The relationship between respiratory impairment and asbestos-related pleural abnormality in an active workforce

A thesis submitted to the
Faculty of Graduate Studies and Research
in partial fulfillment of the requirements for the degree of
Master of Science

March 1988

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Impairment and asbestos-related pleural abnormality

ABSTRACT

Due to generally improved environmental controls in workplaces where asbestos is used, there are now fewer workers who develop asbestosis while an increasing number exhibit isolated pleural plaques. Whether these are associated with respiratory impairment independently of underlying parenchymal disease (usually mild in degree and extent) remains unresolved. The question was re-investigated using quantitative gallium-67 lung scanning to take into account parenchymal change not evident on the chest radiograph in a cross-sectional study of 110 construction insulators all currently at work. Overall, 58% had pleural abnormality, 52.5% pleural plaques only and 5.5% diffuse pleural thickening as assessed by reading the PA chest radiograph into the ILO 1980 classification. Compared to those without, those with pleural abnormality had significantly reduced forced expiratory volumes. This deficit was related independently to chest wall pleural thickening and to costophrenic angle obliteration, after taking into account age, height, smoking status and the presence of parenchymal abnormality as assessed by chest radiography and gallium uptake. In addition, the complaint of dyspnea with strenuous activities was significantly related to the width and extent of chest wall pleural thickening after taking into account the covariables mentioned above, even though exercise capacity was not different in subjects with and without pleural abnormality. However, on exercise, those with pleural abnormality were shown to use more of their ventilatory reserve and breathe with a higher frequency at selected levels of submaximal exercise. The increase in the sensation of breathlessness on effort in those with pleural abnormality may therefore be related to differences in breathing pattern induced by the pleural changes.

RESUME

Grâce à un meilleur contrôle de l'hygiène industrielle chez les travailleurs exposés à l'amiante, moins de travailleurs développent maintenant l'amiantose et un plus grand nombre d'entre eux présentent des plaques pleurales isolées. La question d'une association entre la présence de plaques pleurales et une dysfonction respiratoire, indépendamment de tous changements parenchymateux, demeure controversée. Cette question fut réévaluée dans une étude transversale de 110 travailleurs calorifugeurs tous au travail, avec l'ajout de la scintigraphie pulmonaire quantitative au gallium-67, pour l'évaluation de tous changements parenchymateux non détectés sur la radiographie pulmonaire standard. Selon une lecture des radiographies pulmonaires postéroantérieures utilisant la classification BIT 1980, 58% des travailleurs avaient des anomalies pleurales, 52,5% des plaques pleurales et 5,5% des épaississements pleurals diffus. Par comparaison aux travailleurs sans anomalies pleurales, ceux avec anomalies pleurales avaient une diminution significative des volumes expiratoires maximaux. De plus, cette diminution était associée à l'étendue des anomalies pleurales et la présence d'une oblitération de l'angle costophrénique après ajustements pour l'âge, la taille, le tabagisme et la présence de changements parenchymateux, tels qu'évalués par la lecture des radiographies et scintigraphies pulmonaires au gallium. Les symptômes de dyspnée en relation avec des activités importantes étaient aussi associés de façon significative à l'étendue des anomalies pleurales après ajustement pour les mêmes covariables ci-haut mentionnées, et malgré le fait que la capacité à l'exercice était semblable chez les travailleurs avec et sans anomalies pleurales. Cependant, à certains niveaux d'exercice, les travailleurs avec anomalies pleurales utilisaient une plus grande proportion de leur réserve respiratoire maximale et respiraient à une fréquence respiratoire plus élevée. L'augmentation de la perception de dyspnée à l'effort chez les travailleurs avec anomalies pleurales pourrait donc être associée à des différences de modes de respiration induits par des changements pleuraux.

ACKNOWLEDGEMENTS

The many steps, from the conception of the protocol, the realisation of the study, the analysis and finally the writing of the thesis required a collaborative effort and an enthusiastic contribution of many hands and minds, and the support and encouragement I received from many persons were greatly appreciated.

It is not possible to overstate my gratitude to my research assistants Fatima Nunes and Yves Blanchet who worked magnificently for innumerable hours and by their collaborative efforts made possible the realisation of the study. The efforts by Fatima Nunes deserve special praise since she handled effectively the tedious and necessarily exacting task of typing the several drafts up to and including the final. The devotion and diligence with which she carried out her tasks was greatly appreciated.

I am indebted to Dan Nguyen not only for his generosity in time spent programming on the computer but also for the benefit of his experience and assistance during the whole data analysis and preparation of the thesis.

Throughout the study, I received much cooperation from the department of radiology, nuclear medecine and the pulmonary function laboratory at the Montreal General Hospital. I am grateful to them and for the collaboration and the expertise of Dr. John Chrome in developing a program for quantifying gallium in the lung, a relatively new imaging technique and an essential modality in the present study.

I am especially grateful to Dr. Pierre Ernst, with whom I had numerous hours of discussion and precious advice throughout the study.

His assistance and help as a collaborator and a friend were always of good support and encouragement during the entire study, the analysis and finally writing the thesis.

I would also like to thank Dr. Ben Armstrong, statistician at the School of Occupational Health, McGill University, who assisted me in many ways in the analysis of the study. I would also like to thank Frances Belland who supported my humour and provided continuous encouragement.

It is not possible to overstate my gratitude to my thesis director, Dr. M.R. Becklake, who advised and assisted me throughout the study and the thesis with her rich experience and her many constructive comments. Her enthusiasm and creative mind were a great inspiration to me.

Finally and with immense gratitude, I recall the patience and understanding displayed by my wife throughout the study and the thesis. Without her encouragement, this thesis would not have been completed, and I acknowledge her many virtues with much love.

TABLE OF CONTENTS

LIST OF TABLES

GLOSSARY OF LUNG FUNCTION TERMINOLOGY USED

FORCED EXPIRATORY VOLUMES

FVC	Forced Vital Capacity
FEV_1	Forced Expiratory Volume in 1 second

FORCED EXPIRATORY FLOW RATES

PEFR	Peak Expiratory Flow Rate
FEF_{50}	Forced Expiratory Flow when 50% of FVC has been expired
FEF_{75}	Forced Expiratory Flow when 75% of FVC has been expired
FEF_{25-75}	Forced Expiratory Flow during the middle portion of the forced expiration

LUNG VOLUMES

TLC	Total Lung Capacity
FRC	Functional Residual Capacity
RV	Residual Volume

DIFFUSING CHARACTERISTICS

DL_{co}	Diffusing Capacity for carbon monoxide
V_A	Alveolar volume obtained from helium dilution in the single breath manoeuvre

EXERCISE TEST

HR	Heart Rate
$\dot{V}O_2$	Oxygen uptake (expressed in l/min or ml/kg/min)
$\dot{V}_E$	Ventilation per minute
O_2 pulse	$\dot{V}O_2$ / HR (a measure of cardiovascular efficiency)
$\dot{V}_E/\dot{V}O_2$	Ventilation per minute / oxygen uptake (a measure of respiratory efficiency)
V_t	Tidal Volume
MVV	Maximal voluntary ventilation estimated from the equation MVV = 30.6 x FEV_1 - 29 l/min

CHAPTER 1. INTRODUCTION

Asbestos is the name given to natural fibrous silicates well known for their wide commercial use since the late nineteenth century. The harmful effects on health of exposure to asbestos were recognized by the early years of this century (1). Since then, extensive investigations have established that asbestos exposure results in an increased risk of nonmalignant as well as malignant pulmonary diseases (2-4). Included in the former are lung fibrosis or asbestosis, rounded atelectasis, benign pleural effusion, diffuse pleural thickening, pleural plaques and airway disease. Included in the latter are lung cancer and malignant mesothelioma.

In the case of non malignant disease, major attention has focused on asbestosis which may be associated with respiratory impairment, disability and death (2), while pleural abnormality has often received only passing attention. Thus pleural plaques, though common, have traditionally been considered the sign post of asbestos exposure with no more than a mild effect on lung function. However, diffuse pleural thickening is generally regarded as more likely to cause lung function impairment, and if extensive, disability (4). Nowadays, with improved environmental control measures, the prevalence and extent of parenchymal abnormality is decreasing (5,6), and more workers remain employed for 20 or more years from onset of exposure, after which time

pleural plaques tend to develope. In consequence there is an increasing number of individuals with pleural plaques as the sole manifestation of exposure. In addition, pleural plaques may also occur as the consequence of non-occupational exposure (2). The effect of isolated pleural plaques on respiratory health is therefore of increasing importance in the practice of pulmonary medicine.

Chapter 2. NON-MALIGNANT ASBESTOS-RELATED PLEURAL ABNORMALITY

2.1 Type of pleural abnormality

2.1.1 General

Pleural thickening as the consequence of an occupational exposure was first described in 1943 by Siegal et al in a study of New York State talc miners (7). It was not until 12 years later, in 1955, that Jacob and Bohlig described pleural thickening and calcification in association with asbestos exposure, and their findings resulted in renewed interest in asbestos-related pleural abnormality (8). Subsequently, two types of pleural abnormality were recognized: diffuse (usually in the form of diffuse pleural thickening) and localized (usually in the form of pleural plaques, which may or may not be calcified). Pleural plaques are rarely seen under 15 years from the date of first exposure to asbestos; most will appear after 30 years or more. In general, the longer and heavier the exposure, the more extensive the plaques; however intermittent, possibly heavy exposure has been implicated as well as slight and short exposure (9).

The association between asbestos exposure and the development of non-malignant exudative effusion was first reported in 1964 (10), and since then, many case series have been reported. Asbestos pleurisy is

the most common asbestos-related lesion during the first two decades after exposure commences (11) but can also occur much later. Those affected are very often symptom free, the abnormality being discovered incidentally by chest radiography (12). Some of the asbestos pleurisies will disappear without trace, but often sequelae will be visible (13,14). There have been several reports of diffuse pleural thickening following acute pleural reactions (12-15). For these reasons, it has recently been the practice of some investigators to include diffuse pleural thickening and benign pleural effusion under one term, namely visceroparietal reactions (17). When followed over some years, some cases of the diffuse pleural thickening show a tendency to increase slowly; more often however, the disease remains unaltered for years, even decades (13,16). Occasionally the clinical course is marked by a sudden deterioration, probably reflecting the recurrence of an acute pleurisy.

2.1.2 Pathology

Pleural plaques (18,19), whether calcified or non-calcified, are typically found on the parietal pleura lining the postero-lateral aspect of the thorax, the vertebral column and the dome of the diaphragm; they are rarely seen over the apices of the lung or in the cost ophrenic angles, or on the visceral pleura. They are usually greyish white and either have a smooth or coarsely nodular surface. Their size and shape vary: whereas plaques on the surface of the

diaphragm are typically round and disk-like, those located over the intercostal spaces tend to be elongated. Microscopically, pleural plaques consist of dense strands of hyalinized collagen with occasional fibers of asbestos; they are lined by a surface of mesothelial cells.

There are few histologic descriptions of diffuse pleural thickening (2). The underlying pathophysiologic process is believed to involve both parietal and visceral pleural surfaces, with varying degrees of obliteration of the pleural space and frequent involvement of the costophrenic angle. Benign asbestos pleural effusion can be clear or hemorrhagic and the cellular content of the fluid is variable (20). On examination at thoracotomy, the pleural surfaces of benign pleural effusion show an active exudative process, characterized by increased vascularity and symphysis. Microscopic examination usually shows variable pleural thickening, pleural carbon dust and iron-positive granules, regenerating mesothelium and extensive collateral vascular circulation (14).

2.1.3 Pathogenesis

The pathogenetic mechanism underlying the development of pleural plaques is still not established; several theories exist (21). Any credible theory will need to explain their location, the long interval between first exposure to asbestos and the development of clinically recognizable abnormality, the absence of adhesions between the two pleural surfaces, and their slow progression. An early theory

postulated mechanical damage caused by the movement during respiration of long thin asbestos fibers projecting from the lung surface. Weaknesses in this theory include the fact that the relative movement of the pleural surfaces is greatest at the most dependent part of the lungs, i.e. in the costodiaphragmatic junction where pleural plaques are seldom if ever found, also the expectation that long thin fibers should give rise to an intense foreign body reaction resulting in pleural adhesions which are seldom found with pleural plaques. Several non-mechanical theories have been published but very little proof has been presented and discrepancies in logic may be found in many of them. It is the theory advanced by Hillerdal (21) which best explains the characteristic features of pleural plaques and it is also supported by some experimental data. This theory holds that short asbestos fibers reach the pleural space by penetrating the pulmonary parenchyma; they then follow the normal lymphatic flow from the pleural space through the parietal pleura. In passing through the parietal pleura, some will be trapped in macrophages, causing a low grade stimulation of the submesothelial fibroblasts, and this process eventually results in visible pleural plaques, twenty or more years later.

The pathogenetic mechanisms underlying the development of diffuse pleural thickening are also obscure, although several case reports suggest that active pleural reaction or noncomplicated pleural effusion may be a frequent precursor (12-15). Of interest is the fact that pleural effusion is more common in younger individuals, often in their 30's, and within 10 years of first exposure (13), a time relationship

consistent with effusion as a precursor of diffuse pleural thickening. However, in the individual case, it is difficult to confirm in retrospect the presence of benign pleural effusion, since typically there are few or no symptoms.

2.1.4 Radiographic features

i) Standard chest radiograph

The posteroanterior (PA) chest radiograph has been the traditional tool used in health surveillance of asbestos-exposed workers to detect asbestos-related disease of the pleura. Several studies suggest that the PA chest radiograph detects only a small proportion of plaques identified at autopsy or thoracotomy (22,23). Plaques are best seen when they are calcified, in which case they stand out clearly wherever they are situated. Common sites are the posterolateral chest wall between ribs 5 to 10 and the middle portion of the diaphragm. Hyaline plaques are best seen tangentially. In profile, they are denser with more distinct borders. If sufficiently thick, even uncalcified plaques can be seen en face as faintly delineated shadows. Distinction between plaques and pleural fat pads may be difficult, especially in overweight persons. Pleural fat pads are usually seen in the flanks, sometimes from costophrenic angle to the apex (24). Unless strict criteria are used, there may be overdiagnosis in reading chest radiographs for pleural changes.

Chest radiographs are usually read according to the ILO International Classification of Radiographs of Pneumoconioses. This system was developed by an International Commission for the purposes of standardizing the interpretation of films obtained for the evaluation of pneumoconioses. It was not until the ILO U/C classification 1972 (25) that pleural abnormality was brought into the main classification; two types of abnormality were recognized, thickening and calcification, while plaques were still recorded only as a symbol "pq". The ILO 1980 classification (26) introduced a further modification to record the sites of pleural thickening (chest wall, diaphragm, costophrenic angle) separately for right and left sides. In addition, pleural change was now classified as parietal pleural plaques and/or diffuse pleural thickening, though the radiographic distinction is hampered by the lack of a uniform definition of diffuse pleural thickening. Nor are specific criteria provided in the more recent 1980 ILO classification to distinguish diffuse pleural thickening from confluent pleural plaques. A recent study on between and within reader variability in the assessment of asbestos-related pleural abnormality using the ILO 1980 classification has confirmed the opinion that confident separation of the 2 types of pleural thickening may be difficult to achieve (27). McLoud et al (15) suggested that involvement of the costophrenic angle was a distinguishing feature, since it was blunted in diffuse thickening secondary to a previous effusion, and usually preserved in diffuse thickening due to confluent plaques. The NIOSH B reader instruction course also suggests that costophrenic blunting be

recognized as a major component of the ILO definition of diffuse pleural thickening, a view supported by other investigators (20).

ii) Oblique chest radiographs

To improve sensitivity of chest radiography in the diagnosis of pleural abnormality, several authors have suggested obtaining oblique views of the chest in addition to the PA films (1,28,29). Oblique radiographs often permit the detection of pleural thickening along an aspect of the lung surface not viewed tangentially in the PA projection and therefore such films should result in a higher detection of pleural abnormality. Baker and Greene reported a 33 percent increase in the prevalence of pleural thickening when two oblique views were added (29); on the other hand, Sheers et al (30) concluded that oblique views did not contribute significantly to detection of pleural plaques, noting an increase in the prevalence of pleural thickening of 2.7 % only. More recently, Greene et al (31) found that the increased sensitivity afforded by the oblique views is largely dependent upon the threshold level of pleural reading, increasing most when a strict threshold criteria of more than 2 mm thickening is used as opposed to one of less than 2 mm. Reger et al (32) have also challenged the use of oblique films; they found that although the use of oblique films with the PA films leads to a much higher detection rate, and the detection using both reading procedures appears to have similar validity in terms of relationship to years of asbestos exposure, there

is less consistency between readers in interpreting oblique films. This in turn would be likely to increase the rate of both false negative and false positive results.

iii) Computer tomography of the chest

It is still unclear as to what is, and should be the role of computerized tomography (CT scan) of the chest in the evaluation of asbestos related pleural abnormality; the question asked whether it is worth the additional cost and radiation exposure. Early studies reporting upon relatively small clinical series of patients suggested that the CT scan leads to earlier diagnosis of pleural thickening (33,34). They also indicated that the method was of value in distinguishing subpleural fat from asbestos-related pleural abnormality, a major problem especially in obese individuals. However another study (35) which compared PA chest radiograph, 4 views of the chest (PA, lateral and oblique films) and CT scan for the evaluation of asbestos-related pleuro-pulmonary abnormality reached different conclusions. Quantifiying the degree of pleural abnormality by a radiological score, the authors found that the highest overall score for pleural thickening without associated calcification was obtained by the 4 views of the chest followed by PA films and CT scan. The CT scan was also insensitive to involvement of the costophrenic angles and diaphragm, though it was much better than the two other methods for detection of pleural calcification. The findings in a more recent

study (36) suggest that CT and conventional chest radiographs should be considered complementary. Thus some pleural plaques visible on conventional films were missed on CT scan and vice versa. However the distinction between subpleural fat pads and pathologic pleural thickening was better done by CT scanning. In all these studies, the assumption is made that the more abnormality detected, the more valid the measurement. This assumption has not been tested against pathology findings.

2.2 Epidemiology of pleural abnormality

Epidemiologic studies have shown that non-malignant pleural abnormality in the form of diffuse thickening or localized plaques may be associated with both occupational and non-occupational exposure to asbestos (2). In occupationally exposed groups, the prevalence of pleural abnormality assessed by the chest radiograph has been shown to increase in relation to estimated level of asbestos exposure, although it is usually difficult to separate age and exposure effects (30,37,38). Some studies have also stressed the importance of the latency period prior to the appearance of pleural abnormality (39-42). Time passed since first exposure appears to be an important determinant of the presence of pleural abnormality, in addition to intensity of exposure including peaks.

All varieties of asbestos fibers have been associated with pleural abnormality but they appear to vary in their ability to evoke pleural

changes (3). In the case of exposure in mining operations, the site and nature of the deposit appear also to be of importance. For instance, in Quebec the prevalence of radiologic pleural changes was higher in the Thetford Mines area compared to the Asbestos mining area, despite the fact that the mining operations are only a few kilometers apart and exploit essentially the same deposits (37). The difference was most marked for pleural calcification which was common in Thetford Mines but virtually absent in Asbestos. Possible explanations include the presence of associated minerals e.g. tremolite in the Thetford deposits. Pleural abnormalities also occur more in miners than among millers (38,43). In addition, attention has been drawn to the high prevalence of pleural abnormality in workers in certain other parts of the industry. For instance, in shipyard workers, the frequency of pleural abnormalities is high and may exceed that of parenchymal abnormalities (30,33,44,45), while the rates for pleural abnormality are also high in construction and insulation workers (40,46,47) where prevalence rates as high as 80% have been reported in those with long exposure.

Pleural plaques may also be caused by talc containing no true asbestos (48) and fibrous erionite such as found in central Turkey (49,50). Nevertheless, most individuals found to have pleural plaques have been exposed to asbestos. Although the occupationally exposed individuals represented the most frequent situation found, the prevalence of pleural abnormality among populations with nonoccupational i.e. environmental exposure, may range from 2 to 28%

(50-55), whereas in a general population not so exposed, it is usually less than 3% (56). In some areas of the world, asbestos deposits contaminate the bedrock and if these fibers become mixed into the soil or are used locally for other purposes (e.g. plastering), an increased prevalence of pleural abnormality can occur. Such endemic areas have been reported from Austria, Bulgaria, Czechoslovakia, Finland, Soviet Union and recently also from Greece (51-55).

2.3 Pleural abnormality and its relationship to respiratory impairment

2.3.1 Introduction

Though a great deal of research has been directed towards clarifying the relationship of asbestos-related parenchymal abnormality to respiratory impairment and disability, the functional impact of asbestos related pleural abnormality has received much less attention until relatively recently. This section contains a review of the published evidence, some of which is summarized in table 1. In the present study, the WHO definition of the terms impairment and disability was used: impairment referring to lung function deficit, and disability to impaired capacity to exercise.

2.3.2 Objective assessment of impairment (see Table 1)

2.3.2.1 Studies with evidence of impairment

Most early studies of the effects of pleural abnormality on lung function did not distinguish the different types of pleural changes. For instance, Becklake et al (1970) studied an age stratified random sample of men currently employed in the asbestos industry of Eastern Quebec, and showed small but consistent adverse changes in lung function in those with any pleural abnormality compared to those with none, for a given grade of severity of parenchymal fibrosis (57). The overall prevalence of plaques in the total population from which the sample was drawn was 3.8 %, of calcification 2.5 % and of costophrenic angle obliteration 5.8 %. Harries et al (1972) also found that the presence of any pleural abnormality was associated with lower lung function (38). Subsequent studies distinguished the various forms of pleural abnormalities and most evidence suggests that while pleural plaques have only modest effects on lung function, pleural thickening, particularly if diffuse, can affect lung function more seriously and may even be associated with disability (58-60).

Thus, Lumley in 1975 reported a cross-sectional study of 194 dockyard employees, stratified on the basis of chest radiograph findings (61). A group of men with diffuse pleural thickening were matched for age and occupation with 4 other groups of men with, respectively, i) lung fibrosis (ILO profusion greater than or equal to

1/1) irrespective of pleural abnormality; ii) non-calcified pleural plaques, iii) pleural calcification and iv) normal chest radiographs. Compared to those with normal chest radiographs, subjects with lung fibrosis, diffuse pleural thickening or pleural plaques had statistically significantly ($p<0.05$) lower values for several resting pulmonary functions (FEV_1, FVC, TLC, DL_{CO}) and also higher values of ventilation during exercise ($\dot{V}E$ at oxygen uptake of 1.0 L/min). There was on average more functional impairment related to lung fibrosis than to diffuse pleural thickening, or to pleural plaques, while pleural calcification was not accompanied by any significant abnormality.

In 1981, Fridriksson et al, using data from a population health survey (62), selected 46 subjects with pleural plaques but no parenchymal abnormality who also reported asbestos exposure, and compared their lung function with that of a reference group of 263 healthy men after adjusting for age, height, weight and smoking habits. Compared to the reference population, those with pleural plaques had lower values (by approximately 14 to 16%) for total lung capacity (TLC) and forced expiratory volumes (FVC, FEV_1); their lungs were also stiffer (reduced compliance) and the transfer factor for carbon monoxide was reduced, all changes consistent with the presence of lung fibrosis. Since no specific assessment of associated parenchymal disease was provided in the study, the findings attributed to pleural disease may in fact have been due to parenchymal fibrosis underlying the pleural changes. The results may also reflect what is already known about the chest radiograph, namely that it is a poor

instrument in detecting early lung fibrosis (63).

Jarvholm and Sanden based their 1986 study on an active workforce in shipyards (64). They restricted their observations to 202 non smoking men, 115 with a normal chest radiograph and 87 with pleural plaques. Those with pleural plaques but no radiographic asbestosis had on average an FVC of 6.9 % lower than that of workers without pleural plaques. After stratification for asbestos exposure, workers with plaques were also found to have lower FVC's than those without plaques, and the difference was larger for those with heavy exposure than for those with light exposure. This finding could also be interpreted as reflecting the presence of lung fibrosis not detected by chest radiography. Nor did the authors provide information on whether the extent of the pleural abnormality was comparable in the two strata of light and heavy exposure.

Using data from a cross-sectional survey of men above the age of 40 from a general population in Denmark and Norway, Hilt et al (65) selected subjects with radiographic changes compatible with asbestos-related disorders, e.g., pleural changes, pleural calcifications or basal pulmonary fibrosis. At a followup examination the medical and occupational history were recorded, and subjects with other current lung disease or other cause for pleural abnormality excluded. Also based on followup chest radiographs which were read according to the ILO classification, subjects were selected to represent the following 4 categories: 1) asbestos-related lung fibrosis only or in combination with pleural abnormality;

2) asbestos-related pleural plaques only; 3) normal chest film with reported asbestos exposure; and 4) normal chest radiograph but no reported asbestos exposure. The men in category 1) or 2) (i.e. with asbestos-related lung fibrosis or pleural plaques only) were found to have lower lung function than the other 2 categories when lung function was expressed as a percentage predicted, using a reference population of the same sex, age, height and same smoking habits as the study population.

Oliver et al in 1987 studied a population of 576 workers exposed to asbestos, 20 % of whom had pleural plaques (66). After exclusion of subjects with diffuse pleural thickening or evidence of parenchymal fibrosis (ILO profusion greater than 1/0), the presence of pleural plaques was associated with a decrement in FVC, when asbestos exposure and smoking was taken into account (p .02). An association between extent of pleural abnormality and decrement in FVC was also shown.

Whether the degree of function impairment associated with pleural plaques demonstrated in the above studies should change the clinical view of plaques as being essentially benign is still unclear. For instance, Jarvholm and Sanden (64) showed that few individuals with pleural plaques had spirometric values (FEV_1, FVC) below the expected values even if as a group their average value was reduced significantly ($p < .05$) below that of men with high exposure only. Hilt et al (65) in their population study found no individuals with pleural plaques had an FVC two standard deviations(SD) or more below the predicted values or an FVC less than 80 % of predicted value.

2.3.2.2 Studies without evidence of impairment (see Table 1)

Hedenstierna et al (1981) reported a study based on subjects identified in a program that includes health screening every second year among Stockholm construction workers. Subjects with and without pleural plaques were selected, using chest radiographs including PA, lateral and oblique films, and conforming to the following criteria; i) age 45-65 years, ii) no disablement and iii) no complicating diseases (67). Although mean values for FEV_1 and FVC were significantly less in exposed subjects with pleural abnormality compared with those nonexposed, when differences in age, height and smoking habits was taken into account by paired matching analysis, the differences were reduced and no longer statistically significant.

Ohlson et al (1985)carried out a four year follow up study of workers at an asbestos cement plant in Sweden. The association of pleural plaques and loss of ventilatory function was examined by comparing subjects with pleural plaques and referents chosen from three plants without exposure to asbestos (68). The comparison was confined to males, actively employed, with at least 10 years of employment; they were classified as smokers and never smokers. Forty three exposed smokers of the 77 originally examined and 32 exposed never smokers of the 48 originally examined took part of the study. The presence of pleural plaques was assessed by a qualified reader, a member of the National Pneumoconiosis Panel, using PA films supplemented by oblique films, read into the ILO classification. No

difference for the four year decrements in lung function were demonstrable between those with and without pleural plaques, after adjustment for age, smoking and fibre years.

2.3.3 Subjective assessment of impairment

Despite the two negative studies cited above, most of the published data provides evidence that lung function is decreased in subjects with pleural plaques. Respiratory symptoms are also an important aspect of health, but surprisingly have attracted almost no attention in studies of pleural plaques. Hedenstierna et al (67) observed an excess of symptoms of chronic bronchitis among workers with pleural plaques compared to exposed subjects without pleural plaques and nonexposed subjects for similar smoking status; there were however no difference in the subjective feelings of suffering from pulmonary abnormality. Hilt et al (65) showed an increase in the prevalence of grade 1 breathlessness in individuals with pleural plaques compared to those without, but no increase of breathlessness of grade 2 or more.

2.4 Underlying parenchymal disease as a cause of impairment attributed to pleural disease: methods of detection

2.4.1 Introduction

An unresolved issue in the studies that provide evidence of an

association between lung function impairment and the presence of pleural plaques is the extent to which any impairment demonstrated is dependant on underlying (if mild) parenchymal abnormality. In most of the studies cited, parenchymal fibrosis was excluded on the basis of conventional chest radiographic findings (57-68). However it is generally accepted that the presence of pleural change makes radiological assessment of the underlying lung parenchyma, particularly mild abnormality, even more difficult to detect. Furthermore, as in other forms of fibrosis, pathologic examination of the lung tissue may reveal the presence of fibrotic changes even when the radiographic changes in the pulmonary parenchyma are, at the most equivocal, and mechanics of breathing are normal (63,69).

2.4.2 Lung function tests

Other methods may be more sensitive than conventional chest radiographs for the detection of early parenchymal change. For instance, the findings in 2 early studies, by Williams & Hugh-Jones (70) and Leathart (71), lead to the suggestion that diffusing capacity might be sensitive to early effects of asbestos dust exposure (70,71). This was not however confirmed in subsequent studies, including those of an epidemiological nature, on larger samples of working populations (72). For instance in the study by Becklake et al (57) of Quebec miners and millers, changes in diffusion capacity at rest and on exercise only occurred in association with radiographic changes of

profusion of small opacities 1/2 or more, i.e. diffuse interstitial disease of at least moderate-degree. On the other hand, a radiologic profusion of only 0/1 was associated with a decrease in vital capacity and of 1/0 with an increase in exercise minute ventilation. However, in patients with pleural abnormality, lung restriction as assessed by decreased lung volume did not contribute to the distinction between parenchymal fibrosis and pleural thickening. Yet other studies (73, 74,75) have led to the suggestion that abnormality in tests of small airway function is an indicator of early parenchymal change; however the findings are not consistent.

2.4.3 Gallium-67 scan of the lung

Gallium-67 scan, a relatively new imaging technique, has been used in the detection of diffuse interstitial lung disease. In the context of pneumoconiosis, this test was first used in characterizing patients with well established asbestosis (76). More recently however, computed gallium-67 lung scanning has been proposed as a sensitive indicator of early asbestos related parenchymal injury (77,78). Begin et al (1982) showed in an experimental sheep model that gallium-67 uptake is related to the intensity of the asbestos induced macrophagic alveolitis (77). In a subsequent study in humans (78), they documented that in the majority of patients with asbestosis, Gallium-67 accumulates excessively in the lung, in keeping with the previous suggestions of Siemson et al (76). Moreover gallium-67 uptake in the

lung was also increased in approximately 43 % of the long term asbestos workers before the conventional criteria for diagnosis of asbestosis were met. In addition, 87 % of the patients in the group without radiographic evidence of asbestosis but with a high cumulative gallium-67 uptake had decreased lung compliance and/or abnormal alveoloarterial oxygen difference ($AaPO_2$) during exercise, in contrast to only 27 % of the patients in the group without radiographic evidence of asbestosis and low cumulative gallium-67 uptake. These 2 groups could not be differentiated by the conventional indicators of early parenchymal fibrosis, such as lung volumes (FVC, TLC, diffusing capacity), presence of rales on clinical examination and radiographic evidence of parenchymal abnormality. However, without longterm follow-up data, it is not possible to conclude that increased gallium-67 uptake in the lungs necessarily predicts the later development of asbestosis..

2.4.4 Computed tomography of the chest

Another new imaging technique proposed for the early detection of parenchymal lung abnormality is computed tomography of the thorax (CT). However, despite some earlier studies (34,35) suggesting that thoracic CT scans could detect early parenchymal fibrosis not seen by conventional xrays, Gerhard et al (37) were unable to confirm these findings in a more recent study; nevertheless, their data did show that fibrosis when present, was more strikingly shown on CT scans than on

conventional radiographs. In another recent study, Begin et al (36) compared the assessment of parenchymal abnormality using the PA radiograph and 4 oblique views with that obtained using chest CT; they showed that in workers with a rigid pressure volume curve and increased gallium-67 lung uptake, CT scan scores for parenchymal abnormality were not significantly higher than in subjects without these markers of early interstitial lung disease.

2.5 Conclusion

At the present time, with the generally improved environmental control measures in workplaces where asbestos is used, there is an increasing number of individuals with isolated pleural plaques. Despite two negative studies, most recently published studies offer evidence of an association between the presence of pleural plaques and lung function impairment (57-68). However, in most of these studies, the extent to which the impairment demonstrated is independent of any parenchymal abnormality remains uncertain. Until recently, early lung injury from asbestos exposure was assessed by conventional chest radiography. Given the new imaging techniques, which enable detection of parenchymal change prior to it becoming evident on the chest radiograph (77-78), it was felt that the question of whether pleural plaques are associated with respiratory impairment indepently of parenchymal abnormality merited re-investigation. The present study had this as its main objective.

Chapter 3. HYPOTHESIS, OBJECTIVES AND DEFINITIONS

3.1 Hypothesis

Asbestos related pleural abnormality is a cause of respiratory impairment independent of parenchymal abnormality.

3.2 Objectives

3.2.1 General objective

To determine whether asbestos related pleural abnormality is a cause of respiratory impairment in the absence of parenchymal abnormality. Available evidence (57-66) suggests this to be the case but the question invites re-investigation using new imaging modalities to exclude the presence of even minimal parenchymal abnormality.

3.2.2 Specific objectives

1) To determine whether there is a relationship between respiratory capacity (measured by questionnaire, lung function at rest and on exertion) and the presence of asbestos-related pleural abnormality, independent of parenchymal abnormality, taking into

account other relevant factors such as age, height and smoking.

2) To determine which features of pleural abnormality best predict respiratory impairment, taking into account other relevant factors such as age, height, smoking and parenchymal abnormality.

3) To determine whether the extent of pleural abnormality relates to degree of respiratory impairment, taking into account the other relevant factors mentioned above.

3.3 Definitions

Asbestos-related pleural abnormality was defined according to the reading of a standard posteroanterior (PA) chest radiograph, by an experienced chest physician, a certified B reader, using the ILO 1980 International Classification of Radiographs of Pneumoconioses. The classification allows pleural abnormality to be described in terms of location, width and extent of pleural thickening and calcification (26). Minimal width for a reading of pleural thickening of the chest wall was 2 mm (32), and diffuse pleural thickening was only classified when there was involvement of the costophrenic angle as suggested by the National Institute of Occupational Safety and Health (NIOSH) and the American College of Radiology.

Parenchymal abnormality was defined in several ways:

1) Small opacities with a profusion of 1/0 or more by a certified B reader according to the ILO 1980 International Classification of Radiographs of Pneumoconioses (26). This radiographic feature in association with a history of asbestos exposure is conventionally used to define "asbestosis".

2) Computer-based quantitative analysis of Gallium 67 uptake of the lung, and referred to in this thesis as the gallium index, was used to indicate early parenchymal reaction. This measurement has been shown to correlate with histopathologic scores of inflammation in lung tissue, both in the sheep model and in human subjects exposed to asbestos (77,78).

Respiratory impairment was defined in several ways using:

1) Responses to a French translation of the ATS-DLD-78 standardized respiratory symptom questionnaire for use in epidemiologic studies (79). A copy of this questionnaire can be found in appendix 1.

2) A recently described clinical index for dyspnea which contains ratings for each of three separate features: magnitude of task, magnitude of effort and functional impairment (80,81). A copy of this clinical index can be found in appendix 2.

3) Resting lung function, described below in greater detail.

4) Maximal and sub-maximal exercise cardiorespiratory function measured during treadmill exercise in the laboratory.

Workplace exposure in the population under study was defined by the number of hours worked as a construction insulator. During this time the subject was likely to be exposed to various amounts of asbestos and man made mineral fibers.

Chapter 4. DESIGN AND RATIONALE

4.1 Design

To achieve these objectives, a cross-sectional study was carried out among members of a union representing construction insulators, all of whom were currently at work. The dependent variable used for hypothesis testing was respiratory impairment, as assessed by both symptom information, and by respiratory function at rest and on exercise. The independent variable of interest was asbestos-related pleural abnormality as assessed by chest radiographic reading using the ILO 1980 International Classification of Radiographs of Pneumoconioses. The relationship between the dependent and independent variables was assessed after accounting for the effect of age, height and smoking status, all well recognized determinants of respiratory function. Since asbestos-related parenchymal abnormality is a potential confounder, its presence, assessed by chest radiographic reading of small pneumoconiotic parenchymal opacities and by a relatively new imaging modality, the gallium index, was also taken into account in the analysis.

4.2 Rationale

The rationale of selecting, as a basis for the present study, an active workforce of construction insulators from a previous survey on respiratory health was based on three considerations:

First, prevalence of pleural abnormality is well known to be high in the insulation trade (30,44,45). In a previous study of chest radiographs of this particular workforce, in which the ILO 1980 International Classification for Radiographs of Pneumoconioses was used, pleural abnormality was found to be present in over fifty percent of the workers (27).

Second, by selecting an active workforce, it was anticipated that there would be few if any subjects with evidence of frank asbestosis, i.e. subjects with a chest radiographic reading of small opacities with profusion of 1/0 or more. By minimizing the chances of encountering subjects with asbestosis, it was hoped to focus on the early functional effects of asbestos-related pleural abnormality.

Third, the availability of the previous survey information on this workforce permitted stratifying by age prior to sampling. The target age group was 35 to 55 years; exclusions were men under 35 years of age in whom it is unusual to find pleural abnormality, and men over 55 in whom other causes of disability such as heart disease and other lung disease are more frequent. The age group 35 to 55 years also represents the most active in the workforce.

A major concern in the present study was to overcome a weakness

of previous investigations in which exclusion for pulmonary parenchymal abnormality was based on radiographic criteria only. A relatively new and more sensitive imaging modality for detecting early asbestos-related parenchymal reaction was therefore used to assess whether or not parenchymal abnormality was present.

Chapter 5. POPULATION

5.1 Previous epidemiological surveys in the insulation trade

The study population for the present research consisted of 110 subjects, identified through previous epidemiological surveys of construction insulators carried out by this laboratory since 1982. The base population consisted of all members of Local 58 of the International Union of Frost and Heat Insulation and Asbestos Workers; this local represents almost all insulators employed in the construction industry in Quebec. The derivation of the study population for the present study is shown in Table 2. In the first survey, carried out in 1982, a respiratory symptom questionnaire was mailed to all the members of the Local 58, 644 men in all; 558 of them (86.6%) workers returned the questionnaire of whom 21 subjects were not considered further because they were receiving compensation for asbestosis, leaving 537 subjects. Subsequently, in 1983-1984, insulators fifty years old or less, who lived within a 30 kilometer radius of Montreal, and who had returned the previous study questionnaire, were invited to take part in laboratory tests of respiratory health; 215 of 246 eligible workers (87.4%) participated by attending the laboratory for lung function tests and measurement of airway reactivity.

5.2 Target population

The target population for the present study was selected from the 215 workers who had participated in the 1983-1984 laboratory study. Only workers of 35 years or more were selected, since asbestos-related pleural abnormality is rare before the age of 35. Of the 129 workers eligible for the present study, 110 agreed to participate, giving a response rate of 85.3%; 19 workers either refused or were unavailable.

Chapter 6. METHOD OF MEASUREMENT

6.1 Measurement of respiratory impairment

6.1.1 General

Respiratory impairment may be assessed subjectively by the subject himself, when it is usually based on his perception of dyspnea particularly on effort, or it may be measured objectively in the laboratory with conventional physiologic measurements of pulmonary function at rest or on exercise. Different measures of pulmonary function have been shown to be related to the sensation of dyspnea but do not alone or in combination explain this complex symptom. Nevertheless, the subjective assessment of dyspnea can be used as an effective supplement to its objective measurement by physiologic tests in the laboratory. In this study, the respiratory symptom information was gathered with particular emphasis the recording of dyspnea on effort.

6.1.2 Respiratory symptom information

A French version of the standardized ATS-DLD-78 questionnaire (79) was administered by an interviewer to each subject. This questionnaire

contains questions concerning the presence and severity of the major respiratory symptoms: cough, phlegm, dyspnea and wheeze; also a complete series of questions about current and past cigarette smoking; and an inquiry into personal and family history of disease(s) of the respiratory system.

There are several clinical scales for quantitating dyspnea. The questions on dyspnea in the ATS-DLD-78 questionnaire allow breathlessness to be rated according to the magnitude of the most taxing task the subject can perform, but no attention is given to the effort expended in performing the task, or to associated functional impairment. A recently proposed clinical index for dyspnea (80) contains ratings for each of three separate features: magnitude of task, magnitude of effort and functional impairment at home and at work. Further specifications have recently resulted in what has been called the Modified Dyspnea Index (MDI) (81). The latter has been shown to be reproducible and easy to administer and it appears to assess the disability associated with dyspnea more comprehensively than other scales. When compared with pulmonary function tests, the MDI has an intermediate to incomplete correlation which suggests that it measures a related but distinctive aspect of respiratory disability. The advantages of the MDI were demonstrated in a randomized placebo-controlled clinical trial on patients with chronic obstructive pulmonary disease, in which aminophylline was shown to produce a statistically significant improvement in the dyspnea index ratings but not in laboratory tests of airflow, gas exchange, or exercise

performance (82). In the present study, the clinical questionnaire upon which the MDI was based was administered by the same physician to each subject.

6.1.3 Cardiorespiratory function tests

i) Lung function at rest

All tests were administered by one of two trained technicians. Spirometry was performed using a Ohio 827 volume displacement spirometer according to the recommendations of the Snowbird Workshop on standardization of spirometry published by the American Thoracic Society in 1979 (83). The best forced expiratory volume in one second (FEV_1) and forced vital capacity (FVC) from any of three forced expiratory trials were retained for the purpose of analysis. To obtain lung volume, the best functional residual capacity (FRC) was selected from three trials carried out using body plethysmography and from this, residual volume (RV) and total lung capacity (TLC) were calculated. Calibration for pressure and volume was performed daily. The gas transfer factor for carbon monoxide, also referred to as pulmonary diffusing capacity (DL_{CO}), was measured using a Collins pulmonary testing system by the single breath method; the test was repeated until three results within 10% of each other were obtained and the average of the best two DL_{CO} results retained for analysis. DL_{CO} calibration was done prior to testing and again after testing 2 subjects. Quality

control measures also included weekly pulmonary function testing (spirometry, lung volume, DL_{co}) of one of two technologists.

ii) Lung function on exercise

All exercise tests were done on a treadmill with on line recording of data using a Sensor-medics automated system (84,85). The subjects breathed through a mouthpiece attached to a low resistance valve with a combined dead space of 200 cc. A noseclip was used for all experiments. Respiratory rate (f), tidal volume (V_t), minute ventilation (VE), oxygen uptake (VO_2), carbon dioxide output (VCO_2), respiratory exchange ratio (RER), and O_2 saturation by ear oximeter were recorded. Cardiac rhythm and heart rate (HR) were also monitored using a modified V5 ECG lead throughout exercise. Complete automatic calibration was performed each day for the gas analysis (O_2, CO_2), volume and temperature. Gas analysis checks and volume verification were also done before each exercise. In the procedure for complete gas analysis calibration, the calibration constants were recalculated based on recorded response to known concentration of oxygen and carbon dioxide; in the procedure for the gas analysis checks, calibrated gas mixtures were passed through the system and instrument response only measured. The volume calibration, which is also automated, was done with known volumes being added manually at a controlled rate. Quality control measures also included weekly exercise testing of one of two technologists.

Incremental exercise testing was performed to maximum on a treadmill. Subjects were attached to the mouthpiece and no work was done for at least 2 minutes until cardiorespiratory variables had stabilized. The subject then walked on the treadmill at zero elevation and 1.5 mph for the first minute, 2.5 mph for the second minute and 3.0 mph for the third minute. Thereafter the speed was kept constant at 3.0 mph and every minute the elevation was increased by 2.5% ; at 15 % elevation, the speed was increased to 3.5 mph and at 20 % elevation the speed was again increased to 4.0 mph. The exercise was continued until the subject could no longer sustain exercise. The subjects were also asked to estimate the magnitude of their dyspnea after each minute. They were requested to concentrate on their breathing and ignore other sensations such as leg fatigue or pain. The intensity of dyspnea was estimated using a category scale as recommended by Borg (86,87). This was done by asking the subject to select a number from 0 to 10 to describe their sensations, zero being no appreciable dyspnea and 10 maximum dyspnea.

6.2 Measurement of pleural abnormality

The chest radiograph is an essential tool in the evaluation of asbestos-related pleural abnormality. For each subject, chest radiographs were taken using the conventional views in posteroanterior (PA), lateral, and 45 degrees left and right anterior oblique positions with a standard high kilovoltage.

First, PA chest radiographs were read blindly by 2 chest physicians, both certified B readers according to the ILO 1980 International Classification of Radiographs of Pneumoconioses (26). Next, during the same reading session, the PA film was supplemented by left and right oblique films and pleural abnormality recorded again according to the ILO 1980 classification. For the present study, the readings of one reader only were used, selected a priori because a preliminary analysis (27) indicated that he achieved a higher level of reproducibility for readings of pleural abnormality than the other reader. A score was also computed according to the site (chest wall, costophrenic angle and diaphragm) and the degree of pleural abnormality. Chest wall pleural thickening was computed by summing the assessment in profile for each site (using the width category a, b or c converted to a numerical score of 1, 2 and 3 multiplied by the extent category 1, 2 or 3) and the assessment en face (using the extent 1, 2 or 3 category). Finally, right and left side were added together for a minimum score of 0 and a maximum of 24. Scores of 1 and 2 were given for obliteration of one or both costophrenic angles and of 1 and 2 for thickening of one or both diaphragms.

6.3 Measurement of parenchymal abnormality

6.3.1 The chest radiograph

Pneumoconiotic parenchymal disease, in particular that related to

asbestos exposure, has traditionally been defined by profusion of small opacities of 1/0 or more according to the ILO International Classification of Radiographs of Pneumoconioses (25,26). Studies of asbestos exposed human subjects and the sheep model of asbestosis (77,78) have provided evidence of an inflammatory process in the alveoli and interstitium surrounding the peripheral airways, which precedes the development of interstitial lung fibrosis. This alveolitis can be detected by Gallium-67 uptake of the lung. In the present study, parenchymal abnormality was assessed both by conventional chest radiograph and also by gallium index of the lung. The chest radiographs were read in the manner described above; i.e. they were read by 2 chest physicians, both certified B readers into the ILO 1980 International Classification of Radiographs of Pneumoconioses (26), but only one set of readings was retained, an a priori selection of the reader who achieved the highest level of reproducibility for pleural abnormality.

6.3.2 Computer-based quantitative Gallium-67 uptake in the lung

Gallium-67 was measured as follows. Forty-eight hours after injection of 4 millicuries of Gallium-67, anterior lung scan, posterior neck to pelvis scan and anterior thigh scan were recorded on a Siemens LFOV Camera system. Software for acquisition and processing of the data was developed at the Montreal General Hospital and has been

previously described by Bisson et al (88).

To calculate the index of the Gallium uptake by the lung, the posterior scan of the chest was used to minimize the variable uptake of soft tissues which is less in the back as compared to the front of the chest. The Gallium index was reported on a relative scale of 0 (background uptake) to 16 (maximum liver uptake). Background radioactivity was assessed from an area of the abdomen below the kidney and free of fecal artifacts. Background radioactivity was given a score of 0 and substracted from all areas. The maximum area of Gallium uptake in the liver was scored as 16. Uptake by the lung was measured over 6 regions (right and left upper, middle and lower lung) excluding the hilar regions. The overall gallium index was obtained by averaging the six regional indices of the lung.

The validity of this method of deriving and index of Gallium uptake was examined by Begin et al in a sheep model of asbestosis (88-91). The gallium index of the lung correlated with bronchoalveolar lavage (BAL) levels of gallium radioactivity and with histopathologic scores of inflammation in autopsy lung tissue. In addition, in non-exposed smoking or non-smoking subjects, the average gallium lung uptake index was significantly lower than in asbestos exposed subjects as assessed in his laboratory.

6.4 Measurement of asbestos exposure

The optimal measurement of exposure should take into account both

duration and level of exposure, preferably assessed by personal sampler of ambient air for total dust and fiber counts in the workplace over representative periods of time since first exposure. This is certainly impractical among construction insulators since workers are employed on a casual basis by a very large number of different employers and no industrial hygiene assessments are available. Accordingly, the estimate of exposure to dust and mineral fiber had to be based on the duration of exposure only (92). Information was gathered from two sources. For the years 1974 and 1984, annual hours worked in the trade were available from a government pension plan. From union records, it was possible to calculate the number of hours worked from 1964 to 1974, on the basis of dues paid, and to obtain the date of first employment in the trade. For subjects who started working as insulators prior to 1964, an estimate of prior exposure was obtained by multiplying the mean annual hours of work from 1964 to 1984 by the number of years in the trade before 1964. A cumulative exposure was thus developed, expressed as total hours worked in the trade (92).

Chapter 7. METHODS OF ANALYSIS

7.1 Dependent, independent and other variables

The hypothesis to be examined in the present study was addressed by investigating the relationship between respiratory function, as assessed by symptoms and measurements of respiratory function, and asbestos-related pleural abnormality.

The dependent variables or outcome variables used in the analysis were selected from three sources:

1) information describing the symptom of dyspnea; this was obtained from 3 sources: a) the subject's answers to the ATS questionnaire; b) a clinical index of dyspnea upon which the MDI score is based and c) dyspnea on a treadmill exercise graded by the subject using the Borg scale at $\dot{V}O_2$ 1 liter and 1.5 liters;

2) pulmonary function at rest as assessed by the following tests: forced expiratory volumes, forced expiratory flow rates, lung volumes and diffusing characteristics;

3) cardiopulmonary capacity on maximal exercise as assessed by $\dot{V}O_2$, $\dot{V}_E$, HR, $\dot{V}_E/\dot{V}O_2$, O_2 pulse, $\dot{V}_E/MVV$, breathing frequency, V_t and

V_t/VC, and at submaximal exercise, using the same parameters but at different exercise levels, including the anaerobic threshold (AT). The same parameters were derived by interpolation at VO_2 1 liter/min, VO_2 1.5 liter/min and VO_2 15 ml/kg/min. MVV was calculated according to Jones et al. MVV = 30.6 x FEV_1 - 29 L/min (85).

The independent variable of interest was asbestos-related pleural disease defined from chest radiographic reading into the ILO 1980 International Classification of Radiographs of Pneumoconioses and expressed as a discrete variable and also as a continuous variable.

The other variables of interest were age, height, weight, smoking habit and asbestos-related parenchymal abnormality as assessed by chest radiographic reading and gallium uptake of the lung. All are determinants of pulmonary function and hence potential confounding variables which were therefore taken into account in the present analysis.

7.2 Specific Analysis

The analysis was approached in a sequence of two major steps. The first step of the analysis sought to confirm the main hypothesis that asbestos-related pleural abnormality is associated with respiratory impairment. The independent variable of interest, asbestos-related pleural abnormality, was dichotomized as present or absent, first according to the PA chest radiograph reading in the manner described, then according to the PA radiograph reading

supplemented by oblique films. The crude relationship between asbestos-related pleural abnormality so defined and lung function was first described without taking into account parenchymal abnormality and other potential confounding variables. There were next taken into account using a multiple regression analysis (ANCOVA). The relationship between asbestos-related pleural abnormality and dyspnea was examined by logistic regression. Confounders considered were age, height, weight, smoking status and parenchymal abnormality as assessed by chest radiograph reading and gallium uptake of the lung.

In the second step of the analysis, an attempt was made to characterize in greater detail the effect of pleural abnormality in the different sites on lung function. A multiple regression analysis (ANCOVA) was again used for the lung function tests and a logistic regression for dyspnea after accounting for age, height, smoking status and parenchymal abnormality as assessed by chest radiograph reading and gallium scan of the lung. The independent effect of pleural abnormality in different sites (diaphragm, costophrenic angle and chest wall) and of different degrees of chest wall pleural thickening (width and extent) was examined. Though the presence of asbestos-related pleural abnormality on the chest radiograph has often been translated into a score, this has not previously been assessed with any rigour in relation to respiratory impairment; the present data provided an opportunity to validate a score of this nature in relation to pulmonary function.

Chapter 8. RESULTS

8.1 General outline

In this chapter the results are presented as follows:

First, descriptive statistics are presented: these include subject characteristics, measurements of resting lung function, and cardiorespiratory function on exercise in relation to smoking status (Tables 3a to 3g).

Second, the same information is presented in relation to the presence or not of pleural abnormality assessed radiographically in two ways as follows: i) from the PA chest radiograph read by the standard method into the ILO 1980 classification, (Tables 4a to 4g) and ii) by the PA chest radiograph read as above but supplemented by the right and left anterior oblique chest radiographs (Tables 5a to 5c).

Third, analytical statistics are presented describing the relationship of dyspnea and lung function to pleural abnormality (assessed by PA chest radiograph reading) after accounting for relevant anthropometric characteristics, smoking status and parenchymal abnormality (Tables 6a to 6c).

Fourth, analytic statistics are presented, describing the relationship of dyspnea and lung function to sites, extent and width of pleural thickening after accounting for relevant anthropometric characteristics, smoking status and parenchymal abnormality (Table 7a to 7c).

8.2 Descriptive statistics (univariate analysis)

8.2.1 Findings in relation to smoking status

8.2.2.1 Personal and exposure characteristics

The mean, standard deviation and range of the personal characteristics (i.e. age, height and weight), and the exposure characteristics (i.e. smoking habits and asbestos exposure) are shown in Table 3a. The population was composed exclusively of men currently at work, aged 35 to 52 years and mainly smokers or exsmokers. Smokers were on average slightly taller than the non or ex-smokers, but weighed slightly less. Asbestos exposure in years, calculated on the basis of 2000 hours of work per year, varied from 9 to 36 years and tended to be on average slightly less in smokers.

8.2.1.2 Prevalence of pleural and parenchymal abnormality

Prevalences of pleural and parenchymal abnormalities in the study population, assessed from reading the PA chest radiograph, are shown in table 3b, with the subjects divided according to smoking status. Overall, 58 % of the study population was identified as having any pleural abnormality. The major site for pleural thickening was the chest wall; in 44.5 % of subjects, the abnormality was read as pleural

plaques and in only 5.5 % as diffuse pleural thickening. The pleural thickening of the chest wall was between 2 to 5 mm thick in more than 25 % of subjects, between 5 to 10 mm in less than 7 % of subjects, and more than 10 mm in less than 2 % of subjects. The diaphragm was involved in 17.3 % of subjects, costophrenic angle blunting reported in 5.5 % of subjects and pleural calcification in 13.6 %.

Parenchymal abnormality was relatively uncommon, with only 10 % of radiographs classified as profusion category 1 or more, and 90 % as category zero, i.e. 0/0 or 0/1. On average, smokers had a higher prevalence of pleural abnormality of any type and also of parenchymal abnormality than the non and exsmokers. Other associations with smoking were a higher prevalence of plaques in smokers and exsmokers compared to nonsmokers; a tendency for pleural thickening to occur more frequently on the left side than on the right side, and more frequent involvement of the costophrenic angle. Indeed, the absence of costophrenic angle involvement in nonsmokers was striking; by contrast a higher prevalence for pleural calcification were found in nonsmokers compared to smokers and exsmokers.

The Table also shows the gallium index which varied from 0 to 8.3 (potential range of 0 to 16) with a mean of 3.7. Exsmokers had a mean gallium index slightly higher than the nonsmokers and smokers. Values up to 3.5 are found in the absence of disease (77,78).

8.2.1.3 Prevalence of respiratory symptoms

The prevalences of respiratory symptoms for the study population as a whole and by smoking status are presented in Table 3c. Usual cough and phlegm were common (31.8 and 43.6 % respectively), in this largely smoking population. Ever wheeze (56.4%), persistent wheeze (24.5%) and dyspnea grade 1 or more (35%) were also prominent symptoms. Smokers were also characterized by higher prevalences of all respiratory symptoms, compared to exsmokers and non smokers. Respiratory diseases associated with residual pleural thickening, such as tuberculosis or pleurisy, did not seem to be of importance in the present study population; none of the subjects reported having had tuberculosis and overall only 5.5% reported a history of pleurisy.

Prevalence percent of dyspnea as reported by subjects in relation to smoking status is shown in Table 3d, using the 3 methods of assessment described above under methods (the ATS-DLD-78 questionnaire, the clinical questionnaire, and dyspnea on treadmill exercise graded by the Borg scale from 0 for minimum to 10 for maximum). Overall, the prevalence of reported dyspnea was high considering all subjects were active workers in a physically demanding job. In general, dyspnea was related to smoking status, being more frequent in smokers or exsmokers compared to nonsmokers. Thus, based on the ATS-DLD-78 questionnaire there was a higher prevalence of dyspnea grade 1 or more in current smokers compared to ex or nonsmokers, and dyspnea grade 2 or more in exsmokers than in current smokers or non smokers. In response to the

clinical questionnaire, dyspnea with functional impairment at work and at home was more commonly reported by smokers than exsmokers and nonsmokers. Using the same questionnaire, the prevalence of reported dyspnea with major activities (such as walking up a steep hill or climbing two flights of stairs and more), was again surprisingly high considering the active working status of the study population, and was also higher in smokers than exsmokers and non smokers. The prevalence of a modified dyspneic index (MDI) composite score of 10 or less incorporating all the responses to the clinical questionnaire, was also highest for current smokers, intermediate for exsmokers and lowest for non smokers. Dyspnea during exercise, assessed by the Borg scale, increased as the level of exercise increased, but did not differ in relation to the smoking habit at a $\dot{V}O_2$ of 1 L/min, at a $\dot{V}O_2$ of 1.5 L/min it was slightly less in nonsmokers than in the other 2 groups.

8.2.1.4 Lung function at rest and cardiorespiratory function on exercise

Measurements of lung function at rest are presented in Table 3e in relation to smoking status. Absolute values are shown, uncorrected for age or height; though the average age was similar for subjects in all 3 smoking categories, smokers were on average taller than ex and nonsmokers, and in consequence would be expected to have slightly larger lung functions. Despite this, there was a tendency for FEV_1 and FEV_1/FVC to be lower in smokers and exsmokers compared to non smokers;

all forced expiratory flow rates at low lung volumes, FEF_{50}, FEF_{75}, FEF_{25-75} were also lower in smokers compared to exsmokers and non smokers. However, for lung volumes and diffusing characteristics there was no obvious relationship to smoking.

The mean and standard deviation of measurements of cardiorespiratory function at maximal and submaximal exercise are shown in Table 3f and 3g in relation to smoking status. It was not possible to be certain every subject achieved his maximum level of exercise, and results at maximal exercise should be interpreted with this reservation in mind. In general, cardiovascular capacity at maximal exercise as reflected by HR, VO_2 and O_2 pulse did not appear to be related to smoking status, whereas respiratory capacity did, with higher values for V_E being achieved in nonsmokers compared to exsmokers and smokers. The pattern of breathing at maximal exercise also showed a higher frequency of breathing in nonsmokers than in exsmokers and smokers. However respiratory efficiency as reflected by V_E/VO_2 did not appear to vary in relation to smoking status, nor did V_t and V_t/VC.

None of the measurements of cardiorespiratory function at submaximal exercise (whether measured at anaerobic threshold (AT), at a VO_2 of 1L, 1.5L, or 15 ml/kg/min) appeared to be related to smoking status (see Table 3g).

8.2.2 Findings in relation to pleural abnormality (PA radiograph)

8.2.2.1 Personal exposure characteristics and indicators of parenchymal abnormality

Personal characteristics (age, weight and height), exposure characteristics (smoking status and asbestos exposure), and indicators of parenchymal abnormality on chest radiograph and by gallium scan, are given in Table 4a in relation to the presence or not of pleural abnormality. Despite the limited age range (35 to 52 years old) from which subjects were selected, the mean age of the subjects with pleural abnormality was 1.3 years older than of subjects without pleural abnormality. Subjects with pleural abnormality also weighed slightly more and smoked more heavily than had subjects without pleural abnormality. On average, exposure years or years since first exposure were similar between subjects with and without pleural abnormality, and the range of values was wide, from under 5 to over 35 years, for both measures. The prevalence of parenchymal abnormality, as defined by profusion 1/0 or more on chest radiograph reading was higher in subjects with pleural abnormality than in those without pleural abnormality. Also, on average, the gallium index was higher in subjects with pleural abnormality compared to subjects without.

8.2.2.2 Prevalence of respiratory symptoms

The prevalence of respiratory symptoms in relation to pleural abnormality in the study population is presented in Table 4b. Subjects with pleural abnormality had a higher prevalences of usual cough, ever wheeze, persistant wheeze and a reported history of pleurisy than subjects without pleural abnormality. However, usual phlegm was more frequent in subjects without than in those with pleural abnormality.

Prevalence percent of reported dyspnea in relation to pleural abnormality is shown in Table 4c, using the 3 methods of assessment already described. Thus based on grade 1 or more, (i.e. when hurrying on the level or walking up a hill), was present in 34.4 % of subjects with and in 28.3 % of subjects without pleural abnormality. Dyspnea grade 2 or more, (i.e. dyspnea when walking on the level with others of the subject's own age), was present in 17.2 % of subjects with and in 6.5 % of the subjects without pleural abnormality. The prevalence of dyspnea with functional impairment at work was similar in both groups, but dyspnea with functional impairment at home and with major activities (i.e. when walking up a steep hill and climbing two flights of stairs and more), was more frequent in those with compared to those without pleural abnormality. By contrast dyspnea on treadmill exercise graded by the Borg scale was slightly higher on average in those without compared to those with pleural abnormality at a level of exercise of a $\dot{V}O_2$ at 1 liter/min, but similar at a $\dot{V}O_2$ at 1.5 liter/min. However, the subjects with pleural abnormality were on

average older, heavier, smoked more, and presented more parenchymal abnormality (i.e a higher prevalence of chest radiograph profusion of more than 1/0 and average gallium index). These factors may partly explain the difference in prevalence of dyspnea and will be taken into account in a further analysis using a logistic regression.

8.2.2.3 Lung function at rest and cardiorespiratory function on exercise

The mean and standard deviation of lung functions at rest are shown in Table 4d in those with and without pleural abnormality. On average, subjects with pleural abnormality had lower forced expiratory volumes (FEV_1, FVC) and forced expiratory flow rates (PEFR, FEF_{50}, FEF_{75}, FEF_{25-75}) than subjects without; they also had lower lung volumes (TLC, FRC, RV) and diffusing characteristics (DL_{CO}, V_A, DL_CO/V_A). These measurements are not adjusted for age and height differences (those with pleural abnormality were older, shorter, smoked more and presented more parenchymal abnormality than those without), factors which may have contributed to these lung function differences. These factors will be taken into account in a further analysis using a multiple regression.

The mean and standard deviation of the measurements of cardiorespiratory function at maximal and submaximal exercise in relation to pleural abnormality in the study population are given in Table 4e and 4f. Measurements reflecting respiratory and

cardiovascular capacity at maximal exercise were similar in the two groups, as were most measurements at submaximal exercise, (i.e. anaerobic threshold, $\dot{V}O_2$ at 1 L, 1.5 L and 15 ml/kg/min); however heart rates (HR) achieved were slightly lower in subjects with compared to those without pleural abnormality. The pattern of breathing at maximal exercise was also different in the two groups; those with pleural abnormality attained on average a greater maximum frequency with a slightly lower V_T and a higher V_T/VC ratio than those without pleural abnormality. Similar findings were obtained in respect to respiratory symptoms and pulmonary function tests when pleural abnormality was assessed from radiographic readings by a second reader, reading independently. The results of the second reader are not presented here.

8.2.3 Findings in relation to pleural abnormality (PA supplemented by oblique radiographs)

The use of PA chest radiographs supplemented by right and left anterior oblique views as opposed to PA chest radiograph alone did not alter the findings. For this reason, and for reasons of brevity, only selected data is presented. For the convenience of the reader, and to facilitate comparisons, selected data from Tables 4a to 4g is included in Table 5a and 5c. Although the number of subjects read as having pleural abnormality may be the same when assessed by PA reading as compared to PA reading supplemented by oblique views, the subjects

themselves are different.

The main feature brought out in these Tables is that findings were remarkably similar whether or not oblique films were used to detect the presence of pleural abnormality. The prevalence of dyspnea (assessed by the ATS-DLD-78 questionnaire, the clinical questionaire and on the Borg scale treadmill exercise) is shown in Table 5a. The mean and standard deviation of selected lung functions at rest in relation to pleural abnormality assessed by the two methods is shown in Table 5b, and again of note is the similarity of the findings. The same is evident for the mean and standard deviation of measurements of cardiorespiratory function at maximal and submaximal exercise presented in Table 5c.

8.3 Influence of pleural abnormality (PA radiographs) on respiratory status taking into account parenchymal abnormality and other relevant factors

8.3.1 Influence of pleural abnormality on dyspnea

Table 6a presents the odds ratio with the confidence limits for the symptom of dyspnea being present, given the presence of pleural abnormality, after taking into account age, smoking habit and parenchymal abnormalities. Also presented are the odds ratio of dyspnea for the other determinants in the model, i.e. for a difference

of 15 years of age, of 10 pack years of cumulative smoking, and of 3 points (equivalent of 1 category) on the scale of profusion on chest radiograph and 3 points on the scale of gallium index (range from 0 to 16). Logistic regression analysis was used to determine these odds ratios. The analyses indicate that after adjusting for other relevant determinants, the presence of dyspnea, assessed by any one of the methods used, was not consistently related to the presence of pleural abnormality. Thus though some of the odds ratios exceeded 1, the range of 95% confidence limit is wide and always included 1. This can be interpreted as showing that the odds of the symptom of dyspnea being present can be less, the same or more, in relation to the presence of pleural abnormality.

8.3.2 Influence of pleural abnormality on lung function at rest

Table 6b presents the mean differences in lung function at rest, in ml, between subjects with and subjects without pleural abnormality, after accounting for age, height, smoking habit, and parenchymal abnormality assessed by chest radiograph and gallium uptake. Also included in the Table are the standard errors of the differences, the 95% confidence limit and the p-value. The analysis indicates that the presence of pleural abnormality (as defined by PA radiograph reading) is associated with an average decrease in the FEV_1 of 222 ml ($p < .05$) and in the FVC of 402 ml ($p < .05$) after accounting for other relevant

factors. The presence of pleural abnormality did not affect TLC or DL_{CO}. Also shown on the Table are the regression coefficients of other relevant determinants included in the model. Those for age, height and smoking were significant in the model for FEV_1; those for age and height were significant in the model for FVC, and those for height and smoking in the model for DL_{CO}. In the present analysis, there was no evidence that either of the indicators of parenchymal abnormality (i.e. the profusion on the chest radiograph or gallium scan) affected lung function.

8.3.3 Influence of pleural abnormality on cardiorespiratory function on maximal and submaximal exercise

Table 6c presents the mean differences in parameters related to cardiorespiratory capacity on exertion between subjects with and without the presence of pleural abnormality, after accounting for age, height, weight, smoking habit and parenchymal abnormality. Also included in the Table are the standard error of the difference, the 95% confidence limits and the p-value. In the present analysis, the presence of pleural abnormality as defined by PA radiograph did not contribute to the cardiorespiratory capacity on maximal or submaximal exercise, after accounting for age, height, weight, smoking and parenchymal abnormalities by chest radiograph and gallium uptake. However, the breathing frequency was higher on submaximal exercise and the ratio $\dot{V}_E/MVV$ higher on maximal and submaximal exercise in subjects

with pleural abnormality as compared to those without, after accounting for other important determinants. The Borg scale at maximal and submaximal effort (VO_2 1L and 1.5 L) was not related to pleural abnormality, after accounting for other important determinants (not shown in the table).

8.4 Influence of the site and extent of pleural abnormality (PA radiographs) on respiratory status, taking into account parenchymal abnormality and other relevant factors

8.4.1 Influence of the site and extent of pleural abnormality on dyspnea

Table 7a presents the odds ratio for the symptom of dyspnea being present in relation to the site and extent of pleural abnormality) given a difference of 4 points for chest wall pleural thickening (on a maximum of 24 point scale), 1 point for each side with costophrenic angle obliteration (on a 2 point scale) and 1 point for each side with diaphragmatic thickening (2 point scale), after taking into account age, smoking status and parenchymal abnormalities. Also presented are the odds ratio of dyspnea for the other determinants in the model, calculated for the following ranges: 15 years of age, 10 pack years of cumulative smoking, 3 points on the 12 point scales of profusion (equivalent of 1 category on the ILO scale for the chest radiograph) and 3 points on the scale of gallium index (range of 0 to 16).

Logistic regression analysis was used with site and extent of pleural disease expressed as a continuous variable according to a score computed at each different site (diaphragm, costophrenic angle and chest wall). Both analyses indicate that after adjusting for other relevant determinants the presence of dyspnea with major activities was related to the extent of chest wall pleural thickening, and the presence of dyspnea with functional impairment at home was related to the presence of diaphragmatic thickening. The presence of dyspnea assessed by the ATS-DLD-78 questionnaire and dyspnea with functional impairment at work was not related to the different sites and extent of pleural abnormality.

8.4.2 Influence of the site and extent of pleural abnormality on lung function at rest

Table 7b shows the regression coefficients describing the independent effect of pleural abnormality at the different sites (diaphragm, costophrenic angle and chest wall) on FEV_1 and FVC (as the dependent variables) after accounting for age, height, cumulative smoking, and parenchymal abnormality assessed by chest radiograph reading and by the gallium index. Also included in the Table are the standard error, the 95% confidence limit and the p-value. In the analysis, chest wall pleural thickening and extent, costophrenic angle obliteration and diaphragmatic thickening were all included in a multiple regression model using a stepwise procedure, after having

accounted for other relevant determinants. As described in section 8.4.1, pleural abnormality was also used as a continuous variable according to a score computed at different sites. The results indicate that after accounting for anthropometric characteristics, smoking habit and parenchymal abnormality, both chest wall pleural thickening and costophrenic angle obliteration independently affected FVC but diaphragmatic thickening did not. For FEV_1, costophrenic angle obliteration showed a significant relationship, and also the effect of chest wall pleural thickening approached statistical significance.

8.4.3 Influence of the site and extent of pleural abnormality on cardiorespiratory function on maximal and submaximal exercise

Table 7c shows the regression coefficient describing the independent effect of pleural abnormality at different sites (diaphragm, costophrenic angle and chest wall) on different parameters related to cardiorespiratory function on exercise, after accounting for age, height, weight, cumulative smoking and parenchymal abnormality assessed by chest radiograph reading and by the gallium uptake of the lung. Also included in the Table is the standard error and the p-value. As previously described, pleural abnormality was used as a continuous variable according to a composite score including abnormality in different sites. The results indicate that pleural disease did not affect the cardiorespiratory capacity on exercise.

However, on maximal exercise chest wall pleural thickening and costophrenic angle obliteration independently affected V_E/MVV, which increased according to the degree of pleural abnormality. At submaximal exercise, costophrenic angle obliteration independently affected V_E/MVV, and chest wall pleural thickening affected V_t/VC. Neither of the sites of pleural abnormality was found to be independently related at a significant level to breathing frequency at maximal or submaximal exercise.

Chapter 9. DISCUSSION

9.1 General

The results of this study indicate that in an active workforce of insulators, the presence of asbestos-related pleural abnormality was associated with a decrease in FEV_1 of on average 222 ml ($p < .05$) and in FVC of 402 ml ($p < .05$) after taking into account other relevant determinants such as age, height, smoking status and parenchymal abnormality. This decrease in FEV_1 and FVC was due to independent effect of pleural abnormalities at the costophrenic angle and the chest wall. The association could also be demonstrated after exclusion of subjects with diffuse pleural thickening (5.5% of the total population) defined by the presence on chest radiograph reading of a costophrenic angle obliteration, i.e. when the comparison was confined to subjects with pleural plaques only and those without pleural abnormality. However analysis (not presented here), which were limited to workers with pleural abnormality, failed to show a dose response relationship between the presence of asbestos related pleural abnormality and FEV_1 and FVC. However, the power of the analyses was reduced substantially as the number of workers with pleural abnormality only was 64, i.e. is less than 60% of the initial number.

The reduced FEV_1 and FVC did not appear to be explained by the

presence of subclinical pulmonary fibrosis since neither of the indicators of parenchymal abnormality (i.e. the conventional chest radiograph reading into the ILO 1980 classification and the quantitative assessment of gallium uptake in the lung), was found to be related to the resting lung function level.

Despite the evidence that pleural abnormality resulted in lower levels FEV_1 or FVC, its presence did not appear to affect the maximum exercise capacity nor cardiorespiratory function during submaximal exercise. However, the complaint of dyspnea associated with major activities was related to the extent of chest wall pleural thickening even though the prevalence of dyspnea complaints assessed by any one of the methods used was not different between subjects with as compared to those without pleural abnormality after taking into account age, smoking status and parenchymal abnormality. Of interest was the fact that on exercise those with pleural abnormality were shown to have a higher V_E/MVV, and a higher breathing frequency and/or V_t/VC at certain selected levels of submaximal exercise. Thus, the relationship between the sensation of dyspnea during major activities and the extent of chest wall pleural thickening may be due to a difference in breathing pattern imposed by the pleural abnormality, resulting in the utilization of proportions of maximum ventilatory capacity.

9.2 Potential sources of bias in the present study

9.2.1 Selection bias

Consideration must be given to potential sources of bias in the present study that may have exaggerated or attenuated the observed effect of pleural abnormality on respiratory function. The survivor effect results from the well recognized selection bias inherent in the study of an active workforce, namely that those with better health are likely to have remained active, while those with less good health are likely to have changed jobs or quit work for health reasons. Obviously there is no way of knowing from a cross-sectional study to what extent this factor was operative. If present (and one must assume it was), this source of bias would be likely to have attenuated the demonstrated effects of pleural abnormality on respiratory function, not exaggerate them. Indeed, in this particular workforce the survivor effect has more than likely attenuated the demonstrable effects, given i) the high prevalence (52.5%) of pleural plaques (which are usually associated with at most mild respiratory impairment and rarely with disability (59-66)), and ii) the low prevalence (5.5%) of diffuse pleural thickening which is more likely to cause impairment and even disability (58-61), and iii) the fact that this is a relatively young population.

9.2.2 Misclassification

Misclassification due to measurement error in the explanatory (independent) variable is certainly an important consideration for which unfortunately there is no good solution. A valid instrument should measure what it is intended to measure in addition to being reproducible. Unfortunately, for the assessment of pleural abnormality, even using the ILO 1980 International Classification of Radiographs of Pneumoconioses and a B reader, trained and certified by the NIOSH, there is still important variability between and within readers (27). Furthermore, the posteroanterior chest radiograph has been shown to detect only a small proportion of pleural abnormalities identified at autopsy (23,93). In addition, the use of the oblique chest radiograph, though shown by several investigators to increase the detection rate of pleural abnormality (28-30), may also increase the rate of false positives (33). The presence of subpleural fat, especially in obese individuals, can also easily be misinterpreted as pleural abnormality on standard chest radiograph even when supplemented by oblique films, and can only be distinguished with certainty using computer tomography of the chest (93). Despite these potential weaknesses inherent to the instrument used to measure the independent variable of interest, the consistency of the relationship found between FEV_1 or FVC reduction and pleural abnormalities measured in several ways (i.e. using the PA reading or the PA reading supplemented by oblique chest radiographs, and using readings provided by a second

reader) makes it more likely that the association demonstrated is a true reflection of the data.

9.2.3 Measurement error

Bias arising from a defect in method of measurement of the response variable can also give rise to artifactual association. The measurements of respiratory function were not carried out by observers blind to the independent variable of interest, namely the presence or not of pleural abnormality. However, since these measurements are carried out using calibrated instrumentation, it is most unlikely that observer bias could account entirely for the respiratory function differences at rest between those with and without pleural disease. The assessment of respiratory function, reported by the subjects as the complaint of dyspnea, is obviously subjective, and could have been influenced by knowledge of an abnormal radiography.

9.2.4 Confounding variables, including parenchymal lung abnormality

Biases may also result from failure to control for important confounding variables. In the present study, the most important determinants of respiratory impairment (age, smoking and parenchymal abnormality) and hence potentially important confounding variables were accounted for in the analysis. Previous investigators (64,68) have

suggested, for instance, that the relationship between pleural plaques and respiratory impairment assessed objectively could be obscured by the presence of subradiographic parenchymal changes. If this were so, pleural plaques would only indirectly affect lung function through their being associated with asbestos-related parenchymal changes. New imaging techniques including gallium scan, judged to be sensitive in assessing early parenchymal reaction (77,78) not seen on the PA chest radiograph, were used in the present study, and indeed, there was a good correlation between the gallium index and pleural abnormality on the chest radiograph, suggesting that either parenchymal and pleural abnormality commonly coexist, or that the gallium index reflects the active pleural process. A relationship between enhanced uptake of gallium and pleural abnormality is plausible but unlikely, in view of the findings by Lambert et al who were unable to show a significant correlation between the gallium uptake in the lung and the radiographic scores of pleural abnormality (94). Nevertheless, after accounting for parenchymal change assessed by combining radiographic readings and gallium scan, there was still a statistically significant relationship between pleural abnormality and a reduction in FEV_1 or FVC in the present study. This supports the hypothesis that asbestos-related pleural abnormality is a cause of respiratory impairment independant of parenchymal abnormality. Furthermore, the presence of pleural plaques without other pleural abnormalities was also associated with respiratory impairment which could not be explained by the presence of parenchymal change, even early parenchymal

reaction detected by quantitative gallium uptake of the lung in the absence of radiographic changes.

9.3 Comparison with previous studies

9.3.1 Lung function impairment.

In line with previous studies on the relationship of pleural plaques and lung function at rest, the present study has found that on average subjects with pleural plaques have a lower FEV_1 (222 ml) and FVC (402 ml) compared to those without pleural abnormality. However, these average differences in FEV_1 and FVC are small between subjects with and without pleural plaques, and do not appear to have affected most cardiorespiratory measurements on submaximal and maximal exercise. This also is in keeping with the common clinical opinion that pleural plaques are little more than a sign of asbestos exposure, and rarely of clinical importance.

Only one other study, that by Lumley (61) reviewed earlier in this thesis, examined the relationship between respiratory parameters during exercise and pleural plaques. In dockyard employees between 28 and 64 years of age, selected on the basis of chest radiographs, and matched for age and occupation, he found a significant ($p < .05$) increase in minute ventilation at a $\dot{V}O_2$ of 1 liter in subjects with pleural plaques compared to those without. However subjects were not matched for smoking and body habitus, nor were these factors taken into account in

analysis, and the findings may therefore have been the consequence of confounders. The present study appears to confirm what most studies have shown that pleural plaques per se do not impair lung function at rest or on exercise to any important degree.

As already discussed some recent studies (64,68) have suggested that the difference in lung function between subjects with pleural plaques compared to those without may have been in part explained by the confounding effect of heavier asbestos exposure associated with subradiographic parenchymal changes among subjects with pleural plaques. Thus given an exposure-response relationship with parenchymal fibrosis, the higher the exposure, the more likely the presence of subradiographic parenchymal fibrosis (2). Consistent with this view are the findings in studies by Ohlson et al (68) and Jarvholm et al (64) found that the difference in lung function between subjects with and without pleural plaques was larger for those with heavy exposure to asbestos. However Jarvholm et al found that even after stratification for asbestos exposure, men with plaques had a lower FVC than men without plaques. In these studies, the larger differences in lung function associated with plaques in subjects with heavy exposure compared to light exposure may be due to more extensive pleural plaques, information not provided to the reader.

In the present study, a sensitive indicator of the alveolitis of asbestosis (the pulmonary uptake of gallium-67) was used (77,78), and pleural plaques were shown to be associated with a lower FEV_1 and FVC independently of any parenchymal change. This finding of an independant

effect of pleural abnormalities on lung function is in line with those of Becklake et al (57) who, in an age stratified random sample of men currently employed in the asbestos industry of Eastern Quebec in 1970, showed a small but consistent adverse change in lung function in those with any pleural abnormality compared to those with none, for any given grade of severity of parenchymal fibrosis.

9.3.2 Dyspnea

Few studies have looked at the prevalence of dyspnea in relation to the presence of plaques (61,65). Hilt et al (65) reported an increase in prevalence of grade 1 breathlessness in individuals with pleural plaques. Lumley also found that subjects with pleural plaques reported a higher level of dyspnea during exercise than those without pleural plaques. In the present study, assessment of dyspnea by all three methods used (ATS-DLD-78 questionnaire, clinical questionnaire and the Borg scale during exercise) showed in general a higher prevalence of dyspnea in subjects with compared to those without pleural plaques though the differences were not statistically significant after accounting for difference in age, smoking habit and parenchymal abnormality. Clearly confounding factors contributed to the complaint of dyspnea of subjects with pleural abnormality who were older and smoked more than those without pleural abnormality. However, the higher prevalence of dyspnea associated with pleural abnormality may also be a genuine reflection of a biological effect minimized because

the population was young and at work and on average did not have extensive disease. Also of importance is the power of the present study; for predicting dyspnea, given the sample size of 50-60 subjects in each group and prevalences of dyspnea in subjects with and without pleural abnormality of 15% and 5% respectively; power was estimated to be only 50% with an alpha error of 5%. This compared unfavorably with the power of the present study to detect abnormalities of lung function at rest which was 80%. Nevertheless, in the present study dyspnea with major activities such as walking up a steep hill was significantly related to the extent of chest wall pleural thickening ($p<.05$), after adjusting for other relevant factors.

9.4 Potential mechanisms of dyspnea

In the present study, as already mentioned, the complaint of dyspnea associated with major activites was related to the extent of chest wall pleural thickening. Although this study was not designed to investigate the potential mechanisms of dyspnea in patients with pleural abnormality, the finding of a possible relationhip between dyspnea and extent of chest wall pleural thickening should not be underestimated and indeed invites further study of these relationships. Even though overall cardiorespiratory capacity on exercise was not different in subjects with and without pleural abnormality, Table 8 (which summarizes information from several previous tables for the convenience of the readers) shows that those

with pleural abnormality had a higher V_E/MVV at maximal and submaximal exercise, and a higher breathing frequency or V_t/VC at certain selected levels of submaximal exercise.

The underlying mechanisms responsable for the presenting symptoms of effort dyspnea are still a subject of controversy, and several mechanisms have been discussed. First, pleural abnormality might impair inspiratory depth and alter the breathing pattern as seen in subjects with interstitial fibrosis (96). This mechanism is likely to be of more importance in subjects with extensive pleural abnormality, but might also play a role in subjects with limited pleural plaques as seen in the present study population.

Second, an increased elastic load to the respiratory muscles because of chest wall changes has been proposed as limiting the exercise capacity through fatigue of the respiratory muscles (95). Picado et al explored this possibility in six subjects with varying degrees of asbestos-related pleural abnormality who all reported dyspnea as the reason for effort limitation (95). Fatigue of the diaphragm on exercise assessed by electromyographic techniques in three subjects was not found to be present. Without similar measurement of chest wall muscle fatigue, this cannot be excluded as a possibility.

Third, pleural abnormality might lead to altered proprioceptive information, an abnormal ventilatory pattern, and excessive perception of inspiratory effort (97). Evidence suggest that elastic loads are poorly tolerated and provoke an increased sense of effort and discomfort (98). It has been shown that subjects with elastic loads

employ a breathing pattern characterized by increased inspiratory flow rates (99,100). Peak inspiratory pleural pressure accounted for the greatest increase in sensory perception of the elastic load (97). Picado et al (95) have shown that subjects with pleural abnormality who complained of shortness of breath had maximum exercise capacity limitation, increased minute ventilation and an abnormal pattern of breathing with increased breathing frequency as well as inspiratory flow rates, and a decreased tidal volume..

In the present study, the sensation of breathlessness in subjects with pleural plaques was associated with a difference in breathing pattern and use of a higher proportion of maximum ventilatory capacity, changes which may have been imposed by the pleural abnormality through its effect in reducing FEV_1 and/or FVC. However, this association is also biologically plausible, in keeping with the hypothesis that pleural abnormality might lead to alter proprioceptive information, an abnormal ventilatory pattern and excessive perception of inspiratory effort (97). Alternatively the abnormal breathing pattern could be accounted for by increases in chest wall impedance due to reduced compliance of the parietal pleura (95). The physiologic measurements made in the present study are not complete enough to identify which of these mechanisms of dyspnea might have been operative in the subjects with pleural abnormality studied here and therefore leave the researcher not only with speculation but, more important, with directions to further research.

Chapter 10. CONCLUSIONS

In the present study of insulators, aged 35 to 53, all currently at work, a reduced FEV_1 and FVC was found in subjects with pleural abnormality compared to those without pleural abnormality. Pleural plaques were the most common pleural abnormality (44.5% of subjects) and diffuse pleural thickening less frequent (5.5%) in the present study population. A sensitive indicator of subradiographic parenchymal reaction, the computed gallium uptake of the lung, was used to take into account subradiographic parenchymal abnormality related to asbestos exposure, and enabled the analysis to demonstrate an independent effect of pleural plaques on lung function at rest.

However, this functional impairment did not seem to alter the cardiorespiratory parameters during exercise though it was associated with a higher prevalence of dyspnea in those with compared to those without pleural abnormality. Although this difference was not statistically significant ($p > .05$) after accounting for other relevant determinants, the association was significant when related to the extent of chest wall pleural thickening ($p = .09$ for dyspnea as defined by the ATS-DLD-78 questionnaire and $p = .01$ for dyspnea with major activities by the clinical dyspnea questionnaire).

Previous studies have provided evidence suggesting that the presence of pleural abnormality alters the pattern of breathing and may be responsible for the increased sensation of breathlessness during physical activities. Further investigation should focus on the prevalence of dyspnea in subjects with pleural plaques, ranging from limited to extensive in their involvement of the pleural surfaces, and should be designed to elucidate the potential mechanisms underlying dyspnea particularly that experienced during physical activities.

TABLE 1

Summary of the published literature on the mean difference of lung function when comparing group of subjects with and without pleural abnormality

First author year (rf)	Source population	Age mean	No. studied (% with plaque)	FEV_1 diff. (% or ml)	FVC diff. (% or ml)	TLC diff. (% or ml)	V_E diff. (l/min)
Studies with evidence of impairment:							
i) Any pleural disease							
Becklake [+] 1970 (57)	miners	--	1069	-5% *	-3%	-4% *	Not reported
ii) Pleural plaques							
Lumley [Φ] 1977 (61)	dockyard employees	48.5	194 (24)	-330 *	-340 *	-280 *	+ 2.0 *
Fredriksson [§] 1981 (62)	general population	62.5	45 (100)	-14% *	-15% *	-16%	Not reported
Jarvholm [¶] 1986 (64)	shipyard employees	53.3	202 (43)	-7.6% *	-6.9% *	Not reported	Not reported
Hilt [Ψ] 1987 (65)	general population	66.1	634 (57)	-200	-200	Not reported	Not reported
Olivier [††] 1987 (66)	not reported	--	576 (20)	Not reported	*	Not reported	Not reported
Studies without evidence of impairment (pleural plaques):							
Hedenstierna [§§] 1981 (67)	construction workers	45-65	72 (50)	-80	-230	Not reported	Not reported
Ohlson [¶¶] 1985 (68)	cement plant workers	--	75 (32)	-7%	-6%	Not reported	Not reported

continued.../

TABLE 1 (continued)

Summary of the published literature on the mean difference of lung function when comparing group of subjects with and without pleural abnormality

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* Statistically significant ($p < .05$) on the basis of analysis carried out by the author.

+ The effect of pleural changes is reported for subjects without small opacities (profusion 1/0 or less) after adjusting for age, height, and weight.

Φ The effect of pleural plaques is reported for subjects without small opacities (profusion 1/0 or less) and compared to exposed individuals without pleural abnormality.

§ The effect of pleural plaques is reported for subjects without parenchymal abnormality (not defined here) and compared to a reference group of 263 healthy men after adjusting for age, height, weight and smoking habits.

¶ The effect of pleural plaques is reported for subjects without parenchymal abnormality (not defined here) and compared to exposed subjects without pleural abnormality. Analysis was restricted to lifetime nonsmoking men also taking into acount age and height.

Ψ The effect of pleural plaques is reported for subjects without parenchymal abnormality (not defined here) and compared to predicted values calculated from a reference population with same age, height and smoking habit. There was also higher proportion of subjects with pleural plaques only who were below 90% of the predicted FVC than the reference population.

†† The effect of pleural plaques is reported for subjects without parenchymal abnormality (profusion 0/1 or less) and compared to exposed individuals without definite pleural plaques. Absolute value of FVC decrements is not given in the abstract.

§§ The effect of pleural plaques is reported for subjects without parenchymal abnormality (not defined here) and compared to non exposed subjects matched on sex, age, height and smoking habit.

¶¶ The effect of pleural plaques is reported for subjects without parenchymal abnormality (not defined here) and compared to referent workers of three plants without exposure to asbestos. The four year declines in FVC and FEV_1 were larger than in the referents, significantly so for FEV_1.

TABLE 2

Derivation of the study population for the present research

		Description	Number of subjects
Questionnaire Survey 1982			
Target population	:	All construction insulators who were members of the union local 58	644
Responders	:	Those who returned their questionnaire	558
		Exclusions: 21 subjects who had been diagnosed as having asbestosis by a pneumoconiosis board	
Study population	:	Those remaining workers who answered the mailed questionnaire	537
Lung function survey 1983 - 1984			
Target population	:	Those participants in the 1982 questionnaire, who were 50 years old or less and living in Montreal area	246
Responders	:	Those who agreed to participate	215
Present study 1986 - 1987			
Target population	:	All participants in the 1983-84 survey who were 35 years or more	129
Responders	:	Those who agreed to participate	110

TABLE 3a

Personal and exposure characteristics * of the study population in relation to smoking status

		All	Non-smokers	Ex-smokers	Smokers
Subjects	n	110	13	42	55
Personal:					
Age	yr	43.8 (5.3) 35-52	44.0 (6.0) 36-52	45.0 (5.0) 37-52	43.0 (5.0) 35-52
Weight	kg	76.1 (11.6) 50-113	76.3 (16.5) 55-113	78.6 (9.9) 62-102	74.0 (11.4) 50-101
Height	cm	169.9 (5.8) 158-183	168.8 (7.0) 158-180	169.8 (5.4) 160-183	170.3 (5.8) 160-182
Exposure:					
Cumulative smoking, pack years		19.1 (12.6) 0 - 56	0.0 -	19.2 (12.9) 1 - 51	23.5 (9.3) 7 - 56
Exposure +, years		17.8 (8.7) 2 - 40	20.2 (9.8) 5 - 38	19.2 (9.7) 2 - 40	16.0 (7.2) 4 - 31
Years since first exposure		23.3 (6.6) 9-36	24.6 (6.4) 13-35	24.0 (6.5) 9-36	22.3 (6.6) 10-34

* Values shown are mean, SD in parentheses, and range to the nearest integral.

+ Calculated on the basis of 2000 hours of work per year.

Table 3b

Chest radiographic abnormalities (% prevalence) and mean value gallium index in relation to smoking status

	All	Non-smokers	Ex-smokers	Smokers
Subjects n	110	13	42	55
Pleural abnormality:				
Any pleural abnormality	58.2	53.9	54.8	61.8
Chest wall:				
pleural plaques	44.5	30.8	45.2	47.3
diffuse thickening	5.5	7.7	2.4	7.3
in profile:+				
width a, right	25.5	7.7	26.2	29.7
left	27.3	23.1	23.8	30.9
width b, right	4.5	0.0	7.1	3.6
left	6.4	0.0	9.5	5.5
width c, right	0.9	7.7	0.0	0.0
left	1.8	0.0	4.8	0.0
en face, right	11.8	15.4	14.3	9.1
left	12.7	0.0	19.1	10.9
Diaphragm	17.3	23.1	7.1	23.6
Costophrenic angle obliteration	5.5	0.0	7.1	5.5
Pleural calcification	13.6	23.1	4.8	18.2
Parenchymal abnormality:				
Profusion 0/0	84.5	92.3	85.7	81.8
0/1	5.5	0.0	7.1	5.5
1/0 or less	10.0	7.7	7.1	12.7
Gallium index *	3.7 (2.0) 0 - 8	3.7 (2.0) 0 - 8	4.2 (2.0) 0 - 8	3.4 (1.9) 0 - 7

* Values shown are mean, SD in parentheses, and range to the nearest integral.

+ Thickness or width read as a < 5mm, b = 5-10 mm and c > 10 mm.

TABLE 3c

Prevalence % of respiratory symptoms * in relation to smoking status (n = 110)

	All	Non-smokers	Ex-smokers	Smokers
Usual cough +	31.8	15.4	9.5	52.7
Usual phlegm Φ	43.6	15.4	31.0	60.0
Ever wheeze§	56.4	23.0	47.6	70.9
Persistant wheeze¶	24.5	15.4	14.3	34.6
Dyspnea ΨΨ††				
Grade 1 or more	31.8	15.4	28.6	38.2
Grade 2 or more	12.7	7.7	16.7	10.9
Tuberculosis §§	0.0	0.0	0.0	0.0
Pleurisy §§	5.5	0.0	4.8	7.3

* Respiratory symptoms according to a French translation of the ATS-DLD-78 questionnaire (see appendix I for details): The symptoms shown are:

+ Usual cough: cough with first smoke or on first going out of doors but not clearing of the throat.

Φ Usual phlegm: phlegm with the first smoke or on first going out of doors but not phlegm from the nose.

§ Ever wheeze: wheeze with a cold.

¶ Persistent wheeze: wheeze most days or nights.

ΨΨ Dyspnea grade 1 : hurrying on the level or walking up a hill.

†† Dyspnea grade 2 : dyspnea walking on the level with normal people of own age.

§§ Tuberculosis or pleurisy: ever had either of these.

TABLE 3d

Dyspnea in relation to smoking status

	All	Non-smokers	Ex-smokers	Smokers
Prevalence % dyspnea (based on the ATS questionnaire) *:				n = 110
Grade 1 or more	31.8	15.4	28.6	38.2
Grade 2 or more	12.7	7.7	16.7	10.9
Prevalence % dyspnea (based on the clinical questionnaire) +:				n = 104
dyspnea with functional impairment:				
at work	15.7	0.0	10.5	22.6
at home	5.9	0.0	0.0	11.3
dyspnea with major activities	29.4	9.1	23.7	37.7
Composite MDI score Φ (of 10 or less)	22.5	0.0	18.4	30.2
Dyspnea on treadmill exercise (graded by the Borg scale) §:				n = 102, 98
at $\dot{V}O_2$ of 1.0 L/min	1.6 (1.3) 0 - 6	1.7 (1.6) 0 - 5	1.6 (1.2) 0 - 6	1.6 (1.3) 0 - 6
at $\dot{V}O_2$ of 1.5 L/min	3.3 (2.0) 0 - 10	2.6 (2.3) 0 - 7	3.3 (1.6) 0 - 9	3.5 (2.2) 0 - 10

* Dyspnea grade 1 : dyspnea when hurrying on the level or walking up a hill. Dyspnea grade 2 : dyspnea walking on the level with normal people of own age.

+ Functional impairment: any level of home or work-related activities impaired because of dyspnea. Dyspnea with major activities such as walking up a steep hill, climbing two flight of stairs or more, carrying a heavy bag on the level.

Φ MDI score incorporates all the information in the questionnaire (see Appendix II).

§ Values shown are mean, SD in parentheses, and range to the nearest integral.

TABLE 3e

Lung function at rest* in relation to smoking status

		All	Non-smokers	Ex-smokers	Smokers
Forced expiratory volumes: n = 110					
FEV_1	L	3.5 (0.6)	3.8 (0.6)	3.5 (0.6)	3.5 (0.6)
FVC	L	4.5 (0.7)	4.5 (0.8)	4.4 (0.7)	4.5 (0.6)
FEV_1/FVC	%	79.0 (7.0)	83.0 (5.0)	80.0 (5.0)	77.0 (7.0)
Forced expiratory flow rates: n = 110					
PEFR	L/min	9.0 (1.9)	9.2 (1.9)	9.2 (2.1)	8.8 (1.8)
FEF_{50}	L/min	4.5 (1.5)	5.1 (1.3)	4.7 (1.4)	4.1 (1.6)
FEF_{75}	L/min	1.5 (0.6)	1.8 (0.7)	1.5 (0.5)	1.4 (0.7)
FEF_{25-75}	L/min	3.6 (1.3)	4.2 (1.2)	3.7 (1.1)	3.3 (1.3)
Lung volumes: n = 84					
TLC	L	6.8 (1.0)	6.6 (0.9)	7.1 (1.0)	6.7 (1.0)
FRC	L	3.8 (0.8)	3.3 (0.6)	4.0 (0.9)	3.7 (0.7)
RV	L	2.4 (1.1)	2.0 (0.9)	2.8 (1.1)	2.2 (0.8)
Diffusing characteristics: n = 106					
DL_{CO}	ml/min/mm	28.8 (5.3)	29.7 (2.4)	30.2 (5.0)	27.6 (5.8)
VA	L	6.4 (0.9)	6.4 (0.8)	6.5 (1.0)	6.5 (0.8)
DL_{CO}/VA		4.5 (0.9)	4.7 (0.5)	4.7 (0.8)	4.8 (1.0)

* Values shown are mean, SD in parentheses.

TABLE 3f

Cardiorespiratory function on maximal exercise* in relation to smoking status (n = 102)

		All	Non-smokers	Ex-smokers	Smokers
HR	/min	165.6 (14.8) 125-195	167.6 (18.3) 130-195	166.8 (15.8) 125-194	164.2 (13.2) 137-186
VO_2	L/min	2.4 (0.4) 1 - 4	2.5 (0.6) 2 - 4	2.5 (0.5) 2 - 3	2.4 (0.4) 1 - 3
VO_2	ml/kg/min	31.6 (5.7) 15 - 46	31.9 (3.7) 25 - 36	31.6 (5.6) 20 - 44	31.5 (6.2) 15 - 46
VE	L/min	77.1 (18.7) 41 - 137	83.2 (22.0) 41 - 112	79.4 (19.0) 47 - 127	77.9 (17.8) 47 - 137
O_2 pulse		14.6 (2.6) 9 - 21	14.9 (2.8) 10 - 21	14.9 (2.9) 10 - 20	14.3 (2.3) 9 - 19
VE/VO_2		32.6 (6.8) 23 - 75	33.2 (5.9) 24 - 44	32.5 (8.0) 21 - 75	32.6 (6.1) 23 - 44
V_E/MVV +	%	96.1 (29.4) 43 - 210	89.2 (27.3) 62 - 138	96.6 (27.9) 61 - 210	97.2 (31.4) 43 - 191
Breathing frequency		35.3 (6.6) 22 - 55	37.1 (7.1) 24 - 45	34.9 (6.2) 24 - 55	35.3 (6.8) 22 - 53
V_t		2.1 (0.4) 1 - 4	2.0 (0.5) 2 - 3	2.1 (0.5) 1 - 4	2.0 (0.4) 1 - 3
V_t/VC		0.5 (0.1) 0.3 - 0.8	0.5 (0.1) 0.3 - 0.6	0.5 (0.1) 0.4 - 0.8	0.5 (0.1) 0.3 - 0.7

* Values shown are mean, SD in parentheses, and range to the nearest integral. Exercise tests were done by 105 subjects and maximum by 102 subjects (3 subjects did not complete the exercise test because of physical limitation other than respiratory).

+ Predicted estimated for MVV were derived from Jones'equation (Jones et al, Am Rev Respir Dis 1985; 131: 700-708).

TABLE 3g

Cardiorespiratory function on sub-maximal exercise* in relation to smoking status

	All	Non-smokers	Ex-smokers	Smokers
At anaerobic threshold: n = 96				
$\dot{V}O_2$ L/min	1.4 (0.3)	1.5 (0.4)	1.4 (0.3)	1.3 (0.3)
HR min	118.5 (13.9)	120.3 (15.3)	120.0 (14.6)	116.9 (13.2)
$\dot{V}E$ L/min	34.3 (7.0)	36.1 (10.0)	33.8 (7.4)	34.4 (6.2)
$\dot{V}_E/\dot{V}O_2$	25.6 (4.6)	25.5 (7.2)	24.6 (4.1)	26.4 (4.3)
At $\dot{V}O_2$ 15 ml/kg/min: n = 103				
HR min	110.4 (13.9)	109.7 (10.2)	112.8 (16.9)	108.6 (11.6)
VE L/min	28.5 (6.5)	29.6 (8.8)	28.6 (6.8)	28.2 (5.8)
V_E/VO_2	25.0 (5.0)	25.3 (5.8)	24.2 (4.3)	25.7 (5.3)
At $\dot{V}O_2$ 1 Liter: n = 102				
HR min	106.8 (13.8)	106.0 (7.7)	107.6 (17.6)	106.4 (11.2)
$\dot{V}E$ L/min	24.7 (4.1)	25.4 (6.6)	24.1 (4.1)	25.1 (3.4)
$\dot{V}_E/\dot{V}O_2$	24.7 (4.1)	25.4 (6.6)	24.1 (4.1)	25.1 (3.4)
At $\dot{V}O_2$ 1.5 Liters: n = 98				
HR min	126.1 (16.3)	123.2 (9.2)	125.3 (18.9)	127.5 (15.2)
$\dot{V}E$ L/min	38.9 (6.3)	39.7 (8.9)	37.8 (6.1)	39.6 (5.9)
$\dot{V}_E/\dot{V}O_2$	25.9 (4.2)	26.4 (5.9)	25.2 (4.0)	26.4 (4.0)

* Values shown are mean, SD in parentheses.

TABLE 4a

Personal and exposure characteristics* of the study population in relation to pleural abnormality (PA reading)

		Without pleural abnormality	With pleural abnormality
Subjects	n	46	64
Personal:			
Age	yr	43.0 (5.9) 35 - 52	44.3 (4.8) 35 - 52
Weight	kg	75.2 (11) 50 - 96	76.8 (12) 55 - 113
Height	cm	170.7 (5.5) 162 - 183	169.3 (6.0) 158 - 182
Exposure:			
Smoking	%		
Current		45.7	53.1
Ex		41.3	35.9
Non		13.0	11.0
Cumulative smoking pack years		15.0 (10.6) 0 - 38	22.0 (13.2) 0 - 56
Exposure	yrs	18.5 (10.2) 4 - 40	17.3 (7.4) 2 - 36
Years since first exposure		23 (7.8) 9 - 36	24 (5.6) 10 - 34
Indicators of parenchymal abnormality:			
Chest radiograph profusion > 1/0		1.8	8.2
Gallium index +		3.5 (2.1) 0 - 8	4.2 (1.5) 1 - 8

* Values shown are means, SD in parentheses, and range to the nearest integral except for smoking and chest radiograph of small profusion which are represented by a prevalence percent.

\+ Possible range 0 -16.

TABLE 4b

Prevalence % of respiratory symptoms* in relation to pleural abnormality (PA reading)

	Without pleural abnormality	With pleural abnormality
	n = 46	n = 64
Usual cough	26.1	35.9
Usual phlegm	50.0	39.1
Ever wheeze	54.4	57.8
Persistant wheeze	21.7	26.6
Dyspnea:		
grade 1 or more	28.3	34.4
grade 2 or more	6.5	17.2
Tuberculosis	0.0	0.0
Pleurisy	2.2	7.8

* See footnote of Table 3c for definition of respiratory symptoms.

TABLE 4c

Dyspnea* in relation to pleural abnormality (PA reading)

	Without pleural abnormality	With pleural abnormality
Prevalence % dyspnea (based on the ATS questionnaire):		
	n = 46	n = 64
Grade 1 or more	28.3	34.4
Grade 2 or more	6.5	17.2
Prevalence % dyspnea (based on the clinical questionnaire):		
dyspnea with functional impairment:		
	n = 37	n = 60
at work	17.5	14.5
at home	0.0	9.7
dyspnea with major activities	22.5	33.9
composite MDI score (10 or less)	17.5	25.8
Dyspnea on treadmill exercise graded by (Borg scale) + :		
	n = 42	n = 60
At $\dot{V}O_2$ 1 liter	1.9 (1.3) 0 - 6	1.4 (1.2) 0 - 5
	n = 40	n = 56
At $\dot{V}O_2$ 1.5 liters	3.3 (2.0) 0 - 10	3.3 (2.0) 0 - 10

* Table shows prevalence % not standardised for age, smoking status and parenchymal abnormality.

+ Values shown are mean, SD in parentheses, and range to the nearest integral.

TABLE 4d

Lung function at rest* in relation to pleural abnormality (PA reading)

		Without pleural abnormality	With pleural abnormality
Forced expiratory volumes:		n = 46	n = 64
FEV_1	L	3.8 (0.5)	3.3 (0.6)
FVC	L	4.8 (0.6)	4.2 (0.6)
FEV_1/FVC	%	79	79
Forced expiratory flow rates:		n = 46	n = 64
PEFR	L/min	9.2 (1.7)	8.9 (2.1)
FEF_{50}	L/min	4.7 (1.4)	4.3 (1.6)
FEF_{75}	L/min	1.6 (0.6)	1.4 (0.7)
FEF_{25-75}	L/min	3.7 (1.1)	3.5 (1.4)
Lung volumes:		n = 38	n = 46
TLC	L	6.9 (0.9)	6.7 (1.0)
FRC	L	3.7 (0.7)	3.8 (0.8)
RV	L	2.2 (1.0)	2.5 (1.8)
Diffusing characteristics:		n = 44	n = 62
DL_{co}	ml/min/mm	30.0 (5.6)	28.0 (5.0)
V_A	L	6.7 (0.9)	6.4 (0.9)
DL_{co}/V_A		4.5 (0.97)	4.5 (0.99)

* Values shown are means and SD in parentheses not taking into account differences in age, height smoking status and parenchymal abnormality.

TABLE 4e

Cardiorespiratory function on maximal exercise* in relation to pleural abnormality (PA reading)

		Without pleural abnormality	With pleural abnormality
		n = 43	n = 59
$\dot{V}O_2$	L/min	2.4 (0.4) 2 - 3	2.4 (0.5) 1 - 4
$\dot{V}O_2$	ml/kg/min	32.2 (5.6) 20.0 - 43.6	31.1 (5.8) 14.5 - 45.7
HR	/min	167.5 (14.6) 135 - 195	164.3 (15.0) 125 - 194
$\dot{V}_E$	L/min	79.9 (17.5) 47 - 127	78.5 (19.6) 41 - 137
O_2 pulse		14.5 (2.6) 10 - 19	14.7 (2.6) 9 - 21
$\dot{V}_E/\dot{V}O_2$		33.2 (7.5) 26 - 75	32.6 (4.2) 21 - 44
$\dot{V}_E$/MVV		0.8 (0.2) 0.4 - 1.4	1.1 (0.1) 0.6 - 2.1
Breathing frequency	/min	33.8 (5.4) 23 - 45	36.4 (7.2) 22 - 55
V_t	L	2.2 (0.5) 1 - 4	2.0 (0.4) 1 - 3
V_t/VC		0.45 (0.07) 0.3 - 0.6	0.48 (0.1) 0.3 - 0.8

* Values shown are mean, SD in parentheses, and range, not taking into account differences in age, height, smoking status and parenchymal abnormality.

TABLE 4f

Cardiorespiratory function on submaximal exercise* in relation to pleural abnormality (PA reading)

		Without pleural abnormality	With pleural abnormality
At anaerobic threshold:		n = 39	n = 57
$\dot{V}O_2$	L/min	1.4 (0.3) 1 - 2	1.3 (0.3) 1 - 2
HR	/min	116.2 (15.0) 93 - 153	120.1 (13.1) 89 - 147
$\dot{V}_E$	L/min	33.8 (7.5) 22 - 48	34.6 (6.8) 23 - 54
At VO_2 15 ml/kg/min:		n = 42	n = 61
HR	/min	107.2 (13.2) 80 - 137	112.6 (14.1) 78 - 165
$\dot{V}_E$	L/min	27.6 (6.6) 18 - 50	29.1 (6.5) 19 - 47

* Values shown are mean, SD in parentheses, not taking into account differences in age, height, smoking status and parenchymal abnormality.

TABLE 4f (continued)

Cardiorespiratory function on submaximal exercise* in relation to pleural abnormality (PA reading)

		Without pleural abnormality	With pleural abnormality
At $\dot{V}O_2$ 1 liter:			
		n = 41	n = 61
HR	/min	103.8 (12.9) 79 - 132	108.9 (14.1) 70 - 155
$\dot{V}_E$	L/min	24.6 (4.0) 19 - 34	24.8 (4.2) 18 - 41
$\dot{V}_E$/MVV	%	28.0 (7.0) 18 - 46	38.0 (14.0) 16 - 86
Breathing frequency		19.5 (4.6) 12 - 30	22.1 (6.9) 12 - 55
V_t		1.3 (0.3) 1 - 2	1.2 (0.4) 1 - 4
V_t/VC		0.26 .18 - .47	0.28 .15 - .55
At $\dot{V}O_2$ 1.5 liter:			
		n = 39	n = 57
HR	/min	123.9 (17.2) 93 - 166	127.7 (15.7) 92 - 168
$\dot{V}_E$	L/min	38.6 (6.1) 26 - 55	39.0 (6.5) 23 - 56
$\dot{V}_E$/MVV	%	44.0 (11.0) 30 - 66	57.0 (23.0) 25 - 78
Breathing frequency		24.0 (5.0) 13 - 35	26.0 (7.0) 16 - 48
V_t		1.6 (0.2) 1 - 2	1.6 (0.3) 1 - 3
V_t/VC		0.34 .22 - .47	0.37 .26 - .75

* Values shown are mean, SD in parentheses to the nearest integral and are not standardized for age, height, smoking status and parenchymal abnormality.

TABLE 5a

Dyspnea* in relation to pleural abnormality assessed from the PA chest radiograph alone, and from the PA chest radiograph supplemented by oblique films

	PA reading		PA-oblique reading +	
	Without pleural abnormality	With pleural abnormality	Without pleural abnormality	With pleural abnormality
Prevalence % dyspnea (based on the ATS questionnaire):				
	n=46	n=64	n=46	n=64
Grade 1 or more	28.3	34.4	28.3	34.4
Grade 2 or more	6.5	17.2	8.7	15.6
Prevalence % dyspnea (based on the clinical questionnaire MDI score):				
	n=37	n=60	n=35	n=62
dyspnea with functional impairment:				
at work	17.5	14.5	15.4	15.9
at home	0.0	9.7	5.1	6.4
dyspnea with major activities	22.5	33.9	25.6	31.8
composite MDI score (10 or less)	17.5	25.8	17.9	25.4
Dyspnea on treadmill exercise graded by Borg scale:Φ				
	n=42	n=60	n=40	n=62
At $\dot{V}O_2$ 1 liter	1.9 (1.3) 0 - 6	1.4 (1.2) 0 - 5	1.7 (1.1) 0 - 4	1.6 (1.4) 0 - 6
	n=40	n=56	n=38	n=58
At $\dot{V}O_2$ 1.5 liters	3.3 (2.0) 0 - 10	3.3 (2.0) 0 - 10	3.0 (1.3) 0 - 6	3.5 (2.3) 0 - 10

* See footnote of TABLE 3d for definition of dyspnea.

+ Although the number of subjects read as having pleural abnormality may be the same when assessed by PA reading as compared to PA-oblique reading, the subjects themselves are different.

Φ Values shown are mean, SD in parentheses and range rounded to the nearest integral.

TABLE 5b

Lung functions at rest* in relation to pleural abnormality assessed from the PA chest radiograph alone and from the PA chest radiograph supplemented by oblique films

	PA reading		PA-oblique reading +	
	Without pleural abnormality	With pleural abnormality	Without pleural abnormality	With pleural abnormality
Forced expiratory volume:				
	n = 46	n = 64	n = 46	n = 64
FEV_1 L	3.8 (0.5)	3.3 (0.6)	3.7 (0.6)	3.4 (0.6)
FVC L	4.8 (0.6)	4.2 (0.6)	4.6 (0.7)	4.4 (0.7)
Lung volumes:				
	n = 38	n = 46	n = 32	n = 52
TLC L	6.9 (0.9)	6.7 (1.0)	6.9 (0.9)	6.7 (1.1)
Diffusing characteristics:				
	n = 44	n = 62	n = 45	n = 61
DL_{CO} ml/min/mm	30 (5.6)	28 (5.0)	29 (5.6)	29 (5.1)

* Values shown are mean, SD in parentheses.

+ Although the number of subjects read as having pleural abnormality may be the same when assessed by PA reading as compared to PA-oblique reading, the subjects themselves are different.

TABLE 5c

Cardiorespiratory function on exercise* in relation to pleural abnormality assessed from the PA chest radiograph supplemented by oblique films

	PA reading		PA-oblique reading	
	Without pleural abnormality	With pleural abnormality	Without pleural abnormality	With pleural abnormality
Maximal exercise:				
	n = 43	n = 59	n = 42	n = 60
$\dot{V}_E$ L/min	79.9 (17.5)	78.5 (19.6)	80.2 (15.2)	78.4 (20.8)
$\dot{V}_E/\dot{V}O_2$	33.2 (7.6)	32.6 (4.9)	33.1 (7.2)	32.7 (5.4)
Submaximal exercise:				
At $\dot{V}O_2$ 1 liter:				
	n = 41	n = 61	n = 42	n = 60
$\dot{V}_E$ L/min	24.6 (4.0)	24.8 (4.2)	24.6 (3.2)	24.8 (4.6)
$\dot{V}_E/\dot{V}O_2$	24.6 (4.0)	24.8 (4.2)	24.6 (3.2)	24.8 (4.6)
At $\dot{V}O_2$ 15 ml/kg/min:				
	n = 42	n = 62	n = 42	n = 61
$\dot{V}_E$ L/min	27.6 (6.6)	29.1 (6.5)	27.1 (4.4)	29.5 (7.5)
$\dot{V}_E/\dot{V}O_2$	24.4 (3.9)	25.5 (5.6)	24.5 (3.3)	25.4 (5.8)

* Values shown are mean and SD in parentheses. integral.

TABLE 6a

Odds ratio for dyspnea* in the presence, or not, of pleural abnormality taking into account other relevant determinants

		Other relevant determinants		Parenchymal abnormality	
	Radiographic pleural abnormality	Age	Smoking	Chest x-ray	Gallium
Dyspnea (based on the ATS questionnaire)					
Grade 1 or more	0.89 .4 to 2	2.4	1.6 Φ	0.83	1.4
Grade 2 or more	1.60 .4 to 7	2.3	1.6 Φ	1.10	1.6
Dyspnea (based on the clinical questionnaire MDI score)					
Dyspnea with functional impairment:					
at work	0.4 .1 to 2	4.5	1.7 Φ	2.70	0.9
at home	---	4.5	1.0	3.0	0.7
Dyspnea with major activities:	1.6 .5 to 5	2.4	1.6 Φ	2.5	0.8
Composite MDI score (10 or less):	1.0 .3 to 3	6.0	1.8 Φ	2.3	0.7

* Logistic regression analysis was used to determine the odds ratios. Values shown are odds ratio of dyspnea. The 95% confidence limit are shown for the effect of pleural abnormality.

+ Odds ratios are calculated for the presence or not of pleural abnormality, a difference of 15 years of age, 10 packyears of smoking, 3 point scales of profusion on chest radiograph and 3 point scales of gallium index.

Φ $p < .05$

TABLE 6b

Mean differences in lung function at rest between subjects with and without pleural abnormality, taking into account other relevant determinants*

	Mean differences between subjects with and without pleural abnormality adjusted for other determinants	Regression coefficients of other determinants in the model: Age (yr)	Height (cm)	Smoking (pack-yrs)	Chest X-ray (10 point scale)	Gallium (16 point scale)
Forced expiratory volumes:						
FEV_1	-222+ (93) -404 to -39	-33+ (9)	49+ (8)	-11+ (4)	-70 (39)	-12 (28)
FVC	-402+ (102) -601 to -202	-21+ (10)	62+ (9)	-5 (4)	-44 (43)	-50 (31)
Lung volumes:						
TLC	-35 (243) -511 to 438	-31 (24)	27 (20)	-18 (10)	-152 (111)	103 (75)
Diffusion characteristic:						
DL_{CO}	-8 (1.2) -2 to 3	-0.14 (0.12)	0.32+ (0.10)	-0.13+ (0.05)	-0.41 (0.55)	-0.32 (0.36)

* Values shown are the regression coefficient in ml after accounting for other relevant determinants, the standard error in parentheses and the 95% confidence limits.

\+ $p < 0.05$

TABLE 6c

Mean differences in cardiorespiratory function on exercise for subjects with and without pleural abnormality, taking into account other relevant determinants *

	Mean differences in subjects with and without pleural abnormality adjusted for other determinants	Regression coefficients of other determinants in the model: Age (yr)	Height (cm)	Weight (kg)	Smoking (pack-yrs)	Chest X-ray (10 point scale)	Gallium (16 point scale)
Maximal exercise:							
$\dot{V}O_2$	0.07 (0.1) -0.1 to 0.2	-0.01 (0.01)	0.01 (0.01)	0.02 (0.006)	-0.006 (0.004)	-0.03 (0.05)	-0.05 (0.04)
$\dot{V}_E$	-2.7 (4.2) -11 to 6	-0.7 (0.5)	1.3 (0.5)	0.2 (0.3)	-0.16 (0.19)	0.73 (2.2)	2.3 (1.9)
$\dot{V}_E/\dot{V}O_2$	0.2 (1.0) -1.8 to 2.2	0.1 (0.1)	0.3 (0.1)	-0.09 (0.06)	0.04 (0.04)	0.4 (0.5)	0.4 (0.4)
$\dot{V}_E$/MVV	11.6 (5.9) + 0 to 23.2	0.7 (0.6)	-1.1$^{\Phi}$ (0.6)	0.5 (0.3)	0.6$^{\Phi}$ (0.2)	6.5$^{\Phi}$ (2.8)	0.6 (2.3)
Breathing frequency /min	1.9 (1.5) -0.8 to 5	0.04 (0.2)	-0.07 (0.1)	-0.04 (0.1)	-0.01 (0.06)	1.1 (0.7)	0.3 (0.6)
V_t/VC %	2.2 (1.7) -1 to 6	-0.03 (0.2)	-0.02 (0.2)	0.03 (0.1)	0.09 (0.07)	0.4 (0.8)	0.2 (0.7)
Submaximal exercise:							
At anaerobic threshold (AT)							
$\dot{V}_E$	-0.12 (1.6) -3.2 to 3.0	-0.09 (0.17)	0.22 (0.17)	0.12 (0.1)	0.02 (0.07)	0.23 (0.78)	0.16 (0.64)
$\dot{V}_E/\dot{V}O_2$	1.17 (0.9) -0.5 to 2.9	0.1 (0.1)	0.08 (0.1)	-0.1 (0.06)	0.004 (0.04)	-0.15 (0.44)	0.2 (0.4)
At $\dot{V}O_2$ 15 ml/kg/min							
$\dot{V}_E$	0.38 (1.1) -1.8 to 2.5	0.04 (0.11)	0.08 (0.11)	0.25 (0.07)	0.004 (0.05)	-0.40 (0.52)	0.92 (0.43)
$\dot{V}_E/\dot{V}O_2$	0.55 (0.9) -1.1to 2.3	0.06 (0.1)	0.07 (0.1)	-0.09 (0.06)	-0.001 (0.04)	-0.24 (0.36)	0.56 (0.36)

Continued.../

TABLE 6c (continued)

Mean differences in cardiorespiratory function on exercise for subjects with and without pleural abnormality, taking into account other relevant determinants *

	Mean differences in subjects with and without pleural abnormality adjusted for other determinants	Regression coefficients of other determinants in the model: Age (yr)	Height (cm)	Weight (kg)	Smoking (pack-yrs)	Chest X-ray (10 point scale)	Gallium (16 point scale)
At $\dot{V}O_2$ 1 liter							
$\dot{V}E$	0.43 (0.93) -1.4 to 2.3	0.17 (0.1)	0.005 (0.1)	-0.05 (0.06)	0.04 (0.04)	-0.47 (0.44)	0.06 (0.36)
$\dot{V}_E/\dot{V}O_2$	0.35 (0.9) -1.4 to 2.1	0.16 (0.09)	-0.004 (0.09)	-0.05 (0.06)	0.04 (0.04)	-0.4 (0.4)	0.05 (0.35)
$\dot{V}_E$/MVV	5.8 (2.3)$^{\Phi}$ 1 to 10	0.6$^{\Phi}$ (0.2)	-0.8$^{\Phi}$ (0.2)	0.007 (0.1)	0.2 $^{+}$ (0.09)	0.9 (1.0)	-0.08 (0.9)
Breathing frequency /min	3.1 (1.3) 0.6 to 6	0.2 (0.1)	-0.03 (0.1)	-0.2$^{\Phi}$ (0.07)	-0.05 (0.05)	-0.02 (0.6)	-0.2 (0.5)
V_t/VC %	0.8 (1.3) -2 to 3	-0.05 (0.1)	-0.3$^{\Phi}$ (0.1)	0.1 $^{+}$ (0.07)	0.07 (0.05)	-0.4 (0.6)	-0.4 (0.5)
At $\dot{V}O_2$ 1.5 liters							
$\dot{V}_E$	0.2 (1.6) -3 to 3	-0.1 (0.2)	0.2 (0.2)	0.1 (0.1)	0.02 (0.07)	0.2 (0.8)	0.1 (0.6)
$\dot{V}_E/\dot{V}O_2$	1.17 (1.4) -2 to 4	0.1 (0.1)	0.07 (0.1)	-0.2$^{\Phi}$ (0.1)	0.04 (0.06)	-0.5 (0.7)	0.3 (0.5)
$\dot{V}_E$/MVV	6.8 (3.8) $^{+}$ -1 to 14	0.9$^{\Phi}$ (0.4)	-1.4$^{\Phi}$ (0.4)	-0.08 (0.2)	0.3$^{\Phi}$ (0.2)	2.0 (1.7)	0.5 (1.4)
Breathing frequency /min	2.2 (1.3) $^{+}$ -0.3 to 5	0.2 (0.1)	-0.2 (0.1)	-0.2$^{\Phi}$ (0.1)	-0.07 (0.05)	-0.6 (0.6)	-0.3$^{\Phi}$ (0.5)
V_t/VC %	1.4 (1.6) -2 to 5	0.1 (0.1)	-0.2 $^{+}$ (0.2)	0.09 (0.08)	0.1$^{\Phi}$ (0.06)	1.6 (0.7)	-0.4 (0.6)

* Values shown are the regression coefficient in L after accounting for the other relevant determinants and standard error in parentheses. 95% confidence limit are given for the effect of pleural abnormality.

$^{+}$ $p < 0.1$

$^{\Phi}$ $p < 0.05$

TABLE 7a

Odds ratio for dyspnea* given the presence, or not, of pleural abnormality at different sites, taking into account other relevant determinants

Radiographic sites of pleural determinants			Other relevant determinants		Parenchymal abnormality	
Chest wall pleural thickening (24 point scale)	Costophrenic angle obliteration (2 point scale)	Diaphragmatic thickening (2 point scale)	Age	Smoking	Chest x-ray	Gallium
Dyspnea (based on the ATS questionnaire)						
Grade 1 or more	2.4	1.3	0.7	2.8	1.4	0.9	1.0
Grade 2 or more	1.6	0.8	1.2	2.7	1.6	1.3	1.4
Dyspnea (based on the clinical questionnaire)						
Dyspnea with functional impairment:						
at work	0.7	0.5	1.0	4.9	1.6 Φ	2.4	1.4
at home	1.4	2.9	8.9 Φ	4.5	1.3	3.5	0.7
Dyspnea with major activities:							
	4.5Φ	2.1	0.7	3.9	1.5Φ	3.2	0.4

* Logistic regression analysis was used to determine the odds ratio of dyspnea given a difference of 4 points for chest wall pleural thickening (24 point scale), 1 point for one costophrenic angle obliteration (2 point scale) and one diaphragmatic thickening (2 point scale). Values shown are odds ratio.

+ See methods of evaluation section for details of pleural score.

Φ $p < 0.05$

TABLE 7b

Regression coefficient in ml of FEV_1 and FVC* on pleural abnormality in different sites, after accounting for other relevant determinants

	Radiographic sites of pleural abnormality			Other relevant determinants			Parenchymal abnormality	
	Chest wall pleural thickening (24 point scale)	Costophrenic angle obliteration (2 point scale)	Diaphragmatic thickening (2 point scale)	Age	Height	Smoking	Chest x-ray	Gallium
FEV_1	-50 $^{+}$ (25) -93 to 3	-590$^{\Phi}$ (183) -596 to -238	-66 (75) -81 to 213	-33 $^{\Phi}$ (9)	45$^{\Phi}$ (8)	-11$^{\Phi}$ (4)	-66 (38)	-3 (29)
FVC	-68$^{\Phi}$ (29) -123 to -9.7	-462$^{\Phi}$ (220) -889 to -35	-153 $^{+}$ (89) -327 to -22	-21 $^{\Phi}$ (11)	60$^{\Phi}$ (9)	- 6 (4)	-46 (44)	-41 (33)

* FEV_1 and FVC were the dependent variables, chest wall pleural thickening and extent, costophrenic angle obliteration and diaphragmatic thickening the independent variables in a multiple regression, after accounting for age, height, smoking and parenchymal abnormality. Values shown are the regression coefficient in ml, standard error in parentheses and the 95% confidence limits. See methods of evaluation section for details of pleural score.

$^{+}$ $p < .1$

$^{\Phi}$ $p < .05$

TABLE 7c

Regression coefficient of respiratory parameters during exercise on pleural abnormality in different sites after accounting for other determinants*

	Radiographic sites of pleural abnormality			Other relevant determinants				Parenchymal abnormality	
	Chest wall pleural thickening (24 point scale)	Costophrenic angle obliteration (2 point scale)	Diaphragmatic thickening (2 point scale)	Age	Height	Weight	Smoking	Chest x-ray	Gallium
Maximal exercise:									
$\dot{V}_E$	0.1 (1.0)	-2.7 (8.0)	0.5 (3.0)	-0.3 (0.4)	1.0 $^{\Phi}$ (0.4)	0.2 (0.2)	-0.009 (0.2)	2.3 (2.0)	0.7 (0.7)
$\dot{V}_E/\dot{V}O_2$	0.2 (0.3)	-0.1 (2.0)	0.02 (0.9)	0.1 (0.1)	0.3 $^{\Phi}$ (0.1)	-0.1 $^{+}$ (0.06)	-0.003 (0.04)	0.3 (0.5)	0.6 (0.4)
O_2 pulse	-0.1 (0.1)	-0.07 (1.0)	-0.04 (0.5)	-0.01 (0.06)	0.07 (0.05)	0.1 $^{+}$ (0.03)	0.01 (0.02)	0.3 (0.3)	-0.2 (0.2)
$\dot{V}_E$/MVV	3.4 $^{\Phi}$ (1.6)	3.5 $^{\Phi}$ (1.1)	1.0 (4.8)	0.4 (0.6)	-0.1 (0.6)	0.3 (0.3)	0.6 $^{\Phi}$ (0.2)	6.0 $^{+}$ (3.0)	0.7 (2.0)

* Values shown are regression coefficients, standard error in parentheses.

$^{+}$ $p < 0.1$

$^{\Phi}$ $p < 0.05$

§ See methods of evaluation section for details of pleural score.

TABLE 7c (continued)

Regression coefficient of respiratory parameters during exercise on pleural abnormality in different sites after accounting for other determinants *

	Radiographic sites of pleural abnormality			Other relevant determinants				Parenchymal abnormality	
	Chest wall pleural thickening (24 point scale)	Costophrenic angle obliteration (2 point scale)	Diaphragmatic thickening (2 point scale)	Age	Height	Weight	Smoking	Chest x-ray	Gallium
Submaximal exercise:									
At $\dot{V}O_2$ 1 Liter									
$\dot{V}_E$	-0.3	1.6	1.1	0.04	0.03	-0.03	0.1	-0.4	-0.06
	(0.3)	(1.7)	(0.8)	(0.1)	(0.09)	(0.05)	(0.03)	(0.5)	(0.3)
Breathing frequency	-0.2	4.0	2.8 Φ	0.2	-0.05	-0.1	-0.01	-0.5	-0.07
	(0.4)	(3.0)	(1.0)	(0.1)	(0.1)	(0.07)	(0.06)	(0.7)	(0.5)
V_t/VC %	0.7 Φ	-0.5	-0.09	-0.03	-0.2 +	0.08	0.06	0.6	-0.3
	(0.3)	(2.4)	(1.0)	(0.1)	(0.1)	(0.07)	(0.05)	(0.6)	(0.5)
$\dot{V}_E/MVV$ %	1.0	16.0	-1.4	0.4 +	-0.7 +	-0.1	0.2 Φ	0.2	-0.001
	(0.6)	(4.4)	(1.8)	(0.2)	(0.2)	(0.1)	(0.09)	(0.1)	(0.8)
At $\dot{V}O_2$ 1.5 Liters									
$\dot{V}_E$	-0.3	2.0	0.5	0.01	-0.02	-0.15 +	-0.0001	-0.015	0.4
	(0.4)	(2.7)	(1.0)	(0.1)	(0.1)	(0.08)	(0.06)	(0.7)	(0.5)
Breathing frequency	-0.1	4.0	1.5	0.1	-0.2	-0.2 Φ	-0.05	-0.8	-0.4
	(0.4)	(2.5)	(1.0)	(0.1)	(0.1)	(0.07)	(0.05)	(0.06)	(0.5)
V_t/VC %	1.0 Φ	-1.0	-0.9	0.1	-0.2	0.05	0.1 +	0.2	0.2
	(0.04)	(3.0)	(1.4)	(0.2)	(0.2)	(0.09)	(0.07)	(0.8)	(0.6)
$\dot{V}_E/MVV$ %	1.8 +	24.0 Φ	0.3	0.7 +	-1.3 Φ	-0.2	0.3 Φ	-1.2	0.5
	(1.0)	(7.0)	(3.0)	(0.4)	(0.4)	(0.2)	(0.1)	(1.8)	(1.4)

* Values shown are the regression coefficient, standard error in parentheses.

\+ $p < 0.1$

Φ $p < 0.05$

§ See methods of evaluation section for details of pleural score.

TABLE 8

Respiratory parameters * on maximal and submaximal exercise in relation to pleural abnormality.

Respiratory parameters	Maximal exercise		Submaximal exercise $\dot{V}O_2$ 1.5 L/min	
	with pleural plaques	without pleural plaques	with pleural plaques	without pleural plaques
$\dot{V}_E$ L/min	78.5 (19.6)	79.9 (17.5)	39.0 (6.5)	38.6 (6.1)
Breathing frequency /min	36.4 (7.2)	33.8 (5.4)	26.0 + (7.0)	24.0 (5.0)
V_t L	2.0 (0.4)	2.2 (0.5)	1.6 (0.3)	1.6 (0.2)
V_t/VC	0.48 (0.07)	0.45 (0.07)	0.37 (0.08)	0.34 (0.06)
$\dot{V}_E/MVV$	1.1 + (0.1)	0.8 (0.2)	0.57 + (0.23)	0.44 (0.1)

* Values shown are mean and SD in parentheses not taking into account differences in age, height, smoking status and parenchymal abnormality.

\+ $p < 0.1$ after taking into account the relevant determinants.

REFERENCES

1. Selikoff IJ, Lee DHK. Asbestos and Disease. New York : Academic Press, 1978; 3: 3-357.
2. Becklake MR. Asbestos-related diseases of the lung and other organs: their epidemiology and implications for clinical practice. Am Rev Respir Dis 1976; 114: 187-226.
3. Becklake MR. Asbestos-related diseases of the lungs and pleura. Current clinical issues. Am Rev Respir Dis 1982; 16: 187-194.
4. Rosenstock L, Hudson LD. Non-malignant asbestos-induced pleural disease. Seminars in Respiratory Medicine 1986; 7: 197-202.
5. Bamblin WP. Dust control in the asbestos textile industry. Ann Occup Hyg 1954; 2: 54-59.
6. Gilson JC. Problems and perspectives: the changing hazards of exposure to asbestos. Ann NY Acad Sci 1965; 132: 696-705.
7. Siegal W, Smith AR, Greenberg L. Report on study of talc miners and millers in St-Lawrence County. NY Indust Bull 1943; 22: 432-468.
8. Jacob C, Bohlig H. Uber Haufigkeit und besonderheiten des lungenkrebs bei asbestose. Arch Geuerbepathol Geuerbehyg 1955; 14: 10.
9. Hillerdal, G. Pleural plaques in a health survey material: frequency, development, and exposure to asbestos. Scand J Respir Dis 1978; 59: 257-263.
10. Eisenstadt HB. Asbestos pleurisy. Dis Chest 1964; 46: 78-81.
11. Mackerzie FAF, Harnies PG. Changing attitudes to the diagnosis of asbestos disease. J R Nav Med Serv 1970; 56: 116-123.

12. Hillerdal G. Non-malignant asbestos pleural disease. Thorax 1981; 36: 669-675.

13. Harnies PG. Experience with asbestos disease and its control in Great Britain's dock yards. Environ Resp 1976; 11: 261-267.

14. Gaensler EA; Kaplan AI. Asbestos pleural effusion. Ann Intern Med 1971; 74: 178-191.

15. McLoud TC, Woods BO, Carrington CB, Epler GR, Gaensler EA. Diffuse pleural thickening in an asbestos-exposed population: prevalence and causes. AJR 1985; 144: 9-18.

16. Navratel M, Dobias J. Development of pleural hyalinosis in long-term studies of persons exposed to asbestos dust. Environ Res 1973; 6: 455-472.

17. Hillerdal G. Nonneoplastic injury to the pleura by fibers. In Chretien J, Bignon J, Hirsch A eds. The pleura and health disease. New York, Marcel Dekker, 1985, 461-485.

18. Sargent EN, Jacobson G, Gordonson JS. Pleural plaques: a signpost of asbestos dust inhalation. Semin Roentgen 1977; XII: 282-297.

19. Craighead JE, Abraham JL, Churg A, et al. The pathology of asbestos-associated diseases of the lung and pleural cavities: diagnostic criteria and proposed grading schema. Arch Pathol Lab Med 1982; 106: 543-597.

20. Hillerdal G. Nonmalignant pleural disease related to asbestos exposure. Clinics in Chest Medecine 1985; 6: 1: 141-152.

21. Hillerdal G. The pathogenesis of pleural plaques and pulmonary asbestosis: possibilities and impossibilities. Eur J Respir Dis 1980; 61: 129-138.

22. Hillerdal G, Lindgren A. Pleural plaques. Correlation of autopsy findings to radiographic findings and occupational history. Eur J Respir Dis 1980; 61: 315-319.

23. Hourihane DO'B, Lessof L, Richardson PC. Hyaline and calcified pleural plaques as an index of exposure to asbestos: a study of 100 cases with a consideration of epidemiology. Br Med J 1966; 1: 1069-1074.

24. Sargent EN, Boswell WD, Ralls PW, Arkovitz A. Subpleural fat pads in patients exposed to asbestos: distinction from non-calcified pleural plaques. Diagnostic Radiology 1984; 152: 273-277.

25. International Labour Office. ILO U/C International Classification of Radiographs of Pneumoconioses 1971. Occupational Safety and Health Series. No. 22 (revised) ILO: Geneva.

26. International Labour Office. ILO U/C International Classification of Radiographs of Pneumoconioses 1980. Occupational Safety and Health Series. No. 22 (revised) ILO: Geneva.

27. Bourbeau J, Ernst P. Between and within reader variability in the assessment of asbestos-related pleural disease using the ILO 1980 International Classification of Radiograph of pneumoconioses. Am J Ind Med 1988 (accepted).

28. Anton HC. Multiple pleural plaques. Br J Radiol 1967; 40: 685-690.

29. Baker EL, Greene R. Incremental value of oblique chest radiographs in the diagnosis of asbestos-induced pleural disease. Am J Ind Med 1982; 3: 17-22.

30. Sheers G and Templeton AR. Effects of asbestos in dockyard workers. Br Med J 1968; 3: 574-579.

31. Greene R, Boggis C, Fantsch H. Asbestos-related pleural thickening: effect of threshold criteria on interpretation. Radiology 1984; 152: 569-573.

32. Reger RR, Ames RG, Merchant JA, Polakoff PP, Sargent EN, Silbigen M, Whittlesey P. The detection of thoracic abnormalities using posterior-anterior (PA) vs PA and oblique roentgenograms. Chest 1982; 81: 290-296.

33. Kreel L. Computer tomography in the evaluation of pulmonary asbestosis, preliminary experiences with EMI general purpose scanner. Acta Radiologica Diagnosis 1976; 17: 405-411.

34. Katz D and Kreel L. Computer tomography in pulmonary asbestosis. Acta Radiologica 1979; 30: 207-213.

35. Begin R, Bocton M, Bergeron D, et al. Radiographic assessment of pleuro-pulmonary disease in asbestos workers: Postero-anterior 4 view films and CT scan. British J Ind Med 1984; 41: 373-383.

36. Gerhard K, Sluis-Cremer GK, Thomas RG and Schmaman B. The value of computerised axial tomography in the assessment of workers exposed to asbestos. Am J Ind Med 1984; 6: 27-35.

37. Rossiter CE, Bristol LJ, Cartier PH, Gilson JG, Grainger TR, Sluis-Cremer GK, McDonald JC. Radiographic changes in chrysotile asbestos mine and mill workers of Quebec. Arch Environ Health; 24: 388-400.

38. Harries PG, Mackenzie FAF, Sheers G, Kemp JH, Oliver TP, Wright DS. Radiological survey of men exposed to asbestos in naval dockyards. Br J Ind Med 1972; 29: 274-279.

39. Selikoff IJ. The occurence of pleural calcification among asbestos insulation workers. Ann NY Acad Sci 1965; 132: 351-367.

40. Anderson HA, Selikoff IJ. Pleural reactions to environmental agents. Federation Proc 1978; 37: 2496-2500.

41. Cordier S, Theriault G, Provencher S. Radiographic changes in a group of chrysotile miners and millers exposed to low asbestos dust concentration. Br J Ind Med 1984; 41: 384-388.

42. Copes R, Thomas D, Becklake MR. Temporal patterns of exposure and nonmalignant pulmonary abnormality in Quebec chrysotile workers. Arch Environ Health 1985; 40: 80-87.

43. Gibbs GW. Etiology of pleural calcification: a study of Quebec chrysotile asbestos miners and millers. Arch Environ Health 1979; 34: 76-82.

44. Sheers G. Asbestos associated disease in employees of Devonport dockyard. Ann NY Acad Sci 1979; 300: 281-288.

45. Selikoff IJ, Lilis R, Nicholson WJ. Asbestos disease in United States shipyards. Ann NY Acad Sci 1979; 330: 295-312.

46. Hedenstierna G et al. Pleural plaques and lung function in construction workers exposed to asbestos. Eur J Resp Dis 1981; 62: 111-122.

47. Langlands HM, Wallance WFM, Simpson MJC. Insulation workers in Belfast. Br J Ind Med 1971; 28: 217-225.

48. Gamble J, Greife A, Hancock J. Cross-sectional epidemiology and industrial hygiene survey of talc workers mining ore from Montana, Texas, and North Carolina. In Proceeding of the National Workshop on Substitutes for Asbestos. Environmental Protection Agency Publication no. EPA-560/3-80-001. Washington, D.C., Government Printing Office, 1980, 570 pages.

49. Baris YI, Sabin AA, Ozesmi M. An outbreak of pleural mesothelioma and chronic fibrosing pleurisy in the village of Karain/Ungup in Anatolia. Thorax 1978; 33: 181-192.

50. Artvinli M, Baris YI. Environmental fiber-induced pleuropulmonary diseases in an Anatolian village: an epidemiologic study. Arch Environ Health 1982; 37: 177.

51. Wagner JC, Elmes PC. The mineral fibre problem. In: McDonald JC, ed, Recent Advances in Occupational Health. Edinburgh: Churchill, Livingston, 1981: 1-14.

52. Bazas TB, McDonald JC. Pleural calcification in North-West Greece. Lancet 1981; 2: 254.

53. Meurman LO. Pleural fibrocalcific plaques and asbestos exposure. Environ Res 1968; 2: 30-46

54. Zolov C, Burelkov T and Babdjov L. Pleural asbestosis in agricultural workers. Environ Res 1967; 1: 287-292.

55. Yaziciogly S. Pleural calcification associated with exposure to chrysotile asbestos in southeast Turkey. Chest 1976; 70: 43-47.

56. Anderson HA, Lilis R, Daum SM, Selikoff IJ. Asbestosis among household contacts of asbestos factory workers. Ann NY Acad Sci 1979; 330: 387-401.

57. Becklake MR, Fournier-Massey G, McDonald JC, Siemiatycki J, Rossiter CE. Lung function in relation to chest radiographic changes in Quebec asbestos workers. Bull Physiopath Resp 1970; 6: 637-659.

58. McGavin CR, Sheers G. Diffuse pleural thickening in asbestos workers: disability and lung function abnormalities. Thorax 1984; 39: 604-607.

59. Wright PH, Hanson A, Kreel L, Capel LH. Respiratory function changes after asbestos pleurisy. Thorax 1980; 35: 31-36.

60. Miller A, Teirstein AS, Selikoff IJ. Ventilatory failure due to asbestos pleurisy. Am J Med 1983; 75: 911-919.

61. Lumley KPS. Physiological changes in asbestos pleural disease. In: Walton WH, ed. Inhaled particles IV. Pergammon Press 1977; 781-788.

62. Fridriksson HV, Hedenstrom H, Hillerdal G, Malmberg P. Increased lung stiffness in persons with pleural plaques. Eur J Respir Dis 1981; 62: 412-424.

63. Epler GR, McLoud TC, Gaensler EA. Normal chest roentgenograms in chronic diffuse infiltrative lung disease. New Engl J Med 1978; 27: 934-939.

64. Jarvholm B, Sanden A. Pleural plaques and respiratory function. Am J Ind Med 1986; 10: 419-426.

65. Hilt B, Lien JT, Lund-Larsen PG. Lung function and respiratory symptoms in subjects with asbestos-related disorders: a cross-sectional study. Am J Ind Med 1987; 11: 517-528.

66. Oliver LC, Eisen EA, Green R, Sprince NL. Asbestos-related pleural plaques, exposure, and lung function. Am Rev Respir Dis 1987; 135 (abstract): A19.

67. Hedenstierna G, Alexandersson R, Kolnodin-Hedman B, Szamosi A, Tollqvist J. Pleural plaques and lung function in construction workers exposed to asbestos. Eur J Respir Dis 1981; 62: 111-122.

68. Ohlson G, Bodin I, Rydman T, Hogstedt C. Ventilatory decrements in former asbestos cement workers: a four year follow-up. Br J Ind Med 1985; 42: 612-616.

69. Sluis-Cremer GK. Pathoradiologic correlation on 108 cases of asbestosis proved at post mortem. XIV Internation Congress on Occupational Health, Madrid, 1963, p.608-610.

70. William R, Hugh-Jones P. The significance of lung function changes in asbestosis. Thorax 1960; 15: 109-119.

71. Leathart GL. Pulmonary function tests in asbestos workers. Transactions of the Society of Occupat Med 1968; 18: 49-59.

72. Becklake MR. Lung function. Biological effects of Asbestos, 1973, Lyon, International Agency for Research on Cancer, p. 31-39.

73. Jodoin G, Gibbs GW, Macklem PT, McDonald JC, Becklake MR. Early effects of asbestos exposure on lung function. Am Rev Respir Dis 1971; 104: 525-535.

74. Churg A, Wright JL, Wiggs B, Pare PD, Lazar N. Small airway disease and mineral dust exposure. Am Rev Respir Dis 1985; 131: 139-143.

75. Begin R, Masse S, Sebastien P, Bosse J, Rola-Plezczynski M, et al. Asbestos exposure and retention as determinants of airway disease and asbestos alveolitis. Am Rev Respir Dis 1986; 134: 1176-1181.

76. Siemsen JK, Grebe SF, Sargent EN, Wentz D. Pulmonary concentrations of 67Ga in pneumoconiosis. AJR 1974; 120: 815-20.

77. Begin R, Cantin A, Drapeau G, Lamoureux G, Boctor M et al. Pulmonary uptake of Gallium-67 in asbestos exposed humans and sheep. Am Rev Respir Dis 1983; 127: 623-630.

78. Begin R, Rola-Pleszczynski M, Drapeau G, Lamoureux G, Masse S. Pulmonary accumulation of Gallium-67 in asbestos; what does it mean? Chest 1982: 216.

79. Ferris BG, ed. Epidemiology Standardization Project. Am Rev Respir Dis 1978; 118 (suppl II): 1-88.

80. Mahler DA, Weinberg DH, Wells CK, Feinstein AR. The measurement of dyspnea: contents, interobserver agreement, and physiologic correlates of two new clinical indexes. Chest 1984; 85: 751-758.

81. Stoller JK, Ferranti R, Feinstein AR. Further specification and evaluation of a new clinical index for dyspnea. Am Rev Resp Dis 1986; 134: 1129-1134.

82. Mahler DA, Matthay RA, Snyder PE, Wells CK, Loke J. Sustained released theophylline reduces dyspnea in non-reversible obstructive airway disease. Am Rev Respir Dis 1985; 131: 22-25.

83. American Thoracic Society. Snowbird workshop on standardization of spirometry. Am Rev Respir Dis 1979; 119: 881-888.

84. Jones NL, Campbell EJM. Clinical exercise testing, 2nd ed. Philadelphia, WB Saunders Co. 1982.

85. Jones NL, Makrides L, Hitchcock, Chypchan T, McCartney N. Normal standards for an incremental progressive cycle ergometer test. Am Rev Respir Dis 1985; 131: 700-708.

86. Borg GAV, Noble B. Perceived exertion. In: Wilmore JH, ed. Exercise and sports science reviews. Vol 2. New York: Academic Press 1974; 131-152.

87. Borg GAV. Medicine and Science in Sports and Exercise 1982; 14: no.5 377-381 and 406-411.

88. Bisson G, Drapeau G, Lamoureux G, Cantin A, Rola-Pleszczynski M, Begin R. Computer based quantitative analysis of Ga-67 uptake in normal and diseased lungs. Chest 1983; 84: 513-518.

89. Begin R, Rola-Pleszczynski M, Sirois P, Masse S, Nadeau D, Bureau MA. Sequential analysis of the bronchoalveolar milieu in conscious sheep. J Appl Physiol Respir Environ Exercise Physiol 1981; 50: 665-671.

90. Begin R, Rola Pleszczynski M, Masse S et al. Asbestos induced lung injury in conscious sheep: the initial alveolitis. Environ Res 1983; 30: 193-210.

91. Begin R, Rola Pleszczynski M, Masse S, Nadeau D, Drapeau G. Assessment of progression of asbestosis in the sheep modely by bronchoalveolar lavage and pulmonary function tests. Thorax 1983; 38: 119-157.

92. Ernst P, Shapiro S, Dales RE, Becklake MR. Determinants of respiratory symptoms in insulation workers exposed to asbestos and synthetic mineral fibers. Br J Ind Med 1987; 44: 90-95.

93. Sargent EN, Boswell WD, Ralls PW, Markovitz A. Subpleural pads in patients exposed to asbestos: distinction from non-calcified pleural plaques. Radiology 1984; 152: 273-276.

94. Lambert R, Bisson G, Lamoureux G, Begin R. Gallium-67 Thoracic scan and pleural disease in asbestos workers. J Nucl Med 1985; 26: 600-603.

95. Picado C, Laporta D, Grassino A, Cosio M, Thibodeau M, Becklake MR. Mechanisms affecting exercise performance in subjects with asbestos-related pleural disease. Lung 1987; 165: 45-57.

96. Burdon JGW, Killian KJ, Jones WC. Pattern of breathing during exercise in patients with interstitial lung disease. Thorax 1983; 38: 778-784.

97. Killian KJ, Bucens DD, Campbell EJM. Effect of breathing patterns on the perceived magnitude of added loads of breathing. J Appl Physiol 1982; 52: 578-584.

98. Pope H, Holloway R, Campbell EJM. The effect of elastic and resistive loading of inspiration on the breathing of conscious men. Respir Physiol 1968; 4: 363-372.

99. Bland S, Lazaron L, Dyck G, Cherniack RM. The influence of the chest wall on respiratory rate and depth. Respir Physiol 1967; 3: 47-54.

100. Grimby G, Goldman M, Mead J. Respiratory muscle action inferred from rib cage and abdominal V-P partitioning. J Appl Physiol 1976; 41: 739-751.

ATS - DLD - 78-A Questionnaire

Pour l'usage du bureau

1 2 3

NUMERO D'IDENTIFICATION

4 5 6 7 8 9

NUMERO DE CARTE

1
10

NOM _____

ADRESSE _____

_____

_____

(code postal)

11 12 13 14 15 16

NUMERO DE TELEPHONE _____

INTERVIEWEUR _____

17 18 19

DATE _____

20 21 22 23 24 25

(année) (mois) (jour)

Pour l'usage du bureau

RENSEIGNEMENTS DEMOGRAPHIQUES

i. Date de naissance _____ _____ _____
année mois jour

26 27 28 29 30 31

ii. Lieu de naissance _____

32 33

iii. Sexe 1. masculin _____
2. féminin _____

34

iv. Etat civil 1. célibataire ____
2. marié(e) ____
3. veuf(ve) ____
4. séparé(e) ____
5. divorcé(e) ____

35

v. Race 1. blanche ____
2. noire ____
3. orientale ____
4. américidienne ____
5. autres (spécifiez) _____

36

vi. Langue maternelle 1. français ___
2. anglais ___
3. autres(spécifiez)___

37

vii. Dernière année scolaire terminée _____

Exemple: a complété l'école secondaire 11
a complété le CEGEP 13

38 39

viii. Vous considérez-vous bilingue (français-anglais)?

1. non ___
2. un peu ___
3. moyen ___
4. beaucoup ____

ix. Nom et adresse de votre employeur.

_____
_____
_____

x. Titre d'emploi: _____
_____

SYMPTOMES RESPIRATOIRES

Les questions suivantes concernent principalement vos poumons. Vous êtes prié de répondre autant que possible par "oui" ou "non". Si vous hésitez entre "oui" et "non", répondez "non".

1. TOUX

A. Toussez-vous habituellement? (tenez compte de la toux en fumant la première cigarette de la journée ou lors de la première sortie à l'extérieur. Excluez le nettoyage de la gorge).

1. oui ___ 2. non ___ 40

Si vous avez répondu "non", passez à la question C.

B. Toussez-vous habituellement au moins 4 à 6 fois par jour pendant 4 jours ou plus par semaine?

1. oui ___ 2. non ___ 41

C. Toussez-vous habituellement en vous levant ou en vous réveillant le matin?

1. oui ___ 2. non ___ 42

D. Toussez-vous habituellement pendant le reste de la journée ou pendant la nuit?

1. oui ___ 2. non ___ 43

Si vous avez répondu "oui" à au moins une des questions précédentes (soit 1A, B, C ou D), répondez aux questions suivantes. Si non, passez à la question 2A.

E. Toussez-vous habituellement comme cela la plupart des jours pendant au moins trois mois de suite chaque année?

1. oui ___ 2. non ___ 44

F. Depuis combien d'années avez-vous cette toux?

Nombre d'années _____ 45 46

2. EXPECTORATIONS (crachats)

A. Ramenez-vous habituellement des crachats qui viennent des poumons? (Tenir compte des crachats en fumant la première cigarette de la journée ou lors de la première sortie à l'extérieur. Négligez les crachats venant du nez. Tenir compte des crachats avalés).

1. oui ___ 2. non ___ 47

(Si vous avez répondu "non", passez à la question C.)

B. Ramenez-vous habituellement des crachats qui viennent des poumons au moins 2 fois par jour pendant 4 jours ou plus par semaine?

1. oui ___ 2. non ___ 48

C. Ramenez-vous habituellement des crachats qui viennent des poumons en vous levant ou en vous réveillant le matin?

1. oui ___ 2. non ___ 49

D. Ramenez-vous habituellement des crachats qui viennent des poumons pendant le reste de la journée ou pendant la nuit?

1. oui ___ 2. non ___ 50

Si vous avez répondu "oui" à au moins une des questions précédentes (soit 2A, B, C, ou D), répondez aux questions suivantes. Si non, passez à la question 3A.

E. Ramenez-vous habituellement des crachats comme cela la plupart des jours pendant au moins trois mois de suite chaque année?

1. oui ___ 2. non ___ 51

F. Depuis combien d'années produisez-vous ces crachats?

Nombre d'années ___ 52 53

3. EPISODES DE TOUX ET DE CRACHATS

A. Avez-vous déjà eu des périodes ou des épisodes de toux et de crachats (augmentés*) d'une durée de trois semaines ou plus chaque année?

* (pour les personnes qui habituellement toussent et/ou ramènent des crachats de leurs poumons).

1. Oui ___ 2. non ___ 54

Si "oui" à la question 3A

B. Pendant combien d'années avez-vous eu au moins un tel épisode par année?

Nombre d'années ___ 55 56

Pour l'usage du bureau

4. SIFFLEMENT DANS LES POUMONS (Respiration sifflante)

Vous arrive-t-il parfois en respirant d'entendre des sifflements ou des "ailements" dans vos poumons?

A. Lorsque vous avez un rhume?

1. oui ___ 2. non ___ 57

B. Parfois, même lorsque vous n'avez pas de rhume?

1. oui ___ 2. non ___ 58

C. La plupart des jours ou des nuits?

1. oui ___ 2. non ___ 59

Si "oui" à 4A, B, ou C

D. Depuis combien d'années cela vous arrive-t-il?

Nombre d'années ____ 60 61

5. A. Avez-vous déjà eu une crise de sifflements (ailements) qui vous ait essoufflé?

1. oui ___ 2. non ___ 62

Si "oui" à 5A

B. Quel âge aviez-vous lors de la première crise?

Age ____ 63 64

C. Avez-vous déjà eu plus d'une crise?

1. oui ___ 2. non ___ 65

D. Avez-vous déjà eu besoin de médicaments ou de traitements pour cette (ces) crise(s)?

1. oui ___ 2. non ___ 66

6. ESSOUFFLEMENT

Si vous êtes handicapé par une condition autre que cardiaque ou pulmonaire qui vous empêche de marcher normalement, décrivez-la.

Nature de la condition _____ 67

_____

_____

A. Devenez-vous essoufflé quand vous vous dépêchez sur un terrain plat ou quand vous montez une pente légère?

1. oui ___ 2. non ___ 68

Si "oui" à la question 6A

B. Devez-vous marcher plus lentement que les gens de votre âge sur un terrain plat parce que vous devenez essoufflé?

1. oui ___ 2. non ___ 69

C. Vous arrive-t-il de vous arrêter pour reprendre votre souffle quand vous marchez à votre rythme sur un terrain plat?

1. oui ___ 2. non ___ 70

D. Vous arrive-t-il de vous arrêter pour reprendre votre souffle après avoir marché environ 100 verges (300 pieds) (ou après quelques minutes) sur un terrain plat?

1. oui ___ 2. non ___ 71

E. Etes-vous trop essoufflé pour quitter la maison ou devenez-vous essoufflé en vous habillant ou en vous déshabillant?

1. oui ___ 2. non ___ 72

F. Depuis combien d'années êtes-vous essoufflé comme cela?

Nombre d'années _____ 73 74

7. RHUMES DE POITRINE ET MALADIES PULMONAIRES

A. Lorsque vous attrapez un rhume, s'agit-il la plupart du temps d'un rhume de poitrine? (La plupart du temps veut dire ici plus de la moitié du temps).

1. oui ___ 2. non ___ 8. je n'ai jamais de rhume ___ 75

B. Au cours des trois dernières années, avez-vous eu une maladie des poumons qui vous ait empêché de travailler ou obligé à rester à la maison ou au lit?

1. oui ___ 2. non ___ 76

Si "oui" à 7B

C. Avez-vous ramené des crachats de vos poumons lors de l'une ou l'autre de ces maladies pulmonaires?

1. oui ___ 2. non ___ 77

D. Au cours des trois dernières années, combien de ces maladies, avec une quantité des crachats augmentés, ont duré une semaine ou plus?

Nombre de maladies ___ Aucune maladie ___ 78 79

NUMERO DE CARTE

Pour l'usage du bureau

2
10

ANTECEDENTS MEDICAUX

8. Avez-vous souffert de maladie(s) des poumons avant l'âge de seize ans?

1. oui ___ 2. non ___ 11

9. A. Avez-vous déjà souffert de bronchite aigüe?

1. oui ___ 2. non ___ 12

Si "oui" à 9A

B. Un médecin vous a-t-il dit que vous aviez cette maladie?

1. oui ___ 2. non ___ 13

C. A quel âge remonte votre première bronchite aigüe?

1. Age ___ 14 15

10. A. Avez-vous déjà souffert de pneumonie? (inclure les broncho-pneumonies).

1. oui ___ 2. non ___ 16

Si "oui" à 10A

B. Un médecin vous a-t-il dit que vous aviez cette maladie?

1. oui ___ 2. non ___ 17

C. A quel âge avez-vous eu votre première pneumonie?

Age ___ 18 19

11. A. Avez-vous déjà souffert de fièvre des foins?

1. oui ___ 2. non ___ 20

Si "oui" à 11A

B. Un médecin vous a-t-il dit que vous aviez cette maladie?

1. oui ___ 2. non ___ 21

C. A quel âge avez-vous commencé à en souffrir?

Age ___ 22 23

12. A. Avez-vous déjà souffert de bronchite chronique?

1. oui ___ 2. non ___ 24

Si "oui" à 12A

B. En souffrez-vous toujours?

1. oui ___ 2. non ___ 25

C. Un médecin vous a-t-il dit que vous aviez cette maladie?

1. oui ___ 2. non ___ 26

D. A quel âge avez-vous commencé à en souffrir?

Age ___ 27 28

13. A. Avez-vous déjà souffert d'emphysème?

1. oui ___ 2. non ___ 29

Si "oui" à 13A

B. En souffrez-vous toujours?

1. oui ___ 2. non ___ 30

C. Un médecin vous a-t-il dit que vous aviez cette maladie?

1. oui ___ 2. non ___ 31

D. A quel âge avez-vous commencé à en souffrir?

Age ___ 32 33

14. A. Avez-vous déjà souffert d'asthme?

1. oui ___ 2. non ___ 34

Si "oui" à 14A

B. En souffrez-vous toujours?

1. oui ___ 2. non ___ 35

C. Un médecin vous a-t-il dit que vous aviez cette maladie?

1. oui ___ 2. non ___ 36

D. A quel âge avez-vous commencé à en souffrir?

Age ___ 37 38

E. Si vous n'en souffrez plus, à quel âge votre asthme a-t-il cessé?

Age ___ 39 40

F. Avez-vous actuellement besoin de traitements ou de médicaments pour l'asthme?

1. oui ___ 2. non ___ 41

15. A. Avez-vous déjà souffert de tuberculose pulmonaire?

1. oui ___ 2. non ___ 42

Si "oui" à 15A

B. Un médecin vous a-t-il dit que vous aviez cette maladie?

1. oui ___ 2. non ___ 43

C. A quel âge avez-vous commencé à en souffrir?

Age ___ 44 45

D. Quelle sorte de traitement avez-vous suivi?

1. aucun ____
2. médicaments ____
3. opération ____
4. autres (spécifiez) _____ 46

E. Quelle a été la durée du traitement?

1. En mois ____ 47 48

16. A. Avez-vous déjà souffert de pleurésie?

1. oui ___ 2. non ___ 49

Si "oui" à 16A

B. Un médecin vous a-t-il dit que vous aviez cette maladie?

1. oui ___ 2. non ___ 50

C. A quel âge avez-vous eu votre première pleurésie?

Age ___ 51 52

17. A. Avez-vous déjà souffert de troubles des sinus?

1. oui ___ 2. non ___ 53

Si "oui" à 17A

B. Un médecin vous a-t-il dit que vous aviez cette maladie?

1. oui ___ 2. non ___ 54

C. A quel âge avez-vous commencé à en souffrir?

Age ___ 55 56

18. Avez-vous déjà:

A. Eu d'autres maladies des poumons?

1. oui ___ 2. non ___ 57

Si oui, spécifiez _____

_____

Age ____

B. Subi une opération à la poitrine ou aux poumons?

1. oui ___ 2. non ___ 58

Si oui, spécifiez _____

_____

Age ____

C. Subi des blessures à la poitrine?

1. oui ___ 2. non ___ 59

Si oui, spécifiez _____

_____

Age ____

19. A. Un médecin vous a-t-il déjà dit que vous aviez des troubles cardiaques?

1. oui ___ 2. non ___ 60

Si "oui" à 19A

B. Avez-vous été soigné pour des troubles cardiaques au cours des 10 dernières années?

1. oui ___ 2. non ___ 61

Si "oui" spécifiez _____

_____

20. A. Un médecin vous a-t-il déjà dit que vous faisiez de l'hypertension? (haute pression)

1. oui ___ 2. non ___ 62

Si "oui" à 20A

B. Avez-vous été soigné pour de l'hypertension (haute pression) au cours des 10 dernières années?

1. oui ___ 2. non ___ 63

Pour l'usage du bureau

CIGARETTE

21. A. Avez-vous déjà fumé la cigarette? ("non" signifie moins de 20 paquets de cigarettes ou 400 grammes de tabac au cours de votre vie, ou moins d'une cigarette par jour pendant un an).

1. oui ___ 2. non ___ 64

Si "oui" à 21A

B. Fumez-vous actuellement la cigarette ou avez-vous fumé depuis un mois?

1. oui ___ 2. non ___ 65

C. Quel âge aviez-vous lorsque vous avez commencé à fumer la cigarette régulièrement?

Age ___ 66 67

D. Si vous avez complètement cessé de fumer la cigarette, quel âge aviez-vous quand vous avez arrêté?

Age ___

Cochez si vous fumez toujours ___ 68 69

E. Combien de cigarettes fumez-vous par jour actuellement?

Nombre de cigarettes par jour ___ 70 71

F. Pendant tout le temps que vous avez fumé, combien de cigarettes fumiez-vous par jour en moyenne?

Cigarettes par jour ___ 72 73

G. Est-ce que vous respirez ou respiriez la fumée?

1. pas du tout ___
2. peu ___
3. modérément ___
4. profondément ___ 74

H. Pendant tout le temps que vous avez fumé la cigarette, fumiez-vous des bouts filtres?

0. jamais ___
1. moins que la moitié du temps ___
2. la moitié du temps ___
3. plus que la moitié du temps ___
4. toujours ___ 75

I. Pendant tout le temps que vous avez fumé la cigarette, quelle sorte fumiez-vous la plupart du temps?

1. régulier ___
2. King size ___
3. rouleuse (roulée à la main) ___ 76

NUMERO DE CARTE

Pour l'usage du bureau

3
10

PIPE

22. A. Avez-vous déjà fumé la pipe régulièrement?

("oui" signifie plus de 400 grammes ou 8 blagues de tabac durant votre vie).

1. oui ___ 2. non ___

11

Si "oui" à 22A

B. Fumez-vous actuellement la pipe ou l'avez-vous fumée depuis un mois?

1. oui ___ 2. non ___

12

C. Quel âge aviez-vous lorsque vous avez commencé à fumer la pipe régulièrement?

Age ___

13 14

D. Si vous avez complètement cessé de fumer la pipe, quel âge aviez-vous quand vous avez arrêté?

Age ___ Cochez si vous fumez toujours la pipe ___

15 16

E. Combien de tabac fumez-vous par semaine actuellement?

___(blague(s) par semaine (une blague de tabac contient 50 grammes).

17 18

F. Pendant tout le temps que vous avez fumé la pipe, quelle quantité de tabac fumiez-vous par semaine en moyenne?

___blague(s) par semaine (une blague de tabac contient 50 grammes).

19 20

G. Est-ce que vous respirez ou respiriez la fumée de pipe?

1. pas du tout ___
2. peu ___
3. modérément ___
4. profondément ___

21

CIGARE/CIGARELLO

23. A. Avez-vous déjà fumé le cigare ou le cigarello régulièrement? ("oui" signifie plus d'un cigare ou cigarello par semaine, pendant un an).

1. oui ___ 2. non ___ 22

Si "oui" à 23A

B. Fumez-vous actuellement le cigare ou l'avez-vous fumé depuis un mois?

1. oui ___ 2. non ___ 23

C. Quel âge aviez-vous lorsque vous avez commencé à fumer le cigare régulièrement?

Age ___ 24 25

D. Si vous avez complètement cessé de fumer le cigare, quel âge aviez-vous quand vous avez arrêté?

Age ___ Cochez si vous fumez toujours le cigare ____ 26 27

E. Combien de cigares fumez-vous par semaine actuellement?

Nombre de cigares ___ 28 29

F. Pendant tout le temps que vous avez fumé le cigare, combien de cigares par semaine fumiez-vous en moyenne?

Nombre de cigares ___ 30 31

G. Est-ce que vous respirez ou respiriez la fumée du cigare?

1. pas du tout ___
2. peu ___
3. modérément ___
4. profondément ___ 32

H. Pendant tout le temps que vous avez fumé le cigare, quelle sorte fumiez-vous la plupart du temps?

1. mini (grandeur cigarette) ___
2. petit (cigarello) ___
3. grand (vrai cigare) ___ 33

ANTECEDENTS FAMILIAUX

24. Le médecin a-t-il déjà dit à un membre de votre famille qu'il souffrait d'une maladie pulmonaire chronique telle que:

	Père	Mère	Frères & Soeurs	
	1. oui	1. oui	1. oui	
	2. non	2. non	2. non	
	3. ne sais pas	3. ne sais pas	3. ne sais pas	
A. Bronchite chronique	____	____	____	34 35 36
B. Emphysème	____	____	____	37 38 39
C. Asthme	____	____	____	40 41 42
D. Cancer de poumons	____	____	____	43 44 45
E. Tuberculose	____	____	____	46 47 48
F. Autres maladies respiratoires	____	____	____	49 50 51
G. Eczéma ou urticaire	____	____	____	52 53 54
H. Fièvre des foins	____	____	____	55 56 57

25. Vos parents sont-ils toujours en vie?

Père	Mère	
1. oui ___	1. oui ___	
2. non ___	2. non ___	
3. ne sais pas ___	3. ne sais pas ___	58 59

26. Si vos parents sont morts, veuillez spécifier la cause de leur décès.

Père _____ 60 61

Mère _____ 62 63

27. Veuillez spécifier l'âge actuel de vos parents ou de leur décès.

Père _____ 64 65

Mère _____ 66 67

NUMERO DE CARTE

Pour l'usage du bureau

4
10

HISTOIRE PROFESSIONNELLE

28. A. Avez-vous déjà travaillé à plein temps (30 heures par semaine ou plus pendant 6 mois ou plus)?

1. oui ___ 2. non ___ 11

Si "oui" à 28A

B. 1. Avez-vous déjà travaillé dans un lieu poussiéreux durant un an ou plus?

1. oui ___ 2. non ___ 12

2. Spécifiez le travail et l'industrie _____

_____

3. Nombre d'années de travail ___ 13 14

4. L'exposition à la poussière était-elle

1. légère ___ 2. modérée ___ 3. sévère ___ 15

C. 1. Avez-vous déjà été exposé à des gaz ou des fumées chimiques à votre travail?

1. oui ___ 2. non ___ 16

2. Spécifiez le travail et l'industrie _____

_____

3. Nombre d'années de travail ___ 17 18

4. L'exposition était-elle

1. légère ___ 2. modérée ___ 3, sévère ___ 19

D. Quelle était votre profession habituelle, celle que vous avez eue le plus longtemps?

1. Profession _____

2. Nombre d'années de travail dans cette profession _____

3. Poste et titre de l'emploi _____ 20 21

3. Domaine ou industrie _____

E. Quel est votre travail actuel ou votre travail le plus récent?

1. Profession _____

2. Nombre d'années de travail dans cette profession _____ 22 23

3. Poste et/ou titre de l'emploi _____

4. Domaine ou industrie _____

5. Exercez-vous toujours cette profession?

   1. non ____
   2. oui, à temps plein ____
   3. oui, à temps partiel ____

6. Si vous n'exercez plus cette profession, quel âge aviez-vous au moment où vous l'avez quittée?

   ____

29. Maintenant que vous avez complété ce questionnaire, seriez-vous capable d'y répondre en anglais?

   1. Oui ___
   2. Non ___ 24

APPENDIX 2

Questionnaire sur la dyspnée (MDI)

Numéro d'identification	0 1 ___ ___ ___ (25 26 27 28 29)
Numéro de visite	0 1 (30 31)
Intervieweur	___ ___ ___ (32 33 34)
Date	___ ___ ___ ___ ___ ___ (35 36 37 38 39 40) (année) (mois) (jours)

1- INCAPACITE FONCTIONNELLE AU TRAVAIL

Les questions suivantes concernent vos activités au travail.

A. Avez-vous une incapacité physique autre que l'essoufflement, vous limitant dans vos activités au travail? 41

1-oui ___ 2-non ___

si OUI à 1A

Veuillez inscrire la nature de la condition limitante et passez à 2A: _____

_____

_____

B. Travaillez-vous présentement? 42

1-oui ___ 2-non ___

si NON à 1B

C. Avez-vous cessé de travailler ou pris votre retraite prématurée à cause d'essoufflement?

83

1. oui___ passez à 2A
7. non___ donnez la raison pour laquelle vous avez quitté le travail et passez ensuite à 2A

_____

_____

si OUI à 1B

D. Etes-vous capable d'accomplir vos activites habituelles au travail sans essoufflement?
4. oui___ passez à 2A, si "non" passez à 1E

E. Avez-vous à cause d'un problème d'essoufflement dû modifier vos activités au travail? (par exemple, devez-vous faire une de vos tâches régulières plus lentement qu'avant?)
3. oui___ passez à 2A, si "non" passez à 1F

F. Avez-vous à cause d'un problème d'essoufflement :
(1) abandonné une partie de votre travail, ou
(2) changé pour un travail moins difficile, ou
(3) diminué le nombre d'heures de travail par semaine.
2. oui ___ passez à 2A, si "non" passez à 1G

G. Avez-vous une incapacité dans vos activités au travail sans qu'il vous soit cependant possible de spécifier à quel degré?
8. oui___ passez à 2A
9. je ne sais pas____

2. INCAPACITE FONCTIONNELLE A LA MAISON

Les question suivantes concernent vos activité à la maison

A. Avez-vous une incapacité physique (autre que l'essoufflement) limitant vos activités à la maison.

1.oui___ 2.non___ 44

si OUI à 2A

Veuillez inscrire la nature de la condition limitante et cessez le questionnaire:

_____

_____

B. Pouvez-vous toujours faire vos activités habituelles à la maison à votre rythme normal sans être essoufflé? 45

4. oui___ passez à 3A

si NON à 2B

C. Avez-vous dû abandonner toutes ou la plupart de vos activités habituelles à cause d'essoufflement?
(par exemple êtes-vous dépendant d'une autre personne pour accomplir des tâches telles que le magasinage, la cuisine, l'entretien ménager ou avez-vous besoin d'aide pour vous vêtir ou même vous laver?)
1.oui___ passez à 3A, si "non" passez à 3D

D. Votre essoufflement vous a-t-il obligé à abandonner plusieurs (mais non toutes) de vos activités habituelles ou devez-vous faire presque toutes vos activités plus lentement.
2.oui___ passez à 3A, si "non" passez à 2E

E. Votre essoufflement vous a-t-il obligé à modifier vos activités à la maison? (par exemple, même si vous n'avez pas abandonné aucune de de vos activités faites-vous ces mêmes activités plus lentement ou moins fréquemment à cause de votre essoufflement?)
3.oui___ passez à 3 A , si "non" passez à 2F

F. Avez-vous une incapacité dans vos activités à la maison sans qu'il vous soit cependant possible de spécifier à quel degré?
8.oui___ passez à 3A
9.je ne sais pas_____

3. IMPORTANCE DE LA TACHE

Nous allons maintenant essayer de déterminer les tâches qui vous essoufflent.

A. Devenez-vous essoufflé lorsque vous êtes couché, assis ou que vous vous tenez debout? 46
0. oui___ passez à 4A, si "non" passez à 3B

B. Devenez-vous essoufflé lorsque vous vous habillez, vous vous lavez ou lorsque vous marchez pour aller à la salle de bain ou que vous marchez sur un terrain plat à pas lent.
1. oui___ passez à 4A, si "non" passez à 3C

C. Devenez-vous essoufflé lorsque vous faites certaines activités comme transporter un léger fardeau sur un terrain plat, marcher vigoureusement sur un terrain plat, monter une pente douce ou monter deux étages d'escalier?

2. oui___ passez à 4A, si "non" passez à 3D

D. Devenez-vous essoufflé lorsque vous faites certaines activités comme monter une pente abrupte, monter plus de deux étages d'escalier ou transporter un lourd sac d'épicerie sur un terrain plat?

3. oui___ passez à 4A si "non" passez à 3E

E. Devenez-vous essoufflé <u>seulement</u> lorsque vous faites certaines activités comme transporter de lourds paquets sur un terrain plat, transporter des paquets légers en montant des escaliers ou en courant?
4. oui___ passez à 4A

4. IMPORTANCE DE L'EFFORT

A. Etes-vous essoufflé au repos, assis ou couché. ___ 47
0.oui___ terminez le questionnaire ici,
si "non" continuez ci-dessous.

Nous allons maintenant essayer de déterminer la tâche la plus difficile que vous êtes capable de faire pendant au moins 5 minutes.
Inscrivez ici _____

B. Diriez-vous que vous faites cette tâche très lentement et en vous arrêtant plusieurs fois avant de la terminer ou d'abandonner?
1.oui___ terminez le questionnaire ici,
si "non" passez à 4C

C. Diriez-vous que vous faites cette tâche lentement avec une ou deux pauses pour reprendre votre souffle avant de la terminer ou d'abandonner?
2.oui___ terminez le questionnaire ici,
si "non" passez à 4D

D. Diriez-vous que vous faites cette tâche lentement mais sans pause pour reprendre votre souffle?
3.oui___ terminez le questionnaire ici,
si "non" passez à 4E

E. Diriez-vous que vous faites cette tâche vigoureusement, sans devoir vous arrêter pour reprendre votre souffle ou sans devoir ralentir pour vous reposer?
4.oui___ terminez le questionnaire ici.

APPENDIX 3

Borg Scale

Perception du niveau de difficulté de l'effort

0	non perceptible
0.5	très très facile (à peine perceptible)
1	très facile
2	facile
3	quelque peu difficile
4	moyennement difficile
5	
6	
7	très difficile
8	
9	très très difficile (quasi maximum)
10	maximum