doubtful normal	16	37	0
Normal	18	28	6

all 7 showed radiological abnormality, 5 with asbestosis (linear markings and/or pleural thickening), 2 with healed tuberculosis. Of the 7, 5 also had pulmonary function abnormality (diffusing capacity for carbon monoxide <75% of predicted normal without significant obstruction) and 2 had extensive basal rales.

The mean longitudinal curvature for all digits of both hands measured directly on the 50 subjects is shown in fig. 3.

Discussion

The correlation between the physicians' score and the hyponychial angle was so striking that the procedure was examined in detail for methodological bias. This could be excluded in the physicians' appraisal since they were given no information about the subjects. However, the

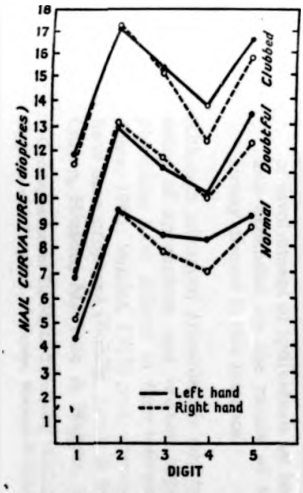

Fig. 3—Mean longitudinal curvature of normal, doubtful, and clubbed fingers.

measurement of the angle might be biased if made by persons familiar with the deformity. To obviate this, the measurement was repeated by two non-medical observers who were not familiar with clubbing. Both found a similar degree of separation (5° and 2°) between normal and clubbed groups and reported comparable misclassification-rates.

The normal group had been exposed to asbestos dust and its normality could therefore be questioned. Some check was obtained here by repeating all four measurements on finger casts of 10 healthy manual workers on the staff of this school. The mean, and range, of this group (186·1, 178·5–192·0°) accorded well with the test group (187·0, 176·5–192·0°). The pooled standard error of the difference was 1·967°.

The difference between Lovibond's (1938) figures for his profile angle and those reported here may be due to his use of the thumb rather than the index finger, or to other variations in technique. Like Lovibond (1938), Bigler (1958) did not describe his method of measuring the

profile angle in sufficient detail to permit comparison with our results. The spherometer provides a rapid, accurate assessment of curvature and has obvious advantages over the brass disc described by Stavem (1959).

It is often claimed (Lovibond 1938, Just-Viera 1964) that clubbing begins in the first two digits and spreads later to the other digits. Fig. 3 indicates that although there are inherent differences in curvature between the digits, the thumb being least and the index finger most curved, the abnormality seems to advance uniformly in all digits and in both hands. Thus although clubbing may be measured on any digit, comparison between individuals must be made on the same fingers.

The hyponychial angle, which from these results seems to be the best discriminator, may be superior because it combines to some extent the measurement of curvature and profile angle. The three points defining this angle may be readily obtained from a shadow of the live finger cast by any system giving parallel light, for example, a torch.

We thank Dr. J. C. Gilson for taking and reading the X-ray films, Miss Joan Walford for statistical advice, Mrs. O. L. Wade who devised the method for making the finger casts, and Dr. J. Colley, Dr. J. E. Cotes, Dr. J. H. M. Langlands, Dr. C. B. McKerrow, Dr. D. Muir, Dr. N. C. Oswald, Dr. W. R. Parkes, Dr. G. A. Rose, Prof. J. G. Scadding, Dr. W. J. Smither, Prof. O. L. Wade, Dr. W. F. M. Wallace for grading the casts. This study was supported by a research grant from the Medical Research Council.

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THE RELATIVE IMPORTANCE OF CLINICAL, RADIOLOGICAL AND PULMONARY FUNCTION VARIABLES IN EVALUATING ASBESTOSIS AND CHRONIC OBSTRUCTIVE AIRWAY DISEASE IN ASBESTOS WORKERS

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SUMMARY

1. The relative power of sixteen clinical, radiological and pulmonary function variables for evaluating asbestosis and chronic osbtructive airway disease has been assessed by principal component analysis of the data from a survey of 201 asbestos workers.

2. A decrease in the transfer factor (diffusing capacity) for carbon monoxide followed by a decrease in the vital capacity had the greatest power to measure the severity of both types of disease but had little ability to distinguish between the two.

3. In decreasing order of potency, the best indicators for distinguishing between asbestosis and obstructive airway disease were forced expiratory volume as a proportion of vital capacity, phlegm, radiological pleural thickening, cough and finger clubbing. Low values in FEV/VC and high values in phlegm and cough indicated obstructive airway disease: high values of pleural thickening and finger clubbing indicated asbestosis in the present context.

4. The analysis also provided numerical scores for each individual that could be plotted on a two-dimensional diagram. Orientation along one axis showed the degree of involvement of individuals by lung disease, whereas separation along the other axis depended on the nature of the disease process, asbestosis and obstructive airway disease in this instance.

Although advanced asbestosis is readily recognized, there is wide disagreement about the order of appearance and relative importance of the initial manifestations. Experienced physicians have differed in their interpretation of the same chest films (Williams & Hugh-Jones, 1960; Sander, 1955) and, although several radiological classifications of the disease have been proposed (Bohlig, Jacob & Muller, 1960; Sluis-Cremer & Theron, 1960; Caplan, Gilson, Hinson, McVittie & Wagner, 1965), none has yet been generally adopted. Finger

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clubbing and crepitations at the lung bases, although common in asbestosis, may be absent even in advanced stages of the disease. The usefulness of functional measurements has recently been stressed (Bader, Bader & Tierstein, 1968), but unless pre-exposure data are available their value is decreased by the considerable scatter which occurs even among normal subjects of the same sex, age and body size.

An objective method is required of ascertaining the relative importance of the clinical, radiological and pulmonary function variables and integrating them to provide a more reliable diagnosis and assessment of the severity of the disease. Since there is no firm criterion of asbestosis the method of discriminant analysis is not appropriate. Faced with the problem of evaluation, many authors have used the radiological category as a yardstick of the disease and have compared clinical and pulmonary function findings with it. This obscures the true relationship between these indices. Agreement in detail between these may enable a firm diagnosis of asbestosis to be made, but this is only likely in a proportion of cases or at a late stage of the disease.

The method of principal component analysis (PCA) (Hotelling, 1933; Kendall, 1961) used in this study makes no *a priori* assumptions but looks for communalities or trends in the results. The meaning of any such trends must, however, be determined by means external to the analysis. This paper describes the application of principal component analysis to the results from a comprehensive field survey of asbestos workers in whom all stages of the disease were believed to be present.

METHODS

Population

The study group comprised 201 Caucasian males who had been working with raw asbestos in three factories for at least 3 years. They made brake linings and insulating materials. They formed 69% of the total population (291) defined by these criteria, of whom 256 (88%) volunteered to be examined. The remaining fifty-five (21%) had one or more missing observations (fifty), or had been exposed to known inhalation hazards other than asbestos (five). (In twenty-eight the missing observation was *D*m; of the five with other exposures, three were to cotton, one to cotton plus chemicals and one in coalmining.) At the time of the survey examination fourteen of the 201 (7%) had been certified by the Medical Panels of the Pneumoconiosis Board as having asbestosis and were in receipt of compensation. A further ten were certified 1–3 years later.

Exposure

The duration of exposure to the dust was expressed as the 'number of years from first exposure' whether or not this was continuous. This has been shown to correlate more highly with asbestosis than 'years of exposure' (Knox & Beattie, 1954), no doubt because of the progressive nature of this disease.

Clinical

The presence or absence of crepitations and rhonchi was recorded (each coded 1, 0). A comparison was made between the findings of the experienced and highly competent factory physician and M.L.T., in which both examined independently twenty subjects, some of

whom had asbestosis, on the same morning. There was substantial agreement between these observers; the mean difference in respect of crepitations was not significant. Also noted were any deformities of the rib cage or cardiac abnormality that might cause pulmonary function or radiological change simulating asbestosis. Finger clubbing was measured as the hyponychial angle (Regan, Tagg & Thomson, 1967). Cough, phlegm and dyspnoea were coded as in the U.K. Medical Research Council's long questionnaire (Medical Research Council, 1960) which was completed with detailed attention to the occupational history. Electrocardiograms were made with thirteen leads, the correct positioning of which was facilitated by a special device (Rose, 1961). Early morning sputum samples were examined for asbestos bodies and fibres (UICC, 1965). In all, 156 specimens were obtained of which forty-six (30%) had asbestos bodies and ninety-eight (63%) had asbestos fibres.

Radiological

AP films were taken by the Pneumoconiosis Research Unit's (Penarth) mobile unit. They were read independently by three observers who later met and agreed on a final assessment. Abnormality of pattern, whether linear, reticular or blotchy and whether in one or both lungs, was coded 1, 2, 3 for the lower, mid and upper zones respectively. Pleural thickening was coded 1 if it was present only in the wall or diaphragm or both and 2 if it was present also in the mediastinum or fissure, whether in one or both lungs.

Before deciding on this coding many combinations of types of abnormalities and areas of involvement of both pleural and pulmonary radiological abnormality were plotted against the transfer factor, finger clubbing and crepitations. None of these alternative gradings appeared to be superior to the above simplified coding; it is clearly possible, however, that improvements may be made in these gradings on larger populations.

Pulmonary function

The vital capacity (VC) and residual volume (RV) were measured by spirometry and closed-circuit helium-dilution (Gilson & Hugh-Jones, 1949). Tne forced expiratory volume in 1 s (FEV_1) was obtained with a Gaensler-type spirometer (McKerrow, McDermott & Gilson, 1960) and the peak flow rate on a Wright–McKerrow meter (Wright & McKerrow, 1959). Since VC is decreased in asbestosis FEV as a proportion of VC (FEV/VC) was used as the most appropriate index of airway patency. The transfer factor (diffusing capacity) for carbon monoxide (Tl) and its membrane (Dm) and blood components were determined by the single-breath method in duplicate (McNeill, Rankin & Forster, 1958); the alveolar volume being obtained from the single-breath helium-dilution (Thomson, McGrath, Smither & Shepherd, 1961). The specific conductance (conductance/thoracic gas volume) was measured by constant-volume body plethysmograph (Dubois, Botelho & Comroe, 1956).

Principal component analysis

The aim of this analytical technique is to condense the data by finding those factors that represent independent attributes of lung disease. A linear transformation is applied to the original set of correlated variables to produce a new set of uncorrelated variables or components. Each component is extracted in the order of the magnitude of its contribution to the total variance of the original variables. The first few components usually account for most of the total variance and reveal the underlying nature of the variability in which

case the remainder can be ignored. A component score for each individual is calculated as a weighted sum of the values of the original variables after they have been standardized by subtracting the mean and dividing by the standard deviation. The individual scores plotted against the axes of the components may then show meaningful trends. The computer program used was No. BMDOIM, Health Sciences computing facility, UCLA.

RESULTS

The ECG, rhonchi and specific conductance were omitted after a preliminary principal component analysis which indicated that they had very low weightings on the important first and second components. (The ECGs were reported as being substantially similar to those of a normal population.) Sputum asbestos bodies and fibres were omitted because the counts showed little correlation with the main indicators of asbestosis or with exposure to asbestos. The peak flow rate was not used because it correlated highly with the more reliable FEV and FEV/VC.

TABLE 1. The sixteen variables used in the final analysis with their means and standard deviations for 201 asbestos workers

No.	Mean	SD
1. Age (years)	44·3781	10·0909
2. Height (cm)	169·3781	6·4200
3. FEV/VC (%)	71·3632	9·9771
4. VC (litres)	4·2066	0·9016
5. RV/TLC (%)	35·6219	9·3897
6. *T*l (ml/mmHg × min)	24·5383	6·7207
7. Exposure	51·9950	7·0735
8. Crepitations	0·1542	0·3621
9. Clubbing (degrees)	188·1294	7·7996
10. Cough	0·6965	0·7632
11. Phlegm	0·5572	0·7402
12. Dyspnoea	1·4229	0·7248
13. Smoking	98·7164	33·1656
14. *D*m (ml/mmHg × min)	53·3682	20·4264
15. X-ray pattern	0·4950	0·9022
16. X-ray thickening	0·4000	0·6799

X-ray thickening refers to pleurae and fissures; X-ray pattern, parenchymal abnormality; FEV/VC, forced expiratory volume (1 s)/vital capacity; RV/TLC, residual volume/total lung capacity; *T*l and *D*m, Transfer factor (diffusing capacity) of the lung and membrane respectively; exposure, year in this century when exposure commenced; clubbing as hyponychial angle (Regan *et al.*, 1967). Coding of remaining variables in the text.

The percentage of the total variance accounted for by the sixteen components was: (1) 26, (2) 13, (3) 10, (4) 7, (5) 7, (6) 5, (7) 5, (8) 5, (9) 4, (10) 4, (11) 3, (12) 4, (13) 2, (14) 2, (15) 2, (16) 1.

TABLE 2. Correlation coefficient matrix for the principal component analysis

	1 Age	2 Height	3 FEV/VC	4 VC	5 RV/TLC	6 TI	7 Exposure	8 Crepitations	9 Clubbing	10 Cough	11 Phlegm	12 Dyspnoea	13 Smoking	14 Dm	15 X-ray (pattern)	16 X-ray (thickening)
1. Age	1·0000															
2. Height	−0·1793	1·0000														
3. FEV/VC	−0·4163	0·1295	1·0000													
4. VC	−0·4945	0·4689	0·1567	1·0000												
5. RV/TLC	0·5558	−0·0959	−0·4578	−0·4484	1·0000											
6. TI	−0·5400	0·3109	0·3429	0·5643	−0·3736	1·0000										
7. Exposure	0·3272	−0·0408	−0·1720	−0·2244	0·2721	−0·2737	1·0000									
8. Crepitations	0·2239	−0·1352	−0·0287	−0·3817	0·1125	−0·4166	0·1035	1·0000								
9. Clubbing	0·0427	−0·1598	0·0886	−0·1830	0·0178	−0·2903	0·0466	0·3190	1·0000							
10. Cough	0·0600	−0·0836	−0·3123	−0·0872	0·1267	−0·2297	0·1023	0·1377	0·0024	1·0000						
11. Phlegm	0·0347	−0·1069	−0·2903	−0·0042	0·1324	−0·1017	0·0845	0·0355	−0·0150	0·5564	1·0000					
12. Dyspnoea	0·2615	−0·0673	−0·2642	−0·3317	0·1984	−0·3491	0·2117	0·1994	0·1397	0·3436	0·2300	1·0000				
13. Smoking	0·0626	−0·0740	−0·1780	−0·0580	0·0695	−0·2677	0·1703	−0·0015	0·1827	0·2496	0·1765	0·1483	1·0000			
14. *Dm*	−0·2789	0·2139	0·0549	0·3873	−0·1297	0·7030	−0·1330	−0·3832	−0·2448	−0·1346	−0·0260	−0·2351	−0·1772	1·0000		
15. X-ray (pattern)	0·1460	−0·0120	0·0633	−0·1903	−0·0231	−0·1688	0·1293	0·2631	0·2388	0·0586	0·0624	0·1352	0·0454	−0·1989	1·0000	
16. X-ray (thickening)	0·1325	−0·0920	0·0154	−0·3458	0·0644	−0·3626	0·2135	0·3216	0·3126	0·0618	−0·0831	0·1602	0·1155	−0·3329	0·4166	1·0000

The sign of 'Exposure' has been changed throughout to convert into 'years since first exposure'.

The first two components therefore accounted for only 39% of the variance. To find if the remaining components were meaningful the weights given to the variables in components 3–5 were examined in conjunction with the first two components. For each of the three factories co-ordinate points were plotted against two component axes for all combinations of the five components. Comparison between the factories showed no consistent trends, nor was the distribution of the variables about the axes meaningful.

TABLE 3. Relative power of sixteen clinical, radiological and pulmonary function variables to assess lung disease (component I) and to separate asbestosis from chronic obstructive airway disease (component II) in 201 asbestos workers

Component I			Component II		
Variables	Standardized weightings	Raw weightings	Variables	Standardized weightings	Raw weightings
*T*1	+0·416	+0·0613	FEV/VC	+0·416	+0·0416
VC	+0·356	+0·3948	Phlegm	−0·380	−0·5133
Age	−0·320	−0·0317	X-ray (thickening)	+0·350	+0·5147
*D*m	+0·309	+0·0151	Cough	−0·345	−0·4520
RV/TLC	−0·263	−0·0283	Finger clubbing	+0·315	+0·0403
Crepitations	−0·258	−0·7125	X-ray (pattern)	+0·293	+0·3247
Dyspnoea	−0·257	−0·3545	Rales	+0·288	+0·7954
X-ray (thickening)	−0·234	−0·3441	RV/TLC	−0·272	−0·0289
FEV/VC	+0·214	+0·0214	*D*m	−0·170	−0·0083
Exposure	−0·207	−0·0381	Dyspnoea	−0·152	−0·2097
Height	+0·193	+0·0300	Age	−0·124	−0·0122
Cough	−0·178	−0·2332	VC	−0·111	−0·1231
Finger clubbing	−0·172	−0·0220	Smoking	−0·101	−0·0030
X-ray (pattern)	−0·161	−0·1784	Exposure	−0·074	−0·0104
Smoking	−0·149	−0·0044	Height	−0·059	−0·0091
Phlegm	−0·117	−0·1580	*T*1	−0·035	−0·0052
Constant term		+2·1197			+5·1032

Increasing power to separate lung disease and health

Increasing power to separate asbestosis and obstructive airway disease

Further description of variables is given under Table 1.

The final analysis was done on the remaining sixteen variables which are listed with the means and standard deviations in Table 1. Table 2 gives the correlation matrix for the variables and Table 3 gives their standardized weightings (eigenvectors) in decreasing order of magnitude for components I and II. Fig. 1 is a plot of the 201 individuals, using the scores of component I on the horizontal axis and those of component II on the vertical axis.

The individual scores were calculated as follows:

$$Z_{A1} = \frac{W_1(x_1-\bar{x}_1)}{SD(x_1)} + \frac{W_2(x_2-\bar{x}_2)}{SD(x_2)} \ldots\ldots + \frac{W_{16}(x_{16}-\bar{x}_{16})}{SD(x_{16})}$$

where Z_{A1} is the score for subject A for component I, W_{1-16} are the weightings (eigenvectors) of the variables (Table 3) and x_{1-16} and $\bar{x}_{1-16}$ are respectively their observed values and means. The unstandardized weightings are also listed in Table 3; they enable any further subjects for whom the sixteen variables are known to be plotted on the diagram in Fig. 1.

When the individuals on the extreme right and left of Fig. 1 were identified and their clinical features examined it became clear that component I, which is usually of a general nature in the principal component analysis, was separating the healthy (on the right) from those with lung disease (on the left). Establishing the role of component II involved the argument that the features of severe asbestosis are known and universally agreed although their relative weightings and the order of their appearance in early disease are in doubt. Inspection

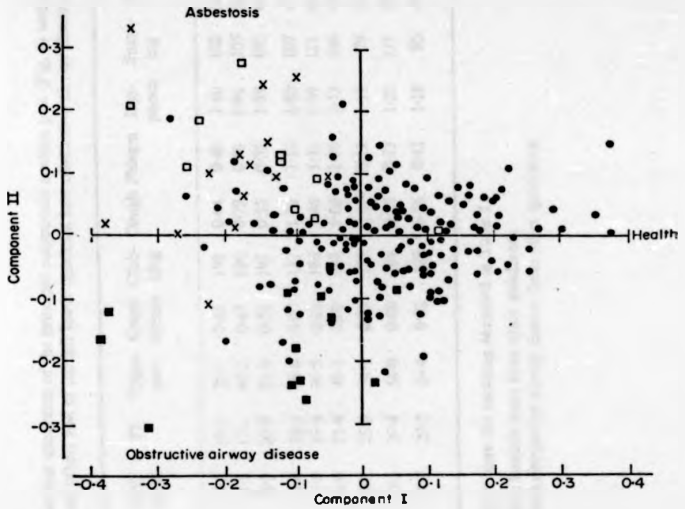

FIG. 1. Plot of 201 asbestos workers on the first two components. ×, Already certified as having asbestosis at the time of the survey; □, certified within 3 years after the survey; ■, presumptive obstructive airway disease.

of individuals on the left of Fig. 1 at the extremes of the vertical range indicated that component II was separating those with lung disease into the restrictive disease asbestosis at the top and chronic obstructive airway disease at the foot. This interpretation is supported by the stratification of the data given in Table 4 and Fig. 2.

Table 4 gives the means of the sixteen variables, unadjusted for age and height for individuals lying in each of the four quadrants of the PCA (Fig. 1). It also gives a further breakdown of those in the left (chest disease) quadrants into certified asbestosis and remainder (upper quadrant) and presumptive airway obstructive disease and remainder (lower quadrant). Without exception there are consistent trends in the means of all variables in both upper and lower quadrants, indicating decreasing health from right to left. Also there are consistent changes from upper to lower quadrants on both sides which conform with the known abnormalities in established asbestosis and chronic obstructive airway disease. Again the

TABLE 4. Means of the sixteen variables for 201 subjects in the four quadrants of the principal component analysis plot (Fig. 1) with further subdivision of the left upper quadrant into certified asbestosis and others and of the left lower quadrant into obstructive airway disease and others

	No.	Age	Height	FEV/ VC	VC	RV/ TLC	*T*1	Expo- sure	Crepi- tations	Club- bing	Cough	Phlegm	Dys- pnoea	Smok- ing	*Dm*	X-ray (pat- tern)	X-ray (thick- ening)
Left upper quadrant	53	49	167	72·7	3·53	37·1	19·3	50·2	0·49	193	0·64	0·40	1·60	103	39·7	1·11	1·09
Certified asbestosis	24*	48	168	73·3	3·55	35·5	17·2	48·2	0·67	196	0·79	0·50	1·96	105	33·7	1·29	1·25
Other	31	50	167	72·3	3·57	38·3	20·9	51·4	0·32	191	0·55	0·35	1·39	103	44·3	0·90	0·94
Left lower quadrant	44	51	168	62·9	3·90	43·4	20·1	48·6	0·07	187	1·20	1·16	1·80	107	47·3	0·33	0·27
Obstructive	13†	50	167	46·7	3·95	47·8	18·4	49·5	0·23	186	1·46	1·31	1·69	111	49·1	0·08	0·23
Other	33	51	167	68·3	3·96	41·6	21·4	48·3	0·00	187	1·06	1·06	1·73	106	49·4	0·42	0·27
Right upper quadrant	54	38	170	77·6	4·60	30·2	29·0	54·7	0·03	187	0·17	0·12	1·12	79	59·1	0·33	0·14
Right lower quadrant	50	41	172	70·0	4·81	33·3	29·4	54·0	0·00	184	0·95	0·73	1·23	111	68·4	0·14	0·05
Mean RUQ and RLQ	104	40	171	73·8	4·71	31·7	29·2	54·4	0·02	186	0·56	0·43	1·18	95	63·8	0·24	0·10

The column headings have the meaning described in Table 1.

* Includes two certified asbestosis cases from other quadrants.

† Includes two cases with obstructive airway disease from other quadrants.

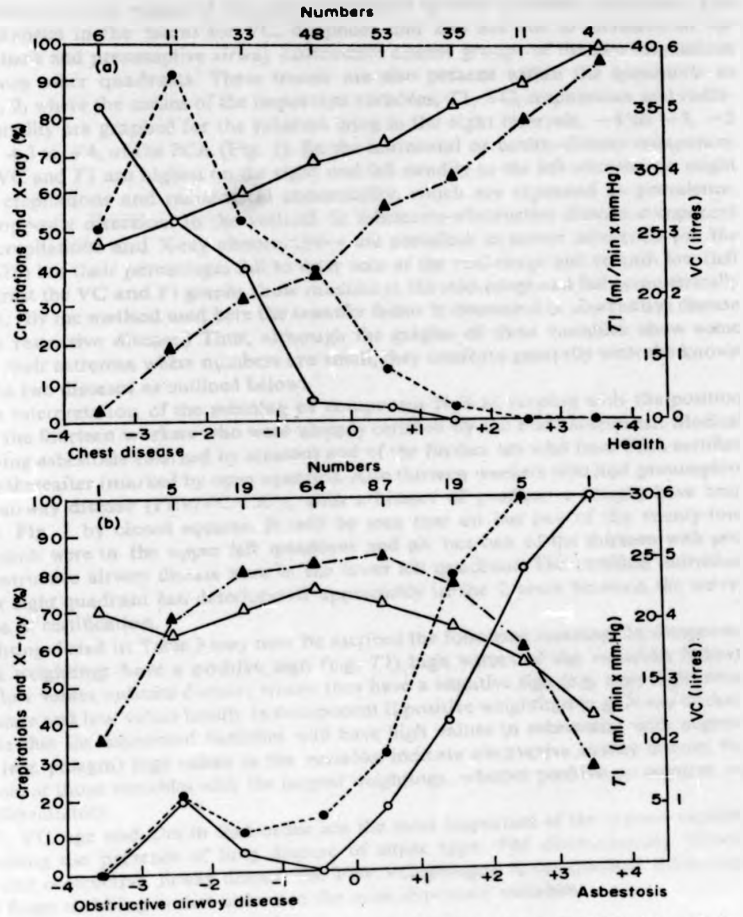

FIG. 2. Unadjusted means of the transfer factor (*TI*) (▲), vital capacity (VC) (△), and the prevalence of X-ray abnormality (●) and crepitations (○) for subjects lying within (a) the horizontal intervals (component I) of the PCA (Fig. 1), and (b) the vertical intervals (component II) of the PCA (Fig. 1).

expected differences in the means of variables are present in both quadrant subgroups. The slight inconsistencies in the means for VC, dyspnoea and *Dm* are due to inclusion in the certified asbestosis and presumptive airway obstructive disease groups of the two anomalous individuals from other quadrants. These trends are also present within the quadrants as shown by Fig. 2, where the means of the important variables, *T*1, VC, crepitations and radiological abnormality are graphed for the subjects lying in the eight intervals, -4 to -3, -3 to -2, ... $+3$ to $+4$, of the PCA (Fig. 1). In the horizontal or health–disease component (Fig. 2a) the VC and *T*1 are highest on the right and fall steadily to the left whereas (as might be expected) crepitations and radiological abnormality, which are expressed as prevalence, slope in the opposite direction. In the vertical or asbestosis–obstructive disease component II (Fig. 2b) crepitations and X-ray abnormalities are prevalent in severe asbestosis (on the right of Fig. 2b) but their percentages fall to near zero at the mid-range and remain low (left side). In contrast the VC and *T*1 graphs show maxima at the mid-range and fall symmetrically on both sides. (By the method used here the transfer factor is decreased in obstructive disease as well as in restrictive disease.) Thus, although the graphs of these variables show some anomalies at their extremes where numbers are small, they conform generally with the known findings in the two diseases as outlined below.

The above interpretation of the meaning of component II is in keeping with the position on Fig. 1 of the fourteen workers who were already certified by the Pneumoconiosis Medical Panel as having asbestosis (marked by crosses) and of the further ten who have been certified up to 3 years thereafter (marked by open squares). Also thirteen workers who had presumptive obstructive airway disease (FEV/VC$<55\%$ with a history of productive cough) have been identified in Fig. 1 by closed squares. It will be seen that all but two of the twenty-four certified subjects were in the upper left quadrant and all but two of the thirteen with presumptive obstructive airway disease were in the lower left quadrant. The certified individual in the upper right quadrant had deteriorated appreciably in the 2 years between the survey and the time of certification.

The weightings listed in Table 3 may now be ascribed the following meaning. In component I where the weightings have a positive sign (e.g. *T*1) high values of the variables indicate health and low values indicate disease; where they have a negative sign (e.g. age) high values indicate disease and low values health. In component II positive weightings (e.g. X-ray thickening) indicate that the associated variables will have high values in asbestosis; with negative weightings (e.g. phlegm) high values in the variables indicate obstructive airway disease. For each component those variables with the largest weightings, whether positive or negative, are the best differentiators.

Thus, *T*1, VC, age and *Dm* in that order are the most important of the sixteen variables for determining the presence of lung disease of either type. For discriminating between asbestosis and obstructive airway disease the FEV/VC, phlegm, X-ray (pleural thickening), cough and finger clubbing in that order are the most important variables.

DISCUSSION

Transfer factor and vital capacity

*T*1 and VC were potent measures of lung disease, heading the list in component I, but were poor differentiators between the two diseases because they were decreased to an equal extent

in both (Fig. 2b). In practice, however, since airway obstruction is usually absent in the diffuse fibroses including asbestosis and can be reliably excluded by the FEV/VC, *T*1 and VC become powerful indicators of disability and progression in asbestosis. Of the two, *T*1 has a somewhat higher weighting in component I, but the error of measurement is almost certainly greater than in the VC. Strictly, *T*1 is not interpretable when there is appreciable airway obstruction because of the associated uneven ventilation (Cadigan, Marks, Ellicott, Jones & Gaensler, 1961); in practice in the method of measurement used here it is usually decreased (Palmer & Diament, 1969), especially when hyperinflation supervenes (Fig. 2b).

Transfer factor of the membrane

In theory *D*m should be more discriminating than *T*1 where, as in asbestosis, the contribution of the membrane resistance to the total resistance should outweigh that of the blood component (McNeill *et al.*, 1958). In practice the technique is difficult and time consuming. It is greatly affected by error in the determination of CO; for example, the presence of carboxyhaemoglobin causes error in both indices but whereas its effect is small and can be neglected in *T*1, it must be measured and allowed for in *D*m. Airway obstruction causes greater artifact in the *D*m than in the *T*1. In the present study group twenty-eight subjects were omitted because the *D*m was not obtained for technical reasons. When a further principal-component analysis was done without *D*m but including these twenty-eight subjects the ranking of the remaining variables was unaltered and the weightings were substantially the same as in the first analysis. It was concluded that no bias had been introduced by their omission.

Total lung capacity

Like the FEV/VC the TLC is polarized about the mean since airway obstruction tends to increase it and restrictive disease to decrease it. It was not included, however, in the final variables for the analysis for the following reasons. Its value was lessened in field conditions because practical considerations imposed a limit on the length of time that could be allowed for equilibration of the inert gas. This must have caused it to be underestimated in some cases of airway obstruction. A PCA was in fact done with the same sixteen variables as in Table 3 including the TLC; the distribution of the individuals in the plot was little altered, the obstructive airway disease and asbestosis patients having almost identical relationships to each other and to the axes of the PCA.

FEV/VC

In asbestosis the increased elastic retraction exerted on the airway walls by the pulmonary fibrosis tends to widen and support them, with the result that the FEV/VC is normal or increased (Thomson, Pelzer & Smither, 1965). In obstructive airway disease FEV/VC is decreased. Like the TLC therefore this index is polarized above and below normality which may account for its great power to separate the two diseases.

RV/TLC

As airway obstruction becomes more severe the residual volume/total lung capacity (RV/TLC) ratio increases; this occurs as the result of a marked increase in RV in spite of a slight rise in TLC (Burrows, Fletcher, Heard, Jones & Wootliff, 1966). On the other hand, in

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asbestosis, as in most diffuse fibroses, there is a proportionate decrease in lung volumes with RV forming a normal proportion (<45%) of the TLC until a late stage of the disease when this ratio may rise to 50 or 60%. Thus it is not surprising that in early disease as found in these working men a raised RV/TLC is ranked by the principal component analysis as being more indicative of obstructive disease than of asbestosis, but that its power to differentiate between them is less than the FEV/VC.

X-ray films

The three film readers reported abnormality of X-ray pattern as blotchy, reticular or linear, of which expressions all three at one time or another had been considered indicative of asbestosis. The decision to score them equally was taken after preliminary correlation had shown no difference between them as indicators of asbestosis. In the same way bilateral pleural thickening was found to be no more indicative of asbestosis than unilateral (i.e. excluding the costophrenic angle). The increased score given to 'central' pleural thickening (mediastinum and fissure) as compared with wall and diaphragm is in keeping with the findings of Meurman (1966) on autopsy material that mediastinal involvement in asbestosis is relatively rare and only occurs in conjunction with peripheral pleural thickening. Since this paper was written a new international radiological classification of asbestosis has been proposed (UICC Committee, 1970) which describes all pattern abnormalities under the heading 'regular and irregular opacities'. It is clearly possible that different gradings arising from the classification may enhance the value of radiology in asbestosis.

Age and exposure

Age had a high negative weighting (−0·320) in component I and a low negative weighting in component II (−0·124). When all other variables were held constant therefore older persons were more likely to have lung disease, and of the two diseases they were somewhat more likely to suffer from airway obstructive disease than asbestosis. The same was true, to a lesser extent, of exposure (−0·207 in component I and −0·074 in component II). Due to the paucity in the group of young individuals who had a long exposure and of old individuals who had a short exposure it is probable that the analysis was unable to disentangle the effects of age and exposure. In practice, however, so long as the correct values for both are used in calculating the coordinates these two variables will be jointly allowed for in determining the location of subjects on the plot (Fig. 1).

Assessment of disability

For diagnosis of asbestosis the Pneumoconiosis Medical Panel (McVittie, 1965) requires that there has been adequate exposure to asbestos and also positive findings in at least two of the following: (1) basal crepitations, (2) finger clubbing, (3) radiological appearances, and (4) pulmonary function. The implication is that these four criteria occur randomly in any case and are of equal value in characterizing the disease. The analysis indeed showed that crepitations, clubbing and X-ray abnormalities had high and almost equal weightings as indicators of asbestosis but goes further in grading objectively according to their value the individual variables within the X-ray and pulmonary function categories. For example it is capable of indicating the relative merits of blotchy, reticular and linear forms of pattern

abnormalities although this was not attempted in this study because reticular and linear types were infrequently reported.

It is in the complex pulmonary function category, however, that the PCA has been of most help, enabling a more quantitative estimate of disability for assessing prognosis and, if applicable, the level of compensation and common law damages for which there have recently been many claims.

In the positive sense, the analysis agrees well with certification of asbestosis by the Panel (the misclassified subject in the upper right quadrant of Fig. 1 had deteriorated rapidly in the 2 years between the survey and the time of certification). The analysis, however, has anticipated by 1–3 years the diagnosis of the disease in the nine subjects lying in the upper left quadrant who have been certified since the survey. Also the position in that quadrant furthest to the left and upwards of at least seven more individuals who were not certified at the time this paper was written strongly suggested that they had asbestosis. Depending on their distances from the two axes the remaining thirty-one individuals in this quadrant were either disabled with features of both asbestosis and obstructive airway disease (near the X axis) or mainly had those of asbestosis but were less disabled (nearer to the Y axis).

Since chronic bronchitis is not at present compensatable by itself it is difficult to decide whether to compensate these subjects with mixed impairment and at what level. That three who were in fact already certified in addition to the anomalous individual in the lower left obstructive disease quadrant, may illustrate the difficulty. Thus, although it is not easy to define zones based on probability levels, the principal component analysis offers objective help in reaching this decision at least in the population of which this study group is a sample.

The rate of progression of asbestosis is probably more faithfully indicated by change in serial measurements of function than by extension of crepitations or finger clubbing or increase in radiological abnormality. Further information on this problem should be provided by a follow-up study after 3 years of the workers at present being analysed. Meanwhile the precision of functional data would be greatly increased by pre-exposure tests which should be mandatory for the FEV and VC before employment in dangerous atmospheres.

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