THE IMPORTANCE OF IRREGULAR OPACITIES ON THE CHEST RADIOGRAPH OF COALWORKERS

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ABSTRACT

The aim of this work is to examine the importance of small irregular opacities on the chest radiograph of coalworkers, in terms of their physiological and pathological relationships and their frequency and relation to coalwork exposure. A method of obtaining a numerical score for irregularity of radiographic opacities is described and thereafter used when comparing radiological irregular opacities with other variables.

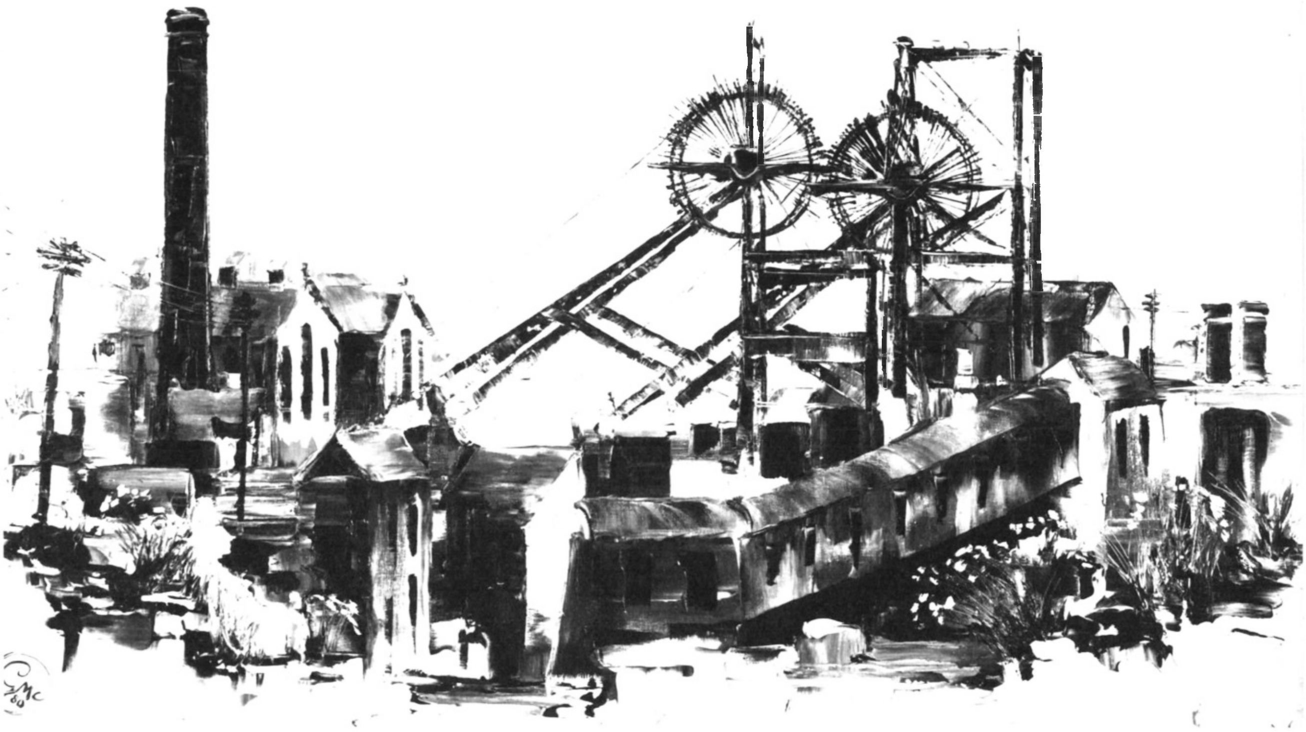
Radiographs were compared with lung function tests in 357 coalworkers who had attended the Cardiff Pneumoconiosis Medical Panel. Men with more irregular opacities had reductions in ventilatory capacity and gas transfer factor, after taking account of age, height, overall profusion of small opacities and smoking.

A method for quantitative assessment of post-mortem lung pathology in coalworkers is described. Amongst 123 deceased South Wales coalworkers, emphysema was common and was related to length of underground exposure in smokers. For 67 men radiographs within ten years of death were available. The degree of irregularity of radiological opacities, but not their overall profusion, was related to the amount of emphysema in the lungs. A group of 39 of the deceased coalworkers were compared with 48 deceased non-coalworkers, the men in both groups having died of ischaemic heart disease between the ages of 50 and 70 years. A separate study established that for these men the amount of

emphysema should not differ if there was no occupational effect. The coalworkers had a significant excess of emphysema, taking age and smoking into account.

The frequency of irregular opacities was studied among 124 coalworkers with pneumoconiosis routinely reattending the Cardiff Pneumoconiosis Medical Panel. Irregular opacities were common (present on two thirds of the current radiographs) and were related to age, smoking and length of underground exposure. A case-referent study of 515 men attending chest clinics in coalmining areas was undertaken and revealed an increased relative risk of irregular opacities (of moderate profusion) among coalworkers.

Taken together, the results of these studies indicate that irregular opacities in coalworkers are common and related to coalwork exposure. They are associated with reductions in lung function and with emphysema found at post-mortem. Their importance may have been previously under-estimated.



(Courtesy Miss C Exall)

TY MAUR COLLIERY

CONTENTS

LIST OF TABLES AND FIGURES

TABLES

FIGURES

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LIST OF ABBREVIATIONS

CWP - Coalworkers' pneumoconiosis

Kco - Transfer factor for carbon monoxide per unit lung volume

FEV_1 - Forced Expiratory Volume in One Second

FVC - Forced Vital Capacity

ILO - International Labour Office

NCB - National Coal Board

PFR - Pneumoconiosis Field Research

PMF - Progressive Massive Fibrosis

PMP - Pneumoconiosis Medical Panel

RV - Residual Volume

TL - Transfer factor for carbon monoxide for the lung

TLC - Total Lung Capacity

WLS - Whole Lung Paper Mounted Section

INTRODUCTION

Coalworkers' pneumoconiosis (CWP) has been recognised as an entity in Britain for around forty years, during which time substantial research effort has been aimed at understanding and preventing the condition. Despite this, there remain gaps and inconsistencies in the body of knowledge about coalworkers' pneumoconiosis. The textbook description of the appearance on the chest radiograph in simple coalworkers' pneumoconiosis is of small rounded opacities scattered through the lung fields. Within the last decade or so there has been increased interest in the significance of small irregular opacities on the chest radiograph of coalworkers. Such opacities are an accepted feature of occupational diseases such as asbestosis and berylliosis but their relevance to coalworkers' pneumoconiosis is not yet adequately established.

This work therefore sets out to examine the importance of irregular opacities on the chest radiograph in coalworkers. It aims to establish whether the recognition and quantification of irregular opacities on the radiographs of coalworkers could alter current concepts about simple coalworkers' pneumoconiosis.

The hypothesis put forward is that irregular opacities represent pathological changes and are associated with lung function deficit in coalworkers; and that they are common and related to coalwork exposure. In order to examine the facets of this hypothesis it has been necessary to undertake a number of different studies, using different populations. To avoid confusion, the study population used is clearly stated in each chapter.

It was necessary to develop a numerical way of expressing the 'degree of irregularity' of opacities on the chest radiograph and this is described in chapter two. Chapter four includes a section on the method used for quantifying post-mortem lung pathology. Chapter six is also methodological, describing how study populations for comparison of pathology in coalworkers and non-coalworkers were selected. Other than these methodological chapters, each chapter describes a study designed to test part of the hypothesis about irregular opacities.

The results of all the studies are brought together in the final section, which considers how far the evidence supports the overall hypothesis about irregular opacities.

CHAPTER ONE

BACKGROUND REVIEW

Page no.

Recognition of coalworkers' pneumoconiosis

In the early part of this century in Britain, the only serious respiratory disease resulting from underground coal-mining was thought to be silicosis. Coal miners were included in the Various Industries (Silicosis) Scheme, 1928, but could only have their condition recognised as occupational if they could prove they had been exposed to the dust of silica rock. Compensation was payable for total disablement or death due to the disease. In 1936, the Medical Research Council was asked by the Home Office and Mines Department to investigate the problem of chronic pulmonary disease among coal miners, especially in South Wales. Their report[1] distinguished between the silicosis that occured in men driving through quartz-containing rock (hard-heading workers) and a more common condition in other underground coal miners, particularly coal-face workers, which they called 'pneumoconiosis of coal-miners'. At about the same time, Gough[2] described the post-mortem findings of pneumoconiosis in a group of coal-trimmers on Cardiff docks exposed only to coal, and concluded that coal dust itself could be severely damaging to the lungs. The Workmens Compensation Act, 1943, meant that compensation was payable for 'pneumoconiosis' meaning 'fibrosis of the lungs due to silica dust, asbestos dust, or other dust and includes the condition of the lung known as dust reticulation'. A review of this period when coalworkers' pneumoconiosis first became recognised in Britain is given by Meiklejohn[3].

Radiology in coalworkers' pneumoconiosis

The diagnosis of coalworkers' pneumoconiosis in life depends on radiological features. An International Labour Office (ILO) conference of experts recommended 30 years ago that CWP should be defined in terms of radiological change and not in terms of the amount of dust found in the lungs after death[4]. Thus interpretation of features on the chest radiograph has a central role in the whole question of the definition of CWP. There is now a very large published literature on the radiology of coalworkers' pneumoconiosis.

When CWP was first recognised in Britain, the radiological appearances were classified as reticulation, nodulation, coalescent nodulation, massive shadows and multiple fluffy shadows[1]. Reticulation meant that the lung fields were altered by fine, net-like shadows and was regarded as the earliest sign of CWP. Early work on developing a classification of the radiological appearances came from South Wales[5,6,7,8]. They divided CWP into simple pneumoconiosis and complicated pneumoconiosis, or progressive massive fibrosis (PMF), and subdivided the simple form into categories 1,2 and 3 and the complicated form into categories A,B,C and D. The features characterising simple CWP were small, rounded opacities scattered through the lung fields, whereas PMF was characterised by the appearance of massive shadows mainly in the upper lobes. They produced evidence that the classification was repeatable and discriminating and bore some relation to pathological changes in the lungs[8]. Later work has confirmed that the category of simple pneumoconiosis defined on the basis of profusion of small rounded opacities is related to exposure to coalmine dust[9,9a,9b]. This basic classification has been modified and extended in subsequent years[4,10,11,12,13]. Following work by Liddell[14,15] the classification for simple CWP was expanded to a twelve-point scale. The later versions of the classification[11,12,13] were designed to be suitable for use with a wider spectrum of the pneumoconioses, in particular asbestos-related disease. They provided for the recording of irregular as well as rounded small opacities. The profusion of these irregular opacities was first read separately from that of the rounded opacities[12] and in the latest version of the classification[13] the overall profusion of all small opacities is recorded and then their size and shape is specified (see annexe 2(a)).

A number of workers have investigated the use of the classification, reflecting its position of importance in the diagnosis of CWP. It was recognised early that consistent readings could not be achieved without the use of a set of reference standard films[16]. Film quality has been shown to be an important factor in categorising radiological CWP[16,17,18] and in determining reading consistency[19,20] although some studies have found inter-reader agreement little affected by film quality[21,22]. The importance of liason between readers to improve inter-reader agreement has been stressed[23] and it has been shown that trained 'lay' readers can read as well as experienced physicians[20]. Nevertheless, disagreements between readers are common and therefore the use of a 'panel' of readers is recommended[19]. A study of readings based on the 1970 classification[12] found that agreement between readers for type of opacities (size and shape) was worse than for profusion of opacities[24].

Since the early days when the appearances characteristic of simple coalworkers' pneumoconiosis were agreed[6,8], there has been no real discussion in the literature as to whether these are the best, or exclusive, radiological reflection of the disease occuring in the lungs. Work has been focussed on better methods of detecting these appearances. This position has been changing over the last decade or so, with the suggestion that irregualr as well as rounded opacities ought to be considered in the radiology of CWP[25]. This may lead to a broadening of radiological criteria for diagnosing the condition. Part of the focus of this thesis is to gather evidence on whether irregular opacities should be considered as part of coalworkers' pneumoconiosis.

The agreement between radiology and pathology has varied between studies. While the radiological presence of PMF has been shown to be associated with respiratory disability and increased mortality, little association has been found between radiological category of simple CWP (i.e. profusion of small rounded opacities) and reductions in lung function or increased mortality.

Pathology in coalworkers' pneumoconiosis

Pathologists working in South Wales provided early and detailed descriptions of the lung pathology of CWP. Gough described both massive and nodular fibrosis, distinct from silicosis, in twelve coal-trimmers exposed on the docks exclusively to coal dust [2] though Belt and Ferris [25a] felt that silica was always involved even in the early stages of coalworkers' pneumoconiosis. Heppleston described the detailed structure of the dust foci of simple CWP [25b,26,27] ranging from small focal collections of dust in macrophages to rather larger focal lesions in combination with focal emphysema and occasional confluence of the focal lesions in more advanced cases. A technique was developed of producing paper-mounted whole lung sections which facilitated the study of lung pathology in CWP [28,29]. The pathologists noted that emphysema was invariably related to the dust foci of simple CWP and considered it an integral part of the condition [27,30,31].

There has been disagreement between pathologists about terminology for the emphysema occuring in relation to simple CWP. Heppleston distinguishes between focal emphysema related to dust foci and other types of emphysema that may occur in coalworkers as well as in the general population [27,32]. Recently, in a study of emphysema in coalworkers and non-coalworkers, the term focal emphysema was extended to include even severe grades of destructive emphysema in coalworkers [33]. This use of the term focal emphysema was criticised on the grounds that it would include most emphysema occuring in coalworkers [34]. It has been suggested that focal emphysema, as described by Heppleston, would not lead to any functional impairment [35].

Post-mortem surveys have found an excess of emphysema in coalworkers and ex-coalworkers compared with non-coalworkers [33,36,37]. However, the survey in America [36] used a 'control' group which excluded subjects with chronic respiratory disease and the study in South Wales [33] was criticised on the grounds that the coalworkers in the study were unrepresentative [39,40] of the population from which they derived, with their apparent excess of emphysema due to selection factors.

The pathological features of PMF have been described in detail [41,42] including studies of ultrastructure and biochemical analysis of areas of PMF [43,44,45]. Areas of PMF may give rise to 'scar' emphysema in the lung, but the emphysema in the surrounding lung is often apparently unrelated to the PMF [46].

In some coalworkers coming to post-mortem a severe form of pigmented emphysema, sometimes accompanied by mild interstitial fibrosis, is found either in localised areas or generally through the lungs [32,47]. The dust may no longer be discernible as discrete foci in these circumstances [47]. Wagner has described a type of 'centrilobular interstitial fibrosis' where the dust foci are seen to straggle out into the surrounding tissue [48]. There is disagreement as to whether this condition results from dust accumulation[47] or whether the dust is secondarily laid down in abnormal areas of lung[32]. Evidence from animal studies suggests that less dust accumulates in emphysematous areas of lung[49].

Lung function in coalworkers' pneumoconiosis

Studies of lung function in groups of coalworkers have been numerous and have ranged from large studies of population samples using simple tests of lung function to studies of selected individuals undergoing detailed tests. Direct comparisons between results from different studies are often difficult because of the different selection of subjects and the different tests used. However, some general points emerge.

There is little doubt that coalworkers with PMF have reductions in lung function, and this has been shown repeatedly[50,51,52]. In simple pneumoconiosis the situation is less clear. Early studies reported little or no loss of ventilatory capacity in coalworkers with simple CWP compared with coalworkers without CWP (radiologically) or with non-coalworkers[50,53]. A number of authors have reported defects in gas transfer in groups of coalworkers[54,55,56,57,58,59]. An increased residual volume in coalworkers has been reported[60,61] and abnormalities of frequency dependence of compliance[62] and other indices of small airways function[63] have been found.

Results from the National Coal Board's large Pneumoconiosis Field Research programme [64] indicated that there is a reduction in ventilatory capacity in coalworkers related to their cumulative dust exposure [65,66]. A study of coalworkers in S.W. Virginia reported a fall in ventilatory capacity related to length of underground work after taking account of age, smoking and category of pneumoconiosis [66a]. This suggests that there may be some dust-related loss of lung function which is not reflected by the classical radiological appearances of simple pneumoconiosis, since these have not been found to be associated with reduced lung function.

Since CWP in life is conventionally diagnosed and its severity assessed radiologically, the question of whether lung function abnormalities found in coalworkers are due to CWP inevitably involves comparison between lung function and radiological findings. Attempts to do this are discussed below.

<u>Relations between radiology, lung function and pathology in coalworkers' pneumoconiosis</u>

Radiology and pathology

The radiological category of CWP has been found to be associated with the amount of dust found in the lungs after death [67,68,69,70]. A reasonably good association was reported between radiological category of CWP and number and type of dust foci identified on whole lung paper sections in a group of 238 South Wales coalworkers with chest radiographs within two years of death[71], and a similar result came from a study of 77 coalworkers in the United States[72].

Rossiter reported that the category of CWP was related to both total lung dust content and to the amount of focal emphysema[68]. Leigh and co-workers have reported a significant positive regression of severity of emphysema on severity of radiological pneumoconiosis in a large series of Australian coalworkers[72a,b]. However, a recent post-mortem study of 95 coalworkers in South Wales found that the amount of emphysema in the lungs was not related to the category of CWP on the chest radiograph (in terms of rounded opacities) although it was related to the profusion of irregular opacities on the radiograph[25]. Similar results were reported from a study by the Institute of Occupational Medicine of 500 coalworkers' lungs: emphysema was related to the presence of irregular opacities but not to the profusion of rounded opacities[75]. It has been suggested that the presence of emphysema may tend to mask dust foci radiologically[73,74], so that although the amount of emphysema increases with the dust foci found pathologically, it does not relate to increasing radiological category of CWP. This could explain the findings of a study of 100 coalworkers' radiographs which found less radiological evidence of emphysema on the films with higher categories of simple CWP[74a]. Two studies have reported that the smallest type of rounded opacities ('p' type) are related to more pathological emphysema than the larger rounded opacities[33,75].

Radiology and lung function

Most studies have failed to find an association between radiological category of simple CWP and reductions in ventilatory capacity [53,50,52] although it has been reported from the NCB Pneumoconiosis Field Research programme that they found a very small reduction in ventilatory capacity with increasing category of simple CWP [51] and an increase in respiratory symptoms with category of simple CWP [75a]. A post-mortem study of Australian coalworkers found a significant negative correlation between a measure of ventilatory capacity and radiological pneumoconiosis [72b]. Reductions of other aspects of lung function in coalworkers (see above) have also been found to be unrelated to radiological category of simple CWP [58,62] but two studies have reported an increase in residual volume related to category of CWP [61,75b] These results have been used to argue that simple CWP does not result in any appreciable reduction in lung function [53,50,76,77] since the diagnosis and assessment of progression of CWP is based on radiological criteria.

Other radiological features in coalworkers have been related to abnormalities of lung function. The effect of size of rounded opacities has been studied and a number of authors have reported defects in gas transfer in coalworkers with 'p' type opacities compared with those with larger opacities [57,54,55,78,56,79]. Increased lung compliance [54,79], and increased exercise ventilation [55] and increased size of pulmonary air spaces [79a] have also been reported in men with 'p' type opacities. In 95 coalworkers, the profusion of irregular opacities on the chest radiograph, but not the profusion of rounded opacities, was related to reduction in ventilatory capacity[25]. Later, a large study of working miners in the USA found that amongst smokers those with irregular opacities on the radiograph had a lower ventilatory capacity and a higher residual volume and total lung capacity than those with rounded opacities. This effect was not found amongst the non-smokers[80]. A follow-up study of 125 men with simple CWP recently reported that irregular opacities were associated with a reduction in gas transfer factor[79].

Lung function and pathology

The difficulties involved in trying to relate lung function to post-mortem pathology in coalworkers have recently been reviewed[81]. In a study of 247 coalworkers with CWP, the amount of emphysema at post-mortem was related to the ventilatory capacity measured by the Pneumoconiosis Medical Panel (PMP) during life[33]. A similar finding was reported in Australian coalworkers[82] and recently a study of pathology in 500 coalworkers reported more emphysema in those with reductions in ventilatory capacity, who had also had greater dust exposure[82a]. In Welsh coalworkers no association was found between post-mortem evidence of chronic bronchitis, as judged by the Reid Index[83] and ventilatory capacity in life, nor was the Reid Index any higher among the coalworkers than among a group of non-coalworkers[84]. In Australia, however, an association was found between an index of chronic bronchitis and ventilatory capacity in life in 136 dead coalworkers[85]. A post-mortem study of 108 coalworkers with PMF suggested that both the size of the PMF and the extent of the emphysema in the lungs contributed to the degree of reduction in ventilatory capacity in life, and that the two contributions were mainly independent of one another[46].

From these various studies, the most consistent fact to emerge in regard to simple pneumoconiosis is the relation between post-mortem emphysema and reduction in lung function during life. The question remains as to whether this emphysema is part of the pneumoconiosis or whether it is occuring co-incidentally.

Disability in coalworkers' pneumoconiosis

This controversial and emotive topic is included only because some of the literature about it is relevant to the substance of this thesis. As mentioned above, it is argued by many that simple CWP does not disturb lung function to any great extent and is not therefore a cause of disability[76,77]. This is supported by studies reporting no increase in mortality in relation to category of simple pneumoconiosis, although coalworkers were found to have a higher mortality than non-coalworkers particulary from respiratory diseases[86,87,88]. Others have argued that disability due to simple CWP may be masked by an uneven distribution of chronic bronchitis amongst radiological categories of simple CWP[89,89a], or that much disability in simple CWP is actually due to associated emphysema[90]. The question arises as to whether chronic bronchitis and emphysema can be considered to be 'occupational' in coalworkers. There is evidence from the National Coal Board (NCB) Pneumoconiosis Field

Research (PFR) programme that chronic bronchitis, with reduction in ventilatory capacity, is related to cumulative dust exposure in coalworkers [91,65]. As mentioned above, post-mortem studies have demonstrated an excess of emphysema in coalworkers [33,36,37] and an association between the amount of emphysema at post-mortem and the number of years spent on the coalface has been reported [82].

An excess risk in a group does not prove causation in individuals, particularly for common diseases such as chronic bronchitis and emphysema, and these conditions are not accepted as Prescribed Industrial Diseases in coalworkers. Disability benefit is payable for disability considered to be due to CWP, although disability from chronic bronchitis or emphysema may be partially taken into account when deciding what percentage disability to award [92]. As a result, the disability benefit received by coalworkers is not related to their overall respiratory disability [93,94]. This inevitably causes discontent and the working of the system has been criticised [60,89].

In the case of emphysema, for many years pathologists have described some emphysema as part of simple CWP [30,27] although there is disagreement as to where the dividing line, if any, comes between this emphysema and that unrelated to CWP [32,33]. An argument could be put forward for considering emphysema in coalworkers to be an integral part of coalworkers' pneumoconiosis. If emphysema were to be considered part of CWP for certification purposes, a substantial increase in certifications and in amount of disability benefit paid could be expected. This is because, at present, coalworkers with emphysema but without category 2 simple CWP on the chest radiograph are not certified and for many who are certified their major disability results from emphysema.

<u>Summary of the present position</u>

The current position in coalworkers' pneumoconiosis is that it is diagnosed on the basis of finding small rounded opacities in the lung fields on the radiograph, with a suitable occupational history. While the profusion of small opacities is related to coal mine dust exposure, to dust content of the lungs and to dust foci found pathologically, it is not related to reductions in lung function. The presence of radiological PMF agrees with pathological findings and is an undisputed cause of respiratory disability and increased mortality.

Other radiological features have been related to abnormalities in lung function: the size of rounded opacities and the presence of irregular opacities. Irregular opacities have also been related to post-mortem emphysema.

Understanding the significance of irregular opacities in coalworkers could be important in assessing lung function changes in simple pneumoconiosis and in a critical assessment of the adequacy of the current radiological definition of CWP. The necessity for further studies about irregular opacities was noted in a review of the NCB PFR programme[95].

CHAPTER TWO

IDENTIFICATION AND QUANTIFICATION OF IRREGULAR OPACITIES ON THE CHEST RADIOGRAPH OF COALWORKERS

Recording size and shape of small opacities

The 1980 I.L.O. Classification of Radiographs of the Pneumoconioses [13] provides that the category of profusion of small opacities recorded includes small opacities of all types, rounded and irregular together. The previous classification [12] provided that the profusions of rounded and irregular opacities should be recorded separately. The 1980 classification requires instead that the overall profusion of all small opacities is first recorded and then requires an assessment of their size and shape.

For the readings of radiographs used in this work, the 1980 classification was used. A scheme based on this classification was developed to score the degree of irregularity of opacities at any given category of profusion, ignoring the size of these small opacities. For the pilot study on lung function and lung pathology in relation to irregularity of opacities described in Annexe 1, an early version of this irregularity score was used. For all the subsequent work a later version of the irregularity score was used. The two versions differ only in detail and can be 'translated' one to the other without difficulty.

Having recorded the overall profusion of small opacities the reader, using the 1980 classification, then records their size and shape with a two letter combination. The detailed instructions given in the classification for recording size and shape are reproduced in annexe 2(a). The first letter of the combination denotes the major type of opacity present and the second letter denotes the minority type of opacity present. If the opacities are all, or almost all, of one type then the same letter appears in both first and second position in the combination. Annexe 2(b) shows a specimen 'reading sheet' used by readers for recording their findings according to the 1980 classification.

The irregularity score

The irregularity score is calculated from the two letter combination for size and shape recorded for the opacities on the radiograph. In calculating the irregularity score, only shape is taken into account.

p,q,r are used to denote rounded opacities of increasing size.
s,t,u are used to denote irregular opacities of increasing size.

Letter in first position	Letter in second position	Irregularity Score
p,q or r	p,q or r	0
p,q or r	s,t or u	1
s,t or u	p,q or r	2
s,t or u	s,t or u	3

Thus an irregularity score of 0 indicates that the reader recorded the opacities as all, or almost all, rounded. An irregularity score of 3 indicates that the reader recorded the opacities as all, or almost all, irregular.

In the early version of the irregularity score used in the study described in Annexe 1, the irregularity score for the individual readers was averaged for all the readers. In the later version of the score, used in the main part of the work, the irregularity scores for the three readers were summed to give an overall irregularity score with range 0 - 9. This overall irregularity score was found to be more convenient to work with. Using this later irregularity score, a value of less than 3 indicates practically no irregular opacities, a score of 3-5 indicates that at least some irregular opacities were recorded but were not the predominant type of opacity recorded, a score of 6 or more indicates that irregular opacities were the major type of opacities present. If one or two of the three readers did not record small opacities then the score was calculated from the readers who did give a reading and multiplied appropriately to correspond to three readers. If the median profusion of small opacities recorded by the three readers was 0/0 on the 12 point scale then no irregularity score was recorded for the radiograph.

Validation of the irregularity score

The irregularity score is a new concept and it is necessary to demonstrate that it reflects a particular radiological feature in such a way that increases in the score represent increases in that feature. Evidence is presented in later chapters that the irregularity score is related to both lung function changes and lung pathology features. In the case of lung function there is a linear relationship between increase in irregularity score and decrease in certain lung function variables. This is evidence that increases in the score are very unlikely to be random. Whatever the irregularity score represents, it would seem to be a useful feature to record since it is related to changes in both lung function and lung pathology.

There is some evidence to support the belief [24] that inter-reader agreement on type of opacity is worse than on category of profusion. This was based on readings using the 1970 classification of radiographs. The readings of three readers for one of the studies in this work (see Chapter 3) have been used to check for inter-reader agreement on shape of opacities.

There were 340 films for which all three readers recorded small opacities. The irregularity scores for these films together with the separate scores for the three readers are shown in table 2.1. Except for the extremes, a given score can be produced in several ways. For example, a score of 3 could represent all three readers recording rounded as the dominant type and irregular as the secondary type, one reader recording the opacities as completely irregular and the other two readers as completely rounded, or an intermediate situation. The table shows that within a given irregularity score there was generally (score 6 is the only exception) a predominance of triplets with close agreement between the readers. There was significant evidence of agreement between readers although it was not as good as that for the major categories of profusion of small opacities for the same films. For irregularity 53% of the comparisons between any two of the readers agreed exactly and only 8% differed by two or more categories on the 0 to 3 scale; the corresponding figures for profusion of small opacities were 59% and 2%. Chapter 3 gives details of the study from which these figures have been taken.

The three readers for the study in Chapter 3, and indeed the readers for all the studies in this thesis, had discussed the question of irregular opacities in the radiology of coalworkers' pneumoconiosis among themselves. They were in agreement about interpretation of the instructions in the 1980 ILO classification for recording of size and shape of small opacities. There was thus good reason to believe that they were all 'looking for the same thing' when recording irregularity of opacities so that it was reasonable to combine their readings into a single irregularity score. If other readers were to be used in deriving an irregularity score, it would be important to first check that they were in agreement about interpretation of size/shape recordings of opacities.

Repeatability of the irregularity score

In none of the studies reported in this thesis were the radiographs read more than once by the same panel of readers. Therefore, the repeatability of the irregularity score could not be estimated from these studies. It was possible, however, to have a preliminary look at repeatability of the score using a set of radiographs of slate workers which were read on two occasions, by the same three readers using the 1980 ILO classification of radiographs.

The radiographs were those used as 'trigger' films during two separate reading sessions. 'Trigger' films are read by the readers together before sessions begin and an 'agreed' reading decided. They are then scattered through the films to be read and read in the usual way, except that the clerk then tells the reader the agreed reading compared with his/her present reading. This helps to prevent over- and under-reading tendencies during long reading sessions. There were a total of 58 of these radiographs, of which 28 were read as more than median category of profusion 0/0 on both occasions. These 28 were used to examine repeatability of the irregularity score.

Table 2.2 shows the median category of profusion and the irregularity score on the two occasions for the 28 radiographs. Table 2.3 shows the comparison of irregularity scores on the two occasions. Agreement was generally good: for 10 radiographs the irregularity scores were identical, for a further 12 within one scale point, for another 3 within two scale points, and for only 3 greater than two scale points different.

These data are encouraging but clearly there is a need for more thorough studies of repeatability of the irregularity score under differing circumstances.

Summary

A score was developed to reflect the relative predominance of irregular versus rounded small opacities on chest radiographs. It was derived from assessments of 'size and shape' of small opacities made when using the 1980 ILO Classification to record features of radiographs. Size of the small opacities is ignored in calculating the score. For three readers combined the score ranges from 0 for completely rounded opacities to 9 for completely irregular opacities.

It was found that agreement between readers for irregularity of opacities was not much worse than for major category of profusion of opacities. A small group of radiographs read twice indicated that the irregularity score was repeatable. Later chapters using the irregularity score show that it is related to changes in lung function and lung pathology. This suggests that the score is really reflecting some radiological feature changing in relation to other variables.

The other studies reported in this thesis use the irregularity score as a measure of the degree of irregularity of small opacities on the radiograph. They assume that an increase in score occurs with increase of irregularity of opacities (i.e. that the score is progressive). They do not assume linearity in the relationship between the score and the irregularity of opacities, nor between the score and other variables.

Table 2.1

Contributions to the overall irregularity score by three readers showing the degree of agreement between them.

Overall irregularity score	**Separate scores from the three readers**			**Number of films**	
0	0	0	0	87	
1	1	0	0	74	
2	(1	1	0	49)	
	(2	0	0	9)	58
3	(1	1	1	27)	
	(2	1	0	18)	48
	(3	0	0	3)	
4	(2	1	1	25)	
	(2	2	0	0)	28
	(3	1	0	3)	
5	(2	2	1	11)	
	(3	1	1	3)	16
	(3	2	0	2)	
6	(2	2	2	4)	
	(3	2	1	11)	16
	(3	3	0	1)	
7	(3	2	2	4)	
	(3	3	1	4)	6
8	3	3	2	5	
9	3	3	3	2	

The table only includes the 340 films for which all three readers recorded small opacities. See Chapter 3 for the study from which this data is taken.

Table 2.2

Median category of profusion and irregularity score for radiographs read on two occasions by the same three readers.

First reading		Second reading	
Median Profusion	**Irregularity Score**	**Median Profusion**	**Irregularity Score**
2/2	0	2/2	0
2/3	0	2/3	0
0/1	9	1/0	6
1/1	7	1/1	9
1/2	1	1/2	2
1/1	3	1/1	3
1/0	0	1/1	0
1/2	0	1/2	1
3/3	0	3/3	2
1/0	7	1/0	3
0/1	0	1/1	0
1/1	6	1/1	3
0/1	6	1/0	7
2/2	1	2/2	0
2/3	1	2/2	2
1/1	0	1/2	0
1/2	4	1/1	4
1/0	2	0/1	1
1/0	1	0/1	4
1/1	3	1/1	2
1/0	1	1/0	1
1/1	4	0/1	3
3/3	0	3/2	0
1/2	0	2/2	1
1/2	4	1/0	4
2/3	0	3/3	1
1/1	2	1/1	2
1/2	1	1/1	2

These 28 radiographs were 'trigger' films of slateworkers used on two occasions when reading series of slateworker films. The same three readers read the films on both occasions.

Table 2.3

Comparison of irregularity scores on first and second readings of radiographs.

Irregularity score on 1st reading	Irregularity score on second reading.									
	0	1	2	3	4	5	6	7	8	9
0	6	4	1							
1	1		3		1					
2		1	1							
3			1	1						
4				1	2					
5										
6				1			1			
7				1						1
8										
9								1		

The full readings of the radiographs on the two occasions are given in table 2.2

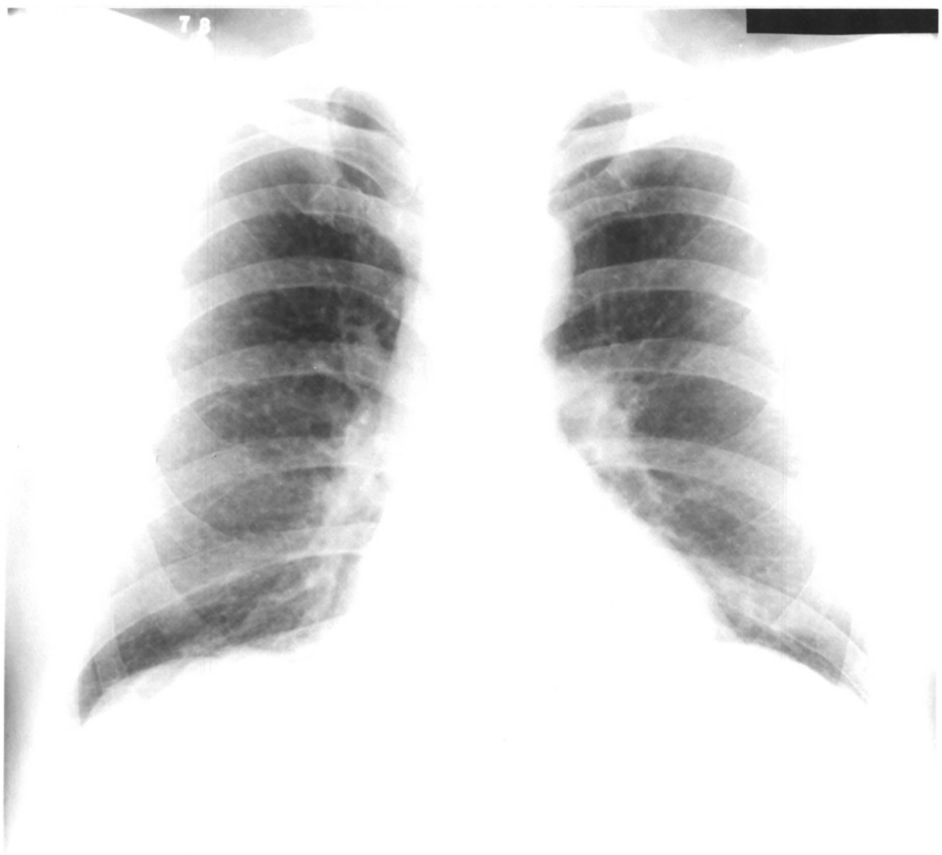


Figure 2.1 (a).
Radiograph read as category 2/1 for profusion of small opacities (median of 3 readers) and with an irregularity score of 0.

Figure 2.1 (b).

Detail from fig. 2.1 (a)

showing rounded opacities

in the right mid-zone.

Figure 2.2 (a)

Radiograph read as category 3/2 for profusion of small opacities (median of 3 readers) and with an irregularity score of 2.

Figure 2.2 (b).

Detail from fig. 2.2 (a)

showing rounded opacities

in the right mid-zone.

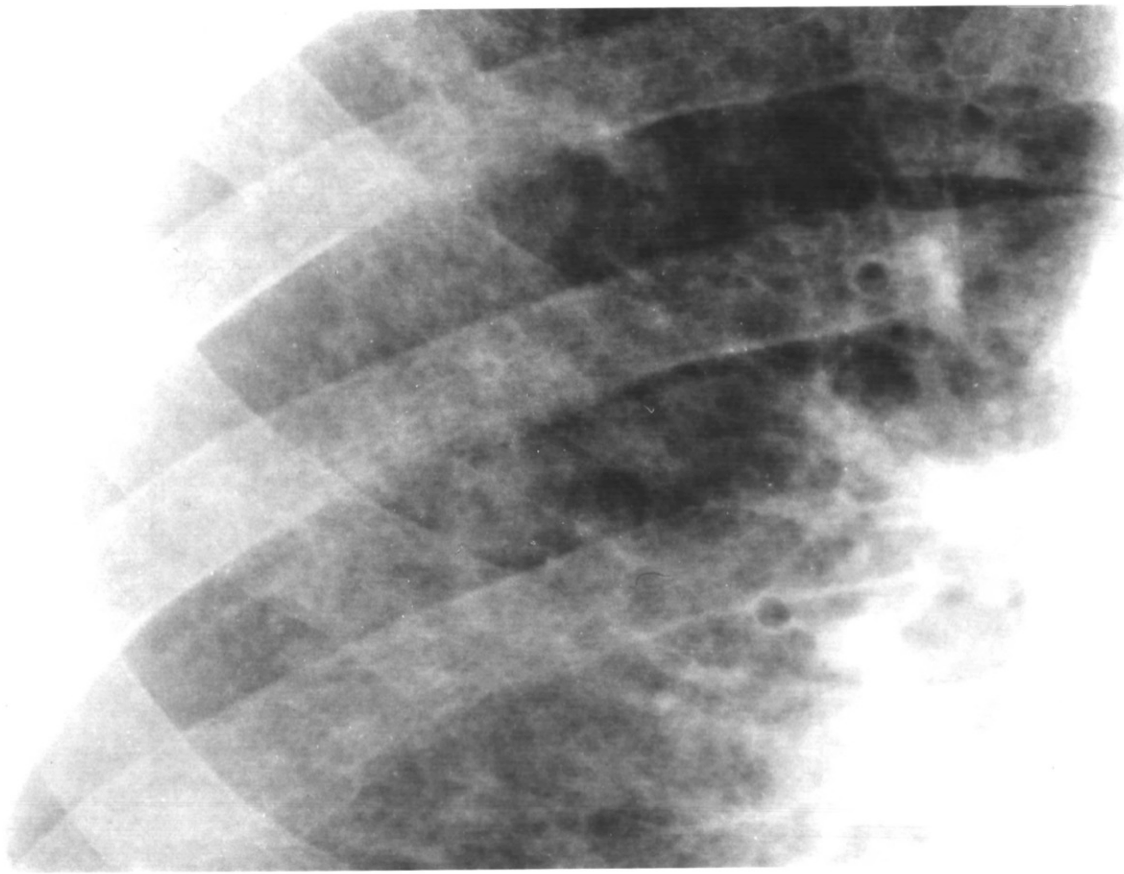


Figure 2/3 (a).

Radiograph read as category 2/2 for profusion of small opacities (median of 3 readers) and with an irregularity score of 6.

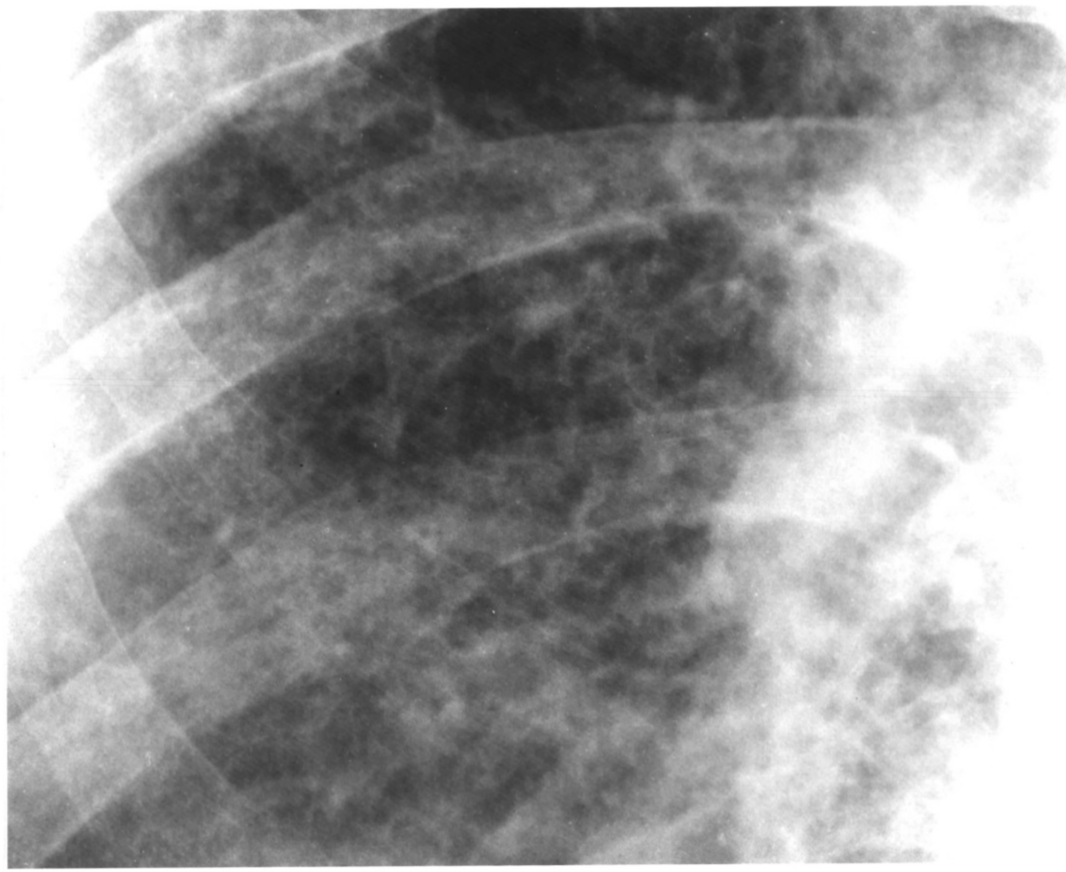
Figure 2.3 (b).

Detail from fig. 2.3 (a)

showing mainly irregular opacities

and some rounded opacities in the

right mid-zone.



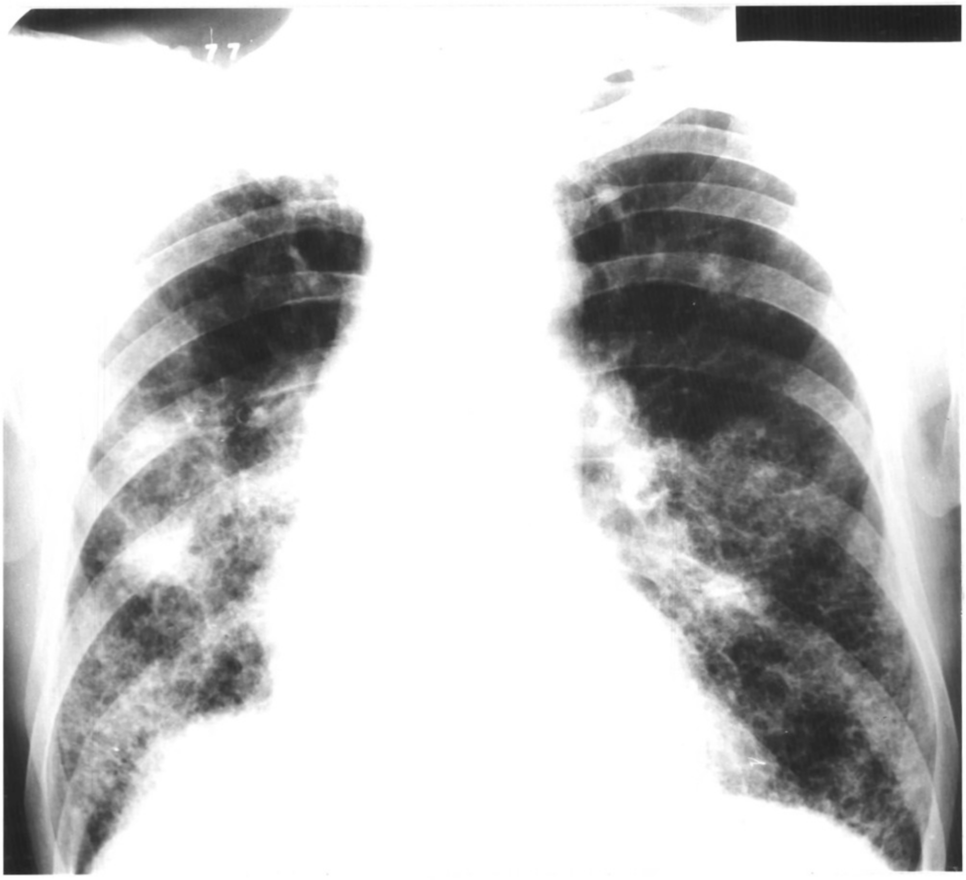


Figure 2/4 (a).
Radiograph read as category 3/3 for profusion of small opacities (median of 3 readers) and with an irregularity score of 8.

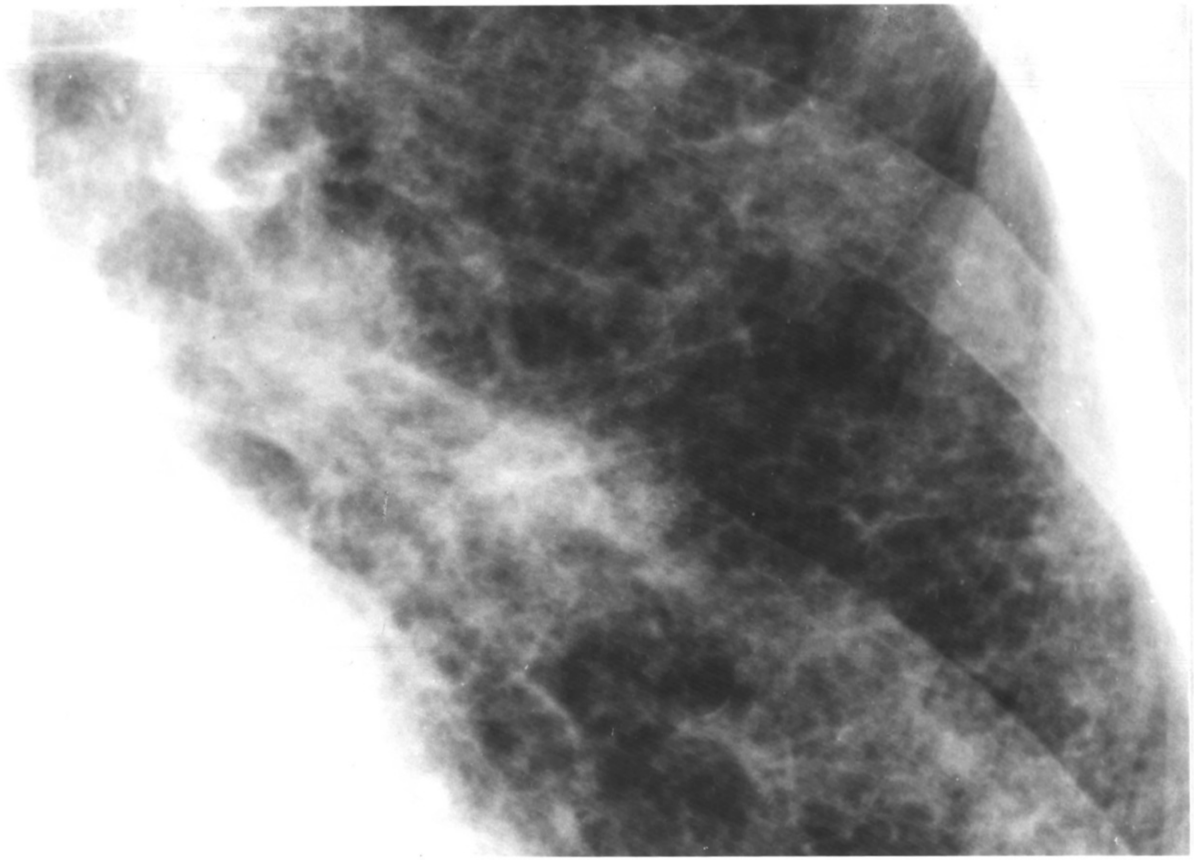


Figure 2.4 (b).

Detail from fig. 2.4 (a)

showing irregular opacities

in the left mid-zone.

CHAPTER THREE

RADIOLOGICAL IRREGULAR OPACITIES AND LUNG FUNCTION IN COALWORKERS

Introduction

In a pilot study of 46 deceased coalworkers irregularity of small opacities on the chest radiograph was found to be associated with reductions in gas transfer factor and total lung capacity (annexe 1). This is in contrast to the many studies which have failed to find any associations between profusion of small opacities and reductions in lung function [53,50,65,62]. In these studies profusion of opacities means profusion of rounded opacities. There is evidence, however, that men with small 'p' type rounded opacities have reductions in gas transfer factor when compared with those with larger 'q' or 'r' opacities [57,78,55,79] as well as increased compliance [54]. Other authors have reported reductions in ventilatory capacity in coalworkers with irregular opacities compared with those with rounded opacities only [25,80].

It seems, then, that the profusion of rounded opacities is not useful for predicting changes in lung function in coalworkers, but that the size of rounded opacities and the profusion of irregular opacities may be more important. The present study was undertaken to examine the effect of shape of small opacities on lung function in a group of coalworkers, taking other factors such as age, smoking, overall profusion of small opacities and presence of progressive massive fibrosis (PMF) into account.

Subjects and methods

The subjects were those coalworkers referred from the Cardiff Pneumoconiosis Medical Panel (PMP) to the MRC Pneumoconiosis Unit for lung function test between 1965 and 1979. They were referred from the PMP for lung function tests particularly if they had 'p' type rounded opacities or irregular opacities on the chest radiograph. Three hundred and fifty-seven of them had a chest radiograph and lung function data available from their first visit to the laboratory and were included in the study. Data from subsequent visits were not included. For each man the age, height and smoking history at the time of lung function testing were extracted from the records. The methods of lung function testing employed at the Pneumoconiosis Unit during the period dealt with in the study have been standard and are described in detail by Cotes[107]. The lung function variables reviewed comprised forced expiratory volume in one second (FEV_1), forced vital capacity (FVC), total lung capacity (TLC), residual volume (RV), gas transfer factor of the lung for carbon monoxide (TL) and gas transfer factor per unit lung volume (Kco). The TLC and RV were measured by helium dilution and the TL and Kco by the single breath method[107].

The 357 radiographs were read independently in random order by a panel of three experienced readers, using the 1980 ILO Classification of Radiographs[13]. In this classification the overall profusion of small opacities is recorded and then their shape and size described by a two letter combination(see annexe 2a). From the size and shape recordings for each radiograph an irregularity score was calculated, as described in Chapter 2.

The lung function variables were analysed by multiple regression to determine whether they were related to the irregularity score. Initially the regressions were on age, height, profusion of small opacities (expressed as dummy variables representing categories 0, 1, 2 and 3) and irregularity score (dummy variables representing the groups 0-2, 3-5 and 6-9). Correction factors for age and height were obtained from the regressions and used in subsequent analyses. The other factors that were considered, in case they influenced the relationships, were smoking and the presence of large opacities. The results are presented as mean values of lung function variables, adjusted for age, height and profusion of small opacities, at different levels of irregularity score. The associations were assessed for statistical significance by fitting a linear trend on irregularity score.

The effect on lung function of size of rounded opacities was examined in the men whose radiographs showed all, or nearly all, rounded opacities (overall irregularity score 0 or 1). The men with predominantly 'p' opacities were compared with those with predominantly 'q' or 'r' opacities for values of TL and Kco. These lung function variables have previously been found to be related to size of rounded opacities[57,55].

Results

The overall characteristics of the 357 men including their radiographic features are given in Table 3.1. Most of the radiographs were recorded as category 2 or 3 for profusion of small opacities and about a quarter as having category B or C PMF. The majority of the men were smokers at the time of lung function testing.

Irregularity score was significantly associated with several lung function variables, so that men whose radiographs showed more irregular opacities had lower values of FEV_1, FVC, TL and Kco and higher values of RV and RV/TLC% than men whose radiographs showed more rounded opacities (Table 3.2). The values shown in Table 3.2 take account of the effects of age, height and profusion of small opacities. Age and height were shown to affect lung function as expected and the correction factors produced were similar to those given by Cotes[107]. Profusion of small opacities had relatively little effect on lung function. The FEV_1 was in fact significantly lower in men with category 0 profusion than in men with category 1-3 profusion. Also, the RV fell with increasing profusion. There was no significant association between irregularity score and profusion of small opacities (Table 3.3).

Smoking history was available for 318 of the men, in the categories of non-smoker, light smoker (< 15 cigarettes/day), heavy smoker (≥ 15 cigarettes/day) and ex-smoker. There was a statistically significant association between smoking and irregular opacities, with smokers having higher irregularity scores than non-smokers ($p < 0.02$) (Table 3.4). As expected, there were associations between smoking history and lung function variables. In particular, smokers had a lower FEV_1 and TL than non-smokers. The regression analysis to examine the effect of irregularity score on lung function was repeated for the 318 men for whom smoking history was available, taking into account smoking effects. There were no material changes to the associations between irregularity score and lung function when this was done.

The assocations between irregularity score and lung function were re-examined separately in the men with and without category B or C PMF. The same trends in lung function related to irregularity score were present in both groups, except for FVC, but were less marked in the men with PMF (Table 3.5). Excluding the men with PMF did not alter the significance of any of the relationships between lung function and irregularity score found in the whole group of 357 men. The magnitude of the PMF effect on ventilatory capcity and TL was less than that of the irregularity score effect.

In the men whose radiographs showed all, or nearly all, rounded opacities (irregularity score 0 or 1), those with predominantly 'p' opacities had significantly lower values of TL and Kco than those with predominantly 'q' or 'r' opacities. The effect is shown in Table 3.6. When the analysis was repeated, taking smoking into account, there were no material changes in these relationships.

Discussion

The results of this study are broadly in agreement with the findings of other investigators. In a group of 95 deceased coalworkers with pneumoconiosis the profusion of irregular opacities, but not the profusion of rounded opacities, was associated with reduction in FEV_1 during life [25]. In a large group of working miners in the United States, those with irregular opacities had a lower FEV_1 and higher RV and TLC than those with rounded opacities but this effect was only present among smokers [80]. Gas transfer factor and Kco were impaired in those with irregular opacities in a follow-up study of 125 men with simple pneumoconiosis [79].

These previous studies used the 1970 ILO Classification of Radiographs [12] in which the profusions of rounded and irregular opacities were recorded separately. In the 1980 ILO Classification [13] overall profusion of small opacities is recorded and size and shape specified. Thus the results of this study, using the 1980 classification, are not directly comparable with the previous studies. Using the 1980 classification meant that it was not possible to allow for different effects of the profusions of the two types of opacity. As there was little association between the overall profusion and lung function it is improbable that separate adjustments, had they been possible, would have made any material difference to the conclusions.

There is evidence that the profusion of irregular opacities in coalworkers is related to the amount of emphysema found at post-mortem[25,75]. Men with irregular opacities were found to have more emphysema and interstitial fibrosis than men with rounded opacities in the pilot study described in Annexe 1. The pattern of lung function impairment found in association with irregular opacities in this study is consistent with a combination of emphysema and interstitial fibrosis. Both processes would produce a reduction in TL and Kco. RV would tend to be reduced in fibrosis and increased in emphysema; the increase found could result from a combination of the two processes. The lack of effect on TLC and the tendency for FEV_1 and FVC to be affected to the same degree argue against emphysema being the only pathology associated with irregular opacities. Musk et al found a reduction in gas transfer factor, no increase in compliance and a tendency towards increased recoil pressure in coalworkers with irregular opacities, again suggesting some fibrosis co-existing with emphysema[79].

The strong associations between irregularity score and a logical pattern of lung function variables in this study are evidence that the score actually reflects a radiological finding that is associated with lung function variables. The associations were not just with the extremes of the score; the whole range related to lung function reductions in a linear manner. This suggests that each increase in the score represents an increase in irregularity of opacities throughout the range although the magnitude of the increase in irregularity may vary over the range of the score.

The effects of several other variables on lung function require comment. The general lack of effect of profusion of small opacities confirms previous findings [53,50,65]. In previous classifications category of pneumoconiosis was recorded on the basis of profusion of rounded opacities only and is therefore not exactly equivalent to the overall profusion of opacities in this study. At least 32 of the men, with irregularity scores 6 or more, would have had a category of pneumoconiosis lower than their overall profusion had the radiograph been read to a previous classification because only the rounded opacities, in a minority on these radiographs, would have been assessed in determining the category. Some men with mainly irregular opacities would have been read as 'Z' and included as category '0' on pre-1970 classifications [10]. It is possible that these men contributed to the previously reported finding of a lower FEV_1 in coalworkers with category 0 than in coalworkers with category 1 simple pneumoconiosis or in non-coalworkers [108]. In the present study the men with category 0 overall profusion also had a lower FEV_1 than those with category 1-3 profusion. This may be because they were all men who had attended the PMP and whereas men with radiological evidence of pneumoconiosis are referred to the PMP on this basis, men without these radiological features attend because of respiratory symptoms. The presence of category B or C PMF produced a fall in RV and TL as is expected with a space-occupying lesion (Table 3.6). However, the effect of PMF on TL was less marked than the effect of irregular opacities.

Smoking affected lung function as expected but, although there was an association between smoking and irregular opacities, the effect of irregularity score on lung function was not materially changed by allowing for the smoking effect. Irregular opacities may sometimes represent smoking-related pathology in coalworkers but in this group this was apparently not their major cause. A study of working miners reported a strong association between smoking and irregular opacities but, nevertheless, amongst smokers lung function was worse in those with irregular than those with rounded opacities and there was an association between irregular opacities and years of underground work [80].

Men attending the PMP and claiming disability benefit may tend to under-estimate their smoking habits. Since all the smoking histories in this study were obtained from PMP notes in the same way any under-estimation should affect them all equally and therefore not affect the results. Smoking history was not available for 11% of the subjects who attended the laboratory, when it was not recorded for a short period. There is no reason to believe that this affected an uneven proportion of men with rounded or irregular opacities on the chest radiograph. The effect of smoking on lung function was taken into account after excluding these 39 men.

Previous work has shown that men with very small ('p' type) rounded opacities have a lower gas transfer factor [57,55] and more emphysema [33] than men with 'q' or 'r' rounded opacities. The results of this study support these findings with regard to gas transfer factor and indeed the effect on TL that was found was of a similar magnitude to that demonstrated previously [55]. The effect of size of rounded opacities in this study was less than the effect of shape of opacities.

The study involved a selected group of coalworkers. They had applied to the PMP and has also been referred for detailed lung function tests. It was initially planned to refer preferentially men with 'p' type or irregular opacities. However, this does not seem to have happened in practice, since the proportion of men with irregular opacities among those included in this study was actually rather less than among a group of coalworkers routinely re-attending the PMP (See Chapter 8). The proportion with 'p' opacities amongst those with rounded opacities in the study was not unduly high at 15% (see Table 3.6). Thus it seems that the findings of this study may reasonably be applied to all coalworkers attending the PMP in South Wales, which will include virtually all coalworkers in the area with radiological evidence of pneumoconiosis [33].

The lung function deficits found here to be associated with irregular opacities on the radiograph could explain the abnormalities of lung function and disability found in some coalworkers with simple pneumoconiosis. The number of men likely to be affected obviously depends on the frequency of irregular opacities among coalworkers with pneumoconiosis; this is explored in Chapter 8. Reduction in lung function usually reflects lung pathology and studies of lung pathology in coalworkers, particularly in relation to irregular opacities, are described in the following chapters.

Summary

Lung function and chest x-rays were reviewed in the 357 coalworkers who had been referred to the Pneumoconiosis Unit from the Cardiff Pneumoconiosis Medical Panel between 1965 and 1979. The chest radiographs were read to the 1980 ILO Classification of Radiographs by three experienced readers. An irregularity score, reflecting shape of the small opacities, was derived from the readings and compared with the lung function variables.

Men with higher irregularity scores had significant reductions in ventilatory capacity and gas transfer factor, with no change in total lung capacity, after taking account of age, height, profusion of small opacities and smoking. The effects were present in men with and without large opacities. Men with rounded opacities had a lower gas transfer factor if they were predominantly 'p' types.

The results are consistent with a combination of emphysema and interstitial fibrosis which has been demonstrated in coalworkers with irregular opacities (see annexe 1). The study does not allow estimation of the frequency of irregular opacities and their associated lung function changes among coalworkers.

Table 3.1

Characteristics of the 357 men in the study

	Mean (Range)
Age (yrs)	55.34 (26-75)
Height (m)	1.70 (1.51-1.86)
FEV_1 (l)	2.20 (0.56-4.50)
FVC(l)	3.50 (1.03-5.78)
TLC(l)	6.30 (3.29-9.30)
RV(l)	2.60 (0.86-5.69)
RV/TLC(%)	40.88 (18.70-70.00)
TL(mmol/min/KPa)	7.58 (1.80-15.0)
Kco(mmol/min/KPa/l)	1.28 (0.33-2.43)

Radiographic Features		No. of radiographs
Median profusion of small opacities	0	10
	1	4
	2	169
	3	137
Irregularity score	0-2	230
	3-5	95
	6-9	32
Category B or C PMF*	Without	266
	With	91

Smoking	Number of men
Non-smokers	47
Light smokers	128
Heavy smokers	76
Ex-smokers	67
Unknown	39

* Recorded by any reader

Table 3.2

Relations between irregularity score and lung function variables

Irreg. Score	Mean FEV1 (l)	Mean FVC (l)	Mean TLC(l)	Mean RV(l)	Mean RV/TLC (%)	Mean TL(mmol/ min/KPa)	Mean Kco(mmol/ min/KPa/l)
0-2	2.30	3.54	6.26	2.54	40.2	8.12	1.37
3-5	2.04	3.46	6.38	2.68	41.7	7.00	1.17
6-9	1.98	3.33	6.37	2.83	42.9	5.48	0.99
Statistical Significance*							
p	<0.001	>0.05	>0.4	>0.05	<0.05	<0.001	<0.001

*From linear regression analysis. In the regression analysis and in calculations of the mean values of the lung function variables the effects of age, height, and profusion of small opacities were taken into account.

Table 3.3

Irregularity score in relation to overall profusion of small opacities

Profusion	Number with Irregularity Score		
	0-2	3-5	6-9
0	6	3	1
1	29	8	4
2	110	47	12
3	85	37	15

Table 3.4

Smoking history in relation to irregularity score

Irregularity Score	Number of Non-Smokers	Number of Light Smokers	Number of Heavy Smokers	Number of Ex-Smokers
0-2	36	81	40	45
3-5	10	31	26	19
6-9	1	16	10	3

Table 3.5

Relationships between lung function and irregularity score in men with and without PMF

Irregularity Score	Number	FEV1 (l)	FVC (l)	RV (l)	TL (mmol/min /KPa)	Kco (mmol/min /KPa/l)
Men without PMF						
0–2	168	2.32	3.56	2.64	8.35	1.39
3–5	68	2.02	3.38	2.82	6.92	1.15
6–9	30	1.92	3.27	2.87	5.45	0.99
Men with PMF						
0–2	62	2.23	3.49	2.26	7.44	1.32
3–9*	29	2.07	3.64	2.38	7.07	1.19

*Only two of the men with PMF had irregularity scores in the range 6-9. Men with PMF are those in whom category B or C PMF was recorded by any reader.

Table 3.6

Effect of size of rounded opacities on TL and Kco

Type of rounded opacities	Number	TL(mmol/min/Kpa)	Kco(mmol/min/KPa/l)
Predominantly 'p'*	24	6.84	1.14
Others	137	8.55	1.44
Significance of difference		$p<0.001$	$p<0.01$

*More 'p' than 'q' and 'r' combined over the three readers where, as in the irregularity score, the first preference is given double the weight of the second.

Only radiographs with irregularity scores 0 or 1 are included.

CHAPTER FOUR

POST-MORTEM LUNG PATHOLOGY IN COALWORKERS

Introduction

Lung pathology in coalworkers has been described by many pathologists, from the 1940s onwards. Descriptions have been mainly qualitative. In order to compare lung pathology between groups of subjects or with other results, say radiographic features or lung function variables, it is necessary to adopt a quantitative approach. The very detailed studies of serial lung sections reported by Heppleston (27,109,32) have yielded valuable information about the anatomy of dust foci in coalworkers' pneumoconiosis but are not practical for studying a large series of lungs. Clinical descriptions of pathological features use terms which do not have exact meanings and cannot be translated reliably into numbers for use in analyses. Different pathologists have different ways of describing what they find and this makes for difficulty when comparing the findings of different studies involving different pathologists. If pathological findings in coalworkers' pneumoconiosis are to be used in epidemiological work in the way that radiological findings are used it is necessary to develop an acceptable quantitative method of recording pathological findings.

It is clearly desirable to study pathology in the whole lung when comparing with other findings, as changes are often distributed unequally through the lung. This means studying post-mortem material. The post-mortem pathology, particularly features such as emphysema, can only reliably be assessed if the lung is inflated and fixed. Suitable techniques for doing this are well established (110). The assessment of post-mortem lung pathology has been greatly helped by the method of preparing whole lung paper-mounted sections described by Gough and Wentworth (28,29) since this allows sections of the whole lung to be stored for review at a later date and by different pathologists.

A number of authors have described techniques for the quantitation of post-mortem lung pathology. Dunnill (111) has reported on a method of taking random tissue blocks from the lung which are then analysed histologically to assess the severity of features such as emphysema. He has also described a 'point counting' method for quantifying pathological features (112). Ryder and co-workers (113) used a grid method for assessing the severity of emphysema on whole lung paper sections. They found that intra- and inter-observer errors were small and of similar magnitude to each other. There is evidence that features on a single slice through the lung correlate very well with the pathology in the whole of the lung (112).

For epidemiological purposes, any technique chosen should ideally be relatively simple and quick to perform, easy to record and to provide information that is useful and reflects pathological features in a repeatable way. The technique that has been used for recording lung pathology in coalworkers in this work was developed by Drs RME Seal and JC Wagner at Llandough Hospital in South Wales. They first defined the features they were looking for and then devised a scheme for scoring them on numerical scales. A description of the technique follows. It was used to assess lung pathology in a group of South Wales coalworkers coming to post-mortem, and this study is described in the rest of the chapter.

Method for assessing and recording lung pathology

The method was designed to allow assessment of features either on a whole lung paper section or on a wet slice of an inflated, fixed lung. Features assessed include dust foci, emphysema of centrilobular, panacinar or irregular type, progressive massive fibrosis and any macroscopic evidence of interstitial fibrosis.

In describing lesions of so-called 'simple pneumoconiosis' the pathologists divide the lesions into three distinct types. First are the central, numerous, widely distributed peribronchiolar lesions, which form the background in simple pneumoconiosis: the primary coal dust foci (figs.4.1 and 4.2). Larger, less numerous lesions, which may be produced by some additional factor such as tuberculous or other infection, increase of quartz in the dust or rheumatoid diathesis, are termed secondary foci. These are divided into stellate secondary foci (fig.4.3) and circumscribed secondary foci. Primary dust foci are graded for size and profusion. The average size of the foci is recorded on a 0-3 scale, with scores 0, 0/1, 1, 1/2 etc.(i.e. a total range of 0 - 6 scale points). The proportion of lobules involved with primary foci is also assessed by eye and graded on a numerical scale as 1 (up to 33%), 2 (33-66%) or 3 (more than 66%), with intermediate grades allowed. Secondary foci are measured using a graticule and recorded as either less than 5mm or 5-20mm. The number of secondary foci of each size is noted. Foci of diameter greater than 20mm are regarded as progressive massive fibrosis (PMF). The total diameter of all lesions above 20mm in diameter is recorded and their position (i.e. upper lobe or lower lobe) noted.

Degree and extent of emphysema are recorded for centrilobular, panacinar and irregular emphysema separately. Severity of emphysema in the average affected lobule is recorded on a 0-3 scale, again with scores of 0, 0/1, 1, 1/2 etc up to 3. The proportion of lobules in the lung affected by emphysema is scored in the same way as for proportion of lobules involved with primary dust foci.

Figure 4.1 is an example of size 1 primary foci with grade 0/1 severity of centrilobular emphysema. Figure 4.2 illustrates size 2 primary foci with associated grade 2 severity of centrilobular emphysema. An example of the more severe lung destruction sometimes found in cases of simple CWP is shown in fig. 4.4. Figure 4.5 illustrates the appearances of simple CWP with minimal surrounding emphysema on a whole lung paper-mounted section (WLS). The WLS in fig. 4.6 has secondary foci and an area of PMF at the apex in addition to the background of simple CWP. Macroscopic appearances are sometimes difficult to interpret with certainty and fig. 4.7 shows the WLS in such a case, with an area in the lower lobe with cystic spaces which could represent lung fibrosis or emphysema or a combination.

The forms used for recording features noted macroscopically on whole lung paper sections or on wet slices of inflated, fixed lungs are reproduced in annexe 3(a). Standard whole lung paper sections demonstrating different grades of dust foci and emphysema have been collected and are available for comparison when making assessments.

Macroscopic examination is supplemented by examination of histological sections. These include large blocks of tissue taken from upper and lower lobes and from areas of particular interest. These blocks are cut, stained and mounted on 5 x 5 cm glass slides for projection with a standard slide projector. The appearances of normal lung tissue on such sections are illustrated in figs. 4.8 and 4.9. Figures 4.10 and 4.11 show minor degrees of dust involvement and emphysema on similarly prepared lung sections.The projected sections are examined to confirm the type of emphysema and to assess whether there is any interstitial fibrosis. In defining types of emphysema, the pathologists regard emphysema which leaves a rim of normal alveoli at the periphery of the lobule as centrilobular, even though there may be very little normal lung tissue left (fig. 4.12). Another feature recorded by the pathologists was termed 'centrilobular interstitial fibrosis.' Centrilobular emphysema in coalworkers often has septa thickened by the presence of dust laden macrophages of the primary dust foci. When this thickening was clearly collagenous this was noted and its extent graded.

The severer forms involved all the septa of the enlarged air spaces right up to the interlobular septa (figure 4.13). The forms used for recording microscopic features are reproduced in annexe 3(b).

This method for assessing and recording lung pathology in coalworkers has been previously reported (105,114). It is used in the pilot study described in annexe 1 and in the pathology studies described in this and the following chapters.

Subjects and methods for study of lung pathology in coalworkers

The death of any man known to have been a coalworker has to be reported to the coroner because of the requirement to report all deaths that might be due to an industrial injury or disease(115). In South Wales at least, nearly all men who are reported to the coroner as having been coalworkers have a post-mortem examination. Exceptions at the discretion of the coroner are elderly men who have worked for a short time underground in their youth and are not certified as having coalworkers pneumoconiosis, and men whose next-of-kin sign a form to the effect that they will not, in the future, make a claim that death was caused or contributed to by pneumoconiosis. After a post-mortem examination on a man known to have been a coalworker, the lungs are sent to the Pneumoconiosis Medical Panel (PMP) in the area. The doctors of the PMP decide whether coalworkers' pneumoconiosis caused or contributed to the man's death. In practice in South Wales, most coalworkers and practically all those certified as having coalworkers' pneumoconiosis come to post-mortem examination.

For this study the lungs of coalworkers coming to post-mortem examination in a group of hospitals in Mid and South Glamorgan were collected. The lungs of such men are usually sent on to the Cardiff PMP, with at least one of the pair of lungs inflated and fixed with formalin using the method of Heard[115a]. For the purposes of the study the PMP agreed to send one inflated, fixed lung from each man to be examined before making their own examination which entails slicing the lung.

Lungs were collected over a period of about a year, from November 1980 to November 1981. Pathologists entering material into the study completed a simple entry form, reproduced in annexe 4(a). Initially lungs of all men known to have been coalworkers, for however brief a period, were included. After several months the PMP were asked to only send lungs of men who had spent at least 10 years working underground, so as not to include a large number of men with very minimal underground exposure. In this way material was collected from 131 men. Eight of these were excluded from the study because there was no trace of them in PMP records and no evidence from other sources(mainly relatives) that they had ever been coalworkers. This left a total of 123 coalworkers in the series.

Information about the men included in the study was sought from PMP records. This included smoking and coalwork exposure histories. The form for recording information from PMP records is shown as annexe 4(b). Some men had never been seen by the PMP during life and therefore had no smoking history available from this source. In such cases a social worker visited relatives two months or more after the man's death and asked about his occupational and smoking history (annexe 4(c)).

One inflated, fixed lung was examined for each man. A sagittal slice was made about midway through the lung, to include both upper and lower lobes. Features were examined on the cut surface of the freshly sliced lungs, under a good light. The features were recorded, as explained above, on the forms reproduced in annexe 3(a). The cut surface of the lung was photographed in colour for future reference. Pouring ethyl alcohol over the surface was found to be helpful in increasing contrast for photography. The sites of blocks of tissue taken to mount on 5 x 5 cm slides were marked and the surface was re-photographed (see fig. 4.14). Five by five cm slices of tissue were taken to produce large paraffin blocks. They were cut at 8μ with a sledge microtome and mounted on 5 x 5 cm slides, stained and covered with 5 x 5 cm coverslips. Such preparations can be projected and also examined under the microscope. The projected material was studied to confirm the type of emphysema and to record any centrilobular interstitial fibrosis (see above) or any generalised interstitial fibrosis.

In view of the good agreement between the two pathologists when they independently assessed features on whole lung paper-mounted sections (see annexe 1) for this study the same two pathologists assessed all the material together and came to agreed decisions on the various scores.

Three other scores were derived from those recorded by the pathologists examining the lungs. The total dust score was calculated as the product of the scores for average size of primary dust foci and proportion of lobules involved with primary dust foci. The new score had a range of 0-36, coming from two scores with range 0-6 (i.e. 0, 0/1, 1, 1/2, 2, 2/3, 3). The total centrilobular emphysema score was the product of the scores for average severity and extent of centrilobular emphysema. It also had a range of 0-36. A total centrilobular emphysema score of 6 or less indicates virtually no emphysema, 6 to 12 mild emphysema, 13 to 18 mild to moderate, 19 to 24 moderate, 25 and above severe emphysema. The total 'centrilobular interstitial fibrosis' score was the product of the scores for severity of centrilobular interstitial fibrosis (as assessed from projected sections) and proportion of lobules involved with primary dust foci. Its range was also 0-36.

The significance of associations was tested by means of χ^2 tests: the Mantel-Haenszel test (116) and the Mantel extension of this procedure (117).

Results

Pathological features

Primary dust foci were found in all the lungs; their size and extent varied considerably within the series. Secondary dust foci were found in 58 of the 123 lungs examined. Progressive massive fibrosis (PMF) was quite a common finding: 31 of the lungs contained areas of PMF greater than 5cm in diameter and a further 18 had areas of PMF of between 2cm and 5cm in diameter (Table 4.1). Emphysema was present to at least a minor degree in virtually all the lungs examined, generally in relation to the primary dust foci. The extent varied from a minimal, non-destructive dilation of air spaces around the dust foci (figs. 4.1 and 4.10) to a severe, destructive lesion with only a thin rim of normal alveoli remaining at the periphery of the lobules (fig. 4.12). According to the definition of centrilobular emphysema used in this study, both these extremes were classified as centrilobular emphysema. On this basis, practically all the emphysema encountered in the lungs of this series was of the centrilobular type.

Table 4.1 shows the distribution of scores for primary dust foci and emphysema. For the few men who had spent less than ten years underground the amount of dust in primary foci was minimal and the lungs were similar to those of elderly town dwellers. It can be seen from the table that primary dust foci were usually widespread: in more than half the lungs they were scored as involving two-thirds or more of the lobules. There was a bigger scatter of scores for size of primary dust foci, with only about a tenth of cases being scored as the largest size and the rest evenly divided between the smallest size and the intermediate size. Six of the lungs were scored as being free from centrilobular emphysema. The emphysema in the rest was generally scored as being widespread. It was scored as severe in fifteen lungs and as mild or moderate in roughly equal proportions of the remainder.

Also in Table 4.1 are given the numbers of lungs in which secondary foci and PMF were found. Stellate secondary foci were more common than circumscribed secondary foci, occuring in over a third of the lungs. It was unusual (four cases) for stellate and circumscribed secondary foci to be found in the same lung. The score for centrilobular interstitial fibrosis was not based on macroscopic assessment as were the other scores in Table 4.1, but rather on assessment of projected 5 x 5cm sections of tissue. It can be seen from table 4.1 that this feature was absent or only present to a minor degree in the majority of the lungs examined. In a few of the lungs it was difficult, on macroscopic examination, to identify individual dust foci; rather there was a more generalised pigmentation of emphysematous lung parenchyma. These were the lungs which, when examined by projection of 5 x 5cm sections, were assessed as having moderate or severe degrees of centrilobular interstitial fibrosis as well as marked centrilobular emphysema around the dust foci.

There was a strong association between primary dust foci (expressed as total dust score) and centrilobular emphysema (expressed as total centrilobular emphysema score) (Table 4.2(a)). Lungs with a total dust score of less than 12 had much lower total centrilobular emphysema scores than those with higher total dust scores ($\chi^2=44.83, p<0.001$) and the association was also strong when comparing lungs with total dust scores of 24 or less with those with scores of 25 or more ($\chi^2=22.59, p<0.001$). Excluding lungs with PMF greater than 5cm in diameter did not materially alter this association between dust foci and centrilobular emphysema; lungs with a total dust score of less than 12 still had much less emphysema than the rest (χ^2=35.16,p<0.001)(Table 4.2(b)). This was despite the fact that lungs with PMF had higher centrilobular emphysema scores than lungs without PMF (Table 4.3, χ^2=12.97,p<0.001).

Lungs in which PMF was found had higher total dust scores than lungs without PMF (χ^2=8.18,p<0.01)(table 4.4). There were also associations between the number of stellate secondary foci and the presence of PMF (χ^2=23.47,p<0.001) and between the number of circumscribed secondary foci and presence of PMF (χ^2=4.13,p<0.05)(table 4.4).

Centrilobular interstitial fibrosis was a relatively uncommon feature (see Table 4.1). The total centrilobular interstitial fibrosis score (centrilobular interstitial fibrosis score X score for proportion of lobules involved with primary dust foci) was used to look for associations with other features. There was a strong association between this score and the total centrilobular emphysema score (Table 4.5). Lungs with a total centrilobular emphysema score of less than 12 were very unlikely to show more than mild centrilobular interstitial fibrosis (χ^2=14.50,p<0.001).

<u>Pathology in relation to other variables</u>

Other information available for most, or all, of the men whose lungs were examined included age at death, smoking history, length of underground work, length of facework, an estimate of whether they had been heavily exposed to quartz dust (for example, working on 'hard-heading'), and what percentage disability benefit for pneumoconiosis (if any) they were receiving before death.

Age at death

There was no excess of PMF in the lungs of older men; nor were there associations between age at death and number of circumscribed secondary foci or severity of 'centrilobular interstitial fibrisis'(table 4.6a). There were associations between the presence of stellate secondary foci and age at death (χ^2=4.76,p<0.05) and between dust in primary foci and age at death (χ^2=2.53,p<0.10) (table 4.6a). Severe centrilobular emphysema was found predominantly in the lungs of older men(χ^2=12.82,p<0.001)(table 4.6a). Excluding men with PMF of 5cm or more in diameter in the lungs made little difference to these results. In particular, there remained an association between severe emphysema and age(χ^2=3.43,p<0.07)(table 4.6b). There was no association between age at death and length of coalface work(table 4.6c) but there was an association between age at death and length of underground work such that older men had spent longer periods working underground(table 4.6c,χ^2=6.01,p<0.02).

Smoking History

Smoking history was available for all but two of the 123 men. Heavy smokers had significantly younger ages at death than light-and ex-smokers combined (χ^2=10.57,p<0.001)(table 4.7). None of the assessments of dust in the lungs : total dust score (primary foci), number of secondary foci, and presence and size of PMF, revealed significant associations with smoking history (Table 4.8).

Centrilobular emphysema in the lungs was weakly related to smoking history (Table 4.9(a)) such that ex-smokers and smokers had more emphysema than life-long non-smokers (χ^2=3.55,p=0.06). The effect was not significant when lungs with PMF were excluded (table 4.9b,χ^2=1.57). From Table 4.9 it can be seen that 3 life-long non-smokers had moderate or severe centrilobular emphysema and in 2 of these men there was no PMF (>5cm in diameter) in the lungs.

Coalwork Exposure

The total dust score (an assessment of the amount of dust in primary foci) was not associated either with years of underground work or with years of facework. This was true whether lungs with PMF were included or not (Table 4.10(a) and 4.10(b)). From Table 4.11(a) it can be seen that stellate secondary foci were more common in men who had spent more than 20 years working underground (χ^2=5.39,p<0.05) and particularly in men who had spent more than 40 years working underground (χ^2=8.97,p<0.01). In addition, coalface work for more than 20 years was associated with more stellate secondary foci in the lungs (χ^2=10.91,p<0.001). There was an association, significant at the

10% level, between stellate secondary foci and likely quartz exposure (χ^2=2.49,p<0.1). These associations were still found when lungs with PMF lesions greater than 5cm in diameter were excluded (Table 4.11(b)). Stellate foci were associated with longer underground exposure (χ^2=5.12,p<0.05), longer coalface exposure (χ^2=5.82,p<0.05) and likely quartz exposure (χ^2=5.07,p<0.05). Circumscribed secondary dust foci were less common than the stellate type and did not appear to be associated with length of underground work, length of facework or likely quartz exposure (Table 4.12(a) and 4.12(b)).Neither the presence of PMF nor the size of the PMF lesions was associated with length of coalface exposure or length of underground exposure (table 4.13).

Centrilobular emphysema in the lungs was not associated with length of underground work or length of facework, taking the group as a whole, whether or not those lungs showing PMF were included (Table 4.14a and 4.14b). Similarly, there were no obvious associations between the total centrilobular interstitial fibrosis score and coalwork exposure (Table 4.15).

When the relationship between centrilobular emphysema and length of underground work was examined, stratifying by smoking history, there was an association between centrilobular emphysema and length of underground work in smokers (χ^2=4.24,p<O.05)) but not in ex-smokers or non-smokers (Table 4.16). Smokers who had worked for more than 20 years underground were nearly six times more

likely to have centrilobular emphysema (score >12) than smokers who had worked for shorter periods underground (Odds ratio=5.93, 95% Confidence Intervals 1.09-32.26).

Percentage Disability Benefit

Fifty three of the men whose lungs were included in the study had not been certified as having coalworkers' pneumoconiosis during life and were not receiving any disability benefit. A further 31 had been receiving 10% or 20%, 30 had been receiving 30-60% and only 9 had been receiving 70% or more. The pathological feature most strongly associated with percentage disability benefit received during life was PMF (Table 4.17(a)). None of the men whose lungs did not contain PMF had been receiving more than 60% disability benefit and the majority of such men (50 out of 74) had not been certified as having coalworkers' pneumoconiosis. Three men with small PMF lesions had not been certified during life. The association between the presence of PMF and amount of disability benefit was significant at the 0.01% level (χ^2=61.43). There was also an association between the score for dust in primary foci (total dust score) and the amount of disability benefit being received. Men not certified during life usually had light dust loads as assessed by the total dust score but two of them had scores of 25 or more. Men whose lung dust scores were less than 12 had been receiving less disability benefit than those whose lungs showed more dust (χ^2=6.97,$p<0.05$)(Table 4.17(a)).

There was a weak association between centrilobular emphysema score and disability benefit. Men whose lungs were given total centrilobular emphysema scores of less than 12 were less likely than those whose lungs had more emphysema to have been receiving disability benefit for pneumoconiosis (χ^2=3.52,p<0.06) (Table 4.17(a)). Of the men with severe emphysema(score >25) more than half(8 out of 13) had been receiving 20% disability benefit or less. There was a tendency, significant at the 12% level, for men who had spent more than 20 years underground to be receiving more disability benefit than those with shorter exposure histories (χ^2=2.38) (Table 4.17(a)). Longer coalface exposures were associated with higher levels of disability benefit (χ^2=3.71,p<0.06) (table 4.17(a)).

Considering only lungs without areas of PMF >5cm in diameter (Table 4.17(b)) there were the same associations between disability benefit for pneumoconiosis and total dust score (χ^2=5.12,p<0.05), total centrilobular emphysema score (χ^2=2.78,p<0.10), length of underground work (χ^2=3.25,p<0.08) and length of coalface work (χ^2=2.47,p<0.12) as in the whole group. Table 4.17(b) also shows that of 8 men whose lungs were scored as having severe centrilobular emphysema, only one had been receiving more than 20% disability benefit and 3 had not been certified as having coalworkers' pneumoconiosis so were not receiving any disability benefit.

Discussion

The legal requirement for a post-mortem examination in deceased coalworkers should mean that the post-mortem rate (number of post-mortem examinations/number of deaths) among coalworkers is high. That this is in fact the case, at least in Mid and South Glamorgan, has been confirmed by the study described in Chapter 6. Thus the coalworkers who provided the material for this study should be representative of all coalworkers dying in the area, who had spent 10 years or more working underground.

The assessment of pathological features on a fresh lung slice was found to be satisfactory. Producing a Gough-Wentworth whole lung paper section [29,118] is a time-consuming and expensive business; a skilled technician has to give time to the procedure personally, the whole process takes about 11 days and costs about £20 per lung. A cheaper, quicker method has been described more recently [119] but this still requires 24-48 hours and the attention of a skilled technician. Assessing features on the cut surface of a freshly-sliced fixed, inflated lung avoided these problems but required organisation to bring everyone together at the same time. There is also the problem of recording the appearances for future review. This was overcome by taking good quality colour transparencies of the lung slice. When projected these transparencies could be assessed quite accurately as compared to the assessment of the wet lung slice. This was checked informally during the course of the study.

The method used for quantifying and recording features of interest was simpler and more 'subjective' than previously described methods (112,111,113). However, in a comparison of the 'point-counting' method (112), the 'grid' method (113) and the 'panel of standards' method for assessing pulmonary emphysema Thurlbeck and co-workers (120) found that the 'panel of standards' method was as good as the other two methods. This method was essentially similar to that used in this study. The quantification of dust foci in the lungs has been previously attempted (71) and a report in 1979 discusses setting pathology standards for coalworkers' pneumoconiosis (121). The method used in this study aims to give a complete, repeatable, quantitative assessment of type and extent of dust foci and associated features in the lung.

The validity of assessing pathology in the whole lung by studying features on a single slice may be questioned, but there is evidence (82a,112) that the findings on a single slice are a good reflection of the pathology of the whole lung.

The study indicates that PMF is still a common finding in coalworkers dying in South Wales having worked for 10 years or more underground. Forty percent of the lungs examined contained PMF and in nearly two thirds of these the PMF was greater than 5cm in diameter. PMF occured more often in lungs with a heavy load of dust in primary foci. This is in keeping with the theory that the main causative factor for PMF is the total amount of dust in the lungs[67] and the findings that men who develop PMF have more background simple pneumoconiosis[122] and have had more dust exposure[123] than those who do not develop PMF. This association between dust in primary foci and PMF means that the exclusion of lungs with PMF limits any comparisons between dust in primary foci and other variables, since most of the lungs with high scores for dust in primary foci will also have been excluded.

The amount of centrilobular emphysema in the lungs was associated with the amount of dust in primary foci. This confirms the visual impression that emphysema occurs predominantly around the dust foci. This pattern has been consistently described by pathologists for over 30 years[30,27,31]. There is disagreement about what extent of emphysema should be considered an integral part of the dust lesions and about terminology. Heppleston[27,108,32] distinguishes between focal emphysema associated with dust foci and other forms of emphysema occuring in coalworkers. On the other hand, Ryder and co-workers[33] have used the term focal emphysema to include even severe grades of emphysema in coalworkers. This use of the term has been criticised[34] and in the most recent edition of his book on occupational chest diseases Parkes[124] questions whether any form of emphysema is specific to coalworkers. In this study the term centrilobular emphysema has been used as defined at the Ciba symposium in 1959[125]. The mildest degrees of this centrilobular emphysema around dust foci would be equivalent to the classical focal emphysema.

From this study it is not possible to say which came first: the dust foci or the emphysema surrounding them. It has been suggested that coal dust may be laid down on damaged areas of lung so that emphysematous areas become pigmented incidentally [32]. However, there is evidence from animal studies that less dust accumulates in emphysematous areas of lungs [49]. Most coalworkers begin work underground in their youth when they are unlikely to have any degree of emphysema and are likely to be unable to continue underground work if they develop substantial emphysema. This makes it difficult to see how coal dust can be accumulating to any extent on already emphysematous areas of lung. The Institute of Occupational Medicine has recently reported on a post-mortem study of 450 coalworkers [125a]. They found an association between life-time dust exposure and emphysema and no evidence that the emphysematous lungs cleared dust less efficiently.

There was an association, in the present series of lungs, between PMF and centrilobular emphysema. Nevertheless, Table 4.3 shows that in more than half the lungs with severe emphysema PMF >5cm in diameter was absent. In about half the lungs with PMF >5cm in diameter there was moderate or severe emphysema. Lyons and Campbell [46] have suggested that the disability associated with PMF is due as much to the concommitent emphysema in the rest of the lung as to the PMF lesions themselves. The emphysema found in the lungs with PMF in this series was centrilobular and not particularly anatomically related to the PMF lesions themselves. This tends to support Lyons and Campbell[46] who found that the emphysema and PMF in their series of lungs were contributing independently to reduction in lung function.

Centrilobular interstitial fibrosis was an unusual but definite finding in the lungs in this series. It tended to occur particularly in lungs which also had considerable centrilobular emphysema (see Table 4.5). In such cases the dust foci were surrounded by cystic air spaces whose walls contained dust-laden macrophages and collagen.

Recent work has led to an increased understanding of the cellular basis for fibrosis[126] and emphysema[127] in the lungs. Keogh and Crystal[126] point out that lung destruction and fibrosis co-exist in a number of conditions, such as idiopathic pulmonary fibrosis, and that the effects of an insult to the lung depend on the lung defences as well as on the nature of the insult. The alveolar macrophage is reported to produce a factor stimulating collagen formation by fibroblasts when it is activated by silica[128]. The dust foci in silicosis are fibrotic and the silica content of coal dust may be responsible for the centrilobular interstitial fibrosis found around the dust foci in this series of coalworkers. This does not explain, however, the emphysema also found around the dust foci. Such emphysema is said to be rare in silicosis[129] and it has been reported that there is less emphysema found in coalworkers who have a higher proportion of quartz in lung dust[82a]. The alveolar macrophage has been shown to release elastase when stimulated. This elastase may be either previously internalised polymorphonuclear leucocyte enzyme or synthesized and secreted by the macrophage itself[130,131].

Either of these enzymes could be potent in the production of emphysema in vivo[127]. Cigarette smoke is known to activate alveolar macrophages[130,131] but there has been little work on the effect of exposure of these cells to coaldust; although a recent report from France[132] raised the possibility that macrophages in the lungs of men with coalworkers' pneumoconiosis may be secreting more collagenase and elastase-like enzymes than normal.

The type of emphysema that might be a result of enzyme release from these activated cells apparently depends on their location; centrilobular emphysema is due to activation of cells in the centre of the lobule[133] whereas panacinar emphysema may result from cellular accumulation in the pulmonary microcirculation[134]. The findings in the present series are compatible with the activation of dust-laden macrophages in the centrilobular dust foci leading to centrilobular emphysema. There is clearly a need for more work on the cellular pathology of coalworkers' pneumoconiosis. This may throw more light on the question of whether the emphysema found around dust foci in coalworkers is co-incidental or results from cellular effects of the dust.

The association between emphysema and smoking found in this series was not unexpected. There is good evidence for an association between smoking and emphysema[135] and this can be explained at a cellular level, as mentioned above[130,131]. It was notable, however, that some severely emphysematous lungs in this series were those of men who had never smoked. The possibility that these men had alpha-1 antitrypsin deficiency could not be investigated directly but this seems unlikely as they had centrilobular emphysema and the emphysema found in association with alpha-1 antitrypsin deficiency is panacinar[136].

Although there was no overall association between centrilobular emphysema and length of underground work, among smokers there was such an association. This implies that there may be some sort of interaction between the effects of smoking and coalwork exposure. It could be argued that the finding is spurious, and simply due to the fact that men who have worked longer underground will have smoked for longer since both these exposures are related to age. This possibility was investigated indirectly by looking to see if older smokers had more emphysema than younger smokers. Table 4.18 shows that they did not have more than 14 percent more with 95% confidence (χ^2=0.04, OR 1.01, 95% CI 0.90-1.14). It therefore seems unlikely that smokers with longer underground exposure had more emphysema simply because they were older. Support for an association between underground exposure and emphysema comes from a study of 500 dead coalworkers: those with reductions in FEVi and more dust exposure had more emphysema than the others[82a]. An extension of this work from the IOM has shown a clear association between life-time dust exposure and emphysema[125a]. The authors conclude that their findings indicate a causal relationship between exposure to respirable coal dust and emphysema, at least in men with dust foci of simple CWP in the lungs.

Length of underground work and length of coalface work are rather crude indices of coaldust exposure but more detailed measurements were not available. The crudity of the indices may explain the lack of associations between them and pathological features. The score for dust in primary dust foci or the presence of PMF may actually be better indicators of total lifetime dust exposure. On the other hand, other exposures underground, such as nitrous fumes[137] have been suggested as a possible cause of emphysema and would be ignored if only dust exposure were considered.

It was surprising to find that stellate, rather than circumscribed, secondary foci were associated with quartz exposure, since the circumscribed type are thought to be more typical of silicosis. It may have been because there were too few circumscribed foci to establish an association, or because the estimation of whether there had been significant quartz exposure was crude. Alternatively, it may be because the secondary foci of anthraco-silicosis tend to be stellate rather than circumscribed like those of pure silicosis.

The associations found with disability benefit were interesting. Disability benefit must be distinguished from actual disability; the former is given for disability considered (by the PMP) to be due to coalworkers' pneumoconiosis. PMF is accepted as a cause of disability and clearly attracts disability benefit. Simple pneumoconiosis, on the other hand, is not accepted as a cause of disability (92) and thus few men with only simple pneumoconiosis receive more than 20% disability benefit. Some men with severe emphysema, who would certainly have been disabled as a result, were not receiving any disability benefit at all because emphysema is not a prescribed disease in coalworkers (or other occupational groups) in the absence of certifiable pneumoconiosis. Nor is it considered to be part of coalworkers' pneumoconiosis when this is diagnosed; its effects in this situation are only taken into account in terms of their aggravation of the effects of CWP when assessing what percentage disability benefit to award. The increase in benefit from emphysema aggravation is only a small amount - usually 10 or 20%. It is clear that the amount of disability benefit received by men with simple pneumoconiosis would be increased if emphysema were to be considered as part of pneumoconiosis and its effects fully taken into account.

The overall aim of this thesis is to examine the importance of radiological irregular opacities in coalworkers. Study of the pathology of coalworkers' pneumoconiosis is relevant because it allows an understanding of what processes are occurring in the lungs and being reflected on the chest radiograph. The quantitative approach used here is essential to allow comparison with radiological features. From the work of other authors [25] and the pilot study described in annexe 1, it is particularly important to look for associations between emphysema in the lungs and radiological irregular opacities. In this regard it is interesting to see in this study that emphysema was a common finding in the lungs of coalworkers in this series and that it was closely associated with dust foci in the lungs. Later chapters examine the relationship between pathology and radiology in these coalworkers (Chapter 5) and whether the emphysema in the coalworkers is in excess of that found in similarly selected non-coalworkers (Chapter 7).

Summary

A method of recording pathological features is described which allows quantitative data on lung pathology in coalworkers to be produced for comparison with radiological findings.

An inflated, fixed lung was collected from each of 123 coalworkers coming to post-mortem examination in an area of South Wales. Most of the men had spent at least 10 years working underground. Pathological features were assessed on the cut surface of each lung according to a set protocol and scored on numerical scales. Smoking and occupational histories of the men were obtained, mainly from records of the Cardiff Pneumoconiosis Medical Panel (PMP).

A wide range of degrees of dust-related pathology was found, ranging from a few small primary dust foci to severe involvement of the whole lung parenchyma with primary dust foci with additional secondary foci and areas of PMF. Emphysema was common. It was almost entirely of centrilobular type and the amount was strongly associated with the score for amount of dust in primary foci. Older men and smokers (current and ex-) tended to have more emphysema. In smokers only, there was an association between emphysema and length of underground work.

The amount of disability benefit being received before death was related mainly to the presence of PMF. Some men with severe

emphysema had received no disability benefit during life, having not been certified as suffering from CWP.

Table 4.1

Distribution of primary dust foci scores, centrilobular emphysema scores, secondary dust foci and PMF in the 123 lungs.

For:	0	Number with scores 1-2	3-4	5-6
Size of primary dust foci	0	52	59	12
Proportion of lobules involved with primary dust foci	0	17	39	67
Average severity of centrilobular emphysema	6	56	46	15
Proportion of lobules involved with centrilobular emphysema	6	14	47	56
Severity of centrilobular interstitial fibrosis	65	35	19	4

Secondary dust foci	None	<10	≥10
Stellate	75	42	6
Circumscribed	109	10	4

PMF	Absent	2-5cm diameter	> 5cm diameter
	74	18	31

Note: (1) The centrilobular interstitial fibrosis score is a microscopic assessment, whereas all the others are macroscopic.

(2) In four lungs both stellate and circumscribed secondary foci were found. They are included within the figures for each type in the table.

Table 4.2

Relationship between primary dust foci and centrilobular emphysema.

(a) In whole group of 123 lungs

	Number with total centrilobular emphysema score		
Total dust score	≤12	13-24	≥25
≤12	55	8	0
13-24	15	26	7
≥25	1	5	6

(b) In lungs without PMF of >5cm diameter (n=92)

	Number with total centrilobular emphysema score		
Total dust score	≤12	13-24	≥25
≤12	43	7	0
13-24	9	21	4
≥25	1	3	4

Table 4.3

Centrilobular emphysema and PMF

Total centrilobular emphysema score	Number with PMF		
	Absent	2-5cm diameter	>5 cm diameter
≤12	50	3	16
13-24	21	10	10
≥25	3	5	5

Table 4.4

Associations between PMF and primary and secondary dust foci.

	Number with PMF	
Total dust score	Absent	Present
≤12	46	17
13-24	23	25
≥25	5	7
Stellate secondary foci		
None	58	17
<10	15	27
≥10	1	5
Circumscribed secondary foci		
None	69	40
<10	4	6
>10	1	3

Table 4.5

Total centrilobular interstitial fibrosis score and total centrilobular emphysema score.

Total centrilobular emphysema score	Number with total centrilobular interstitial fibrosis score		
	≤12	13-24	≥25
≤12	67	0	2
13-24	30	10	1
≥25	5	7	1

Table 4.6

(a) Age at death and pathological findings in the lungs (n=123)

	Number dying aged			
	<60	60-69	70-79	≥80
PMF				
Absent	8	25	32	9
2-5cm diameter	0	7	8	3
>5cm diameter	2	13	9	7
Total dust score				
≤12	8	22	26	7
13-24	2	17	18	11
≥25	0	6	5	1
Stellate secondary foci				
None	8	31	27	9
<10	1	13	20	8
≥10	1	1	2	2
Circumscribed secondary foci				
None	10	40	41	18
<10	0	2	7	1
≥10	0	3	1	0
Total centrilobular interstitial fibrosis score				
≤12	9	36	42	15
13-24	0	7	6	4
≥25	1	2	1	0
Total centrilobular emphysema score				
≤12	7	22	31	9
13-24	3	18	14	6
≥25	0	5	4	4

Note: There were no men dying aged less than 40 years and only one man dying aged less than 50 years.

Table 4.6 (contd)

(b) Associations between age at death and centrilobular emphysema in lungs without PMF >5cm in diameter. (n=92)

Total centrilobular emphysema score	Number dying aged <60	60-69	70-79	≥80
≤12	6	17	25	5
13-24	2	13	12	4
≥25	0	2	3	3

Table 4.6 (contd)

(c) Associations between age at death and coalwork exposure

	Number dying aged <60	60–69	70–79	≥80
Length of underground work (yrs)				
≤20	4	12	3	3
21–40	4	22	21	8
≥41	2	10	24	8
Length of coalface work (yrs)				
≤20	5	19	19	9
21–40	3	16	15	8
≥41	2	3	6	1

Note: Length of underground work unknown for 2 men, length of coalface work unknown for 17 men.

Table 4.7

Smoking history and age at death

Smoking history	Number dying aged <60	60–69	70–79	≥80
Lifelong non-smokers	2	5	5	4
Ex-smokers	1	12	14	6
Light smokers	2	15	23	8
Heavy smokers	5	11	6	1
Smokers-unknown amount	0	1	0	0

Table 4.8

Smoking history and dust foci in the lungs

	Number with smoking history as				
	Lifelong non-smkrs	Ex-smokers	Light smokers	Heavy smokers	Smoker ? amt
Total dust score					
≤12	12	17	18	14	1
13-24	4	13	25	5	0
≥25	0	3	5	4	0
Stellate secondary foci					
None	10	20	26	16	1
<10	5	11	20	6	0
≥10	1	2	2	1	0
Circumscribed secondary foci					
None	14	27	44	21	1
<10	1	4	4	1	0
≥10	1	2	0	1	0
PMF					
None	9	20	29	14	1
2-5cm diam	2	4	9	3	0
>5cm diam	5	9	10	6	0

Note: Ex-smokers were of at least 5 years' standing. Light smokers <15 cigarettes per day, heavy smokers ≥15 cigarettes per day.

Table 4.9

Centrilobular emphysema and smoking history

(a) In whole group of 123 lungs

	Number with total centrilobular emphysema score		
Smoking history	≤12	13-24	≥25
Life-long non-smokers	13	2	1
Ex-smokers	17	11	5
Light smokers	23	19	6
Heavy smokers	14	8	1
Smokers ? amount	1	0	0

(b) In lungs without PMF >5cm diameter (n=92)

	Number with total centrilobular emphysema score		
Smoking history	≤12	13-24	≥25
Life-long non-smokers	9	1	1
Ex-smokers	12	9	3
Light smokers	20	15	3
Heavy smokers	11	5	1
Smokers ? amount	1	0	0

Note: Smoking history could not be obtained for 2 men, one of whom had PMF. Ex-smokers were of at least five years' standing. Light smokers up to 15 cigarettes/day and heavy smokers 15 or more cigarettes/day.

Table 4.10

Dust in primary foci and coalwork experience

(a) Whole group of 123 lungs

	Number of lungs with total dust score		
	⩽12	13-24	⩾25
Length of underground work (yrs)			
⩽20	14	7	1
21-40	28	21	6
⩾41	19	20	5
Length of facework (yrs)			
⩽20	28	20	4
21-40	20	18	4
⩾41	3	7	2

Note: For two men the length of underground work was unknown and for 17 men the length of facework was unknown.

(b) Lungs without PMF >5cm diameter (n=92)

	Number of lungs with total dust score		
	⩽12	13-24	⩾25
Length of underground work (yrs)			
⩽20	12	5	0
21-40	19	14	5
⩾41	17	15	3
Length of facework (yrs)			
⩽20	22	16	3
21-40	13	10	4
⩾41	3	5	0

Note: For two men the length of underground work was unknown and for 16 men the length of facework was unknown.

Table 4.11

Stellate secondary dust foci and occupational exposure

(a) In whole group of 123 lungs

	Number with stellate secondary foci		
	Absent	<10	≥10
Length of underground work (yrs)			
≤20	18	4	0
21-40	35	19	1
≥41	20	19	5
Length of coalface work (yrs)			
≤20	38	13	1
21-40	18	22	2
≥41	4	6	2
Heavy quartz exposure likely			
No	52	33	2
Yes	13	8	4

Note: Length of underground work unknown for 2 men, length of facework unknown for 17 men. Whether or not likely to have been exposed to quartz unknown for 11 men.

Table 4.11 (contd)

Stellate secondary dust foci and occupational exposure

(b) Lungs without PMF >5cm diameter (n=92)

	Number with stellate secondary foci		
	Absent	<10	≥10
Length of underground work (yrs)			
≤20	14	3	0
21-40	26	12	0
≥41	19	13	3
Length of coalface work (yrs)			
≤20	30	11	0
21-40	13	14	0
≥41	4	2	2
Heavy quartz exposure likely			
No	43	21	0
Yes	9	6	3

Note: Length of underground work unknown for 2 men, length of coalface work unknown for 16 men and likelihood of quartz exposure unknown for 10 men.

Table 4.12

Circumscribed secondary dust foci and occupational exposure

(a) In whole group of 123 lungs

	Number with circumscribed secondary foci		
	Absent	<10	≥10
Length of underground work(yrs)			
≤20	21	1	0
21-40	49	3	3
≥41	37	6	1
Length of coalface work(yrs)			
≤20	47	4	1
21-40	36	3	3
≥41	26	3	0
Heavy quartz exposure likely			
No	78	6	3
Yes	21	3	1

Note: Length of underground work unknown for 2 men, length of coalface work unknown for 17 men, likelihood of quartz exposure unknown for 11 men.

Table 4.12 (contd)

Circumscribed secondary dust foci and occupational exposure

(b) Lungs without PMF >5cm diameter (n=92)

	Number with circumscribed secondary foci		
	Absent	<10	≥10
Length of underground work (yrs)			
≤20	17	0	0
21-40	36	2	0
≥41	29	5	1
Length of coalface work (yrs)			
≤20	39	2	0
21-40	24	2	1
≥41	6	2	0
Heavy quartz exposure likely			
No	60	3	1
Yes	15	3	0

Note: Length of underground work unknown for 2 men, length of coalface work unknown for 16 men and likelihood of quartz exposure unknown for 10 men.

Table 4.13

Presence of PMF in the lungs and coalwork exposure

	Number with PMF		
	Absent	2-5cm in diameter	> 5cm in diameter
Length of underground work (yrs)			
⩽20	14	3	5
21-40	31	7	17
⩾41	27	8	9
Length of coalface work (yrs)			
⩽20	33	8	11
21-40	20	7	15
⩾41	6	2	4

Note: Length of underground work unknown for 2 men, length of coalface work unknown for 17 men.

Table 4.14

Centrilobular emphysema and coalwork experience

(a) Whole group of 123 lungs

	Number with total centrilobular emphysema score		
	≤12	13-24	≥25
Length of underground work (yrs)			
≤20	14	5	3
21-40	28	19	8
≥41	25	17	2
Length of coalface work (yrs)			
≤20	30	15	7
21-40	23	14	5
≥41	6	6	0

Note: Length of underground work unknown for 2 men, length of coalface work unknown for 17 men.

(b) Lungs without PMF >5cm diameter (n=92)

	Number with total centrilobular emphysema score		
	≤12	13-24	≥25
Length of underground work (yrs)			
≤20	13	3	1
21-40	18	15	5
≥41	20	13	2
Length of coalface work (yrs)			
≤20	25	12	4
21-40	14	9	4
≥41	4	4	0

Note: Length of underground work unknown for 2 men, length of coalface work unknown for 16 men.

Table 4.15

Centrilobular interstitial fibrosis and coalwork exposure

	Number with total centrilobular interstitial fibrosis score		
	$\leqslant 12$	13–24	$\geqslant 25$
Length of underground work (yrs)			
$\leqslant 20$	18	3	1
21–40	47	7	1
$\geqslant 41$	35	7	2
Length of coalface work (yrs)			
$\leqslant 20$	43	8	1
21–40	36	4	2
$\geqslant 41$	8	3	1

Note: Length of underground work unknown for 2 men, length of coalface work unknown for 17 men.

Table 4.16

Centrilobular emphysema and coalwork experience, stratified by smoking history

Total centrilobular emphysema score	Number with length of underground work(yrs)					
	Non-smokers		Ex-smokers		Smokers	
	≤20	>20	≤20	>20	≤20	>20
≤12	2	11	2	14	10	27
13-24	0	2	4	7	1	26
≥25	1	0	1	4	1	6

Note: For two men the length of underground work was unknown and for a further two men smoking history was unknown.

Table 4.17

(a) Associations between disability benefit received during life and pathological features and coalwork exposure in whole group.

	Number who had been receiving percentage disability benefit			
	None	10-20%	30-60%	>60%
PMF				
None	50	19	5	0
2-5cm diameter	3	6	8	1
>5cm diameter	0	6	17	8
Total dust score				
⩽12	36	11	13	3
13-24	15	16	12	5
⩾25	2	4	5	1
Total centrilobular emphysema score				
⩽12	35	15	16	3
13-24	15	11	12	3
⩾25	3	5	2	3
Length of underground work (yrs)				
⩽20	13	5	2	2
21-40	21	16	14	4
⩾41	17	10	14	3
Length of coalface work (yrs)				
⩽20	24	15	9	4
21-40	13	10	14	5
⩾41	4	2	6	0

Note: Length of underground work unknown for 2 men, length of coalface work unknown for 17 men.

Table 4.17 (cont)

(b) Associations between disability benefit received during life and pathological features and coalwork exposure, excluding lungs with PMF >5cm diameter.

	Number who had been receiving percentage disability benefit			
	None	10–20%	30–60%	>60%
Total dust score				
≤12	36	7	7	0
13–24	15	15	3	1
≥25	2	3	3	0
Total centrilobular emphysema score				
≤12	35	11	7	0
13–24	15	10	5	1
≥25	3	4	1	0
Length of underground work (yrs)				
≤20	13	3	1	0
21–40	21	12	5	0
≥41	17	10	7	1
Length of coalface work (yrs)				
≤20	24	13	4	0
21–40	13	7	6	1
≥41	4	2	2	0

Table 4.18

Centrilobular emphysema and age at death, including only lungs of smokers

	Number dying aged			
	<60	60-69	70-79	≥80
Total centrilobular emphysema score				
≤12	5	13	16	4
13-24	2	11	10	4
≥25	0	3	3	1

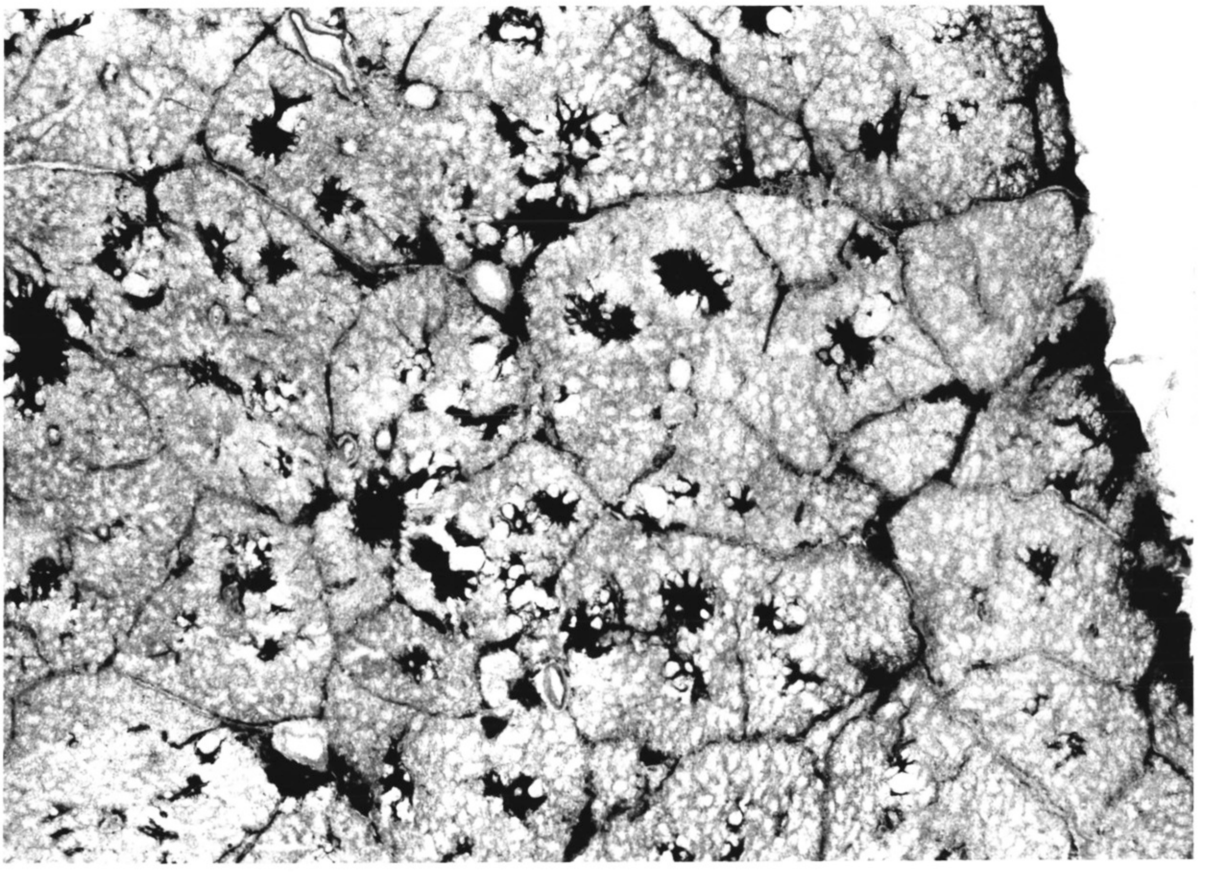


Figure 4.1

Photograph from whole lung paper-mounted section showing small primary dust foci (size 1) and minimal surrounding emphysema (grade 0/1).

Magnification X 3

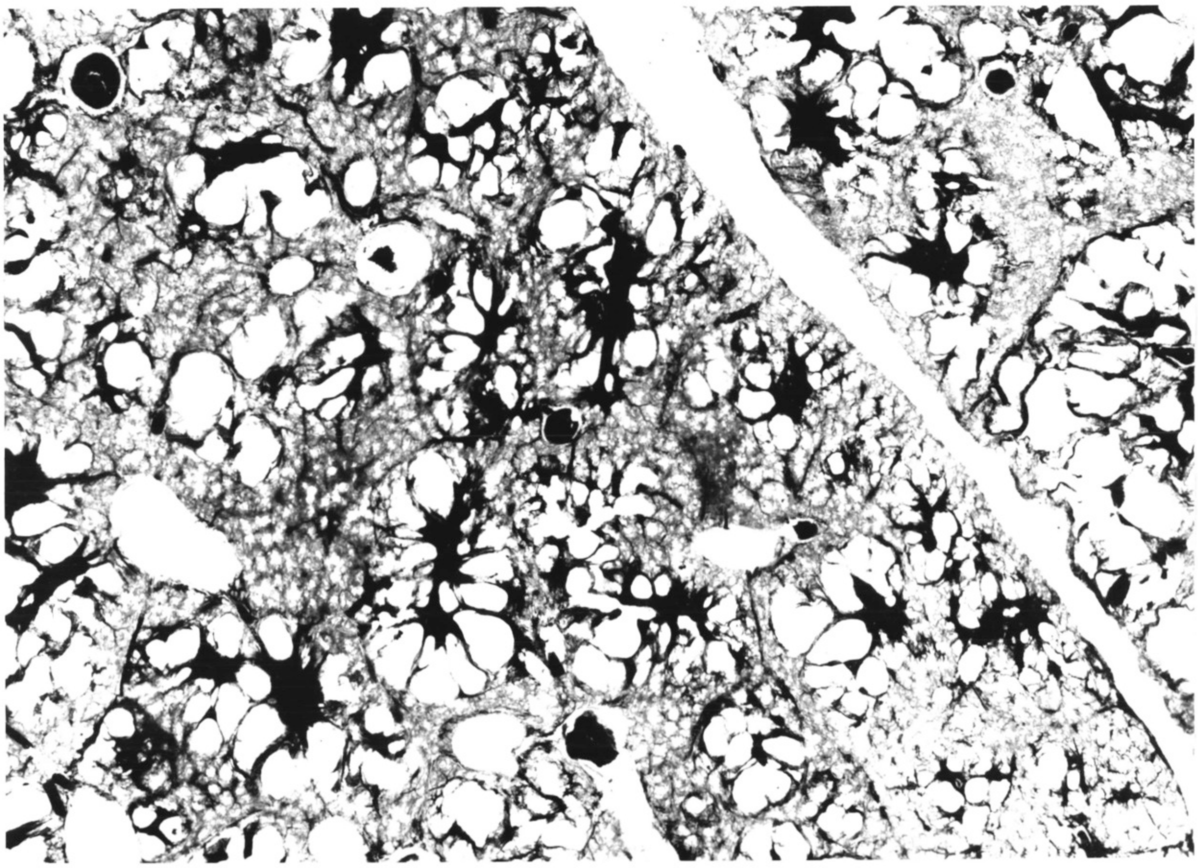


Figure 4.2

Photograph from whole lung paper-mounted section showing moderate primary dust foci (size 2) with moderate surrounding emphysema (grade 2).

Magnification X 3

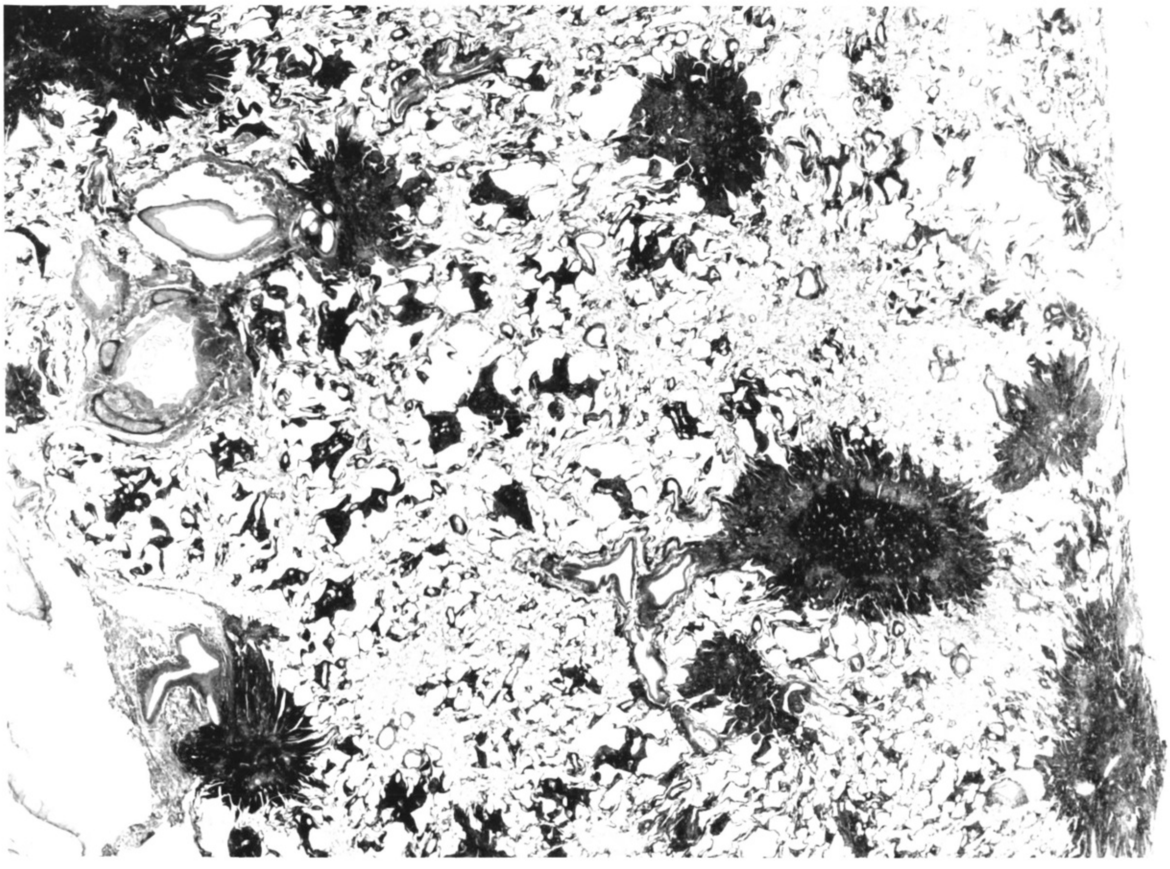


Figure 4.3

Photograph from 5X5 cm tissue section showing primary dust foci with surrounding emphysema and larger stellate secondary dust foci. Magnification X 4

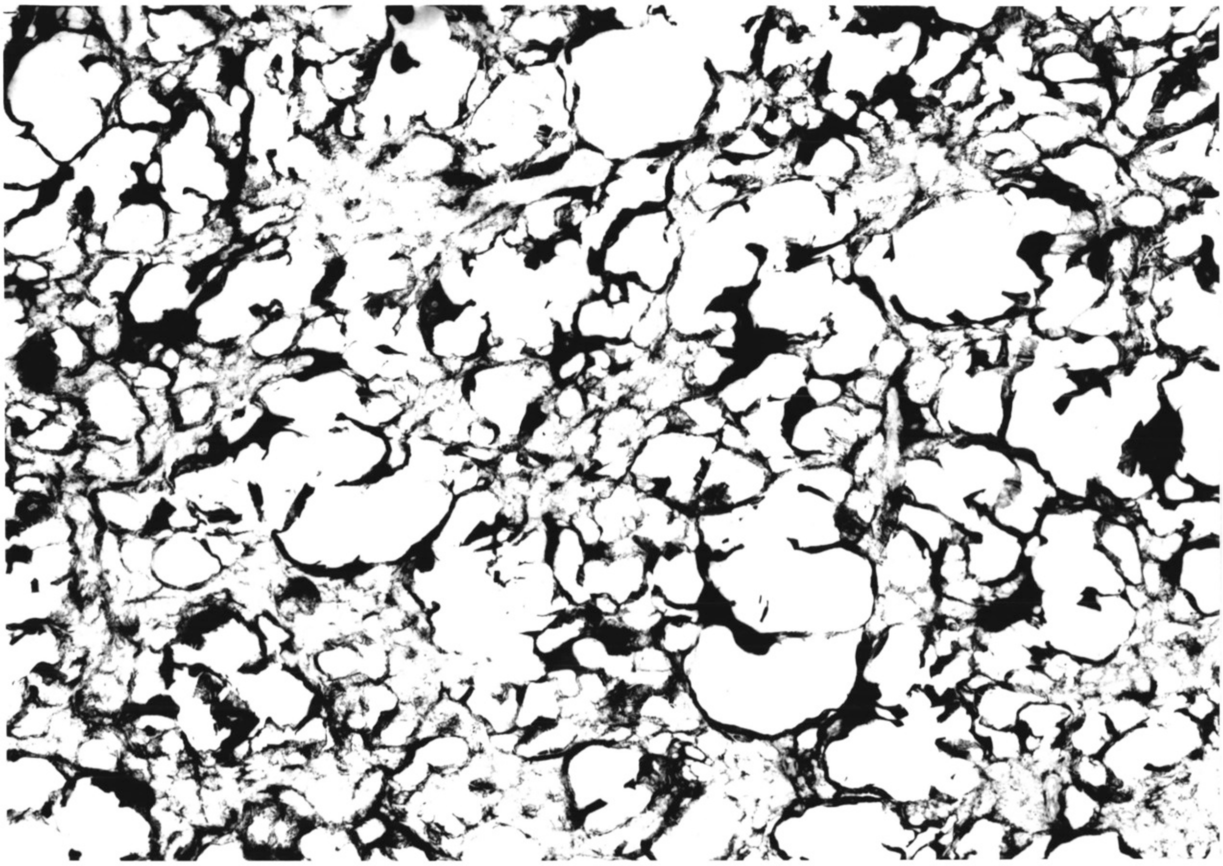


Figure 4.4

Photograph from whole lung paper-mounted section showing large primary dust foci (size 3) and severe surrounding emphysema (grade 3).

Magnification X 3

Figure 4.5

Photograph of a whole lung paper-mounted section. Simple pneumoconiosis is present with widespread small primary dust foci and minimal surrounding emphysema.

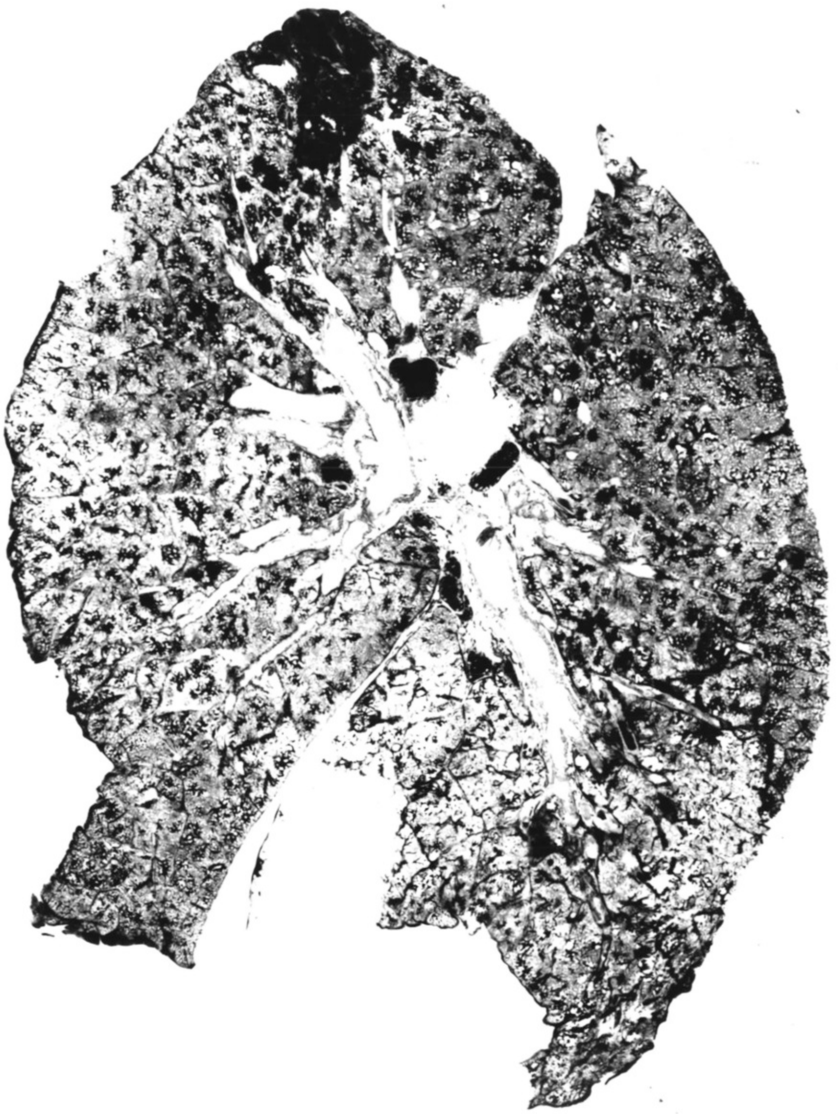


Figure 4.6

Photograph of a whole lung paper-mounted section showing a background of primary dust foci, some larger secondary foci and an area of PMF at the apex.

Figure 4.7

Photograph of a whole lung paper-mounted section. Simple pneumoconiosis is present with primary dust foci and surrounding emphysema, well seen in the upper lobe. The area in the periphery of the lower lobe appears cystic and pigmented. It is difficult to tell, macroscopically, whether this represents fibrosis, emphysema or a combination.

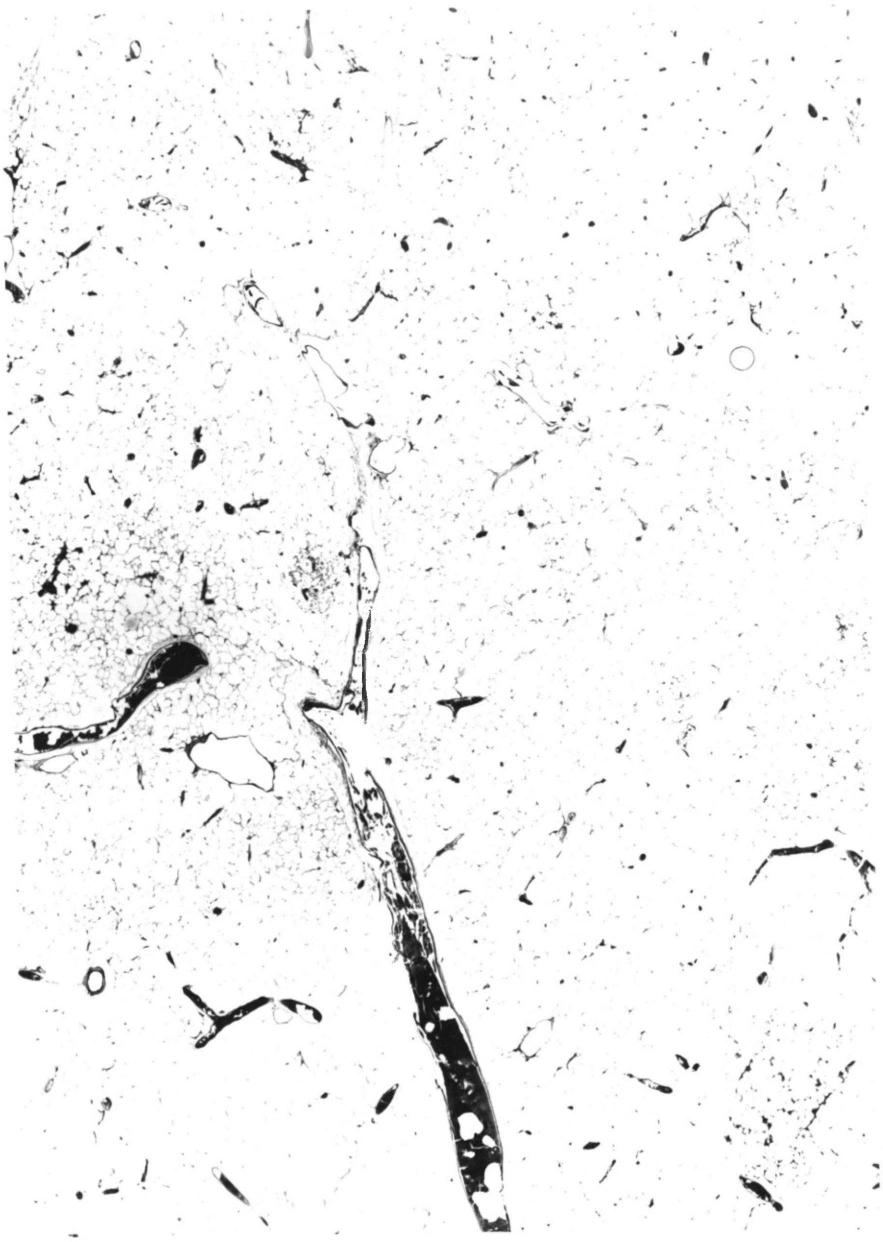


Figure 4.8

Photograph from 5X5 cm tissue section showing the appearances of a normal lung from a relatively young person on this type of section.

Magnification X 4

Figure 4.9

Photograph from 5X5 cm tissue section showing a normal lung from an older person. The air spaces are larger than in figure 4.8 and this could be regarded as minimal panacinar emphysema.

Magnification X 4

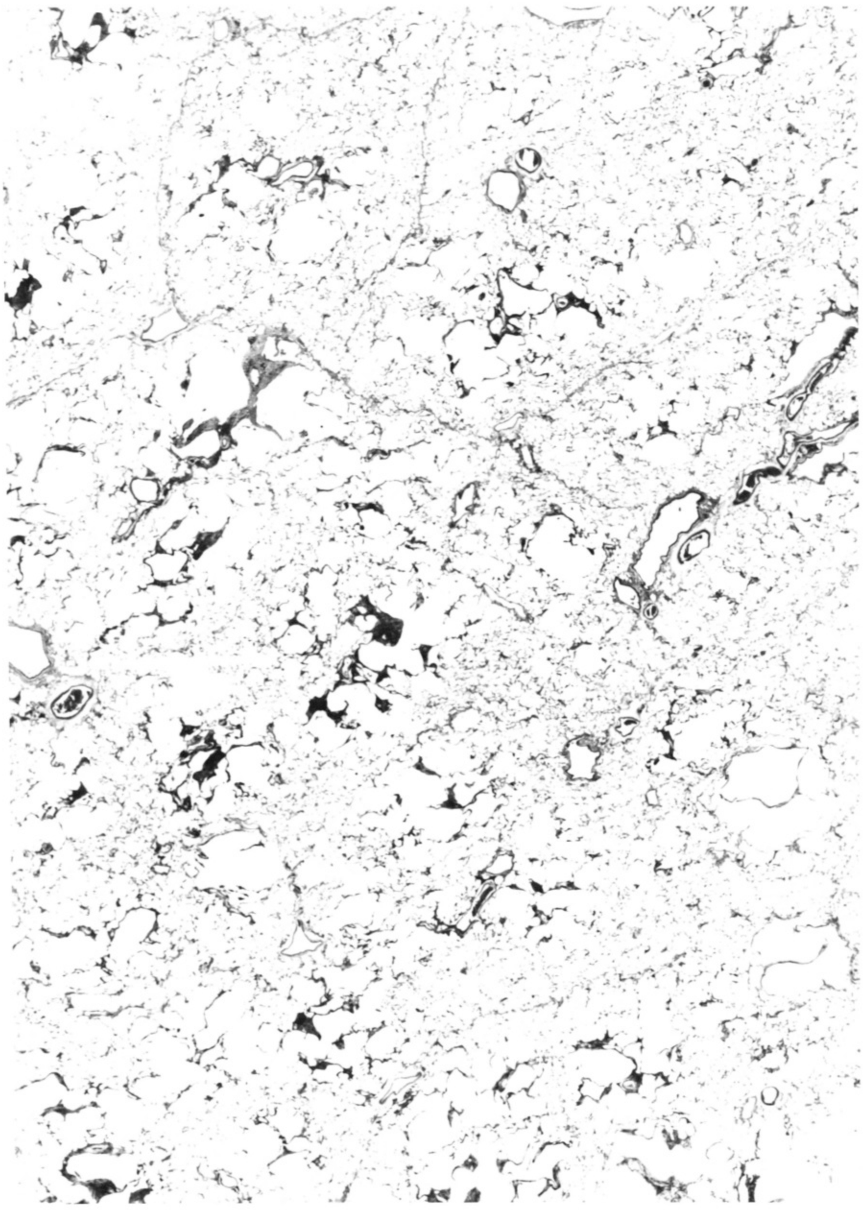


Figure 4.10

Photograph from 5X5 cm tissue section. There are small primary dust foci with a little surrounding emphysema but normal lung structure is generally well preserved. Magnification X 4

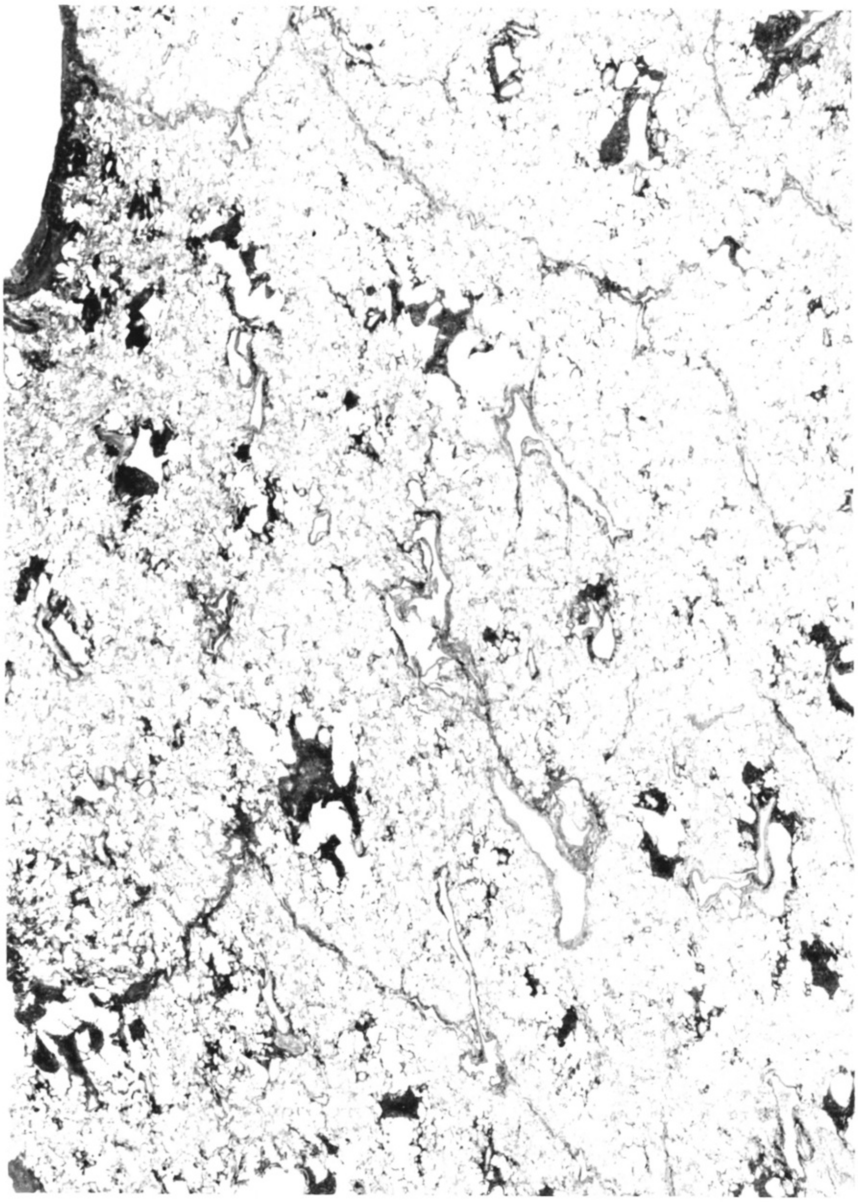


Figure 4.11

Photograph from 5X5 cm tissue section. Primary dust foci with some emphysema are present. Much of the lung architecture is normal.

Magnification X 4

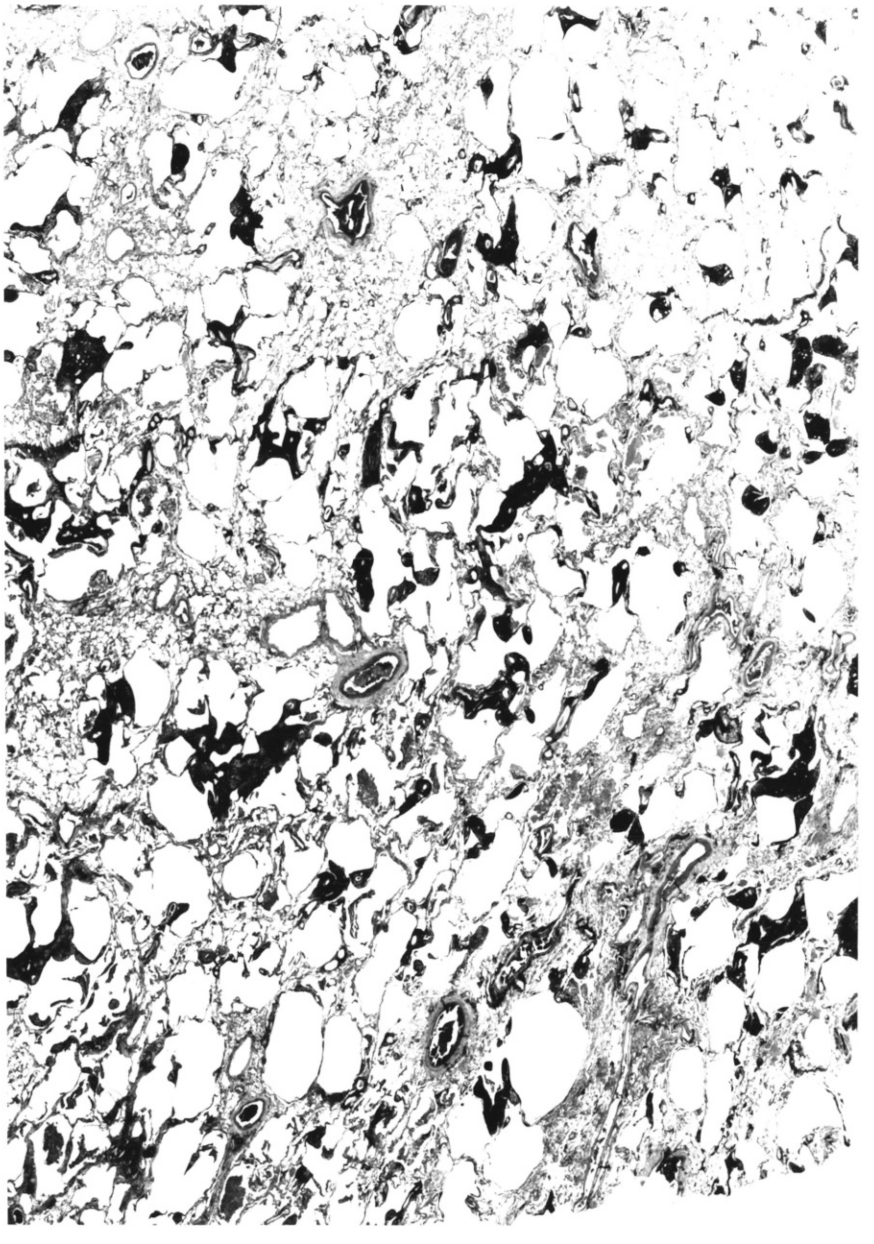


Figure 4.12

Photograph from 5X5 cm tissue section. Primary dust foci are surrounded by severe emphysema. Some of the walls of the large air spaces are thickened and pigmented. A 'rim' of apparently normal alveoli is present at the periphery of the lobules, confirming that this is centrilobular emphysema.

Magnification X 4

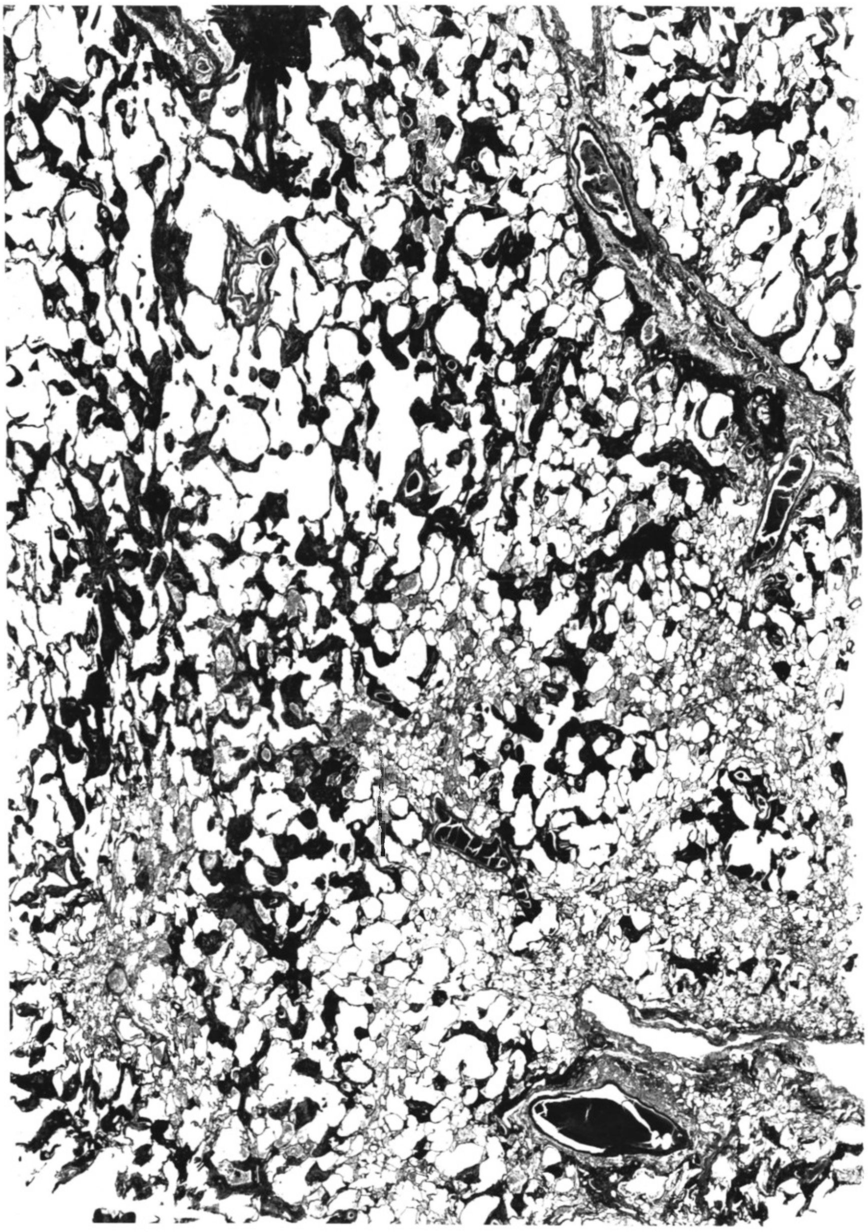


Figure 4.13

Photograph from 5X5 cm tissue section. Individual primary dust foci are hard to distinguish. Air spaces are severely enlarged throughout most of the lobules, with their walls thickened and pigmented. Areas of relatively normal alveoli are seen at the periphery of the lobules.

Magnification X 4

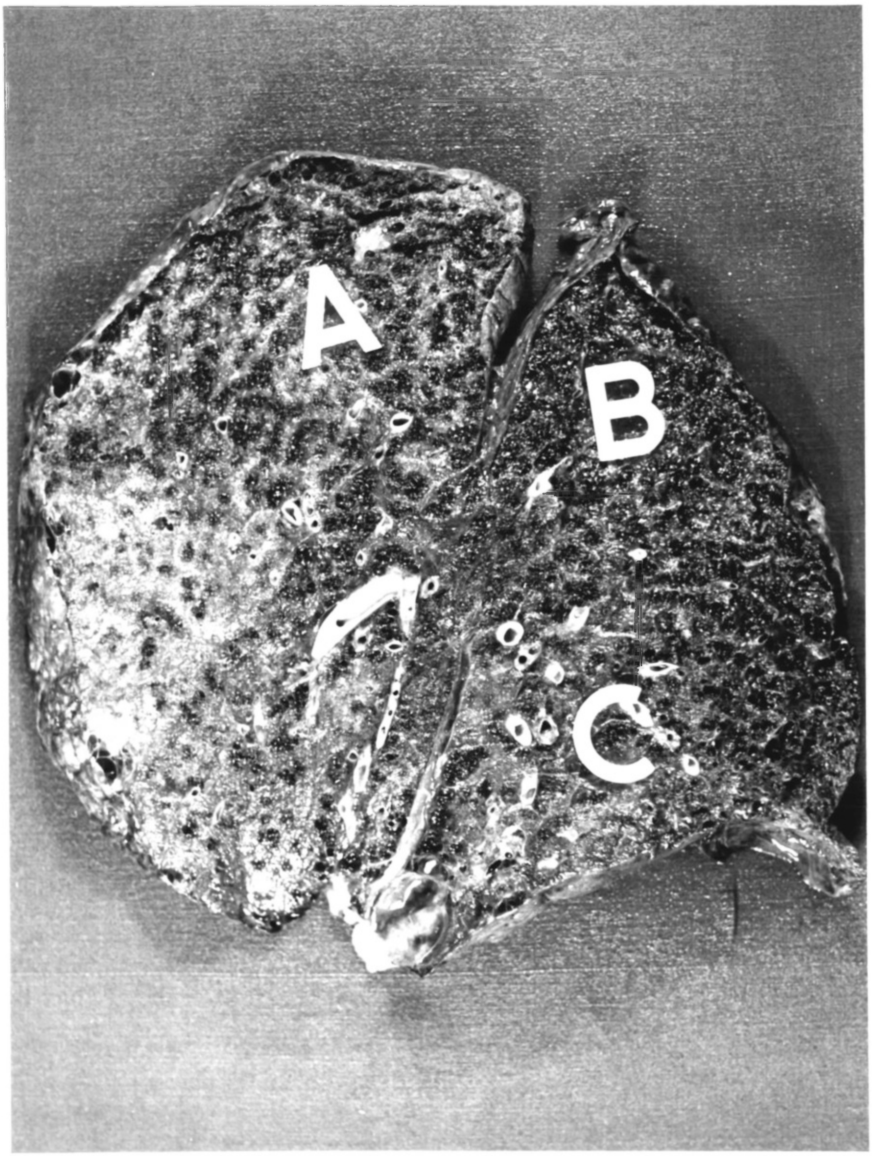


Figure 4.14

Photograph of a freshly sliced, fixed, inflated lung. The cut surface shows heavy simple pneumoconiosis and emphysema with some sub-pleural bullae. The sites for 5X5 cm tissue blocks are marked A, B and C.

CHAPTER FIVE

RADIOLOGICAL IRREGULAR OPACITIES AND POST-MORTEM LUNG PATHOLOGY IN COALWORKERS

Introduction

Radiological features are important in coalworkers' pneumoconiosis, since in Britain at least they form the basis of diagnosis of the condition during life for compensation purposes [92] and have also been used extensively in epidemiological research work. Radiology is used to define both the presence and severity of pneumoconiosis. The actual effects of dust on the lungs are seen in pathological specimens but these cannot be obtained during life; open or transbronchial biopsies would not be feasible for routine purposes and in any case only show a tiny part of a process which may vary considerably through the lungs.

The valid use of radiological features to define pneumoconiosis depends on their being related to the actual underlying lung pathology and a number of authors have reported on various aspects of this relationship. There is evidence that the category of profusion of small rounded opacities on the chest radiograph is associated with the weight of dust present in the lungs [70,67,68,69] and with the profusion of dust foci identified on whole lung paper-mounted sections [71].

The radiological reflection of lung damage related to dust foci (mainly emphysema) is more problematic. Rossiter [68] reported that focal emphysema contributed to the category of profusion of small rounded opacities on the chest radiograph, whereas Lyons and co-authors [25] found that emphysema was not related to the category of profusion of rounded opacities but rather to the profusion of irregular opacities. Recent work from the Institute of Occupational Medicine reports that there is more emphysema in men with irregular opacities and with the smallest, 'p' type, rounded opacities on the radiograph than others[75].

The aim of the work reported here was to examine the relationships between radiological features and lung pathology in a group of dead coalworkers, using numerical scores for pathological features as described in the previous chapter. The relationship, if any, between irregularity of radiological small opacities and lung pathology was of particular interest.

Subjects and Methods

The study was based on the 123 coalworkers' lungs, collected from Mid and South Glamorgan as described in Chapter 4. For 67 of these lungs a chest radiograph of the coalworker taken within 10 years of his death was available for review. These lungs and the corresponding radiographs were included in this study. The radiographs were obtained from the Pneumoconiosis Medical Panel (PMP) in Cardiff, which was also the source of occupational and smoking histories. Not all the men whose lungs were included in the study had been certified with pneumoconiosis during life, despite having all visited the PMP within 10 years of death.

The lungs were received fixed and inflated with formalin; they were sliced in a sagittal plane and features were examined on the cut surface. The features noted were primary dust foci, secondary dust foci, areas of progressive massive fibrosis (PMF), and emphysema of panacinar and centrilobular types. Scores for the features were recorded on numerical scales. Details of the methods of recording pathology are given in Chapter 4 and the forms for recording macroscopic features are reproduced in annexe 3(a). A score for 'centrilobular interstitial fibrosis' (see Chapter 4) was recorded after examination of projected 5x5 cm sections of tissue mounted on glass slides. Annexe 3(b) gives the form used for recording microscopic features.

The 67 radiographs were read in random order by a panel of three experienced readers who were unaware of the identity of the various radiographs. They used the 1980 ILO Classification of Radiographs[13]. The category of profusion of small opacities was taken as the median of the profusions recorded by the three readers. An irregularity score was derived from their recordings for size and shape of small opacities. In the 1980 classification, overall profusion of small opacities is recorded and then their size and shape are specified. Details of this are shown in annexe 2(a) and the derivation of the irregularity score is described in Chapter 2.

Scores for radiological and pathological features were compared to look for associations. Variables such as smoking were taken into account by stratification. The significance of associations was tested by means of χ^2 tests: the Mantel-Haenszel test[116] and the Mantel extension of this test[117].

Results

Figure 5.1 shows the distribution of some of the features on the chest radiographs. All were within 10 years of death and half were within 2 years of death. Twenty five of the radiographs were recorded as showing category B or C Progressive Massive Fibrosis (PMF) by at least one of the three readers. Most of the radiographs showed category 2 or 3 pneumoconiosis (42 out of 67), most had at least some irregularity of opacities (irregularity score of 3 or more) but only 11 had mainly irregular opacities (irregularity score of 6 or more). The median category of profusion of opacities on the radiographs was not related to the irregularity score recorded for them (Table 5.1). In particular, there was no tendency for radiographs with higher profusions to have higher irregularity scores.

Higher categories of profusion of small opacities on the radiographs were associated with a larger average size of primary dust foci scored pathologically (Table 5.2(a), $\chi^2=12.53, p<0.01$) and with a higher proportion of lobules involved with primary dust foci (Table 5.2(b), $\chi^2=4.63, p<0.05$). Accordingly, the category of profusion of opacities was associated with the score for total dust in primary foci (Table 5.2(c), $\chi^2=9.42, p<0.05$). Details of the calculation of the total dust score appear in Chapter 4 (p.77). When men with radiological PMF, category B or C, were excluded from analysis there was an association between profusion of small opacities and score for total dust in primary foci (Table 5.2(d), $\chi^2=6.78, p<0.05$).

The radiological irregularity score was not related to the pathological score for total dust in primary foci (Table 5.3(c) nor to the score for the proportion of lobules involved with primary dust foci. Higher radiological irregularity scores were associated with the smallest size of primary dust foci (Table 5.3(a), $\chi^2=6.65, p<0.01$). When lungs with radiological PMF (category B or C by any reader) were excluded, there was an association, significant at the 0.1% level, between higher irregularity scores and higher scores (≥13) for total dust in primary foci (Table 5.3(d), $\chi^2=10.64, p=0.001$).

The category of profusion of small opacities on the radiographs was not associated with the pathological score for centrilobular emphysema (represented by the total centrilobular emphysema score, which is the product of the scores for average severity of centrilobular emphysema and proportion of lobules involved with emphysema, see Chapter 4(p.78). This is shown in Table 5.4. On the other hand, there was an association significant at the 5% level between radiological irregularity score and centrilobular emphysema such that higher irregularity scores were associated with emphysema scores of 13 or more (Table 5.5(a) and (b), combined $\chi^2=4.04, p<0.05$). An emphysema score of 12 or less indicates little or no emphysema on the scoring system used (see Chapter 4). This association between irregularity score and emphysema score held for both radiographs with category 0 and 1 profusion of opacities (Table 5.5(a), $\chi^2=2.37, p<0.12$) and radiographs with category 2 and 3 profusion of opacities (Table 5.5(b), $\chi^2=3.16, p<0.08$). In the latter case, the association with irregularity score was mainly when emphysema scores of 25 or more (i.e. severe) were compared with lesser scores. The relative risk of having an emphysema score of 13 or more was 2.47 for those cases with an irregularity score of 3 or more on the radiograph (Table 5.5(a) and (b), combined O.R. = 2.47, $\chi^2=2.12$). An irregularity score of 3 or more means that three readers recorded at least a minority of the opacities on the radiograph as irregular. For the calculation of the odds ratio the tables 5.5(a) and 5.5(b) had to be reduced to 2X2 tables, with a consequent loss of power in the analysis reflected in the reduced χ^2 value. When cases with radiological PMF were excluded, there was a tendency among the remainder for more emphysema among those with more irregular opacities (Table 5.5(c), $\chi^2=2.40, p<0.12$).

In this group of lungs there was no association between age at death and total centrilobular emphysema score (Table 5.6) but the tendency for an association between radiological irregular opacities and emphysema was present in both younger (Table 5.6a, $\chi^2=2.55$) and older (Table 5.6b, $\chi^2=1.65$) men. For combined age categories, the association was significant at the 5% level (Table 5.6a and b, combined $\chi^2=4.17, p<0.05$).

The radiological irregularity score had no particular associations with smoking history in this group (Table 5.7a), but was weakly associated with age such that men over 70 had higher irregularity scores (Table 5.7b, χ^2=3.13,p<0.08).

There was good agreement between the recording of PMF on the radiograph (category B or C by at least one reader) and the finding of PMF after death (Table 5.8,χ^2=33.73,p<0.001). In two instances category B or C PMF was recorded on the radiograph without PMF being recorded pathologically. Only one lung was examined pathologically per subject and in these two instances the PMF may have been, as happens rarely, unilateral. In three cases PMF of greater than 5cm in diameter was recorded pathologically but none of the 3 readers noted category B or C PMF on the radiograph. This could be because of development, or increase in size, of PMF between the time of the radiograph and the time of death.

Discussion

A problem in interpreting the results of this work is the selection of the cases. It may be that coalworkers and ex-coalworkers who have had a chest radiograph within 10 years of death are importantly different from all those who have not. The 67 coalworkers in this study derived from an original group of 123 coalworkers coming to post-mortem (see Chapter 4): about half were excluded because they did not have a radiograph within 10 years of death. The potential bias resulting from this selection is not known. It may be that those with radiographs had more severe degrees of radiological pneumoconiosis and were therefore attending the PMP every 3 years after being certified with pneumoconiosis. Not all the 67 were certified with pneumoconiosis in life (16/67 were not); men not certified can apply to the PMP and visit with a radiograph at any stage. The cases then are mainly men certified with pneumoconiosis, of whom they are probably reasonably representative, and few un-certified men who had nevertheless visited the PMP within 10 years of death.

It was not surprising that the category of profusion of radiological small opacities was associated with scores for size and profusion of primary dust foci. A similar association has been reported by Caplan[71] and several authors have noted an association between profusion of radiographic opacities and weight of dust present in the lungs[70,67,68,69]. The inability to demonstrate an association between irregularity of opacities and the size and profusion of dust foci was expected, since the irregularity score was not a score for separate profusion of irregular opacities but a score for degree of irregularity of opacities of a given overall profusion.

There was no significant association, in this study, between profusion of small opacities on the chest radiograph and the degree of pathological emphysema found in the lungs, whereas there was an association between the irregularity of radiological opacities and emphysema. Men whose radiographs had at least a minority of irregular opacities were roughly two and a half times more likely than those with only rounded opacities to have emphysema present in their lungs. These findings are in accord with those of Lyons and co-workers [25]. They reported on a study of deceased South Wales coalworkers. Using the 1971 Classification of Radiographs [12] and therefore obtaining separate scores for profusions of rounded and irregular small opacities, they found that the profusion of rounded opacities was unrelated to post-mortem emphysema but that the amount of emphysema was related to the profusion of radiological irregular opacities. In addition, they found that a reduction in FEV_1 in life was related to profusion of irregular opacities but not to profusion of rounded opacities. In another study, profusion of rounded opacities was unrelated to the degree of emphysema in the lungs of 261 coalworkers but there was a significant increase in emphysema in those men whose radiographs showed irregular opacities [75].

A reasonable interpretation of these findings is that small rounded opacities, which are the predominant radiological feature of CWP, reflect fairly well the amount of dust retained in the lungs of coalworkers but do not reflect the tissue reaction to this dust, in the form of emphysema. The degree of irregularity of opacities seems to be better able to reflect pathological emphysema occuring in association with the dust load. This fits with the well-known lack of association between profusion of rounded opacities and reduction in lung function in coalworkers [53,50]. The association between irregularity of opacities and emphysema is what is predicted from the pattern of lung function deficit found in men with more irregular opacities compared with those with only rounded opacities (see Chapter 3).

In this particular group of men there was no association between age at death and pathological emphysema although such an association may be expected and was noted for the whole group of 123 men from which they were drawn (see Chapter 4). The degree of irregularity of opacities was only weakly related to age. Despite this, irregular opacities apparently had the same pathological significance in both older and younger men, since they were associated with emphysema in both age groups separately and rather more convincingly in the younger men. Thus, the evidence does not suggest an incidental association between irregular opacities and emphysema through age as the common factor but rather a real association occuring in both younger and older men alike.

It was encouraging to find good agreement between radiological and pathological assessments of PMF, since it is usually an obvious feature and large discrepancies may have pointed to errors in recording. Such discrepancies as did occur were explicable on the basis of PMF appearing or increasing after the last radiograph or because of only one lung being examined pathologically.

The results of this study confirm those of the pilot study reported in annexe 1 with regard to the association between irregular opacities and emphysema. Too little centrilobular interstitial fibrosis was found in this group to allow comparison with radiographic features, whereas fibrosis was apparently more common in the lungs in the pilot study. This may reflect the selection of cases for that study.

Having established a relationship between irregular opacities and emphysema in coalworkers, including logical associations with lung function, it is then important to establish whether the emphysema is more than would be expected in non-coalworkers (Chapter 7), how commonly irregular opacities occur in coalworkers (Chapter 8) and whether irregular opacities are related to coalwork exposure rather than other factors such as age and smoking (Chapter 9).

Summary

Radiological features were compared with post-mortem lung pathology in a group of 67 deceased coalworkers with chest radiographs within 10 years of death. Features on the radiographs were recorded using the 1980 ILO Classification of Radiographs and pathological features were recorded as described in Chapter 4.

Overall profusion of opacities was related to size and profusion of dust foci but not to pathological emphysema whereas the degree of irregularity of opacities was associated with the amount of emphysema present. This association between irregularity of opacities and emphysema was present in both younger and older men. There was no overall association between age at death and emphysema. There was good agreement between radiological and pathological assessment of PMF.

The results are in agreement with previous investigators who have looked for pathological associations with irregular opacities and would help to explain the lung function deficit found in conjunction with irregular opacities.

Table 5.1

Profusion of opacities and irregularity score.

Irregularity Score	Median category of profusion of small opacities. 0	1	2	3
0–2	0	8	12	5
3–5	1	9	10	10
6–9	2	4	3	2

Table 5.2

Relations between profusion of small opacities and simple dust foci.

	Median category of profusion on radiograph.			
	0	1	2	3
(a) Score for size of primary dust foci				
1-2	4	9	8	1
3-4	0	9	14	12
5-6	0	3	3	4
(b) Score for proportion of lobules involved with primary dust foci				
1-2	1	3	1	0
3-4	2	6	8	3
5-6	1	12	15	14
(c) Score for total dust in primary foci				
≤ 12	4	10	12	2
13-24	0	8	10	11
≥ 25	0	3	3	4

Excluding those with PMF (n=42)

	0	1	2	3
(d) Score for total dust in primary foci				
≤ 12	4	9	6	0
13-24	0	7	5	4
≥ 25	0	3	3	1

Table 5.3

Irregularity score and dust in primary foci

	Irregularity score		
	0–2	3–5	6–9
(a) Score for size of primary dust foci			
1–2	7	10	14
3–4	16	15	4
5–6	2	5	3
(b) Score for prop$^{\bar{n}}$ lobules involved with primary dust foci			
1–2	2	1	1
3–4	5	10	4
5–6	18	19	6
(c) Score for total dust in primary foci			
≤ 12	11	12	4
13–24	12	13	4
≥ 25	2	5	3
Excluding those with PMF			
(d) Score for total dust in primary foci			
≤ 12	9	6	3
13–24	7	7	2
≥ 25	1	4	2

Note: One case did not have an irregularity score because the median profusion of small opacities was 0/0.

Table 5.4

Profusion of opacities and centrilobular emphysema.

Total centrilobular emphysema score	Category of profusion of small opacities on radiograph.			
	0	1	2	3
≤ 12	2	12	12	6
13-24	2	6	8	10
≥ 25	0	3	5	1

Table 5.5

Irregularity score and centrilobular emphysema

Total centrilobular emphysema score	Irregularity score from radiograph 0-2	3-5	6-9
(a) Category 0 and 1 profusion*			
≤ 12	6	5	2
13-24	1	4	3
≥ 25	1	1	1
(b) Category 2 and 3 profusion			
≤ 12	9	8	1
13-24	8	7	3
≥ 25	0	5	1
(c) All profusions - excluding men with PMF (n=41)*			
≤ 12	12	7	3
≥ 13	5	10	4

* One case does not appear because the radiograph was read as category 0/0 and therefore did not have an irregularity score.

Table 5.6

Irregularity score and centrilobular emphysema in different age groups.

Total centrilobular emphysema score	Irregularity score on radiograph.		
	0–2	3–5	6–9
(a) <70 years old			
≤ 12	9	2	1
≥ 13	7	5	4
(b) ≥70 years old			
≤ 12	6	11	2
≥ 13	3	12	4

Table 5.7

Irregularity score in relation to smoking and age

	Irregularity score on radiograph.		
(a) Smoking History	0–2	3–5	6–9
Non-smokers	4	5	1
Ex-smokers*	6	7	8
Smokers	15	18	7
(b) Age (yrs)			
< 70	16	7	5
$\geqslant 70$	9	23	6

* Ex-smokers of 5 years or more.

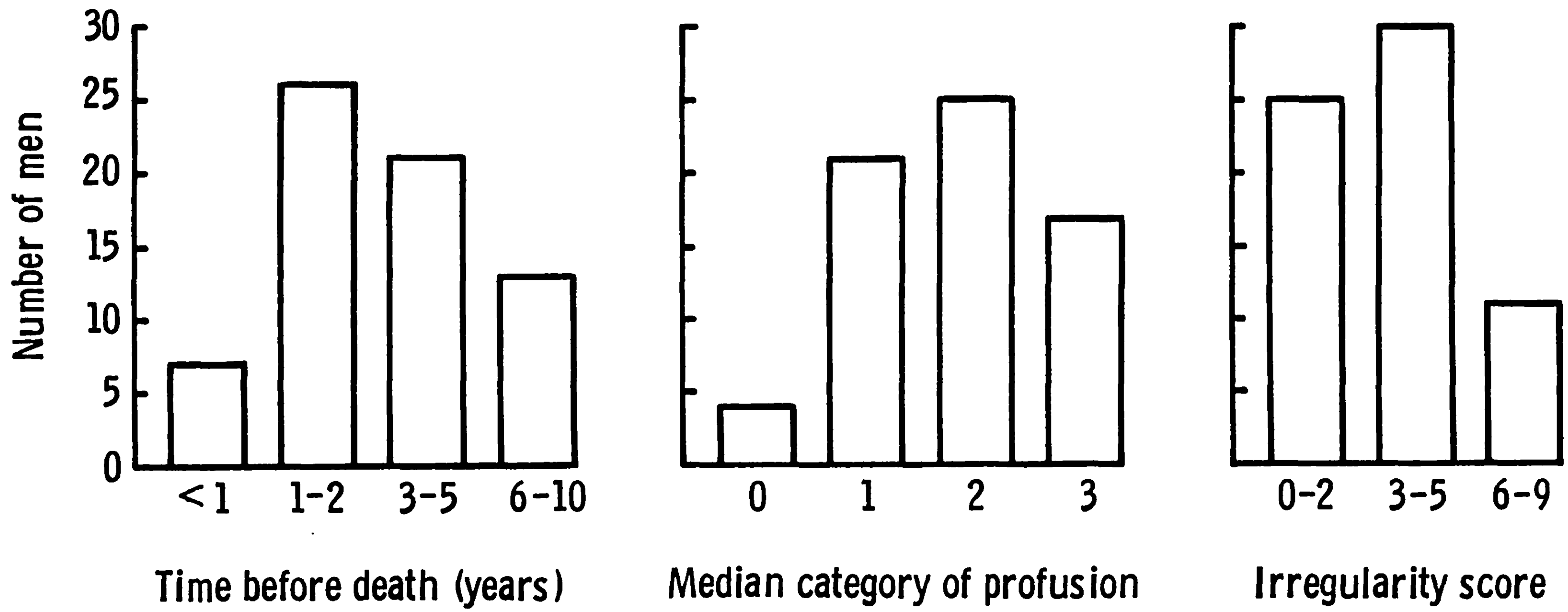
Table 5.8

Association between radiological and pathological PMF

Cat B or C PMF on radiograph	PMF recorded pathologically: Not Present	≤5cm diam.	>5cm diam.
NO	32	7	3
YES	2	6	17

Figure 5.1

Timing of the chest radiographs and distribution of scores for profusion and irregularity of opacities (radiographs of 67 deceased coalworkers).



CHAPTER SIX

SELECTION CRITERIA FOR A STUDY OF POST-MORTEM LUNG PATHOLOGY IN COALWORKERS AND NON-COALWORKERS

Introduction

The finding of an apparently excessive amount of centrilobular emphysema in coalworkers as described in Chapter 4 could theoretically be spurious since non-coalworkers selected in the same way may have an equal amount of emphysema. The problem in making a comparison of post-mortem pathology in coalworkers and non-coalworkers is to get men who are comparable with respect to their chances of having the sort of pathology in question under the null hypothesis (that occupational factors do not play a part).

A simple series of all coalworkers and non-coalworkers coming to post-mortem over a given period (whether age-matched or not) does not solve the problem since it is likely that more coalworkers than non-coalworkers come to post-mortem and the selection factors that bring the non-coalworkers to post-mortem are not known.

The present study set out to look at the post-mortem rates of coalworkers and non-coalworkers to see if criteria for selection could be found which would mean that the lung pathology of coalworkers and non-coalworkers could be validly compared.

Methods

The hospitals which provided post-mortem material for the pathology studies covered an area of Mid and South Glamorgan. A list of all adult male deaths in Mid and South Glamorgan between 1st January and 13st December 1979 was compiled. This involved visiting the Community Health Centres of Mid Glamorgan, where copies of all death returns are kept, and extracting information onto a tape-recorder.

The information extracted was date of birth, date of death, causes of death (as on the death certificate) and occupation (whether ever a coalworker or not). Men were only noted as coalworkers when this was definitely stated on the return. The information from the tapes was later typed onto sheets, with coalworkers and non-coalworkers separated. The staff of the Area Medical Officer extracted similar information from the South Glamorgan death returns.

A second list of all post-mortem examinations over the same period on adult men in the same area was prepared. This was obtained from the post-mortem records of all the hospitals in the area, including hospitals other than those providing material for the pathology studies. The study area had to include the whole of both Mid and South Glamorgan because the post-mortem 'sub-areas' and death return 'sub-areas' did not coincide. One hospital, for example, performed post-mortems on men from both Mid and South Glamorgan. The same information was extracted from the post-mortem records as from the death returns. In this case it was typed onto individual record cards to allow easy categorisation.

The death and post-mortem lists were coded for underlying cause of death according to the International Classification of

Diseases (ICD) Ninth Revision (138). The two lists were then compared and post-mortem rates (number of post-mortems divided by number of deaths) were calculated for coalworkers and non-coalworkers for specific causes of death. The rates for each cause of death were further subdivided into 5 year age categories. The rates were examined in an attempt to find a cause of death/age category where the post-mortem rates were high and similar in coalworkers and non-coalworkers. It was initially hoped to examine the rates in separate sub-areas but this was impossible because of the lack of concordance between death and post-mortem sub-areas, as mentioned above. This is probably a feature in most regions of Britain.

Results

Data were recorded on 1267 deaths among coalworkers and 4476 deaths among non-coalworkers (adult men) during 1979 in Mid and South Glamorgan. Post-mortem examinations were recorded on 886 coalworkers and 1219 non-coalworkers in the area during the study period.

In men up to the age of 69 years, dying of ischaemic heart disease (ICD codes 410 and 414), the post-mortem rates in both coalworkers and non-coalworkers were high. The post-mortem rates, by age, are shown in table 6.1. The rates are high probably because sudden death is relatively common in ischaemic heart disease, making post-mortem examination more likely. Almost all the post-mortem examinations in the survey were at the coroner's request, except in the main teaching hospital in the area.

In some age categories the recorded number of post-mortems for coalworkers was greater than the recorded number of deaths. The probable explanation for this is that the occupation of 'coalworker' or 'ex-coalworker' was under-recorded from the death returns, where strictly the last occupation before death is entered. This failure to record coalworkers as such is known to have occurred in some cases where men dying of coalworkers' pneumoconiosis had the occupation 'labourer' or 'council worker' recorded on the death return. On the other hand the fact of having been a coalworker is more diligently noted at post-mortem examination since the lungs of those men who have been coalworkers have to be sent on to the Pneumoconiosis Medical Panel for examination. The post-mortem rates were corrected to bring those of the coalworkers back to unity. This meant that the proportion of coalworkers who must have been recorded as non-coalworkers on death returns was at least 3% (of deaths of coalworkers). This correction was then applied to all the age categories except the younger ones where failure to record as a coalworker on the death return seemed less likely since many would still have been working as coalworkers at the time of death. The effect of the correction is shown in table 6.2. This estimate of the number of coalworkers not recorded as such on the death return is a minimum and the actual number may be higher.

For other causes of death, post-mortem rates were generally lower and differed more widely between coalworkers and non-coalworkers.

For example, the post-mortem rates for men dying of respiratory diseases (ICD 480-519) are shown in table 6.3. The post-mortem rates were rather low in both groups, particularly the non-coalworkers. In any case, it was thought that respiratory causes of death, unlike ischaemic heart disease, might be related to the lung pathology in question and therefore the differences in post-mortem rates were more important.

On the basis of these findings with regard to post-mortem rates it was decided to include in the study of post-mortem lung pathology in coalworkers and non-coalworkers only those men who died of ischaemic heart disease between the ages of 50 and 70. There is no reason to believe that IHD is related to lung pathology differently in coalworkers and non-coalworkers, and men in the age bracket 50-70 who die of IHD have a high post-mortem rate whether they are coalworkers or not.

Discussion

This study has determined selection criteria which, when applied to coalworkers and non-coalworkers coming to post-mortem, allow a valid comparison of pathology between the two occupational groups. The post-mortem rates in the categories of coalworkers and non-coalworkers chosen for selection were not exactly equal but were high for both groups. A minimum correction was made for coalworkers being recorded as non-coalworkers on the death returns. There is evidence, from comparison of census and death certificate data, that the true number of coalworkers recorded as non-coalworkers on the death certificate is much higher than the correction of 3% that was used (Prof AL Cochrane, personal communication). Thus the post-mortem rates among non-coalworkers are probably higher than calculated, approaching those of the coalworkers. The high rates of post-mortem in both groups, related often to sudden death, mean that in a post-mortem series selected using these criteria (death from IHD, age 50-70) there is relatively little chance for differential selection into the series by occupation. Thus the relative frequency of lung pathology found in the coalworkers and non-coalworkers in such a series should validly reflect the relative frequency in all coalworkers and non-coalworkers dying of IHD in the study area and, by extrapolation, all coalworkers and non-coalworkers in the area.

It could be argued that the perfect post-mortem series would be one where the post-mortem rate for both coalworkers and non-coalworkers was 100%. Such a group may exist but would be small, dying from some relatively rare cause. In such a group the frequency of the pathology under investigation may well not be representative of the overall frequency in the population. Also, although younger age groups may have higher post-mortem rates it is not useful to study people dying below the age when the pathology in question is likely to occur.

It is important that the cause of death selected for inclusion into the post-mortem series should not be related to the pathology in question, particularly not related differently in coalworkers and non-coalworkers. Respiratory causes of death are probably unsuitable because of this, quite apart from the differing post-mortem rates by occupation. Although ischaemic heart disease may be associated with pulmonary emphysema because both are associated with smoking, there is no reason to believe that it is differently related to emphysema in coalworkers and non-coalworkers (under the null hypothesis). Ischaemic heart disease may itself be associated with coalwork but this is not important unless that association depends on an association with the pulmonary pathology in question and there is no reason to suspect this.

The validity of the method assumes that there has been no differential migration out of the area of coalworkers or non-coalworkers with differing rates of the lung pathology in question, who go on to die of ischaemic heart disease. There is no evidence for or against this possibility. In the calculation of post-mortem rates all deaths in the area were included, even those of men not living in the area, and those of men living in the area but dying elsewhere were excluded. This was because information was only available about post-mortems performed on men dying in the area.

The collection and tabulation of data in this study and the calculation of post-mortem rates were performed manually. In future work of this sort, the use of a computer to handle the data would make matters less laborious. The Office of Population Census and Surveys can provide tabulations of deaths by cause and occupation for particular areas on special request. The use of such tabulations would have shortened the period of data collection for the study but would have provided less detailed data. For example, individual men who had clearly been coalworkers (because they had died of coalworkers' pneumoconiosis) but were not recorded as coalworkers on the death returns would not have been picked up.

The use of post-mortem material in epidemiological studies is fraught with difficulties. This was pointed out in a letter[139] criticising a study by Lyons and co-workers based on post-mortem material[90]. Rather than conclude that one has to throw away the valuable information available from the study of post-mortem material because of validity problems, another approach is to identify and attempt to overcome the problems. The work described in this chapter represents such an attempt. It is made use of in the following chapter in a study of post-mortem pathology in coalworkers and non-coalworkers.

Summary

Selection of men to post-mortem examination by occupational factors often causes problems for epidemiological investigation of occupationally related pathology. This study established enrolment criteria which would reduce the effects of this selection bias in the investigation of pulmonary pathology among coalworkers and non-coalworkers. Details of all adult male deaths and post-mortem examinations in the study area over the preceding year were obtained. Post-mortem rates for coalworkers and non-coalworkers were calculated, broken down by age and underlying cause of death.

The rates for coalworkers were generally higher than those for non-coalworkers. For men between 50 and 70 years old, dying of ischaemic heart disease (IHD), post-mortem rates were high for both groups. There is no reason to believe that IHD is differently related to pulmonary pathology in coalworkers and non-coalworkers and it is a common cause of death. It was concluded that men between 50 and 70 years old dying of IHD were relatively unselected to post-mortem with regard to occupation and would therefore provide a realistic basis for comparison of pathology.

The selection criteria determined from this work were used in the study of post-mortem pulmonary pathology in coalworkers and non-coalworkers described in Chapter 7.

Table 6.1

Deaths, post-mortem examinations and post-mortem rates for ischaemic heart disease (ICD 410 and 414) in Mid and South Glamorgan in 1979

	COALWORKERS			NON-COALWORKERS		
Age	No. of Deaths	No. of port-mortem exams.	Post-mortem rate	No. of Deaths	No. of post-mortem exams.	Post-mortem rate
40-44	6	4	0.67	17	13	0.76
45-49	7	5	0.71	47	23	0.49
50-54	14	16	1.14	68	49	0.72
55-59	24	29	1.21	161	81	0.50
60-64	38	41	1.08	152	78	0.51
65-69	73	72	0.99	227	98	0.43
70-74	61	44	0.72	222	67	0.30
75-79	70	47	0.67	200	61	0.31
80-82	37	39	1.05	125	31	0.25
85-89	16	7	0.44	28	14	0.50
90+	-	-	-	-	-	-

Note: Ages under 40 are not shown, as there were no deaths from ischaemic heart disease recorded below 40 years.

Table 6.2

Corrected post-mortem rates for ischaemic heart disease (ICD 410 and 414) in Mid and South Glamorgan in 1979

	COALWORKERS			NON-COALWORKERS		
Age	'Corrected' No. of Deaths	No. of port-mortem exams.	'Corrected' post-mortem rate	'Corrected' No. of Deaths	No. of post-mortem exams.	'Corrected' post-mortem rate
40–44	6*	4	0.67*	17*	13	0.76*
45–49	7*	5	0.71*	47*	23	0.49
50–54	16	16	1.00	66	49	0.74
55–59	29	29	1.00	156	81	0.52
60–64	41	41	1.00	149	78	0.52
65–69	76	72	0.95	224	98	0.44
70–74	64	44	0.67	219	67	0.31
75–79	73	47	0.63	197	61	0.31
80–84	39	39	1.00	123	31	0.25
85–89	16*	7	0.44*	28*	14	0.50*
90+	-	-	-	-	-	-

* Number of deaths and post-mortem rates not corrected (see text)

Table 6.3

Deaths, post-mortem examinations and post-mortem rates for respiratory diseases (ICD 480-516) in Mid and South Glamorgan in 1979

	COALWORKERS			NON-COALWORKERS		
Age	No. of Deaths	No. of port-mortem exams.	Post-mortem rate	No. of Deaths	No. of post-mortem exams.	Post-mortem rate
40-44	0	1	-	3	3	1.00
45-49	1	3	'3'	8	2	0.25
50-54	5	4	0.80	14	4	0.29
55-59	16	19	1.19	35	7	0.20
60-64	26	21	0.81	38	12	0.32
65-69	41	39	0.95	99	17	0.17
70-74	67	48	0.72	119	21	0.18
75-79	69	35	0.51	127	8	0.06
80-84	57	18	0.32	102	4	0.04
85-89	22	11	0.50	85	7	0.08
90+	6	1	0.17	57	2	0.04

CHAPTER SEVEN

POST-MORTEM PULMONARY PATHOLOGY IN COALWORKERS AND NON-COALWORKERS

Page no.

Introduction

Chapter 4 has described the pulmonary pathology found in a group of dead coalworkers. Certain of the features, such as dust foci and Progressive Massive Fibrosis (PMF), are more or less specific to coalworkers and would not be expected in a group of dead non-coalworkers. Non-specific features, such as emphysema and interstitial fibrosis, may or may not be more common in coalworkers than non-coalworkers. The purpose of the work described in this chapter is to compare emphysema in coalworkers and non-coalworkers coming to post-mortem.

Chapter 6 describes a study undertaken to find selection criteria for the present study that would allow a comparison of pathology at post-mortem to reflect the relative frequencies of that pathology in coalworkers and non-coalworkers during life. The criteria derived from that study to allow a valid comparison - i.e. coalworkers and non-coalworkers dying of ischaemic heart disease (IHD, ICD Nos. 410- 414) between the ages of 50 and 70 - were used to select material for this study. In this way, it was hoped to avoid the criticisms of non-representativeness[40,39] levelled at a previous study of post-mortem pathology in coalworkers and non-coalworkers[33].

It is important to establish whether or not there is a real excess of emphysema in coalworkers. Early reports on the pathology of simple coalworkers' pneumoconiosis described emphysema as part of the condition[30,27]. But the importance of this kind of emphysema in producing functional impairment has been questioned (35) and emphysema has been reported to be quite common in post-mortem surveys of the general population (140,141). In a recent article the Senior Medical Officer of the DHSS concluded, on the basis of a 'detailed survey' by Parkes (124) and 'personal clinical experience', that disabling emphysema is not more common in coalworkers than in the general population (141a).

The work described here ties in with the theme of irregular opacities in coalworkers in that in annexe 1 and Chapter 5 evidence was presented that radiological irregular opacities are associated with pathological emphysema in coalworkers. Thus, any excess emphysema that does occur in coalworkers may be identified in life in those with radiological irregular opacities.

<u>Subjects and methods</u>

The study was done in the catchment area of two hospitals in South Wales, covering parts of Mid and South Glamorgan. Selection criteria for entry into the study were those derived from the study described in Chapter 6 - i.e. men dying of ischaemic heart disease, aged between 50 and 70 years. For these men, post-mortem rates were high for both coalworkers and non-coalworkers. These high rates reduced the possibilities for differential selection into post-mortem. There were other advantages of including only men dying of IHD: there is no reason to believe that IHD is related to the frequency of emphysema differently in coalworkers and non-coalworkers; it is a common cause of death so material could be collected over a reasonably short period; and emphysema found incidentally in men dying of IHD is likely to be an unbiased index of the prevalence in the whole male population.

The coalworkers and non-coalworkers fulfilling the selection criteria were consecutive groups from men coming to post-mortem in the study hospitals. The coalworkers were extracted from the larger series of 123 described in Chapter 4, who were the total number of coalworkers coming to post-mortem during the study period. Pathological material from 39 coalworkers and 48 non-coalworkers was collected.

For each subject dates of birth and death, cause(s) of death and occupation ("was he ever a coalworker") were obtained from the post-mortem record. Smoking histories were sought. Most of the post-mortem examinations in the study were at the coroner's request and the coroner's officers were asked to enquire about smoking history during their routine interview with relatives. For some of the coalworkers, smoking information was available from a recent visit to the Pneumoconiosis Medical Panel (PMP). However, a number of the coalworkers had never been seen by the PMP or had only been seen many years previously. When no information about smoking was available from these two sources, a social worker visited the relatives two months or more after the man's death and asked about smoking history. She was asked to visit the relatives of several men for whom recent smoking histories from PMP notes were available. This made possible a comparison between the smoking histories from these two sources. The form used by the social worker to record smoking and occupational history is shown as annexe 4(c).

In each case two pathologists examined one lung, inflated and fixed with formalin. A sagittal slice was made and features were assessed on the cut surface. Findings were scored on numerical scales on standard forms. The method of assessment and the types of features recorded are described in detail in Chapter 4 and the forms used for recording features are shown as annexes 3(a) and 3(b). The scores used in this study were for the size and distribution of simple dust foci, the presence and size of any progressive massive fibrosis (PMF) and the average severity and distribution of centrilobular and panacinar emphysema. From these scores a total dust score (size of foci x proportion of lobules involved) and total emphysema scores (average severity x proportion of lobules involved) were derived. Blocks of tissue from upper and lower lobes of the lungs were prepared and mounted on 5 x 5 cm slides. These were projected using an ordinary transparency projector and examined to confirm the type and severity of emphysema. Occasionally the macroscopic scores were modified as a result. The pathologists were not aware of the men's occupational or smoking histories when they examined the lungs but coalwork experience was usually obvious because of the dust foci.

In analysing the results, counts of subjects with various score levels were compared between groups, with variables such as smoking and age taken into account by stratification. The significance of differences between groups was tested using the Mantel-Haenszel test [116], the Mantel extension of this test [117] or Fisher's Exact test.

Results

The coalworkers had more centrilobular emphysema than the non-coalworkers. The difference between the groups was significant at the 0.01% level (Table 7.1, χ^2=18.14). In Table 7.1 a total centrilobular emphysema score of 6 or less indicates virtually no emphysema, 7 to 12 is mild emphysema, 25 and above is severe emphysema and intermediate scores indicate grades in between.

The coalworkers were older than the non-coalworkers and this difference was significant at the 5% level (Table 7.2, χ^2=5.88). There were more lifetime non-smokers among the non-coalworkers than among the coalworkers (Table 7.2, $p<0.1$, χ^2=2.28). Amongst the coalworkers there was a weak tendency for more centrilobular emphysema in smokers and ex-smokers than in non-smokers (Table 7.2, $p<0.1$, χ^2 =1.89) but the data did not demonstrate any increase in emphysema with age. The range of emphysema scores in the non-coalworkers was too limited to allow the examination of smoking and age effects in them separately.

The difference in amount of centrilobular emphysema between coalworkers and non-coalworkers was still statistically significant at the 1% level when only men more than 60 years old were included (χ^2 =9.64), when only current smokers were considered (χ^2=9.98), and when current and ex-smokers together were considered (χ^2=13.88) (Table 7.2). Considering only men over 60 years old who were current smokers, the excess of centrilobular emphysema amongst the coalworkers was signficant at the 2% level (Table 7.2, χ^2=6.34). The proportion of heavy smokers was not higher amongst the coalworkers than amongst the non-coalworkers (Table 7.3, χ^2=2.88, Odds Ratio=0.38). An excess of heavy smokers among the coalworkers of more than 16% can be excluded with 95% confidence. Table 7.3 also shows centrilobular emphysema in relation to the amount smoked by current smokers amongst coalworkers and non-coalworkers.

Virtually no panacinar emphysema was detected in either group. Eight of the coalworkers had PMF of greater than 5 cm in diameter and two of these had total centrilobular emphysema scores of greater than 19. When men with PMF were excluded the excess of centrilobular emphysema amongst the coalworkers was significant at the 0.1% level.

Of the 39 coalworkers in the study, over half had a total dust score of less than 12, indicating a light dust load (Table 7.4). Many of them were not receiving any disability benefit for pneumoconiosis. Their average length of underground work was 28 years with an average of 22 years of facework. The amount of centrilobular emphysema was strongly associated with the amount of dust in simple dust foci (Table 7.4, $p<0.001$, χ^2=13.95).

Discussion

This study indicates an excess of emphysema in coalworkers compared with a group of similarly-selected non-coalworkers. The finding is in agreement with results reported from other post-mortem surveys [33,36,37]. A previous study from South Wales [33] was of 247 coalworkers and ex-coalworkers, nearly all of whom had been receiving disability benefit for pneumoconiosis, and 247 non-coalworkers coming to post-mortem in the same area and matched for age and sex. It was criticised on the grounds that the results only applied to coalworkers with pneumoconiosis and not to the whole population of coalworkers in the area [142]. It was also claimed that the coalworkers studied may have had a greater amount of emphysema than the population from which they came [40,39]. Another possible bias was that more coalworkers than non-coalworkers dying of respiratory diseases may have been found in the series simply because the post-mortem rate for coalworkers dying of respiratory diseases is higher than for non-coalworkers dying of these diseases (see Chapter 6). This could have produced a spurious excess of emphysema n the coalworkers.

In the present study coalworkers were not selected in terms of a diagnosis of pneumoconiosis or other chest diseases in life. The coalworkers and non-coalworkers were selected similarly with regard to their chances of having pulmonary pathology other than as a result of occupational factors. The emphysema in both groups was incidental and rarely severe, even in the coalworkers, since no men dying of respiratory causes were included. The actual frequency of emphysema found in each of the study groups must be less than that in the whole population of coalworkers and non-coalworkers in the study area. However, the relative frequency comparing the groups reflects or may even underestimate the relative frequency comparing all coalworkers and non-coalworkers in the study area.

As may be expected , there was an association between smoking and emphysema in this study. Although there were less non-smokers among coalworkers than among non-coalworkers, there was still an excess of emphysema in coalworkers when only current smokers, or current and ex-smokers, were considered (Table 7.2). There remained the possibility that current smokers amongst coalworkers smoked more heavily than current smokers amongst non-coalworkers. There was no evidence from the data that this was the case; among coalworkers 10 of 25 current smokers were heavy smokers, compared with 16 of 25 among non-coalworkers (see Table 7.3). The question of accuracy of the smoking histories could be raised, partly because no excess of emphysema was found in coalworkers recorded as heavy smokers compared with those recorded as light smokers (see Table 7.3). About half the coalworkers in the series had smoking histories from PMP notes and about half had histories obtained from relatives. All the non-coalworkers had histories obtained from relatives. Histories were duplicated in some of the coalworkers and this allowed a search for discrepancies between histories given to the PMP and histories given by relatives (figure 7.1). In two men, the histories from PMP notes suggested they were light smokers whereas those from relatives suggested they were heavy smokers. The agreement between histories obtained by the two methods was otherwise complete. Even if the half of the coalworkers who had histories from the PMP had under-estimated in the same proportion (2 out of 5 heavy smokers recorded as light smokers) there would still not have been an excess of heavy smokers amongst the coalworkers compared with the non-coalworkers (see Table 7.3). It is extremely difficult to eliminate recall bias in this type of study but here it has been adequately taken into account and it seems very unlikely that the coalworkers in this series smoked more heavily than the non-coalworkers. Previous studies which have examined smoking habits in coalworkers and non-coalworkers have revealed a pattern similar to that found in this study: more smokers among the coalworkers but a lower proportion of heavy smokers [143,144].

No gradient of emphysema with age was apparent in these small groups but this may be because there was only a 20 year age range.

In this study, as in annexe 1 and Chapters 4 and 5, centrilobular emphysema has been assessed as defined at the CIBA symposium in 1959 [125]. Minimal degrees of this type of emphysema in coalworkers would correspond to focal emphysema. In the coalworkers in this series the emphysema was found around the dust foci and there was an association between the size and distribution of dust foci and the severity and distribution of centrilobular emphysema (see Table 7.3). This in agreement with the findings from the larger series of coalworkers reported in

Chapter 4.

Taken together with Chapter 4, this study provides strong evidence that there is an excess of emphysema in coalworkers related to the coal dust foci in their lungs. This emphysema-in-association with coaldust is reflected radiologically by irregular opacities (see Chapter 5). At present, emphysema is neither a Prescribed Industrial Disease in its own right (for coalworkers or any other occupational group) nor is it considered to be part of simple coalworkers' pneumoconiosis. This situation may change, so that emphysema comes to be considered as an integral part of the disease process in simple CWP. In this case, the identification of irregular opacities on the radiograph of coalworkers would be important, since it is apparently this feature rather than the profusion of opacities (mainly rounded) that best reflects the presence of emphysema. The inclusion of irregular opacities in the radiological definition of coalworkers' pneumoconiosis may result in more men being certified with the condition; the acceptance of the emphysema the opacities represent as part of the condition may result in increases in the percentage disability assessments of men already certified[145].

Particularly in view of these possible implications, it is important to know how many coalworkers display radiological irregular opacities and this is investigated in Chapter 8.

Summary

A post-mortem survey of emphysema in coalworkers and non-coalworkers was carried out. It was determined in Chapter 6 that among men between 50 and 70 years dying of ischaemic heart disease (IHD) selection to post-mortem was similar in coalworkers and non-coalworkers and such men were included in the study. All lungs were examined in the standard way described in Chapter 4 and the amounts of centrilobular and panacinar emphysema were scored on numerical scales. The emphysema was almost entirely centrilobular.

This incidental emphysema in men dying of IHD was of greater frequency in the coalworkers than in the non-coalworkers. The difference was significant at the 0.01% level and remained after age and smoking habits were accounted for by stratification. In the coalworkers the amount of emphysema was related to the amount of dust in simple foci in the lungs.

Because both groups were selected similarly from their parent populations the relative frequency of emphysema found in this study reflects that in the whole populations of coalworkers and non-coalworkers in the study area and supports the hypothesis that an excess of emphysema occurs among coalworkers. The excess is not readily explicable by non-occupational factors. In the coalworkers the emphysema has been found to be associated with radiological irregular opacities (Chapter 5).

Table 7.1

Amount of centrilobular emphysema found at post-mortem in the coalworkers and non-coalworkers

	Number with total centrilobular emphysema score				
	0-6	7-12	13-18	19-24	25-36
Coalworkers	20	8	8	2	1
Non-coalworkers	45	2	1	-	-

Table 7.2

Post-mortem emphysema in coalworkers and non-coalworkers stratified by age and smoking habits

			Number with total centrilobular emphysema score	
			≤6	≥7
Coalworkers	Age <60yr	N-S	0	1
		E-S	0	1
		C-S	3	2
	Age ≥60yr	N-S	4	0
		E-S	3	4
		C-S	10	11
Non-coalworkers	Age <60yr	N-S	4	0
		E-S	2	0
		C-S	11	1
	Age ≥60yr	N-S	7	0
		E-S	1	0
		C-S	14	2

N-S = Non-smokers; E-S = Ex-smokers of 5 years or more; C-S = Current smokers.

In 6 non-coalworkers no smoking history was obtained.

Table 7.3

Centrilobular emphysema and amount smoked in current smokers.

		Number with Total centrilobular emphysema score	
		≤6	≥7
Coalworkers	Light smokers	6	9
	Heavy smokers	6	4
	? Amount	1	0
Non-coalworkers	Light smokers	9	0
	Heavy smokers	13	3
	? Amount	3	0

Light smokers = < 15 cigarettes/day,
Heavy smokers = ≥ 15 cigarettes/day.

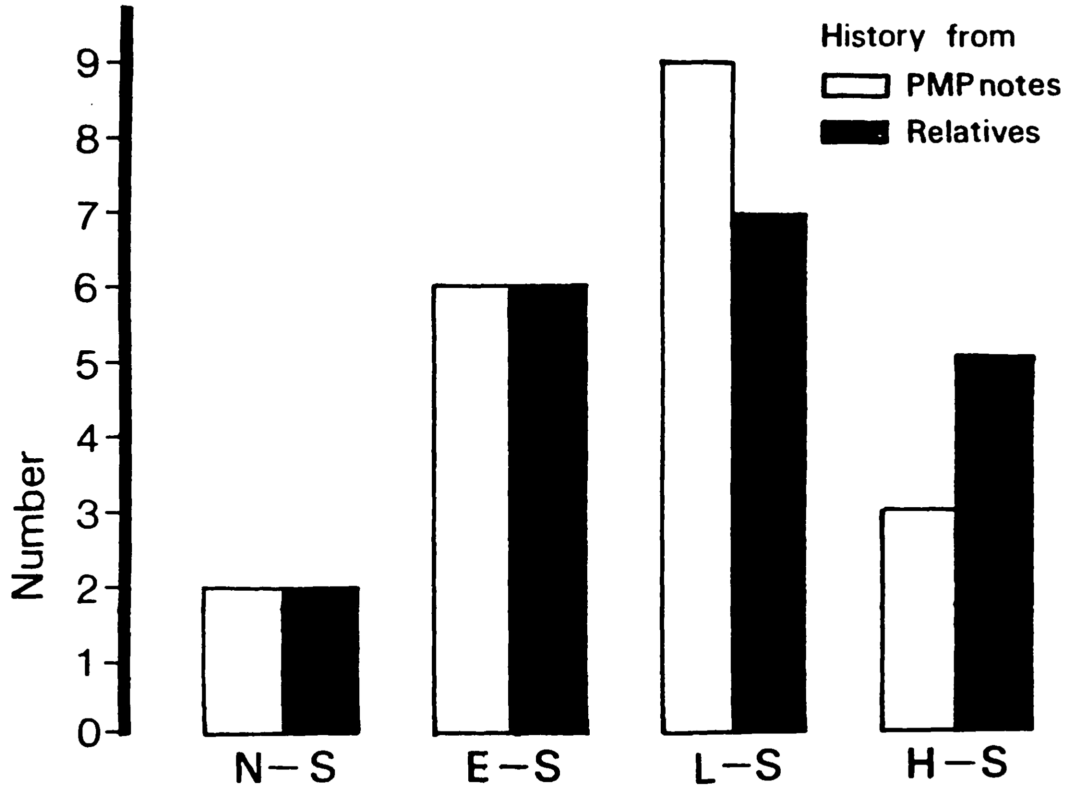
Table 7.4

Relationship between centrilobular emphysema and dust in simple dust foci in the coalworkers

Total dust score	Number with Total centrilobular emphysema score ≤12	>12
≤12	21	1
>12	7	10

Figure 7.1

Comparison of smoking histories obtained from PMP notes and by a social worker from relatives, for 20 men. These include some coalworkers enrolled in the post-mortem survey (chapter 4) but not fulfilling the criteria for the present study. Only PMP histories to within 5 years of death are included.



N-S = life-long non-smokers

E-S = ex-smokers of 5 years or more

L-S = light smokers; <15 cigarettes/day

H-S = heavy smokers; >15 cigarettes/day

CHAPTER EIGHT

PREVALENCE OF IRREGULAR OPACITIES IN COALWORKERS WITH PNEUMOCONIOSIS AND THEIR RELATION TO UNDERGROUND EXPOSURE

Introduction

Previous chapters have demonstrated that coalworkers with radiological irregular opacities have reductions in lung function compared with those who have only rounded opacities (annexe 1 and chapter 3) and that irregular opacities on the radiograph are associated with emphysema found in the lungs (annexe 1 and chapter 5). Whether or not these findings are of much importance depends on the frequency with which irregular opacities are found on the chest radiographs of coalworkers. Studies involving detailed lung function and/or post-mortem material may involve selection so that men with radiological irregular opacities are over-represented. The purpose of the work described in this chapter was to investigate how frequently irregular opacities were found on radiographs of coalworkers with pneumoconiosis who had not been selected for special study in any way.

Another important issue regarding irregular opacities in coalworkers is whether they can be related to coalwork exposure, as can be done for rounded opacities [104,105], or whether they are primarily related to non-occupational factors such as age and smoking. Again, this work aimed to investigate these associations in an unselected group of coalworkers certified with pneumoconiosis.

Subjects and Methods

The great majority of coalworkers and ex-coalworkers certified as having coalworkers' pneumoconiosis are seen by the Pneumoconiosis

Medical Panel (PMP) in their area every two or three years for a chest radiograph and clinical examination. There is evidence that almost all coalworkers with pneumoconiosis are known to the PMP[33]. In the present study, all the certified coalworkers and ex-coalworkers routinely re-attending the Cardiff PMP during January and February 1981 were included. Collection of non-smokers continued into March 1981 to increase their number. Only men with category B or C Progressive Massive Fibrosis (PMF) were excluded. In this way, a group of 124 men was collected.

Two or three chest radiographs were included for each man: the current radiograph and the radiograph at the time of certification as having pneumoconiosis for all men; and the radiograph at the time of stopping coalwork for the 57 men where this fell between the other two radiographs. Information on coalwork exposure and smoking habits was obtained from the PMP notes on the men. The coalwork exposure data comprised the number of years of underground exposure and the date of finishing; more detailed information was not available for most of the men.

The radiographs were read in random order, with dates and other details obscured, by a panel of three trained readers. The 1980 ILO Classification of Radiographs[13] was used and the observations of the three readers were combined for use in analyses. An irregularity score was derived from the size and shape records of the three readers as described in Chapter 2. For profusion of small opacities, the median value of the three readers was used.

The data were analysed by comparing the distribution of irregularity scores in groups with different levels of variables of interest such as age, smoking and underground exposure. Interactions between variables were examined by stratification. The significance of associations was tested using the Mantel-Haenszel test[116] and the Mantel-extension of this test[117].

Results

Of the 124 men in the study, 36 were life-long non-smokers, 73 were current smokers and 15 were ex-smokers of 10 years or more. The average length of underground exposure was 35 years, ranging from 9 to 52 years. Their average age was 39 years at certification and 62 years at the time of the study. The interval between certification and current radiographs ranged from 5 to 36 years, with an average of 22 years.

The median profusion of small opacities on the certification radiographs was 2 or 3 in all but 10 of the 124. On current radiographs, all but 5 were read as category 2 or 3. On both certification and current radiographs, there was a trend for higher irregularity scores with lower categories of profusion of opacities (Table 8.1, $p<0.05$).

Two thirds of the current radiographs had an irregularity score of 3 or more and nearly a fifth had an irregularity score of 6 or more. A score of 3 indicates that a minority of irregular opacities were present and a score of 6 indicates that most of the opacities were irregular. The degree of irregularity on the certification radiographs was much less, and the trend for increasing irregularity between certification and current radiographs was significant at the 0.1% level (χ^2=59.1, see Table 8.2). Figures 8.1 to 8.3 show examples of the change in radiological appearances between certification and current radiographs.

There was a strong association between increasing age and increasing irregularity of small opacities on the chest radiograph. Table 8.3 shows the distribution of irregularity scores by age decade, at certification and on current radiographs. In both cases, men with irregularity scores of 0-2 were significantly younger than men with higher irregularity scores ($p<0.001$).

Considering the men's current radiographs, irregularity scores were significantly higher for smokers than for non-smokers (Table 8.4, χ^2=7.1 $p<0.01$). This could not be accounted for by an age effect, there being no tendency for smokers to be older than non-smokers or ex-smokers.

There was a tendency, significant at the 10% level, for men with more than 40 years underground exposure to have more irregular opacities on current chest radiographs than men with shorter underground exposures (Table 8.5, χ^2=2.55). Length of underground exposure was related to age at the time of the current radiograph. The relationship between underground exposure and irregular opacities could not, however, be explained by the age effect, since an exposure effect was present when only younger men were included (Table 8.6). The exposure effect was actually only apparent in the younger men, as can be seen in Table 8.6. Both smokers and non-smokers separately showed an increase in irregularity of opacities related to underground exposure, with the effect apparently greater in non-smokers.

Radiological changes after ceasing coalwork exposure were examined in the 57 men who stopped coalwork between certification and the time of the study. Comparing their radiographs at the time of stopping coalwork with their current radiographs revealed that there was no tendency for increase in profusion of small opacities but that there was a tendency for the opacities to become more irregular (Table 8.7).

Discussion

This work indicates that small irregular opacities are a common finding in men receiving disability benefit for simple CWP. Two thirds of the study group had some irregular opacities and in nearly a fifth of the men they were the major type of opacity. The irregular opacities seemed to represent a late phase and were a rare finding in the same group of men when they were first certified with CWP. There was probably some selection operating at certification, so that men with mainly irregular opacities when first seen may have been considered to be suffering from a disease other than CWP and not been certified. With increasing age the proportion of men with mainly irregular opacities increased and this was apparently the effect mainly responsible for the increase in irregularity between certification and current radiographs.

There was an association between exposure, taken as number of years of underground coalwork, and increased irregularity of opacities on the chest radiograph. Amandus and co-workers have previously reported an association between underground exposure and irregular opacities in a large group of American coalminers [80]. Despite an association between age and years of exposure in this series, age could not be held responsible for the increasing irregularity with exposure, as the exposure effect was found only in the young men. It could have been masked by the age effect in the older men. The index of exposure used was crude and perhaps estimates of dust exposure would be preferable.

The increase in irregularity of small opacities after ceasing exposure suggests that the pathological process they represent is not dependent on continuing exposure to dust but rather on the effects of dust already in the lungs. There is a belief that simple pneumoconiosis rarely progresses after a man leaves dust exposure [146]. However, although the profusion of radiological small opacities often does not increase, and may sometimes decrease, after ceasing dust exposure this is not to say that the pathological processes set in train by the dust do not continue. There is evidence that profusion of small rounded opacities is related to coal dust content of the lungs [69]. It seems reasonable to suggest that irregular opacities are related to the tissue reaction to inhaled coaldust and that the increase in irregular opacities after ceasing exposure indicates progression of the disease, even though this is not accompanied by an increase in overall profusion of small opacities.

Emphysema has been found in association with irregular opacities in coalworkers previously [25,75] and this has been confirmed in this thesis (annexe 1 and chapter 5). It is a process likely to progress, once started, without requiring any further dust exposure. Emphysema is, of course, likely to be more common in smokers, and this may be part of the explanation for the relationship between irregular opacities and smoking that was found in this study and the study reported in Chapter 3. However, emphysema alone, in a non-dust-exposed individual, would not be expected to produce an increase in irregular opacities but rather a general reduction in lung markings [147]. Also the amount of emphysema in coalworkers is in excess of what would be expected due to smoking (Chapter 7). Smoking may act by enhancement of dust-related disease processes. Evidence for this comes from the finding in Chapter 4 of an association between length of underground work and centrilobular emphysema in smokers only.

The study in the present chapter suggests that irregular opacities are a common finding, even in coalworkers certified on the basis of rounded opacities. It implies that the lung function changes (Chapter 3) and pathology (Chapter 5) associated with irregular opacities are also likely to be common among coalworkers certified with CWP. The finding that irregular opacities were related to underground exposure adds weight to the idea that they should be considered as part of the radiological picture of simple coalworkers' pneumoconiosis.

Further evidence on the question of whether irregular opacities have a particular relationship to coalwork exposure, rather than to age or smoking, is examined in Chapter 9.

Summary

One hundred and twenty four coalworkers and ex-coalworkers receiving disability benefit for coalworker's pneumoconiosis and routinely re-attending the Cardiff Pneumoconiosis Medical Panel during a ten week period were studied, excluding those with complicated pneumoconiosis. Their current chest radiographs and their radiographs at the time of certification were read in random order by three readers using the 1980 ILO classification of radiographs. An irregularity score was derived from the readings. The radiographic findings were examined for changes since certification and for relationships with age, smoking and underground coalwork exposure.

One fifth of the current radiographs showed mainly irregular opacities, whereas nearly all of those from the time of certification showed mainly rounded opacities. Irregular opacities were related to age, smoking and underground exposure. The exposure effect remained after excluding the older men.

The findings suggest that radiological irregular opacities commonly develop in coalworkers with pneumoconiosis, are related to coalwork exposure and should probably be considered part of the condition. This implies that the lung function defects and emphysema found in association with irregular opacities should also be considered as part of the whole picture of simple coalworkers' pneumoconiosis.

Table 8.1

Relation between profusion and irregularity of small opacities on certification x-rays and current x-rays

	Irregularity Score	Category of profusion of small opacities 1	2	3
Certification x-rays	0–2	6	54	27
	3–9	4	27	6
Current x-rays	0–2	1	16	23
	3–9	4	52	28

Table 8.2

Change in irregularity of small opacities between certification and current x-rays.

Irregularity Score	Certification x-rays	Current x-rays
0–2	87	40
3–5	36	64
6–9	1	20

Table 8.3

Relation between age and irregularity of small opacities on x-ray, at certification and at the time of the study.

	Irregularity Score	Age (years)			
		≤29	30–39	40–49	≥50
Certification	0–2	14	41	26	6
x-rays	3–9	0	13	17	7
		≤49	50–59	60–69	≥70
Present	0–2	6	22	10	2
x-rays	3–9	1	21	48	14

Table 8.4

Relation between smoking habits and irregularity of small opacities on x-rays. Current x-rays only.

Irregularity Score	Smokers	Non-smokers	Ex-smokers
0-2	20	14	6
3-5	37	21	6
6-9	16	1	3

Table 8.5

Relation between years of underground exposure and irregularity of small opacities on x-ray. Current x-rays only.

Irregularity Score	Years of underground exposure		
	≤19	20–39	≥40
0–2	6	19	15
3–5	2	34	28
6–9	2	7	11

Table 8.6

Relationship between years of underground exposure and irregularity of small opacities on x-ray, taking age into account. Current x-rays only.

	Age at time of study					
	≤59 years		60 - 69 years		≥ 70 years	
Irregularity Score	0-5	6-9	0-5	6-9	0-5	6-9
Exposure Underground						
<40 yrs	33	0	25	5	2	4
≥40 yrs	13	3	23	5	7	3

Table 8.7

Radiological changes in 57 men after stopping coalwork exposure

	Increase	Decrease	No Change
Category of profusion (> 1 point on 12 point scale)	15	17	25
Irregularity score (> 1 scale point)	39	5	13

Figure 8.1

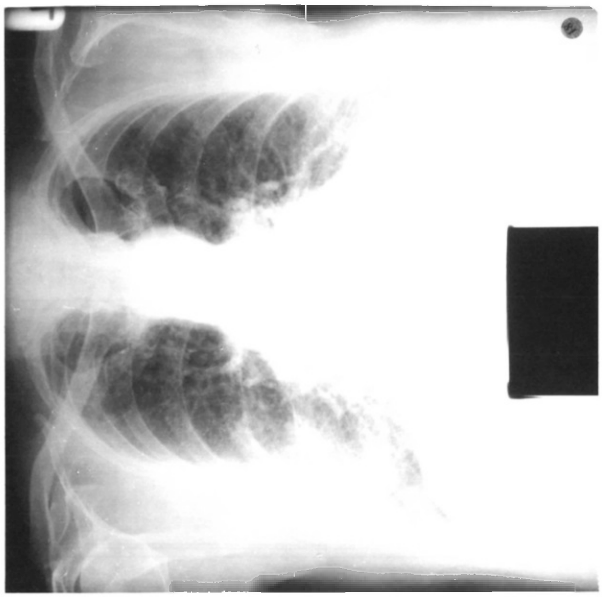
Radiographs of Mr TGE, a smoker, showing progression of irregular opacities.

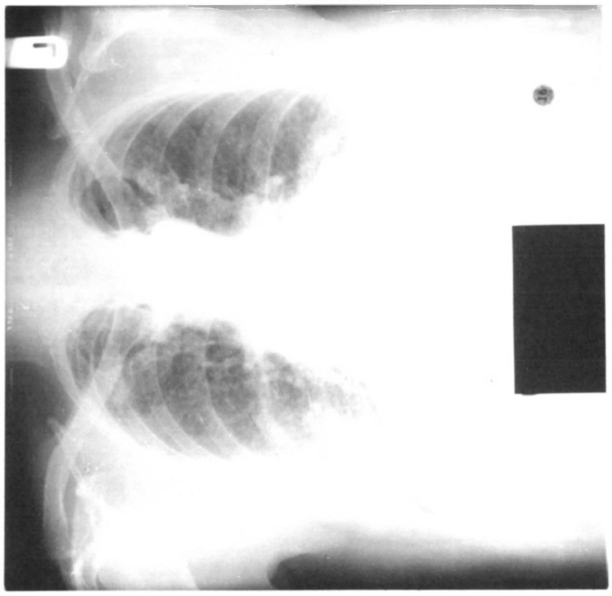
(a) 1949 radiograph at certification aged 37 years.
Read as median profusion 3/2, irregularity score 2.

(b) 1975 radiograph when left coalmining aged 63 years.
Read as median profusion 3/3, irregularity score 3.

(c) 1981 radiograph aged 69 years.
Read as median profusion 3/3, irregularity score 6.

Note that irregularity has progressed after leaving coalmining.





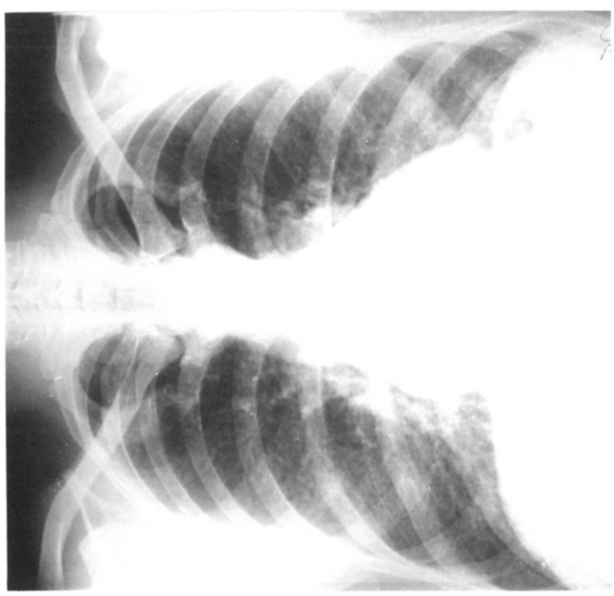


Figure 8.2

Radiographs of Mr RJR, an ex-smoker since 1965, showing progression of irregular opacities.

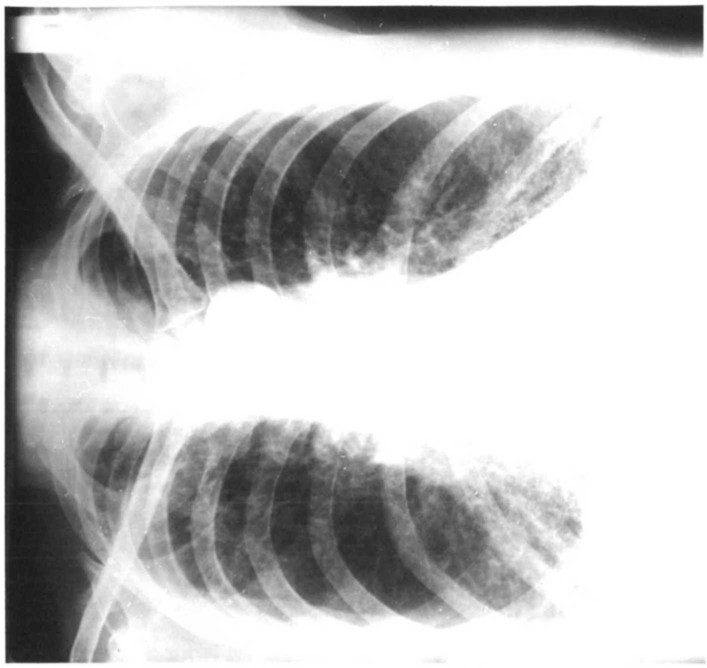
(a) 1960 radiograph at certification aged 54 years.

Read as median profusion 2/3, irregularity score 4.

(b) 1981 radiograph aged 75 years.

Read as median profusion 3/2, irregularity score 7.

There was no coalwork exposure after 1960. Note that profusion of opacities has changed little but their irregularity has increased.



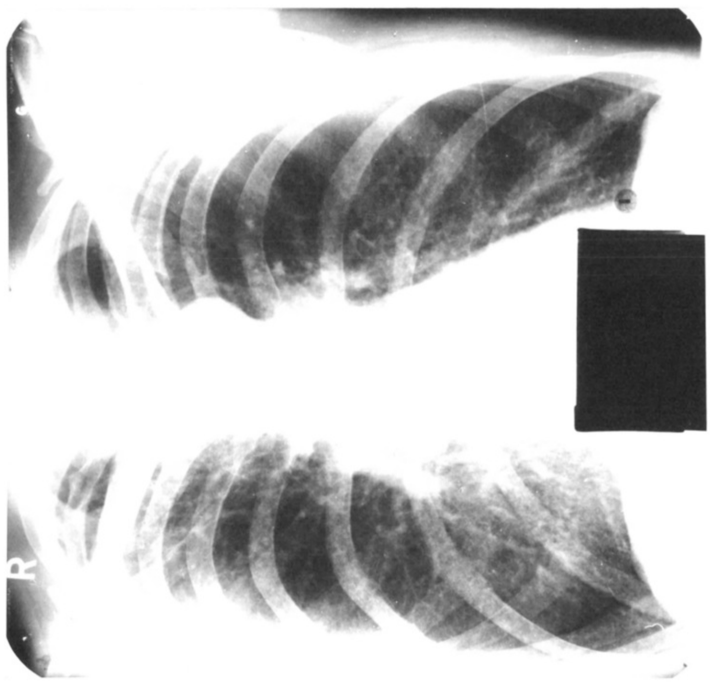


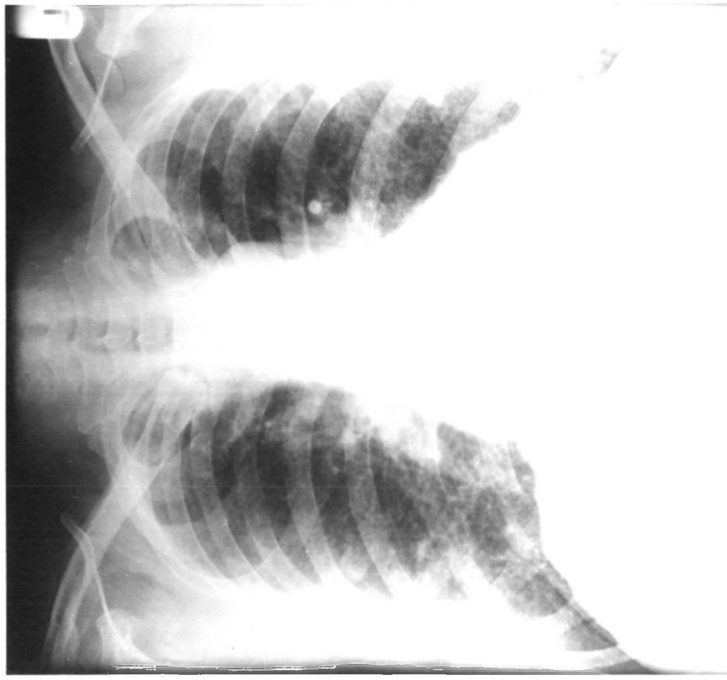
Figure 8.3

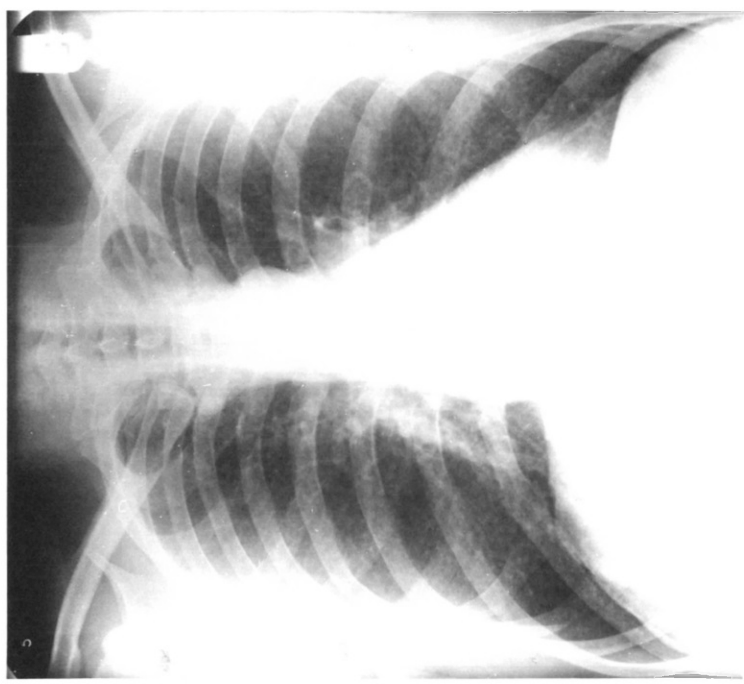
Radiographs of Mr WJW, a life-long non-smoker, showing progression of irregular opacities.

(a) 1963 radiograph at certification aged 40 years.
    Read as median profusion 2/3, irregularity score 0.

(b) 1978 radiograph aged 55 years.
    Read as median profusion 3/3, irregularity score 5.

This is an example of irregular opacities occurring in a relatively young non-smoker.





CHAPTER NINE

A CASE-REFERENT STUDY OF RADIOLOGICAL IRREGULAR OPACITIES AND OCCUPATION IN MEN ATTENDING CHEST CLINICS IN COALMINING AREAS

Introduction

While the lung function and pathology features described in relation to irregular opacities in coalworkers in earlier chapters are interesting, it could be argued that they are nothing to do with coalwork and represent some non-occupational process superimposed on coalworkers' pneumoconiosis. The nature of the associated pathology (Chapter 5), the apparent progression from rounded to irregular opacities and the association between irregular opacities and coalwork exposure (Chapter 8) all suggest that irregular opacities represent part of the process of coalworkers' pneumoconiosis. Nevertheless, the question of association between occupation and irregular opacities needs to be further investigated.

It has been suggested that irregular opacities in coalworkers are mainly associated with smoking [80] and they have been reported in smokers without known occupational exposure to dust [148]. The profusion of opacities in the latter study seems to have been low (probably category 1 or less) but the radiographs were not read using an ILO classification [12,13].

The aim of this case-referent study was to establish whether coalworkers have an increased relative risk of radiological irregular opacities. Cases and referents were men attending chest clinics in coal-mining areas of England and Wales. The study also allowed an estimate of the background frequency of irregular opacities among non-coalworkers.

Subjects and methods

This was a multi-centre study, undertaken in collaboration with chest physicians in a number of centres in coalmining areas of England and Wales. Men were enrolled from Newcastle (two centres), Merthyr Tydfil, Rotherham, Wakefield, Bridgend, Durham, Darlington, Newport, Nottingham, Ashington, Chesterfield and Cardiff. The men entered in the study were all those between the ages of 40 and 80 years attending the Chest Clinic for the first time. For every man eligible for entry the physician completed a Patient Entry Form (PEF) giving the patient's age, name and address and stating whether or not the man was or had been a coalworker. In addition to these data which were obtained on all men in the series, the individual was asked if he would be prepared to fill in a questionnaire about his occupational and smoking history for a research study. If he agreed he was given a questionnaire which he either completed in the clinic and handed in or took home and sent to the Pneumoconiosis Unit in a stamped envelope provided.

The physician examined the man's chest radiograph, as far as possible without knowledge of his occupational history, and stated on the P.E.F. his/her opinion of whether irregular opacities were present or not. All the collaborating chest physicians were sent copies of two radiographs when they agreed to take part in the study: one considered to be 'borderline' for the presence of irregular opacities and the other a good example of heavy profusion of irregular opacities (more than category 2 on the ILO classification). They were asked to use these films for comparison when reading the study radiographs. The P.E.F. and a copy or duplicate chest radiograph were sent to the Pneumoconiosis Unit.

The detailed protocol of the study and copies of the Check List, Patient Entry Form and Questionnaire can be found in annexe 5(a), (b), (c) and (d).

Completed P.E.Fs and questionnaires were collated as they were received in the Pneumoconiosis Unit, keeping the various centres separate. A reminder letter and questionnaire were sent to men for whom no completed questionnaire was received within two months of receiving their P.E.F. and a second reminder and questionnaire was sent if still no questionnaire was received after a further month. No further follow-up was attempted if there was no reply to the second reminder. Copies of the reminder letters are included as annexe 5(e).

The original study protocol aimed for approximately 50 men from each participating centre. In the event, some centres exceeded this number while others had not reached 50 at the time that entry was stopped when a total of 515 men had been entered.

After entry had been completed, all the duplicate radiographs were collected and read as a single series in random order, with identifying marks obscured, by three experienced readers using the 1980 ILO Classification of Radiographs [13]. When recording the comment 'other disease' in regard to a film, the readers were asked to elaborate further, if possible. This was because the ILO classification is designed to quantify features that may be due to occupational chest disease, rather than describe all the features on a chest radiograph. In this series, it was thought likely that many cases of non-occupational lung disease, such as lung cancer, would be encountered and it was hoped to gain some information about these diseases by means of more lengthy comments than are usually given using the ILO classification. The readings of the three readers for shape of small opacities were combined to produce an irregularity score (range 0-9) indicating the degree of irregularity of the opacities. The method of obtaining the irregularity score is described in Chapter 2. Overall profusion of small opacities was taken as the median of the profusions recorded by the three readers.

Cases were those men 'with irregular opacities' on the chest radiograph. For the purposes of this study 'with irregular opacities' was taken as being equivalent to category 2 or more profusion of small opacities, with an irregularity score of 6 or more (i.e. mainly irregular opacities). Case-referent analysis was performed to determine whether there was an excess of men with a history of coalwork exposure among the cases compared with the referents (all men without irregular opacities as defined above). Age and smoking habits were taken into account by stratification. Relative risk was estimated, and the significance of associations was tested, using the Mantel-Haenszel procedures[116].

Results

Of the 515 men entered into the study, radiographs were received for 491 and these formed the study group. A total of 189 of the men were, or had been, coalworkers. The numbers entered from each centre are shown in Table 9.1. Note that the proportion of coalworkers varied considerably between centres. Two of the radiographs were considered 'unreadable' by all three readers because of very poor film quality and therefore only 489 radiographs were included in further analyses.

The panel of three readers identified a total of 19 'cases' of irregular opacities, defined as those radiographs with a median profusion of 2/0 or above and an irregularity score of 6 or above. Coalworkers were significantly more likely than non-coalworkers to be cases of irregular opacities (Odds Ratio 2.84, $\chi^2=3.98, p<0.05$). The figures are shown in Table 9.2.

There was a weak tendency for more coalworkers than non-coalworkers to be smokers rather than ex-smokers ($\chi^2=2.70, p<0.15$, Table 9.3), but among smokers the coalworkers smoked significantly less than the non-coalworkers ($\chi^2=4.67, p<0.05$, Table 9.3). The tendency for an increased relative risk of irregular opacities in coalworkers was found in all smoking categories, being strongest among the heavy smokers (combined $\chi^2=3.00, p<0.10$, Table 9.3).

When the data were stratified by age, the same tendency for increased relative risk of irregular opacities in coalworkers was present in all age decades and was strongest in the oldest men (combined $\chi^2=3.63, p<0.06$, Table 9.4). Analysis after stratification by centre was not possible because of the small number of cases at many of the centres but the breakdown of cases and referents by occupation at the 13 centres is shown in Table 9.5.

The radiographs that were considered by the collaborating chest physicians to show irregular opacities were not all of, or only, those read as 'cases' by the panel of three readers. Table 9.6(a) shows the comparison between 'cases' from the panel readings and the chest physicians' readings. Taking the panel readings as the standard, the chest physicians' readings have a repeatability of 82%, a sensitivity of 42% and a specificity of 20%. The equivalent figures considering only radiographs of coalworkers are 80%, 33% and 29% (Table 9.6(b)); and considering only radiographs of non-coalworkers 77%, 57% and 15% (Table 9.6(c)). In other words, the chest physicians 'missed' less irregular opacities in non-coalworkers, but they also 'over-read' more irregular opacities in non-coalworkers.

Case-referent analysis using the chest physicians' readings of irregular opacities revealed a significantly increased relative risk of irregular opacities in coalworkers (Odds Radio 2.45, $\chi^2=15.5, p<0.001$) (Table 9.7). Note also from Table 9.6 that the number of 'cases' of irregular opacities read by the chest physicians was much greater than that read by the panel of three readers (103 vs 19, see Table 9.2).

The most common 'other disease' noted on the chest radiographs was lung cancer, recorded in 68 cases. Coalworkers were at significantly reduced risk of showing an obvious carcinoma on the radiograph (Odds Radio 0.48, χ^2 =5.54, $p<0.05$) (Table 9.8). For 275 of the radiographs, no 'other disease' was recorded by the panel of readers. Of the remainder, 68 were recorded as showing lung cancer, 32 vascular or cardiac lesions, 31 evidence of tuberculosis, 26 features of emphysema, 20 pleural lesions (thickening, calcification or effusion), 16 enlargement of the hila or hilar nodes, 15 areas of collapse or consolidation, 4 evidence of bronchiectasis and 2 marked distortion of the chest.

Discussion

This study, in revealing an excess relative risk of irregular opacities among coalworkers compared with other men attending chest clinics, has answered two important points. First, it confirms that irregular opacities are indeed more likely to occur in coalworkers and so is consistent with the suggestion (25, Chapter 8) that they are related to coalwork exposure. Secondly, it demonstrates that the phenomenon is not confined to South Wales, where all the other studies in this thesis were carried out. In this, it complements the work of other authors who have discussed the significance of irregular opacities in coalworkers in various parts of Britain[(75)] and in the United States of America[(80)].

The frequency of chest radiograph abnormalities in men attending chest clinics would be expected to be high. Nevertheless, the background frequency of irregular opacities (category 2/0 or above profusion, irregularity score 6 or above) among non-coalworkers in this study was only 2.3%. Coalworkers were nearly three times more likely to show such irregular opacities. It may be that coalworkers with pneumoconiosis are less likely to attend chest clinics as they attribute any respiratory problems to the pneumoconiosis. Because certification with coalworkers' pneumoconiosis is made on the basis of rounded opacities, it could be argued that non-attendance by men with pneumoconiosis would increase the proportion of coalworkers at the chest clinics who had mainly irregular opacities. This is purely speculative, however, as there is no way of knowing whether, or how many, coalworkers with pneumoconiosis do not attend chest clinics because of this diagnosis. Also, there is evidence (Chapter 8) that a fifth of coalworkers certified with pneumoconiosis may show mainly irregular opacities on the radiograph some years later.

Other studies in this thesis have revealed that irregular opacities in coalworkers are more common in smokers and older men. In this study, there was no significant association between smoking and irregular opacities (see Table 9.3) either overall or in coalworkers or non-coalworkers separately. This failure to demonstrate an association may have been due to the small numbers of 'cases' and of non-smokers. The effect of age was confirmed in this study, in that men over 60 years old were more likely than younger men to be 'cases'. This was true overall (Odds Radio 4.42, X^2=5.30, $p<0.05$) and taking coalworkers (X^2=2.30) and non-coalworkers (X^2=1.69) separately. The figures are obtained from Table 9.4. Superimposed on this overall effect of age was that of occupation: the oldest decade showed the strongest association between coalwork and irregular opacities. This is consistent with the hypothesis that coalwork exposure, the duration of which is strongly linked to age (see Chapter 8), is a factor in producing irregular opacities in coalworkers in addition to a general age effect which is also present in non-coalworkers.

The pattern of smoking habits in coalworkers and non-coalworkers found in this study (more smokers but less heavy smokers among coalworkers) is the same as that in the study in Chapter 7 and agrees with the findings of other authors [143,144]. This agreement between studies tends to validate the smoking histories in each one.

It is perhaps not surprising that the readings of the chest physicians of irregular opacities on the radiographs did not correspond very well with the 'cases' of irregular opacities identified from the readings of the panel of three. The chest physicians were asked to state simply whether irregular opacities were present or not, without using any particular scheme of classification. Their lower limit for profusion of opacities could well have been less than category 2/0 and their lower limit for irregularity of opacities may have been higher than the equivalent of an irregularity score of 6. They identified more radiographs as having irreuglar opacities than were identified as 'cases' from the panel readings. This effect was similar in the non-coalworkers (45 vs 7) and the coalworkers (58 vs 12).

It is not certain that the chest physicians were all 'looking for the same thing' when identifying irregular opacities, although an attempt at uniformity was made by sending out 'standard' radiographs showing irregular opacities to use for comparison with films being read. Nonetheless, when the chest physicians' readings for irregular opacities were used there was a significant excess relative risk in coalworkers. The physicians may not have been able to read the radiograph without knowledge of the man's occupation in every case but they would probably have expected rounded rather than irregular opacities on a radiograph known to be that of a coalworker.

The large number of radiographs in this series showing 'other diseases' reflects the fact that all the men were attending chest clinics, so presumably had respiratory symptoms. Obvious evidence of lung cancer was recorded in 14% of the men (see Table 9.8) and clearly those recorded as showing lobar collapse or pleural effusion may also have had primary bronchial carcinomas. The finding of less lung cancer among coalworkers is in line with published statistics [150]. In some instances, the readers noted that it was difficult to read for parenchymal shadows when severe abnormalities were present, for example obscuring one lung. There was nothing to suggest that these difficult radiographs were spread unevenly between coalworkers and non-coalworkers (in 61% of coalworkers and 53% of non-coalworkers no 'other disease' was noted) so that they should not have biased the results.

Clearly a case-referent study of this sort cannot establish that irregular opacities (as defined here) are caused by coalwork exposure. But it does provide support for this hypothesis in that the excess relative risk in coalworkers cannot be explained by smoking or age. It has been suggested that irregular opacities are an age-related pnenomenon, with or without coalwork exposure[151], but there is evidence here of an additional effect in elderly coalworkers, not present in elderly non-coalworkers.

Summary

Five hundred and fifteen men newly attending chest clinics in coalmining areas of England and Wales were entered for study: readable radiographs were received for 489 of them. They completed questionnaires on occupational and smoking history. The radiographs were read for irregular opacities by the collaborating chest physicians and by a panel of three readers using the ILO 1980 classification. 'Cases' were defined as those whose radiographs showed opacities of median category 2/0 or above with irregularity score 6 or above.

Coalworkers had a significant excess risk of nearly three times of having irregular opacities, which remained after stratifying for smoking and age. Older men had more irregular opacities than younger men, but the excess risk in coalworkers was most significant in the oldest age group, suggesting an additional occupational effect. Lung cancer was evident on 14% of the radiographs and was significantly less common in coalworkers than non-coalworkers.

Table 9.1

Entry of men into the study from the different centres.

Centre Number	Total Number entered	Number with radiographs	Number of coalminers with radiographs
1	83	81	15
2	42	42	3
3	35	34	20
4	78	71	39
5	51	51	26
6	27	27	16
7	15	15	13
8	46	40	7
9	3	3	2
10	23	23	4
11	35	35	22
12	44	44	20
13	33	25	2

Note: (1) There were no men for whom it was not known whether or not they had been coalworkers, since even if they did not return the question this information was on the Patient Entry Form completed by the chest physician (see annexe 5(c)).

(2) Two of the radiographs were recorded as 'unreadable' by all three readers and are not included in further analyses; a further 9 were recorded as 'unreadable' by one or two of the three readers and the reading of the remaining reader(s) is used in analysis.

Table 9.2

Case-referent analysis of radiological irregular opacities in coalworkers and non-coalworkers

	Coalworkers	Non-coalworkers
Cases	12	7
Referents	177	293

Note: 'Cases' were those with median category 2 profusion or above and irregularity score 6 or above.

'Referents' were all the remaining men, out of a total of 489.

Table 9.3

Case-referent analysis of radiological irregular opacities in coalworkers and non-coalworkers, stratifying by smoking history.

Smoking History		Coalworkers	Non-coalworkers
Non-smokers	Cases	1	0
	Referents	12	37
Ex-smokers	Cases	2	2
	Referents	38	70
Light smokers	Cases	5	1
	Referents	43	50
Heavy smokers	Cases	3	4
	Referents	62	119

Notes: (1) 'Cases' and 'referents' defined as in Table 9.2

(2) Smoking history was unknown, or incomplete, in 40 men.

(3) Light smokers=<15 cigarettes/day, heavy smokers=≥ 15 cigarettes/day.

Table 9.4

Case-referent analysis of radiological irregular opacities in coalworkers and non-coalworkers, stratifying by age groups.

Age group		Coalworkers	Non-coalworkers
40-49 years	Cases	0	1
	Referents	25	56
50-59 years	Cases	2	0
	Referents	52	80
60-69 years	Cases	6	4
	Referents	69	95
70-79 years	Cases	4	2
	Referents	31	62

Note: 'Cases' and 'referents' defined as in Table 9.2.

Table 9.5

Case-referent analysis of radiological irregular opacities in coalworkers and non-coalworkers, stratified by centre.

Centre Number		Coalworkers	Non-coalworkers
1	Cases	1	0
	Referents	14	66
2	Cases	-	-
	Referents	3	39
3	Cases	-	-
	Referents	20	14
4	Cases	1	2
	Referents	38	30
5	Cases	3	3
	Referents	23	21
6	Cases	-	-
	Referents	16	11
7	Cases	1	0
	Referents	12	2
8	Cases	0	1
	Referents	7	31
9	Cases	-	-
	Referents	2	1
10	Cases	-	-
	Referents	4	19
11	Cases	2	0
	Referents	20	13
12	Cases	4	0
	Referents	16	24
13	Cases	0	1
	Referents	2	22

Notes: (1) 'Cases' and 'referents' defined as in Table 9.2

(2) In centres 2,3,6,9 and 10 no cases were identified.

Table 9.6

Comparison between readings by the panel of three readers and readings by the chest physicians.

(a) Including all the radiographs

	Readings by panel of three readers	
Chest Physicians' readings	Cases	Referents
Irregular opacities present	11	92
Irregular opacities absent	8	363

(b) Including only coalworkers

	Readings by panel of three readers	
Chest Physicians' readings	Cases	Referents
Irregular opacities present	8	50
Irregular opacities absent	4	124

(c) Including only non-coalworkers

	Readings by panel of three readers	
Chest Physicians' readings	Cases	Referents
Irregular opacities present	3	42
Irregular opacities absent	4	239

Note: For the readings by the panel of three readers, 'cases' and 'referents' are defined as in Table 9.2

Table 9.7

Case-referent analysis of radiological irregular opacities in coalworkers and non-coalworkers, using chest physicians' readings of the radiographs.

	Coalworkers	Non-coalworkers
Chest Physicians' readings		
Irregular opacities present	58	45
Irregular opacities absent	128	243

Table 9.8

Radiological evidence of lung cancer in coalworkers and non-coalworks.

	Coalworkers	Non-coalworkers
Lung cancer recorded on radiograph		
YES	17	51
NO	172	249

SUMMARY AND CONCLUSIONS

Summary

While a good deal of research has been aimed at better recognition and quantification of small rounded opacities on the radiographs of coalworkers (i.e. the currently accepted appearances of simple coalworkers' pneumoconiosis) much less has been done on whether these appearances are the best reflection of lung pathology in coalworkers' pneumoconiosis. The profusion of small rounded opacities has not been found to reflect lung function changes in coalworkers. There are reports that small irregular opacities reflect lung function changes in coalworkers and that they are associated with post-mortem emphysema. This work sets out to examine the importance of irregular opacities in coalworkers from several different angles.

A technique for deriving an irregularity score, to reflect the degree of irregularity of small opacities on the radiograph, is described in Chapter 2. The simple calculation of the score is based on readings of radiographs using the 1980 ILO classification of radiographs. Inter-reader agreement for irregularity of opacities was found to be nearly as good as for category of profusion of opacities. The irregularity score is then used throughout the thesis.

A small pilot study of 47 dead coalworkers, who had lung function data and post-mortem material for review (annexe 1), revealed much emphysema related to dust foci and also pigmented interstitial fibrosis in some cases. Cases with more irregular

opacities on the radiograph had lower values of gas transfer factor, total lung capacity and more emphysema than those with mainly rounded opacities. Lungs with higher emphysema scores were from men who had lower values of gas transfer factor during life.

Chapter 3 reports a study of lung function variables in relation to radiographic appearances in 357 coalworkers. The radiographs were read by 3 readers and an irregularity score was produced. Men whose radiographs showed more irregular opacities had significant reductions in ventilatory capacity and gas transfer factor, with no change in total lung capacity, after taking account of age, height, profusion of small opacities and smoking. Profusion of small opacities had little effect on lung function. The results are consistent with emphysema, and possibly additional fibrosis, being the pathology represented by irregular opacities on the radiograph.

The pathology of coalworkers' pneumoconiosis is described in Chapter 4. A technique is described for quantitatively assessing and recording features on suitably prepared post-mortem whole lung specimens. Pathology was studied in 123 coalworkers coming to post-mortem in South Wales. There was a wide range of severity of dust-related pathology. Emphysema, almost entirely centrilobular, was common and the amount was strongly related to the size and profusion of primary dust foci. Older men and smokers had more emphysema than others and in smokers there was an association between the amount of emphysema and the length of underground work. Disability benefit received was mainly related to progressive massive fibrosis and some cases with severe emphysema were receiving little or no diability benefit.

Chapter 5 goes on to describe a comparison between radiology and pathology in 67 of the pathology series who had chest radiographs within 10 years of death. The radiographs were read by three readers and values for median profusion of opacities and irregularity score were obtained. Profusion of opacities was related to size and profusion of dust foci but not to emphysema. The irregularity score was related to the amount of emphysema in the lungs, in both older and younger men, and for both low and high overall profusions of opacities.

A special study to decide criteria for selection of cases when comparing lung pathology in coalworkers and non-coalworkers is described in Chapter 6. Post-mortem rates for different causes of death, at different ages, were calculated for coalworkers and non-coalworkers in the study area. For men dying of ischaemic heart disease, aged 50-70, both groups had high post-mortem rates and additionally IHD is a common cause of death, unrelated to the lung pathology in question (mainly emphysema).

In Chapter 7, the selection criteria derived from Chapter 6 were used to collect fixed, inflated lungs from 39 coalworkers and 48 non-coalworkers. The lungs were examined by the method described in Chapter 4. Emphysema was almost entirely centrilobular and was significantly (0.01% level) more common in the coalworkers. The difference remained after taking account of age and smoking habits. The emphysema was related, both physically and statistically, to dust foci in the coalworkers. Because of the careful admission procedure to avoid selection bias in the study, the result is thought to reflect a greater frequency of emphysema amongst all coalworkers in the area. It suggests that emphysema and the corresponding irregular opacities on the radiograph are occupation-related features in coalworkers.

The prevalence of irregular opacities in coalworkers with pneumoconiosis is sought in the study described in Chapter 8. A group of 124 men certified with simple pneumoconiosis and routinely re-attending the Cardiff Pneumoconiosis Medical Panel were studied. Current radiographs, those at certification and those on ceasing coalwork (where relevant) were read. There was an increase in the irregularity score between certification and current radiographs, with a fifth of current radiographs showing mainly irregular opacities. Irregular opacities were related to age, smoking and underground exposure. The exposure effect was mainly in younger men. After ceasing coalwork, the profusion of small opacities did not change but they became more irregular in shape.

Chapter 9 describes a case-referent study of 515 men attending chest clinics in several coalmining areas to determine whether irregular opacities are more common in coalworkers than non-coalworkers, and whether this finding is confined to South Wales. Occupational and smoking histories were obtained and radiographs were read by 3 readers. 'Cases' were defined as those with median category 2 profusion or above and irregularity score of 6 or more. Case-referent analysis revealed an increased relative risk to coalworkers which was significant at the 5% level. The difference remained after taking account of age and smoking.

Conclusions

The hypothesis that irregular opacities represent pathological change and are associated with lung function deficit in coalworkers, and that they are common and related to coalwork exposure can be examined in the light of the results of the various studies.

The evidence presented is that irregular opacities in coalworkers are of consequence in terms of lung function and lung pathology. Irregularity of opacities was related to reduction in ventilatory capacity and reduction of gas transfer factor in a study of coalworkers who had mainly category 2 or 3 profusion of small opacities. In terms of pathology, irregular opacities mainly reflect emphysema, a feature which is not reflected by straightforward profusion of opacities. Irregularity of opacities could therefore be considered a useful supplementary, perhaps even a better, guide to lung destruction associated with coal dust than is the profusion of opacities, which are usually mainly rounded opacities.

Irregular opacities are surprisingly common in coalworkers with simple pneumoconiosis. In men with mainly rounded opacities at the time of certification with pneumoconiosis, two thirds had some irregular opacities and a fifth had mainly irregular opacities after a mean interval of 22 years between radiographs. It seems a plausible hypothesis that lung changes in the later phase of coalworkers' pneumoconiosis are reflected in increasing irregularity of opacities so that they become more common in older men with the disease.

The question of whether irregular opacities represent part of occupational lung disease of coalworkers is crucial and the body of evidence presented here suggests that the answer is probably affirmative. This is on the understanding that the epidemiological studies described cannot in themselves investigate cause and effect. They can merely investigate associations between disease and certain factors: in aggregate, by excluding effects of certain factors, they imply causation. The pathology studies demonstrated a striking association between emphysema and coal dust foci, and emphysema was reflected by irregularity of opacities on the radiograph. An association between emphysema and underground exposure was demonstrated among smokers, while irregularity of opacities on the radiograph was related to underground exposure in a separate study. Case-referent analysis of men attending chest clinics demonstrated a significant increase in relative risk of coalminers having irregular opacities present on their chest radiographs. There is a plausible biological mechanism for coaldust giving rise to emphysema via effects on the alveolar macrophage and subsequent release of elastolytic enzymes.

In conclusion, it seems that irregular opacities on the chest radiographs of coalworkers may have been incorrectly neglected with respect to their importance. The studies presented here all point to the need for a systematic reappraisal of irregular opacities in coalworkers in areas other than South Wales, to establish whether the findings are generalisable to all coalworkers. It is likely that the 'package' of studies reported here covers the major areas of interest with regard to irregular opacities, so repeating similar studies in other areas would be most informative. Additional studies could examine the question of ease and repeatability of detection of irregular opacities on radiographs of coalworkers, since difficulty of detection would be a possible explanation for their neglect. It would also be of interest to know whether irregular opacities are occuring more frequently in coalworkers in recent years, or are simply detected more readily. This would require comparing similar coalworkers two or three decades apart in age and coalwork exposure.

If further studies in other areas are supportive of the findings reported here, it may be appropriate to consider whether irregular opacities should be officially accepted as part of occupational lung disease (i.e. pneumoconiosis) in coalworkers. Among other things, the criteria for radiological diagnosis of simple coalworkers' pneumoconiosis would require alteration to take this into account. It may also be appropriate, as future evidence accumulates, to consider whether emphysema should be regarded as part of coalworkers' pneumoconiosis.

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Publications involving work from this thesis

1. Cockcroft A, Wagner JC, Seal RME, Lyons JP, Campbell MJ. Irregular opacities in coalworkers' pneumoconiosis - correlation with pulmonary function and pathology. Inhaled Particles V. Ann Occup Hyg 1982; 26(1-4): 767-787.

2. Cockcroft A, Berry G, Cotes JE, Lyons JP. Shape of small opacities and lung function in coalworkers. Thorax 1982; 37: 765-769.

3. Cockcroft A, Seal RME, Wagner JC, Lyons JP, Ryder R, Andersson N. Post-mortem study of emphysema in coalworkers and non-coalworkers. Lancet 1982; 2: 600-603.

4. Cockcroft A, Lyons JP, Andersson N, Saunders MJ. Prevalence and relation to underground exposure of radiological irregular opacities in South Wales coalworkers with pneumoconiosis. Br J Industr Med 1983; 40: 169-172.

Own work

These studies were conceived and arranged by me and I was responsible for the analysis and interpretation of the results. Studies in publications 1 and 3 were done in collaboration with Dr RME Seal and Dr JC Wagner who provided expert opinions in pathology. In the study in publication 2 the lung function measurements were done by technicians at the Pneumoconiosis Unit, Penarth: the computer analysis was overseen by Mr G Berry. Dr JP Lyons referred cases from the PMP in publication 4 and he, with others, read radiographs for this and the other studies. Dr Andersson provided statistical and epidemiological guidance for the studies in publications 3 and 4.

ANNEXES

ANNEXE ONE

Pilot study of lung function and lung pathology associated with radiological irregular opacities in coalworkers

Introduction

It has been reported that the profusion of irregular opacities on the chest radiograph of coalworkers, rather than the profusion of rounded opacities, is associated with reduction in forced expiratory volume in one second (FEV_1) and with emphysema found at post-mortem examination [25]. Another author found that in a large group of working miners reductions in FEV_1 were associated with irregular opacities among smokers [80]. A study of 500 dead coalworkers reported that those with reduced FEV_1 during life had more emphysema [82a].

This study was undertaken in an attempt to relate the degree of irregularity of opacities on the radiograph to lung function during life and to post-mortem lung pathology in a group of dead coalworkers for whom all the necessary material was available for review. The aim was partly to see if there were any associations warranting further study and partly to assess the feasibility of making these sorts of comparisons between irregularity of opacities and other variables.

Material and methods

The Cardiff Pneumoconiosis Medical Panel (PMP) has referred men for detailed lung function tests at the MRC Pneumoconiosis Unit since 1965. Between 1970 and 1979, 126 coalworkers died who had visited for lung function tests during life. Of these, 46 men provided sufficient for this study. Men were only included if their last chest radiograph did not show category B or C progressive massive fibrosis (PMF) and if post-mortem material including a whole lung paper section (WLS) was available for review. The results of lung function tests were extracted from the men's records. In one instance the results were missing and in four others the tests had been performed in another laboratory. The lung function parameters used in the study were the FEV_1, the forced vital capacity (FVC), the gas transfer factor of the lung for carbon monoxide (TL) and the total lung capacity (TLC). The TL was estimated by the single breath method and the TLC by helium dilution. The methods used for lung function testing in the laboratory have been described in detail elsewhere[107]. In the analysis the results were expressed as a percentage of the expected value for age, sex and height.

Smoking history was obtained from the records at the Pneumoconiosis Unit or the PMP. The information was usually available at the time of lung function tests but sometimes there was no information about any changes between then and the time of death.

For each man the chest radiograph nearest to death was reviewed. If lung function testing preceded death by some years a radiograph at the time of this testing was also reviewed. The radiographs were read in random order, independently by a panel of four experienced readers. They used the 1980 ILO classification of radiographs[13] to record their readings.

Annexe 2a gives details of shape/size recording in the classification and annexe 2b is a specimen reading form. An irregularity score was calculated from the shape/size recording of each reader. The method of calculation of the score is described in Chapter 2. The individual irregularity scores of the four readers were meaned to give the overall irregularity score. The category of profusion was taken as the median of the profusions recorded by the four readers.

A whole lung paper-mounted section (WLS) was reviewed for each man by two pathologists independently, recording their findings as scores on numerical scales for a number of features. The features scored included average size of simple dust foci and proportion of lobules involved; average severity and extent of emphysema of centrilobular or panacinar type; size and position of any PMF lesions. The form used for recording these pathological features is reproduced in annexe 3(a). The method of scoring pathology features in this way has been described elsewhere[105] and is discussed in more detail in Chapter 4.

Histological sections, including blocks of tissue 5 x 5 cm, stained and mounted for projection as transparencies, were available for 35 of the men. This material was reviewed by the two pathologists together in order to confirm the type of emphysema present and to assess the degree of interstitial fibrosis, if any. The forms used to score features on this microscopic assessment are reproduced in annexe 1(b). The scores for pigmented interstitial fibrosis, unpigmented interstitial fibrosis and interstitial cellular infiltration were averaged to give an interstitial disease score.

Results

The mean age of the men at the time of lung function testing was 59.7 years and the mean age at death was 64.5 years. The mean interval between the last chest radiograph and death was 2.4 years (range: less than one month to 7 years); between the last lung function tests and death 5.2 years (range: less than one month to 10 years); and between lung function tests and the nearest chest radiograph 0.4 years (range:same day to 2 years). At the time of lung function testing two of the men were two non-smokers, two ex-smokers, 14 light smokers (less than 15 cigarettes/day) and 23 heavy smokers. No smoking history was available for 5 of the men. Perhaps because nearly all the men were smokers at the time of testing, no associations were found between lung function variables or pathological features and smoking history. The mean FEV_1 for the whole group was 1.81 litres (S.D.$\pm$ 0.7), the mean FVC 3.11 litres (S.D.$\pm$ 0.8), and the mean TL 5.8 mmol/min/KPa/l (S.D.$\pm$ 2.2).

The irregularity score tended to be higher on the radiographs nearest to death than on earlier radiographs at the time of lung function testing (χ^2 =4.18 Mantel Extension). This is shown in Table A.1. Note that 11 radiographs appear in both groups in this table, because for 11 men the radiograph nearest to lung function testing and the radiograph nearest to death were one and the same. This tends to decrease differences between the groups. All but one of the radiographs were read as category 2 or 3 for profusion of small opacities and profusion was not considered any further in analysing the results.

Agreement between the two pathologists' assessments of the WLSs was generally good. Table A.2 illustrates this point for average severity of centrilobular emphysema. Note from this table that in all but one instance the readings by the two pathologists were within one major category of each other. Nearly all the emphysema recorded was of the centrilobular type. Review of the histological material revealed some cases of interstitial fibrosis, pigmented, unpigmented or partially pigmented. Sometimes the presence of interstitial fibrosis was not suggested by the macroscopic WLS appearances. Some of these cases with interstitial fibrosis were thought to show features 'typical' of cryptogenic fibrosing alveolitis but in many the appearances were not explained by other diseases and yet were not 'typical' of the expected picture of simple pneumoconiosis (i.e. separate, discrete coal dust foci with a small amount of surrounding emphysema).

Associations between radiology, lung function and pathology

The irregularity score calculated from the radiograph readings was significantly negatively correlated with gas transfer factor ($R=-0.40, p<0.01$) and with TLC ($R=-0.35, p<0.05$). These associations are illustrated in Table A.3. The irregularity score was not associated with changes in FEV_1 or FVC.

Comparing radiology with pathology, the irregularity score correlated closely with the average severity of centrilobular emphysema ($R=0.37, p<0.01$). Table A.4 shows the association between irregularity score and average severity of centrilobular emphysema. The irregularity score also seemed to be associated with the histological interstitial disease score but this did not reach statistical significance at the 5% level.

There were also associations between lung pathology and lung function. These should be interpreted with some caution as there was a 10 year interval between lung function testing and death in some cases. The score for average severity of centrilobular emphysema was significantly negatively correlated with gas transfer factor ($R=-0.38, p<0.02$) and was also associated with TLC, with higher scores in men who had higher values for TLC. This latter association did not reach significance at the 5% level. Table A.5 shows the relationships between pathological emphysema and TL and TLC. Higher scores for interstitial disease were associated with lower values of gas transfer factor ($p<0.05$ by pooled 't' test, Table A.6).

Discussion

A major problem of this study is selection of the material. Not all coalworkers visit the PMP, although practically all those with coalworkers' pneumoconiosis do so [33]. Not all those who visited the PMP during the period were referred for detailed lung function tests; men whose radiographs showed the smallest type of rounded opacities ('p' type) or, later, irregular opacities were referred preferentially so are well-represented in the series. Not all of these men who died had suitable post-mortem material (a WLS) retained for review; the factors determining retention of this material are not standardised. After selection in all these respects the men included in the study cannot be taken as representative of coalworkers overall. This is not to say that internal comparisons between those with more or less irregular opacities are invalid. Another problem is the small numbers of subjects. This is an inevitable feature of including only men who have such detailed information available. The small number may mean that real associations are missed due to a lack of power in the analysis.

Despite these problems, some interesting results have emerged from the study. Irregular opacities were associated with a reduction in gas transfer factor. This would be compatible with more emphysema in cases with irregular opacities. However, the TLC tended to fall with increasing irregularity of opacities, suggesting that emphysema is not the only pathological process involved. Irregular opacities were certainly associated with centrilobular emphysema but also tended to be associated with interstitial disease, although the latter association was not significant at the 5% level. Perhaps in any given case with irregular opacities on the chest radiograph a combination of emphysema and interstitial fibrosis may be present. Both processes would reduce the gas transfer factor but would tend to move the TLC in opposite directions. It is also possible that cases with irregular opacities fall into two different groups: those with emphysema and those with interstitial fibrosis. The association of irregular opacities with emphysema has been described previously [25] but in that study interstitial fibrosis was not specifically looked for. The pathological findings of this present study confirm that a combination of emphysema and fibrosis certainly occurs in some cases.

The present study forms the starting point for the work that is described in the chapters of the thesis. These seek to confirm and expand the suggested associations between irregularity of opacities and lung function and pathology changes. In addition the frequency of irregular opacities in coalworkers and their relation to coalwork exposure are examined in a more representative group of coalworkers since clearly their frequency in the group used in this study cannot be generalised.

Summary

A group of 46 deceased coalworkers who had been referred for lung function tests during life were studied. Radiographs closest to the time of death and to the time of lung function tests were read according to the 1980 ILO Classification by four experienced readers; lung function results were reviewed; and whole lung paper sections were used to score pathological features. A score for irregularity of small opacities was derived from the radiograph readings. The radiological irregularity score was significantly associated with reduction in gas transfer factor, reduction in total lung capacity and with increasing scores for average severity of centrilobular emphysema and interstitial disease. The lung function reductions would be consistent with a combination of emphysema and fibrosis.

Table A.1

Irregularity score on radiographs at the time of lung function testing and on radiographs close to death*

	Number with Irregularity score			
	0	1	2	3
Radiographs at time of lung function testing	13	23	8	0
Radiographs nearest to death	7	24	14	1

*The average time between these radiographs is three years.

Table A.2

Agreement between the two pathologists for scoring of average severity of centrilobular emphysema on the whole lung paper sections

Score by pathologist two	Number with Score by pathologist one						
	0	0/1	1	1/2	2	2/3	3
0	1	2	2	-	-	-	-
0/1	-	3	-	-	-	-	-
1	-	-	-	-	2	1	-
1/2	-	-	-	-	-	1	-
2	-	-	3	5	7	2	2
2/3	-	-	-	-	1	-	1
3	-	-	-	-	1	5	2

Table A.3

Irregularity score related to gas transfer factor and total lung capacity

(a)

	TL/predicted TL x 100%		
Irregularity Score	Mean	S.D.	No.of cases
0	86.6	27.6	12
1	61.1	22.1	23
2	60.5	19.9	7

(b)

	TLC/predicted TLC x 100%		
Irregularity Score	Mean	S.D.	No.of cases
0	106.8	13.2	13
1	99.1	18.7	23
2	89.0	12.3	7

Table A.4

Association between irregularity score and score for average severity of centrilobular emphysema

	Number of lungs with Average severity of centrilobular emphysema*						
Irregularity Score	0	0/1	1	1/2	2	2/3	3
0	1	1	3	0	2	0	0
1	2	3	3	2	9	0	5
2	1	0	0	3	5	3	2
3	0	0	0	0	0	0	1

*The mean of the scores from the two pathologists is used.

Table A.5

Score for average severity of centrilobular emphysema related to lung function changes

(a)

Score for average severity of centrilobular emphysema	TL/predicted TL x 100% Mean	S.D.	No. of cases
0	80.2	14.0	3
0/1	81.1	29.9	4
1	87.4	28.9	6
1/2	80.0	35.6	4
2	61.0	17.7	16
2/3	64.9	27.8	2
3	57.9	26.8	8

(b)

Score for average severity of centrilobular emphysema	TLC/predicted TLC x 100% Mean	S.D.	No. of cases
0	86.3	18.4	3
0/1	95.1	13.3	4
1	99.0	9.6	6
1/2	98.7	20.4	5
2	102.0	17.4	16
2/3	108.8	11.3	2
3	103.6	21.9	8

The association between average severity of centrilobular emphysema and TLC did not reach significance at the 5% level.

Table A.6

Histological interstitial disease score in relation to gas transfer factor

Interstitial disease score	TL/predicted TL x 100%		
	Mean	**S.D.**	**No. of cases**
0	72.4	27.2	4
0/1	78.1	28.8	8
1	76.3	26.5	8
1/2	61.2	27.2	8
2	48.8	15.8	4

ANNEXE 1 (b).

MICRO

CENTRAL DUST FOCI

Assessment of % collagen	Cellular infiltration
0	0
1	1
2	2
3	3

PERILOBULAR

Collagen (Interstitial fibrosis unpigmented)	Collagen (Interstitial fibrosis pigmented)
0	0
1	1
2	2
3	3

Presence of a "rim" of normal lung tissue adjacent to interlobular septa + or -

Interstitial cellular infiltration

0
1
2
3

Dust impregnated interlobular septa including paraseptal dust

0
1
2
3

POLARISABLE PARTICLES

In nodules	In strands
0	0
1	1
2	2
3	3

Do you think there is another clinico-pathological process at work? YES / NO

If YES, what do you suspect?

ANNEXE 2 (a).

Shape and size

The shape and size (Note 10) of small opacities are recorded. Two kinds of shape are recognised: rounded and irregular. In each case, three sizes are differentiated. They are illustrated by standard radiographs which take precedence over the following written definitions. The letters p, q, r denote the presence of small rounded opacities, where

p = diameter up to about 1.5 mm;

q = diameter exceeding about 1.5 mm and up to about 3 mm;

r = diameter exceeding about 3 mm and up to about 10 mm.

The letters s, t, u denote the presence of small irregular opacities, where

s = width up to about 1.5 mm;

t = width exceeding 1.5 mm and up to about 3 mm;

u = width exceeding 3 mm and up to about 10 mm.

To record shape and size, two letters must be used. Thus if the reader considers that all or virtually all opacities seen are of one shape and size, then this should be noted by recording the symbol twice, separated by an oblique stroke (for example, q/q). If, however, another shape (or size) is seen, then this should be recorded as the second letter (for example, q/t). 'q/t' would mean that the predominant small opacity is round and of size q, but that there are significant numbers of small irregular opacities present of size t. In this way any combination of small opacities may be recorded (Note 11).

Standard radiographs illustrating both rounded and irregular shapes should be used for comparisons when the shape of opacity is in doubt or when both shapes are present.

Note 10 Shape and size of small opacities

The 1980 Classification distinguishes between the concepts Shape and Size of small opacities. The symbols used are the same as those defined in previous Classifications under the general heading Type.

For small opacities shape and size are both known to be important. For example, in coalworkers' pneumoconiosis, profusion of p and q opacities relates better to dust content of the lung than the profusion of size r opacities. Also men with small p opacities tend to have lower values of gas transfer of carbon monoxide. Asbestos workers with a "u" pattern have worse prognosis.

Note 11 Mixtures of shapes and sizes

The 1980 Classification permits recordings of mixtures of shapes and sizes of small opacities on the same radiograph. When, as usually occurs, only one shape (and size) is seen, the symbol denoting that shape and size must be recorded twice on the reading sheet (for example, record p/p when only small rounded opacities of size p are seen). This rule avoids ambiguities on the written records and emphasises that not all radiographs with small opacities show mixtures of shapes.

ANNEXE 2 (b).

ILO 19 INTERNATIONAL CLASSIFICATION OF RADIOGRAPHS OF PNEUMOCONIOSES

Film number 1-7

Date of Radiograph 8-13

Reader				14-15
Date of reading				16-21
QUALITY 1 2 3 4				22
If not quality 1, record why				
Parenchyma clearly visible				23
Pleura *Yes = 1, No = 2*				24
SMALL OPACITIES Profusion 0/- 0/0 0/1 1/0 1/1 1/2 2/1 2/2 2/3 3/2 3/3 3/+	/	/	/	25-26
Zones *(Tick) Upper Middle Lower*	R L	R L	R L	27-28 29-30 31-32
Shape-size *p q r s t u (2 symbols)*				33-34
LARGE OPACITIES	None	None	None	35
A B C				36
PLEURAL THICKENING	None	None	None	37
Type: Diffuse Plaques *(Tick)*	R L	R L	R L	38-39 40-41
Width *a b c*				42-43
Face on *(Tick)*				44-45
Extent 1 2 3				46-47
Diaphragm *(Tick)*	None R L	None R L	None R L	48-50
Costophrenic angles *(Tick)*	None R L	None R L	None R L	51-53
PLEURAL CALCIFICATION	None	None	None	54
Site: Diaphragm Wall Other sites *(Tick)*	R L	R L	R L	55-56 57-58 59-60
Extent 1 2 3				61-62
SYMBOLS ax bu ca cn co cp cv di ef em es fr hi ho id ih kl od pi px rp tb	None	None	None	63-65 66-67 68-69 70-71 72-73
COMMENTS *Continue overleaf if necessary - with reader's initials*	None	None	None	74-75 76-77 78-80

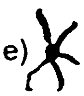
ANNEXE 3 (a).

ASSESSMENT OF CENTRILOBULAR AND PERILOBULAR FEATURES IN DIFFUSE LUNG DISEASE.

NAME: NUMBER:

MACROSCOPIC ASSESSMENT (WET SLICE/WLS/COLOUR PHOTO)

1. CENTRAL DUST FOCI

Type I. (soft, stellate) 

Average size	Proportion of lobules involved
0	0
1	1 (up to 33%)
2	2 (33-66%)
3	3 (66-100%)

Type II. 
Not present
Up to 0.5cm-----
0.5 to 2.5cm-----
Over 2.5cm(PMF)----- Site-----

Type III (dense, 'hard', circumscribed nodules) 
Not present
Up to 0.5cm-----
0.5 to 2.5cm-----
Over 2.5cm(PMF)----- Site-----

2. Dust impregnated interlobular septa including paraseptal dust.
0
1
2
3

3. Generalised pleural thickening.
0
1
2
3

4. EMPHYSEMA

	Severity in average affected lobule	Proportion of lobules involved In W lung	In UL	In LL
Centrilobular	0	0	0	0
	1	1	1	1
	2	2	2	2
	3	3	3	3
Panacinar	0	0	0	0
	1	1	1	1
	2	2	2	2
	3	3	3	3
Irregular plus fine honeycombing	0	0	0	0
	1	1	1	1
	2	2	2	2
	3	3	3	3

5. INTERSTITIAL FIBROSIS

NO/POSSIBLE/PROBABLE

6. CENTRAL LYMPH NODES

0
1 Comment:
2
3
4

7. GENERAL COMMENTS

ANNEXE 3 (b).

NAME:_______________ No.: __________

MICROSCOPIC ASSESSMENT 2x2/Histology Upper lobe/lower lobe

1. Central Dust Foci

Average Size	% Collagen	Cellular infiltration
0	0	0
1	1	1
2	2	2
3	3	3

2. Interstitial fibrosis (perilobular collagen)

Extent	% Pigmented
0	0
1	1
2	2
3	3

3. Interstitial cellular infiltration

0
1
2
3

4. Emphysema - severity

Centrilobular	Panacinar
0	0
1	1
2	2
3	3

'Rim' of normal tissue adjacent to interlobular septa YES/NO

5. Dust impregnated interlobular septa, including paraseptal dust

0
1
2
3

6. Do you think the appearances can be explained by CWP YES/NO
If NO, specify what else:

POST-MORTEM PATHOLOGY STUDY

Please complete this form when you enter a case into the study.

NAME:

DATE OF DEATH:

DATE OF PM:

CAUSE OF DEATH:

COALWORKER: YES/NO

NAME OF PATHOLOGIST:

SMOKING HISTORY: [ ] Non-smoker

[ ] Ex-smoker

Gave up .... months/years ago

[ ] Smoker

........../day cigarettes

other ....

ANNEXE 4 (b).

PATHOLOGY STUDY. PMP details and occupational history

NAME:

PMP live number:

PMP dead number:

Pathology:

Date of birth:

Date of death:

Age at death:

SMOKING

At last board (date:)

Previously:

BOARDS

Last board:

% disability:

First board:

% disability:

Other Boards:

% disability changes:

SPIROMETRY

Dates:

FEV_1/FVC:

Dates:

FEV_1/FVC

CHEST X-RAYS

First:

Last:

Film when left CMI:

OCCUPATIONAL HISTORY

Years of CMI exposure: **UG:**
Surface:

Finished:

Details of Occupational History:

Industry	Precise Occupation	Name & address of employer	Place of employment and check number (if any)	Period of Employment From: To:

ANNEXE 4 (c).

ADDITIONAL INFORMATION

NAME: **NUMBER:**

AGE: **DATE OF DEATH:**

Information from:

SMOKING

Was he ever a smoker? **YES/NO**

If Yes:

When did he start smoking? ----------------

Was he smoking up until he died? **YES/NO**

If No:

When did he stop smoking? ----------------

How many cigarettes (or how much pipe tobacco etc) did he smoke (indicate any big changes) -------

----

COFFEE/TEA

Was he a coffee or tea drinker? ---------------

How may cups/day? --------------- **coffee**
--------------- **tea**

OCCUPATIONAL

When did he work in the mines? ------------------

For how many years? ------------------

If possible, which pits and what jobs ------------------

What were his other major occupations ? ------------------

ANNEXE 5 (a).

Irregular opacities Collaborative Group

Case-control study of irregular opacities and occupation. Preliminary protocol

Aims

To investigate the occupational associations of small irregular opacities on the chest x-ray. In particular to find out if cases, with irregular opacities, have a history of coalworking experience more frequently than controls, without irregular opacities.

Methods Collection of cases and controls

A multi-centred study is proposed. This will increase the number of subjects and allow any geographical variations to be investigated.

Cases and controls will be drawn from new patients attending chest clinics in coalworking areas. A consecutive, complete series of all male patients, aged 40-80 years, attending the clinic for the first time will be entered from each centre. For each subject in the series, the physician will read the chest x-ray with regard to the presence of small irregular opacities. This should be done blind of the subject's occupation if at all possible. The x-ray reading and patient's name, address and age will be entered on a patient-entry form.

Each subject will be asked if he is willing to fill in a questionnaire about his occupational history. If he agrees, he will be given a questionnaire and a stamped envelope, addressed to the MRC Pneumoconiosis Unit. He should complete the questionnaire by himself and then post it. If a subject does not wish to participate he will not be given a questionnaire, but a patient-entry form will still be completed for him, including the fact that he is not participating.

It is envisaged that about 100 subjects will be entered from each centre, usually from several physicians. Many of these will be controls without irregular opacities on chest x-ray. The collection period will be 3-4 months beginning in mid-February 1981.

Analysis

The frequency of coalworking experience will be compared between cases and controls. For each case, several controls will be used, with matching for age. The data for individual centres will initially be analysed separately. The final numbers should be large enough that if a negative result is found it can be reported with confidence.

Organisation

Co-ordination will be from the MRC Pneumoconiosis Unit in South Wales. Each participating physician will have a supply of patient-entry forms and occupational questionnaires. The patient-entry forms will be returned by the physicians throughout the study and the completed occupational questionnaires will be posted by the patients.

Information about the progress of data collection will be circulated to the participating physicians during the study.

ANNEXE 5 (b).

CHECK LIST

IRREGULAR OPACITIES COLLABORATIVE GROUP

Check List for collaborating physicians

1. Enter all male new clinic attenders between the ages of 40 and 80 years.

2. For each of these men fill in a Patient Entry Form, whether or not they agree to fill in a questionnaire

3. For each man read the x-ray, blind of his occupation, for the presence of irregular opacities. A colleague who has not seen the patient may be asked to read the film if it is impossible for you to read it 'blind'. Enter the reading on the Patient Entry Form.

4. Arrange for a duplicate film, or the original film after taking a copy, to be sent to the Pneumoconiosis Unit for reading.

5. At a suitable point in the interview with the patient, ask him if he is willing to take part in a research project which will involve him filling in a questionnaire about his present and previous occupations. Stress that the information on the questionnaire will be treated in strict confidence.

6. If he agrees, give him the questionnaire and attached stamped addressed envelope to take home, complete and post to the Pneumoconiosis Unit. If he refuses, record this on the Patient Entry Form.

7. Return completed Patient Entry Forms to the Pneumoconiosis Unit as soon as possible.

ANNEXE 5 (c).

PATIENT ENTRY FORM

IRREGULAR OPACITIES AND OCCUPATION

PATIENT DETAILS

Name:

Date of Birth:

Address:

Hospital/Clinic:

Date seen:

Consultant:

CHEST X-RAY

Irregular opacities present YES/NO Duplicate film sent ☐

Other comments:

LUNG FUNCTION (IF AVAILABLE)

FEV_1:

FVC:

Other lung function:

THE PATIENT AGREED TO TAKE PART AND HAS BEEN GIVEN A QUESTIONNAIRE ☐

OR

THE PATIENT REFUSED TO TAKE PART ☐

Was the patient ever a coalworker? YES/NO

Number of years ____________________

Physician's signature: ....

ANNEXE 5 (d).

QUESTIONNAIRE

NAME	AGE	DATE OF BIRTH
--------------------	------	---------------

ADDRESS

----

1. Have you ever worked as a coalminer? YES/NO

If YES,

How many years in total did you spend as a coalminer? --------

How many years did you spend underground? --------

How many years did you spend doing face work? --------

What other jobs did you do underground and for how long?

---------------------- ------- years

---------------------- ------- years

How many years did you spend as a colliery surface worker ? -------

How many years ago did you stop working as a miner? -------

2. Please list all the occupations you have had since you left school, beginning with the first and say how many years you spent in each. If you need more space, please use the blank side of this sheet.

Job	From	To	No. of years
---------------------	----	----	----------
---------------------	----	----	----------
---------------------	----	----	----------
---------------------	----	----	----------
---------------------	----	----	----------
---------------------	----	----	----------
---------------------	----	----	----------
---------------------	----	----	----------

3. Have you ever been exposed to asbestos in the course of your work? YES/NO

If YES, how long? --------- years

Other details --------------------------------

----

4. Smoking

Do you smoke? YES/NO

If NO, have you ever smoked as much as one cigarette a day for as long as a year? YES/NO

If YES, to either of the above questions:

How old were you when you started smoking regularly ------- years

How may cigarettes/day do you (or did you) smoke on average? -----------

How many ozs tobacco do you smoke/week? -----------

For ex smokers How long ago did you give up smoking? ------- years

5. Hobbies

Have you ever kept, or been in contact with pigeons or other birds? YES/NO

If YES, How many years? -----------

What kind of birds? -------------------

6. Health

Do you take any medicines or tablets regularly? YES/NO

If YES, please specify ------------------------------

Have you had any serious illnesses in the past? YES/NO

If YES, please specify ------------------------------

Has anyone in your family had chest trouble? YES/NO

If YES, please specify ------------------------------

----

7. Would you like the results of this study to be sent to you when it is completed? YES/NO

Signed ....

Name in block capitals ....

ANNEXE 5 (e).

MRC

Medical Research Council

reference AEC/PJH

MRC Pneumoconiosis Unit
Llandough Hospital
Penarth, S. Glamorgan CF6 1XW

telephone Penarth 708761

Uned Pneumoconiosis
Ysbyty Llandochau
Penarth, De Morgannwg CF6 1XW

ffôn Penarth 708761

January, 1982

At a recent attendance at the chest clinic in your area, you may remember being given a form to fill in about your occupation and smoking habits and a stamped envelope to post it in. We have not received the form back from you and wonder whether you have mislaid it, or if it has been lost in the post.

Another questionnaire and stamped addressed envelope is enclosed. I would be really most grateful if you could spare a few moments to fill it in and put it back in the post. The study we are undertaking will be much more useful if everyone returns the forms. I assure you that all the information on the form will be treated in strict confidence.

I do hope you will be able to help. Please enclose a note with your form if you would like any more information about the study in which you are participating.

Thank you,

Yours sincerely,

Anne E. Cockcroft, MB,MRCP

MRC

Medical Research Council

reference AEC/PJH

MRC Pneumoconiosis Unit
Llandough Hospital
Penarth, S. Glamorgan CF6 1XW

telephone Penarth 708761

Uned Pneumoconiosis
Ysbyty Llandochau
Penarth, De Morgannwg CF6 1XW

ffôn Penarth 708761

January, 1982

I recently sent you a questionnaire about your occupational history but have not yet had a reply. I sent you the questionnaire because you recently attended the chest clinic in your area and we are studying a group of people attending chest clinics to see if certain x-ray changes are associated with certain occupations, such as coalwork. In order that the results of the study are meanginful it is important that we should have an occupational history on everyone. I would be really most grateful if you could find the time to fill in and return the enclosed questionnaire. If you feel that you do not wish to fill in the questionnaire, I would be grateful if you could fill in the small form instead. This will ensure that you are not troubled by further reminders.

I do hope that you will be able to help in this research. Please let me know if you would like more information about the research.

Yours sincerely,

A.E. Cockcroft, MB, MRCP

NAME:

ADDRESS:

Please do not send me any more reminders about the occupational questionnaire.

I have worked (or am working) as a coalminer YES/NO

SIGNED: ....