PULMONARY FUNCTION IN QUEBEC ASBESTOS WORKERS

Relationship to Clinical Symptoms, Pulmonary Radiology Dust Exposure and Smoking

A thesis submitted to the Faculty of
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ABSTRACT

Asbestos is a fibrous silicate which is ubiquitous in modern living because of its many useful qualities. However, its inhalation may be associated with undesirable, even lethal, biological effects. A study of the effect of exposure to asbestos on miners and mill workers was carried out in the chrysotile industry of Quebec; subjects were studied by questionnaire, radiological and pulmonary function studies at rest and on exercise. The results of 1034 workers were related with the dust and effort involved in the jobs of the men.

The analysis of the results was based on a definition of pulmonary function profiles using five tests (residual volume, total lung capacity, maximal breathing capacity, timed vital capacity and maximal mid-expiratory flow rates): 44.3% of the subjects were found to lie in normal limits, 14.9% showed a restrictive profile, 14.3% an obstructive one, and 26.5% a mixed undifferentiated profile. These findings contrast with the conclusions of other series in that the obstructive profile was much more prominent in the present series.

The subjects in obstructive, normal and mixed undifferentiated profiles had as many and often more symptoms and specific radiological changes compared to the restrictive group.

When the subjects in these profile groups were compared in respect of dust, effort and smoking, it was found that the obstructive group had been exposed to more dust, effort and cigarette smoking than the restrictive one.

The differences in the lung function profiles developed by asbestos exposed workers can be explained in theory at least by the dynamic concept of the respiratory system and the laws of deposition, retention and clearance of particles and fibers.

RESUME

L'amiante est une fibre à base de silicates qui, à cause de ses multiples qualités, est indispensable dans le monde moderne. Cependant, l'inhalation de cette substance est associée à des effets biologiques indésirables et souvent mortels. Une étude des effets de la chrysotile chez des travailleurs de l'industrie de l'amiante du Québec a été faite. Les travailleurs ont été soumis à un questionnaire et ont passé une radiographie ainsi que des tests de fonction respiratoire au repos et à l'exercice. Les résultats des tests de 1034 travailleurs ont été ensuite reliés en degré d'exposition à la poussière et à l'effort déployé durant leur travail.

L'analyse des résultats s'est basée sur la définition de profils de fonction respiratoire utilisant cinq tests (volume résiduel, capacité totale, capacité respiratoire maximale, volume expiratoire maximal seconde et débit médian maximal): 44.3% des sujets se trouvaient dans des limites normales, 14.9% avaient un profil restrictif, 14.3% un profil obstructif, et 26.5% un profil mixte non différencié. Ces résultats contrastent avec les conclusions des autres études publiées, en ce que le profil obstructif est plus fréquent.

Les profils obstructif, normal et mixte non différencié avaient autant et souvent plus de symptômes et de changements radiologiques spécifiques que le groupe restrictif. Lorsque l'association de ces profils a été faite avec la poussière, l'effort et la consommation quotidienne de cigarettes, cette association a été plus marquée pour le profil obstructif que le restrictif.

Ces résultats peuvent être expliqués par le concept dynamique du système respiratoire et les lois de déposition, rétention et clearance des particules et des fibres.

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This study was undertaken as one of several in a multidisciplinary approach to the evaluation of the effects of asbestos exposure on health, carried out in the Dept. of Epidemiology and Health, McGill University, under the imaginative direction of Dr. J.C. McDonald. It is evident that the team contributing to the present study brought together administrative staff, epidemiologists, pulmonary physiologists, engineers, pulmonary function technicians, interviewers, industrial physicians, radiologists, programmers, computer experts, industrial hygienist. Adequate acknowledgment of everyone's help is impossible.

The administrative expertise and technical assistance of the following is gratefully acknowledged: Mr. Charles Rossiter, Drs. David Pengelly and Graham Gibbs, Mrs. Jocelyne Rosansky and Misses Margaret Collins and Thérèse Belleau, MM. Allen Greenberg and Jack Siemiatycki, and Drs. Grainger, Cartier and Dussault.

Finally, I would like to present my respects to Vice-Rector G. LaSalle and Deputy Minister M. LeClair who made possible a leave of absence and supported my application to the Medical Research Council for a Fellowship.

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GLOSSARY OF ABBREVIATIONS

ANTHROPOLOGY:

BSA : body surface area
F : female
Ht : height
M : male
Wt : weight

CARDIAC FUNCTION:

ECG : electrocardiogram
LH : left heart
RH : right heart

DUST EXPOSURE:

D : dust
Dust I : dust index expressed in MPPCF years
Dust II : dust index in dust years corrected for the number of pounds lifted during the actual number of working hours
d.y. : dust years
E : exercice or effort
MPPCF : millions of particles per cubic foot
W : work expressed in years

MISCELLANEOUS:

cm : centimeters
Kgs : kilogrammes
M^2 : square meter
no : number
subj : subjects
yrs : years

PULMONARY FUNCTION:

A-a difference : pressure difference between the alveoli and the arterial blood
ccCO/min/mmHg : cubic centimeter of carbon monoxide per minute per mm Hg of partial pressure of CO
C_{dyn} dynamic compliance
cmH_20/LPS : centimeter of water per liter per second
C_{st} : static compliance
$D_{LCO_{SB}}$: single breath diffusion capacity of the lung for CO
$D_{LCO_{SS}}$ rest: steady state diffusion capacity of the lung for CO at rest
$D_{LCO_{SS}}$ 200,400 or 600 : steady state diffusion capacity of the lung for CO at 200, 400, 600 Kilogram Meter per minute
D_{LO_2} : diffusion capacity of the lungs for O_2
ERV : expiratory reserve volume
exp. : expiration
Ext_{CO} : transfer factor or extraction of CO
f : frequency
FEV_1 : forced expiratory volume in one second expressed as percentage of vital capacity

$FEV_1\%$: percentage predicted of FEV_1
FEV_{75} : forced expiratory volume in 0.75 sec.
F_I : inspired concentration of a gas
F_E : expired concentration of a gas
F_A : alveolar concentration of a gas
FRC : functional residual capacity
HbCO : carboxyhemoglobin
IC : inspiratory capacity
insp. : inspiration
K_{CO} : rate of CO uptake
KgmMmin or KMm : kilograms meter per minute
L : liter
L/cmH_2O : liter per centimeter of water
L/min or L/m : liter per minute
L/sec : liter per second
MBC : maximal breathing capacity
ME : mixing efficiency
P_A : partial pressure of alveolar gas
P_a : partial pressure of arterial gas
$P_{el\ max}$: maximal negative intrapleural pressure
%P : percentage predicted
R : rest
RV : residual volume
RV/TLC : residual volume as percentage of total lung capacity
Sat O_2 : hemoglobin saturation in oxygen
S_{CO} : hemoglobin saturation in CO
TLC : total lung capacity
$\dot{V}$: minute ventilation
VC : vital capacity
$\dot{V}_{CO}$: uptake of CO per minute
$\dot{V}_{CO_2}$: carbon dioxide production per minute
V_D : dead space
$\dot{V}_{O_2}$: oxygen consumption per minute
$\dot{V}/\dot{Q}$: ventilation/perfusion ratio
V_T : tidal volume

PROFILES:

def : definite
dom : dominant
obst : obstructive
rest : restrictive
undiff : undifferentiated

QUESTIONNAIRE:

B : breathlessness
C : cough
CI : chest illness
Cig : cigarettes per day
Cr : crepitations
Cy : cyanosis
Sm : smoking

RADIOLOGY:

N : normal
PC : pleural changes alone
SIO : small irregular opacities alone
SIO-PC : combined small irregular opacities and pleural changes

STATISTICS:

S.D. : standard deviation to the mean
TV : total variance

1 - INTRODUCTION

Asbestos is the name given to a group of fibrous minerals composed of the silicates of magnesium and iron. Its unique combination of properties, such as resistance to heat and chemicals and its non-conductivity of electricity as well as modest cost, have resulted in this mineral being increasingly widely-used throughout the world (Gilson, 1965). It is now a common material of every day living and increasing quantities are being produced. The present production is more than four million tons a year, a remarkable increase compared to the three hundred tons of mineral produced in 1879 (Brodeur, 1968).

However, the inhalation of asbestos dust is associated with important undesirable biological effects which include impairment of pulmonary function, asbestosis and cancer (Miner, 1965). As these effects are so little amenable to therapy and can be incapacitating at an early age, there have been many investigations such as the present one examining the nature of this association so that diagnosis, prophylaxis and treatment may be more efficient. Asbestosis is, of course, one stage in the natural history of subjects exposed to asbestos dust and more complete data on the "pre or latent" asbestosis period is of great potential and therapeutic importance. The present study also contributes to this area.

Furthermore, the question has been raised as to whether the different types of asbestos have different biological effects, and to what extent the process during which exposure occurs (i.e. mining, milling or manufacturing) determines the effects on man (Wright, 1969).

The asbestos industry of Quebec lends itself rather well to a study of the effects of exposure during the mining and milling of chrysotile asbestos. As shown in Figure 1-1, the industry is localized to that part of Quebec found to the east of Montreal known as the Eastern Townships, centered around the towns of Asbestos and Thetford-Mines.

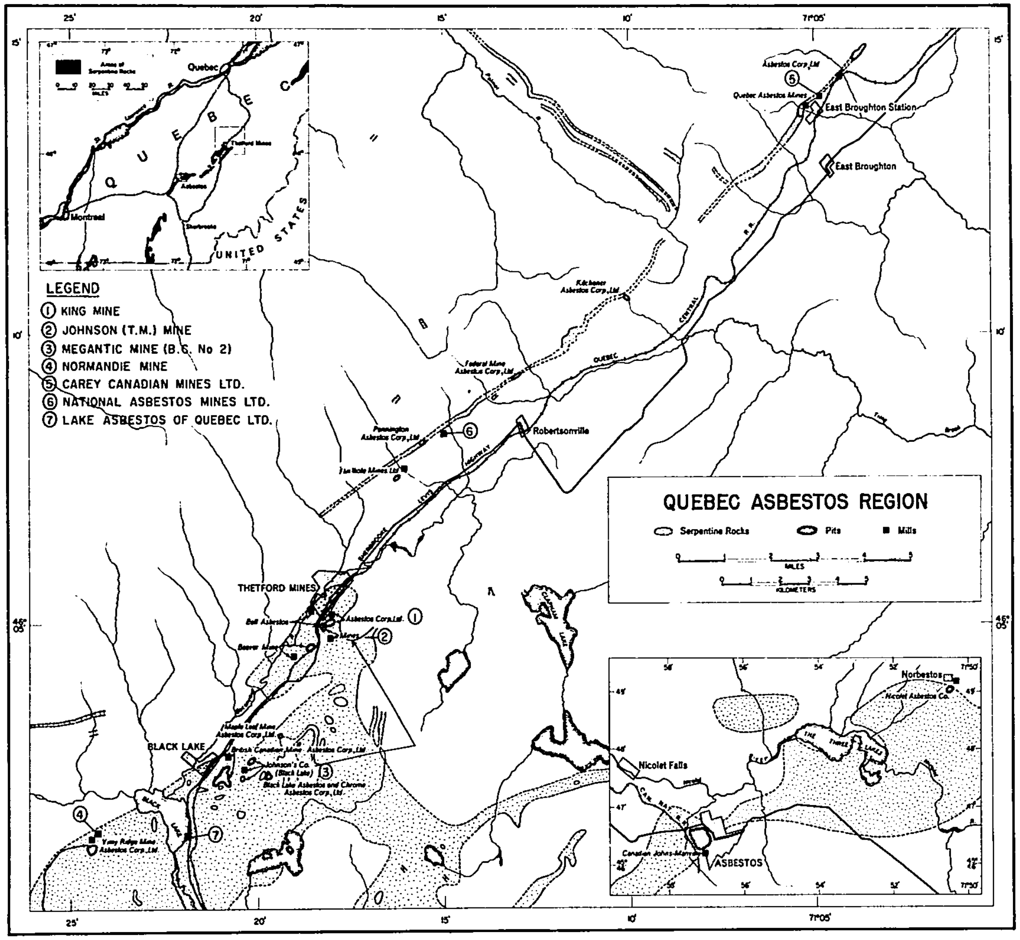
The largest known asbestos deposits outside the Soviet Union are to be found in this area and are entirely chrysotile asbestos. Quebec accounts for approximately one-third of the world's chrysotile asbestos production which implies a reasonably large work force.

In the narrow belt stretching north-eastward from Asbestos to East Broughton are ten mines, eight are of the open pit variety and two are underground operations (Figures 1-2, 1-3, 1-4). The ore is processed locally in mills and there are some manufacturing plants in the area. Thus, the recommendations of a Working Group on Asbestos and Cancer (UICC, 1965) to coordinate epidemiological studies of primary and secondary industry could be followed.

Asbestos has been mined in Quebec for almost 100 years (since 1878) and the labor force has always been remarkably stable. Measurements of health such as questionnaire, physical examination and radiographs and measurements of dust exposure, such as dust concentrations and physical effort, are available on a large number of exposed workers over a long period of time.

FIGURE 1-1 - THE MINING AREA OF EASTERN TOWNSHIPS

Bureau of Mines Information Circular 7880



465673-58 (Face p. 8)

FIGURE 2.—Map of Quebec asbestos region.
(Courtesy of Prentice-Hall Inc.)

FIG. 1-2 - THE JOHNS-MANVILLE MINE, ASBESTOS

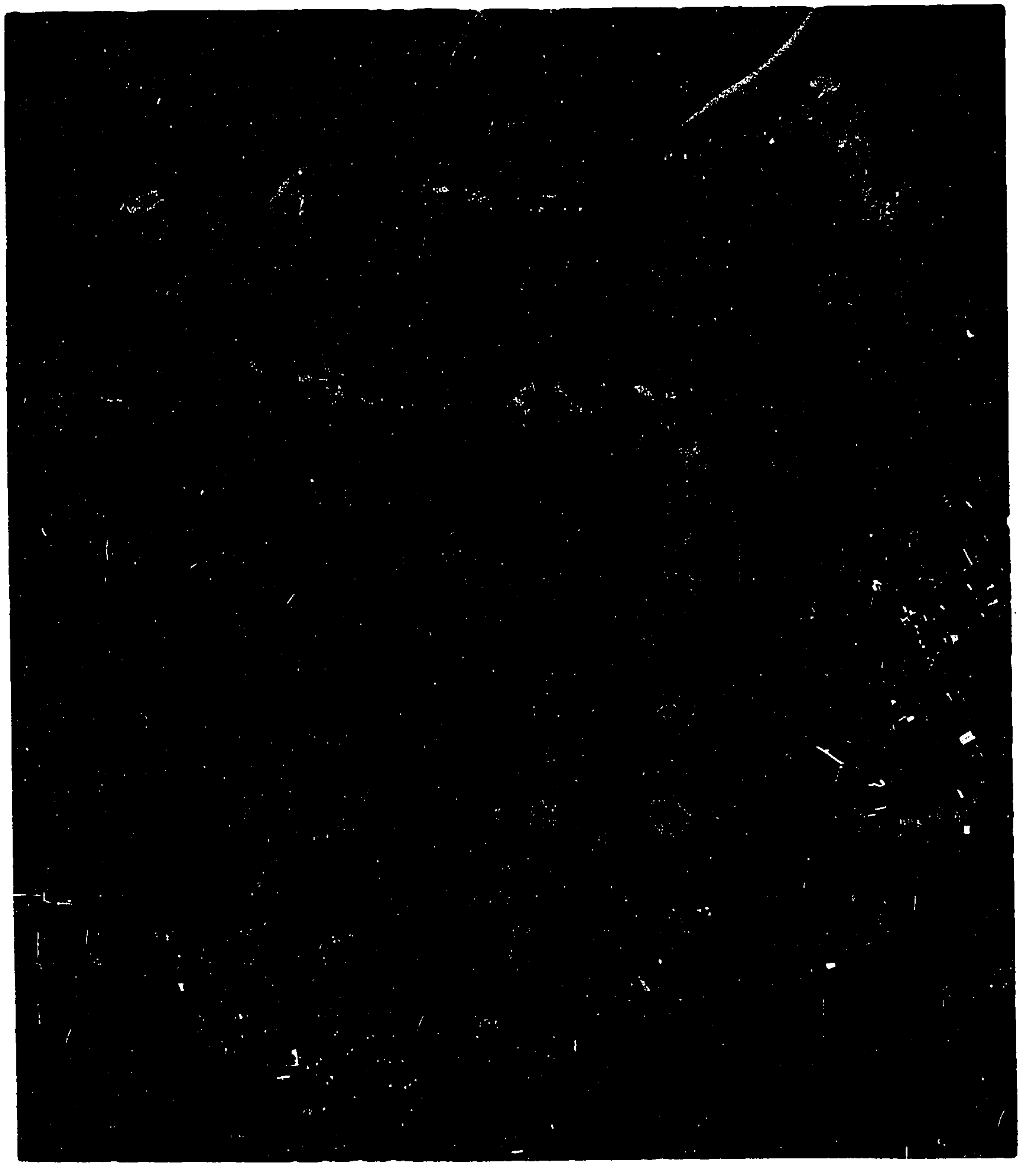


FIG. 1.2 THE JOHNS-MANVILLE MINE, ASBESTOS

FIG. 1-3 - THE KING BEAVER MINE, THETFORD MINE

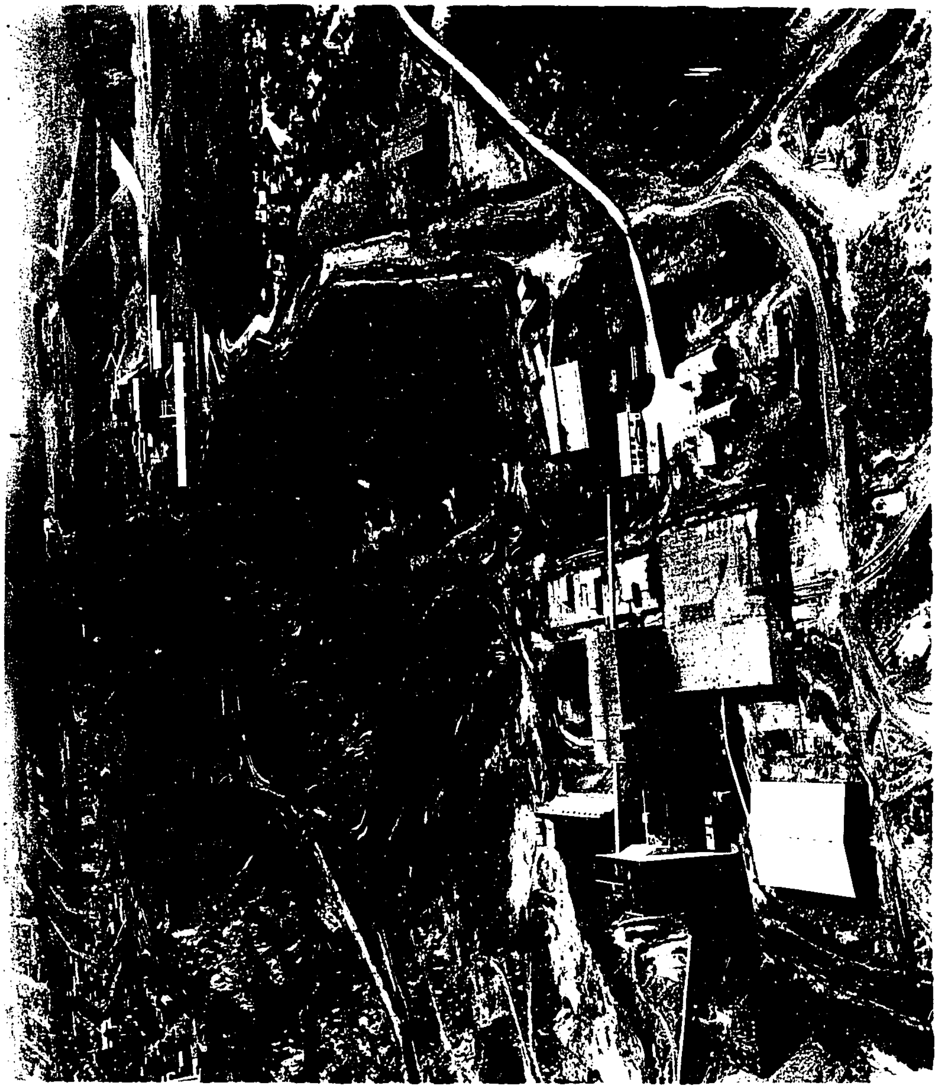


FIG. 1-3 - THE KING BEAVER MINE, THETFORD MINE

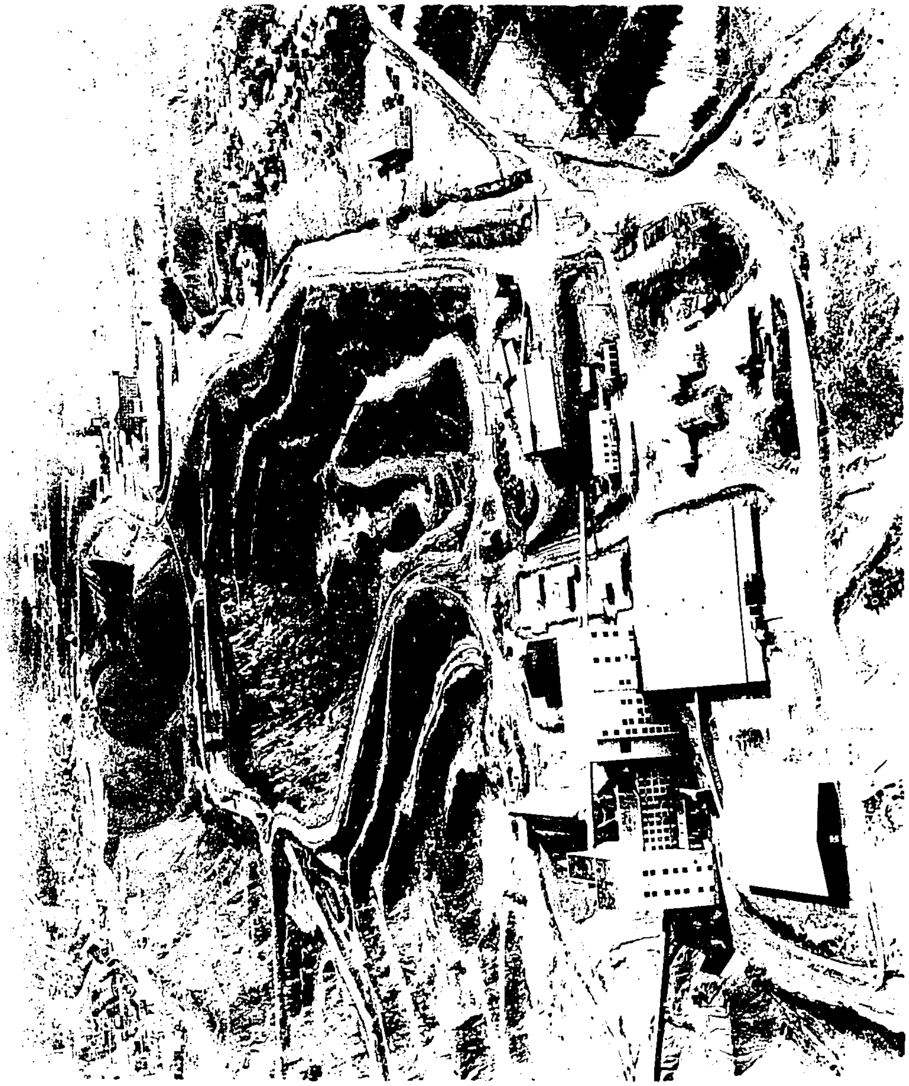


FIG. 1-4 - THE MEGANTIC MINE IN FRONT AND THETFORD MINE IN THE BACK

FIG. 1-4 - THE MEGANTIC MINE IN FRONT AND THETFORD MINE IN THE BACK

In 1966, an epidemiological survey was begun by the Department of Epidemiology and Health of McGill University to study the effects of asbestos exposure on the health of these Quebec workers. Exposure was measured by dust counts and a detailed occupational history, and several aspects of health were examined in relation to dust exposure. Cohort studies examined the mortality rates attributable to respiratory diseases, including lung cancer (McDonald et al, 1971). A review of 11,000 chest radiographs on past and present workers described the relationship of changes in the chest radiograph to dust exposure. In a study of current workers, health was assessed by a questionnaire, chest roentgenogram and tests of pulmonary function (Gibbs et al, 1971; 1972; Becklake et al, 1970, 1972; McDonald et al, 1972; Rossiter et al, 1972). This thesis describes the results of the pulmonary function tests and examines their relationship with clinical findings, dust exposure and smoking.

2 - REVIEW OF THE LITERATURE

1. GENERAL: historical review and definition of "asbestosis"

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4. CONCLUSIONS

1. GENERAL:

Historical Review:

The association between occupation and health has been observed from very early times, for example, an Egyptian papyrus describes the difficulties of those who must work (Sigerist, 1936) and the influence of certain occupations on health was noted in the Greco-Roman world. However, it was only in the late Middle Ages that the relationship was systematically explored. Metal workers and miners were among the earliest occupational groups to be studied because of economic and technological developments. In 1472, Ulrich Ellenbog, a physician of Augsburg, was responsible for the first publication to deal with the hazards facing an occupational group (Rosen, 1964). The purpose of his eight page brochure was to inform goldsmiths and others on how to avoid the poisonous effects of metals such as mercury and lead (Koelsch and Zoepfl, 1927).

The increased volume of trade during the fifteenth century demanded an expanding currency which could only be met by a greater supply of gold and silver. The mines of Central Europe were deepened to meet this need but the occupational hazards also increased, fostering the first books on diseases and accidents of miners. The first such account is to be found in a treatise on mining by Agricola in 1556 (Rosen, 1964). Eleven years later, in 1567, the first monograph devoted exclusively to the occupational diseases of mine and smelter workers appeared at Diblingen in Germany. The etiology, pathogenesis, prevention, diagnosis, and therapy were discussed by Paracelsus in it, and this had a stimulating influence on occupational medicine.

This trend, begun by Agricola and Paracelsus, resulted in Ramazzini's comprehensive Discourse on the Diseases of Workers, published in 1700. It is a synthesis of knowledge on occupational disease from the earliest times to the eighteenth century and established a new branch of medical study in which the patient's occupation was taken into account.

Ramazzini wrote: "It must be confessed that many arts are the cause "of grave injury to those who practise them. Many an artisan has looked "at his craft as a means to support life and raise a family, but all he has "got from it is some deadly disease, with the result that he has departed "this life cursing the craft to which he applied himself." (Wright, 1940). He goes on to say that the lungs of miners are especially affected "since "they take in with the air mineral spirits and are the first to be keenly "aware of injury" and "Hence, the mortality of those who dig minerals in "mines is very great, and women who marry men of this sort marry again "and again". According to Agricola, at the mines in the Carpathian mountains, women have been known to marry seven times (Ramazzini in Rosen, 1964).

Asbestos, the subject of this thesis, has been of increasing interest to the medical profession recently, but it is not a new material. Thousands of years ago, asbestos was in everyday use by Stone Age men and consequently they must have mined it or known where it could be obtained (Kiviluoto, 1965). About 4500 years ago, it was used in Finland as a cementing agent in the preparation of clay pottery and such asbestos ceramics were used over a period of 3000 years. However, at approximately 500 AD, their use in Finland and its neighbouring countries slowly ceased and was only reintroduced some 1000 years later (Meimander, 1954).

Definition of Asbestosis

Exposure to asbestos is associated with a number of biological effects. In 1907, Murray reported the first case of asbestosis, and six years later, in 1913, Marchand and Fahr each presented to the Hamburg Medical Society a subject who died from this disease. Two autopsy series were reported in 1918: that of Hoffmann with 13 cases and that of Pancoast et al comprising 17 patients. Laboratory studies first appeared in 1927 when Cooke described the radiological changes, and in 1929, when Wood reported the first pulmonary function measurement, a fall in Vital Capacity (VC) in one case of asbestosis. Stone confirmed this finding 11 years later in a further 13 patients (1940).

The present concensus concerning asbestosis may be summarized as follows. The inhalation of asbestos fibers and dust over some ten to twenty years can produce a pneumoconiosis known as asbestosis characterised by pulmonary and pleural fibrosis. The gross pathology of advanced asbestosis includes widespread pulmonary fibrosis and diffuse pleural adhesions. Bullae are not infrequent and bronchiectasis may be present (Heard et al, 1961, Leathart, 1965). The microscopic pathology has been recently described as "a diffuse, nonnodular pulmonary fibrosis "which affects alveolar walls, interlobular septums, and pleural "surfaces." (Tepper and Radford, 1970). This is in contrast to earlier reports (Vorwald et al, 1951) which described the early asbestotic lesion as consisting of a dense peribronchiolar fibrosis with dust-containing macrophages with, in some instances, a perivascular fibrosis as well as an endarteritis with intimal hyperplasia (Lanza, 1963).

The principal symptoms reported are dyspnea and cough which increase in severity as the disease progresses (Murray, 1907; Wood et al, 1930; Roemheld et al, 1940; Luton et al, 1946; Bastenier et al, 1953; Gernez-Rieux et al, 1954;Wright, 1955; Sartorelli, 1957; Amsler, 1958; Leathart, 1960; Williams et al, 1960; Scansetti et al, 1960; Bader et al 1961; Thomson et al, 1961; Bollinelli et al, 1963; De Rosa et al, 1964; Pellet et al, 1964; Vaerenberg 1964; Porin, 1965; Schaaning et al, 1965; Kleinfeld et al, 1966a; Gandevia, 1967; Hany et al, 1967; Ferris et al, 1971; Jodoin et al, 1971; Murphy et al, 1971; Smyth et al, 1971). Thoracic pain has also been reported (De Rosa et al, 1964; Pellet et al, 1964; Gracey et al, 1971).

The major recognised signs are limited chest expansion (Wood et al, 1930; Stone, 1940; Roemheld et al, 1940; Luton et al 1946; Sartorelli, 1957; Leathart 1960; De Rosa et al, 1964), decreased breath sounds (Stone, 1940; Porin, 1965; Luton et al, 1946; Sartorelli, 1957; De Rosa et al, 1964; Kleinfeld et al, 1966b; Gracey et al, 1971), basal crepitations(Wood, 1929; Stone, 1940; Roemheld et al, 1940; Bastenier et al, 1953; Gernez-Rieux et al, 1955; Amsler, 1958; Leathart, 1960; Williams et al, 1960; Thomson et al, 1961; De Rosa et al, 1964; Porin, 1965; Kleinfeld et al, 1966a; Hany et al, 1967; Harries, 1971; Murphy et al, 1971; Smyth et al, 1971), cyanosis (Wood, 1930; Roemheld et al, 1940; Bastenier et al, 1955; Leathart, 1960; Williams et al, 1960; De Rosa et al, 1964; Porin, 1965), and clubbing (Wood, 1930; Gernez-Rieux et al, 1954; Leathart, 1960; Williams et al, 1960; Bader et al, 1961; Thomson et al, 1961; Porin, 1965; Kleinfeld et al, 1966a; Gracey et al, 1971; Harries, 1971; Murphy et al, 1971; Regan et al, 1971). Cyanosis and clubbing are usually restricted to the later stages in this disorder.

The chest roentgenograph characteristically reveals the presence of fine irregular opacities, diffusely distributed in the middle and lower lung fields. Involvement of the pleura may be detected as diffuse thickening or calcified pleural plaques and by the "shaggy heart" and loss of definition of the diaphragm (Wood, 1930; Lanza, 1938; Wegelius, 1947; Kiviluoto, 1960; Böhlig et al, 1970).

The associated changes in pulmonary function measurements will be reviewed in detail later.

The sputum may contain asbestos or ferruginous bodies (Wood et al, 1930; Clerens, 1950; Williams et al, 1960; Bader et al, 1961).

The definitive diagnosis of asbestosis is open to doubt in the living subject. Even the histology may not be diagnostic because diffuse pulmonary fibrosis is not uncommon in all walks of life, and because asbestos bodies are found in anywhere from 20% (Hourihane et al, 1966) to 50% (Anjilvel et al, 1966) of random autopsies of adults regardless of their occupation. No relationship was demonstrated by Gross et al (1971) between the number of ferruginous bodies, the number of naked fibers, and the total amount of dust so that such bodies are of little clinical use. McVittie (1964) of the Ministry of Pensions and National Insurance of England lists the following criteria in order to make the diagnosis asbestosis for compensation purposes: an adequate exposure to asbestos dust and two positive findings from the following: presence of basal rales, finger clubbing, radiological appearance and reduced transfer factor in pulmonary function studies.

Asbestosis is frequently associated with chronic bronchitis and emphysema. De Rosa et al (1964) noted chronic bronchitis and acute tracheitis and tracheo-bronchitis in 35 of 85 asbestos workers, and 17 of them were non-smokers. In 42 subjects with asbestosis, 38 had acute tracheobronchitis. Pellet et al (1964)also reported similar findings in their 19 subjects. Leathart (1968) stated that chronic bronchitis is a feature of the later stage of asbestosis. The emphysema associated with asbestosis is thought by some to be of a localized rather than a diffuse obstructive type (Heard et al, 1961), similar to the irregular emphysema described by Heppleston (1969). Cor pulmonale is the major complication and the usual cause of death from the disease (Kleinfeld et al, 1966a). Finally, there is an increased incidence of carcinoma of the lung, of mesothelioma, and of carcinoma of the digestive system in the asbestos exposed individual (Selikoff et al, 1966 ; Enterline et al, 1967; McDonald et al, 1972).

The syndrome of latent or pre-asbestosis is of great interest because in theory recognition of such a stage could lead to measures which might prevent the overt form from developing. Once the clinical picture of asbestosis has developed, only palliative therapy is possible.

Can a latent stage of asbestosis be recognized? The appearance of radiological changes is probably too late, but some workers believe the use of pulmonary function testing is promising. Thus, Williams et al (1960) found a reduction of the diffusing capacity in three of six exposed workers, none of whom showed definite radiological changes. Recent reports suggest that impairment of gas exchange may indeed preceed radiological abnormalities when gas exchange is evaluated by the sensitive measure of A-a oxygen difference (Wallace et al, 1971; Woitowitz, 1972). Brasseur (1963) has shown this to be true for coalworker's pneumoconiosis. Regan et al (1971) using the technique of principal component analysis found that a decrease in D_L followed by a decrease of VC has the greatest power to measure the severity of asbestosis and obstructive disease, but little power in distinguishing between them. The best indicators were FEV_1/FVC, phlegm, pleural thickening, cough and clubbing. Leathart (1968) found basal crepitations before pulmonary function and radiological changes manifested themselves.

Although the recognition of latent asbestosis should help the worker to avoid asbestosis, it must be admitted that the evidence is inconclusive (Holmes, 1964; Hunt, 1965). Furthermore, Leathart in 1968 suggested that loss of function is seldom arrested when the worker is transferred to other work, and that it may deteriorate.

2. PULMONARY FUNCTION IN ASBESTOS WORKERS

In this section, a comprehensive review of the literature of asbestos workers is reported, carried out in order to group the subjects according to their profile of pulmonary function. A discussion of what constitutes each profile is added. The review includes 375 individual cases reported in enough detail to allow them to be grouped in pulmonary function syndromes (Table 2-1), and reference is made to the results of a further 2669 subjects reported by mean and standard deviation or range (Table 2-2, page 28). Finally, reference is made to 777 subjects in whom some measu-

TABLE 2-1 - PULMONARY FUNCTION PROFILES IN INDIVIDUAL CASE REPORTS OF ASBESTOSIS
(Details in Appendix I, Tables I-1 to I-7 inclusively)

REFERENCES		CASES		RESTRICTION			ALVEOLAR-CAPILLARY BLOCK
First Author	Date	Total reported	Total classified	Definite	With Normal RV or TLC	Probable	
Wood	1929	16	1				
Roemheld	1940	19	17				
Baldwin	1949	39	1	1			
Bastenier	1953	1	1	1			
Gernez-Rieux	1954	3	3			2	
Bastenier	1955	9	8	1			
Gaffuri	1957	30	30	7		1	
Marks	1957	31	1				
Sartorelli	1957	1	1				
Read	1959	28	22	12			1
Leathart	1960	21	21				
Williams	1960	40*	18	4			1
Bader	1961	17	17	2	4		6
Heard	1961	6	6	1	1		
Rubino	1961	5	5	3			
Thomson	1961	39	39	6	7		6
Bollinelli	1963	1	1	1			
Bjure	1964	8	8	4		1	
De Rosa	1964	85	42	28			
Pellet	1964	28	28	2			1
Sartorelli	1964	18	17			5	
Vaerenberg	1964	11	11			9	
Vecchione	1964	16	16			14	
Bader	1965	17	13				
Kleinfeld	1966b	21	21	8	3		1
Hany	1967	8	8		1		
Poggi	1970	17	17	1			
Gracey	1971	1	1				
Smyth	1971	1	1				
TOTAL		537	375	82	16	32	16
Percentage of Total				21.9%	12.8%		4.3%

* 22 already reported in 1959 by Read et al.

CASE REPORTS OF ASBESTOSIS
inclusively)

RESTRICTION		ALVEOLAR-CAPILLARY BLOCK	OBSTRUCTION		MIXED		ASSOCIATED DISEASES	NORMAL	INCOMPLETE DATA
With Normal RV or TLC	Probable		Definite	Probable	Dominant Rest.	Obst.			
									1
									17
	2			1					
					4	1			
	1		2	2	2	10		1	1
			6		1				
			1						
		1	5		2		1	1	
									21
		1	7			1	3	2	
4		6		1	2	2			
1					1	2	1		
			1					1	
7		6	4		9	3	4		
	1		2			1			
			5		2	1		6	
		1	7		9	1	5		3
	5			11					1
	9			2					
	14			2					
							3		10
3		1	1		7	1			
1					3	2	2		
				8	2		3		3
							1		
									1
16	32	16	41	27	44	25	23	11	58
12.8%		4.3%	10.9%	7.2%	11.7%	6.7%	6.1%	2.9%	15.5%

rements of specific pulmonary mechanics were carried out (Table 2-3, page 29).

a) Profiles:

Restrictive Profile:

Robin in Harrison's Textbook of Internal Medicine (1970) defines the restrictive disorders in terms of pathophysiology, namely a decreased expansibility of the lung. The diseases responsible involve the chest wall or the pleuropulmonary structures in such a way as to significantly affect pulmonary compliance. Examples in which the chest wall is involved are kyphoscoliosis, thoracoplasty, spondyloarthritis, neuromuscular disorders, pain and phrenic nerve paralysis; examples involving the pleuropulmonary structures are thickened pleura, pneumothorax, pleural effusions, atelectasis, pneumonia and pulmonary fibrosis. He described the associated changes in lung function as a reduction in all volumes with minimal evidence of airflow obstruction and an impairment in intrapulmonary gas mixing.

For the purpose of the present review of the literature, one would have prefered a definition of the restrictive profile more like that of Rubin (1961) with detailed lung function criteria as follows: an increased ventilation ($\dot{V}$) and frequency (f); decreased lung volumes (residual volume, RV and total lung capacity, TLC); normal RV/TLC ratio, flows and distribution (ME); normal or decreased D_L and decreased static compliance (C_{st}); increased elastic recoil ($P_{el\ max}$); and decreased arterial oxygen tension ($P_{\bar{a}_{O_2}}$) and carbon dioxide tension ($P_{a_{CO_2}}$) with a compensated respiratory alkalosis.

However, a definition as detailed as this was impractical for two reasons. When one is reviewing the earlier reports of pulmonary function in asbestos workers, one must be content to diagnose a restrictive profile on much less complete evidence, for example, on decreased lung volumes with maintenance of normal RV/TLC ratio, and normal flow rates, eg the ratio of forced expiratory volume as a percentage of vital capacity ($FEV_1\%$) and Maximum Breathing Capacity (MBC). Furthermore, in the presence of milder degrees of fibrosis, VC may even be normal. In addition, in the present study the large number of individuals tested in a field laboratory precluded the inclusion of such tests as compliance and arterial gases.

In accordance with the suggestions of Robin (1970), it was therefore decided to classify asbestos workers as having the lung function profile of restriction on the following criteria: RV and TLC decreased by 10% and $FEV_1\%$ over 70%.

Eighty-two (82) of the reported cases reviewed were classified as having a restrictive lung function profile (Table 2-1; details of each case in Appendix I, Table I-1). In another 16 cases, certain key tests were normal, such as RV, but a restrictive profile was suspected, based on TLC and $FEV_1\%$ measurements (Table 2-1; Appendix I, Table I-2). A further 32 subjects were classified as having an incomplete restrictive profile, largely because of missing data.

As mentioned previously, the restrictive syndrome may be the consequence of pulmonary or pleural disease or a combination of the two. Since pleural and parenchymal diseases commonly coexist, it is not easy to separate their respective contribution to the pulmonary function profile, particularly in view of high prevalence of pleural disease (fibrosis, plaques and calcification) following asbestos exposure. Among the cases classified as restrictive in Table I-1, pleural changes alone were reported in only one case, and pleural changes associated with small irregular opacities in 16 subjects of the 81 subjects in this group. All other cases were thought to have some evidence of parenchymal disease on the chest radiograph.

Leathart (1965) found no functional abnormality in five patients with plaques, and he attributed the functional changes in the sixth to early parenchymal disease. Worth et al (1968) confirmed this lack of functional change with pleural plaques in 21 patients with asbestosis. Becklake et al (1969) suggested that the non-descript pleural thickening had a small but consistent effect on pulmonary function; in their study for any degree of radiological change in pulmonary parenchyma, additional pleural change was associated with a small but significant reduction in static and dynamic lung function (Becklake et al, 1970). Zolov et al (1968) reported also that radiologically evident plaques were associated with restrictive syndrome. Woitowitz (1971) studied 11 asbestotic subjects without plaques and 11 with plaques. He found a higher VC, a lower $FEV_1\%$, a higher RV and RV/TLC ratio, a higher resistance and a lower P_{O_2} in subjects with plaques, Table I-7).

In summary, one manifestation of asbestos exposure is the restrictive syndrome. It was present in 82 (21.9%) of the 375 reviewed cases; another 48 (12.8%) subjects have a probable restriction. Pleural changes were noted in about 20% of the cases with restrictive syndrome, usually in association with parenchymal changes.

Alveolar-capillary block profile:

The term alveolar-capillary block was introduced by Austrian et al (1951) to describe a pattern of pulmonary dysfunction characterized by " (1) reduced lung volumes, (2) maintenance of a large maximum breathing capacity, (3) hyperventilation at rest and during exercise, (4) normal "or nearly normal arterial oxygen saturation at rest, but a marked reduction "of the arterial oxygen saturation after exercise, (5) normal alveolar oxygen tension, (6) reduced oxygen diffusing capacity and (7) pulmonary "hypertension". The diseases responsible for this syndrome had in common diffuse finely dispersed pulmonary lesions in the alveolar-capillary septa which were thought to alter the properties of the diffusing surface. One of the diseases implicated was asbestosis (Baldwin et al, 1949; Tepper and Radford, 1970).

Baldwin et al (1949) had previously reported 14 cases, including one with asbestosis, which were comparable with Austrian's 12 cases in that the mechanics of breathing were not altered and the distribution of gas was not abnormal. They suggested that "alveolar respiratory insufficiency....results "both from perfusion of large areas of fibrotic tissue which cannot be ventilated and impairment of the adequate diffusion of respiratory gases across "a greatly thickened alveolar septa, or reduction in the area of alveolar-"capillary interface".

In the 12 cases of Austrian et al (1951), the mean VC (% predicted) was 43%; RV, 67%; TLC, 48%; MBC, 91%; and $D_{L_{CO}}$ 45%. Oxygen saturation was 87% at rest and 83% after exercise. They commented that "the low diffusing "capacity may either be due to a reduction of the total area of alveolar "membrane which is available for the diffusion of gases, or to a reduction "in the permeability of the membrane per unit area, or to both". They concluded, however, that "the observation of rather widespread thickening "of the alveolar-capillary septa suggests that the reduction in permeabi-"lity per unit area is the major reason for the low diffusing capacity. "Whether the area of alveolar-capillary interface is also reduced under "resting conditions cannot be determined".

In 1957, Marks et al studied the pulmonary function of 31 patients with diffuse fine parenchymal lesions on radiograph including one with possible asbestosis and found that lung function was less affected than in the cases of Austrian et al (1951). Thus, VC was on the average 80% of the predicted value, RV 119%, TLC 91%, MBC 94% and FEV_1% 75%. Resting O_2 saturation was 93%; D_L for carbon monoxide, steady state method ($D_{L_{CO_{SS}}}$) was 36% and $D_{L_{CO}}$ single breath ($D_{L_{CO_{SB}}}$) was 56% of the value of the control group. The decrease in D_L could not be fully explained by the diminution of the surface area as suggested by Baldwin et al (1949), Thomson et al (1961), and Becklake (1965). Marks et al also stressed the absence of obstruction in their cases.

In 1959, Read et al, in a study of 17 subjects with apparently pure interstitial diseases of the lung (13 with asbestosis) and 11 subjects with interstitial disease complicated by cyst formation or probable emphysema (9 with asbestosis), demonstrated that markedly uneven ventilation in presence of uniform blood flow was found in the former group, and both uneven ventilation and blood flow were common in the latter. Bjure et al (1964) also attributed the decrease of $P_{\bar{a}O_2}$ in their cases to uneven regional distribution of ventilation in relation to blood flow ($\dot{V}/\dot{Q}$), even in those cases with advanced impairment of diffusion.

In the same year, the validity of the term alveolar-capillary block was questioned by Bates and Christie who noted that "there is some doubt "how far the observed lowering of arterial saturation or tension in these "patients is ascribable to the lowered diffusing capacity and how far it "is caused by ventilation-perfusion distribution abnormalities". They referred to a paper by Finley et al (1962) which concluded that an increase in the thickness of the alveolar-capillary membrane of six to eight-fold must occur before an increase in A-a difference of 1 mmHg would be observed.

In addition, the associated pathological changes support the concept of $\dot{V}/\dot{Q}$ disturbance rather than a mechanical alveolar-capillary block. Thus, although Bader et al (1961) and Wright (1955) stated that the major anatomical change was thickening of the alveolar walls, others report that the fibrous tissue is found first around the bronchioles (Vorwald et al, 1951) and arterioles (Lanza, 1963), and that this fibrous tissue extends interseptally toward the periphery of the parenchyma. Furthermore, Scheepers (1965) noted that fibrous tissue does not usually lie between capillaries and alveoli, no fibrotic membrane has been found lining the alveolar surface, except in terminal cases, and extensive alveolar epithelization has rarely been observed.

A review of the literature on asbestos workers has not revealed a single subject with the alveolar-capillary block syndrome precisely as defined by Austrian et al (1951). This was largely because evidence of pulmonary hypertension or changes in some of the other tests were not looked for or at least not reported.

In view of this difficulty, it was decided that for the purpose of this thesis, the term "alveolar-capillary block" would refer to those cases with normal volumes, normal RV/TLC ratio and normal flow rates but in whom there was evidence of impaired gas exchange eg. decreased O_2 saturation or decreased diffusion. Table 2-1 refers to 16 such cases in whom asbestos exposure ranged from 6 to 34 years, and radiological changes were reported in eleven of them, (Details in Table I-3).

In summary, none of the 375 cases reviewed individually were considered to have alveolar-capillary block as defined by Austrian et al (1951) because measures of pulmonary hypertension were lacking, but 16 (4.3%) who had normal volumes, RV/TLC ratio and flows, did show impairment of D_L and/or oxygen saturation.

Obstructive profile:

Although the profiles of restriction and of alveolar-capillary block have been considered to be characteristic of asbestos exposure, there is evidence that the obstructive profile may also be so related.

The concept of the obstructive profile has been recognized in one form or another for many years. Laënnec, in his classical description of emphysema notes the expiratory difficulty encountered in this disorder: "Les poumons au cours de l'emphysème font saillie hors du thorax; il est "difficile de les aplatir et de les rendre flasques." (1819). Rubin (1961) defined the obstructive disorder as a functional disturbance caused by narrowing of the airways. In the chronic state, such as emphysema, the TLC is normal or increased, the two-stage VC may be greater than the one stage, and the RV and RV/TLC ratio are increased. The $FEV_1\%$ is decreased as is the MBC.

When one considers the reports on asbestos workers, there appears to be considerable disagreement on the frequency of the obstructive profile with asbestos exposure: German, Belgian, Italian and French have found it to be common whereas English workers with the exception of Leathart, and American workers consider it to be rare. Thus, Gernez-Rieux et al (1954), Basternier et al (1955), Gaffuri et al (1957), Scansetti et al (1960), Pellet et al (1964), Sartorelli et al (1964), Leathart (1965) and Worth et al (1968), all subscribe to the former point of view, whereas Wright (1955), McGrath et al, (1960), Williams et al (1960), Bader et al (1961) support the latter.

Furthermore, most workers consider the association to be coincidental (Wright, 1966; Bader et al, 1965). For example, Pellet et al (1964) examined 18 subjects exposed to asbestos dust with a reticular pattern on their radiograph and found nine with a predominantly obstructive profile. Despite these findings and while admitting that the pathology of asbestosis might well favor the obstructive syndrome, they concluded that the association was accidental. The following year, in 1965, Pellet gave further details of the function studies in the 18 subjects, eight of which had the obstructive syndrome, and a further five a mixed obstructive and restrictive profile.

From the pathologist's viewpoint, Gloyne (1933) stated that bullae were occasionally seen at autopsy while Wegelius (1947) commented radiological translucency of the upper zones. Heard and Williams (1961) found mild centrilobular emphysema in five cases and severe emphysema in the sixth of their series, but concluded these were incidental findings to asbestosis.

In the present review of the individual cases, the following criteria were used to classify a subject as having the obstructive profile: an increased RV, normal or increased TLC, and decreased $FEV_1\%$ and/or MBC. Using these criteria, 41 subjects were considered to have a definite obstructive profile with no evidence of other associated ones (Tables 2-1, I-4). Another 27 subjects could only be classified as having incomplete obstructive profile, mostly because of missing data. Six out of the 41 subjects in the obstructive group had pleural changes, and only one out of 27 classified as having the incomplete obstructive profile.

In summary, of the 375 case reports of asbestos workers reviewed, 68 (18.1%) with radiological and clinical symptoms of asbestosis have an obstructive pulmonary function profile, definite in 41, suggestive in 27.

Mixed profile:

A certain number of the individually reported cases appeared to have a mixed functional profile i.e. they were not clearly restrictive, alveolar-capillary block or obstructive in nature. The number of subjects falling into this group is 67 (Tables 2-1, I-5) of which 44 were considered to show a predominantly restrictive and 25 a predominantly obstructive profile. It is interesting to note that 13 out of the 42 classified as having a mixed restrictive profile have pleural as well as parenchymal changes, and 5 out of the 25 classified as having a mixed obstructive profile.

Thus 44 (11.7%) of the 375 subjects reviewed had a mixed restrictive, and 25 (6.7%) a mixed obstructive profile.

Normal function:

Only eleven case reports on workers exposed to asbestos (2.9% of the cases reviewed) were found to have pulmonary volumes and flows within normal limits (Tables 2-1, I-6). Nine of these 11 workers had radiological changes. This indicates that the prolonged exposure to asbestos may not necessarily affect function; alternatively this type of pulmonary function may represent a latent phase or the results of two disturbances acting in opposite directions, i.e. restriction and obstruction.

Associated diseases:

In 23 of the case reports reviewed, associated diseases were present which might well have influenced pulmonary function (Tables 2-1, I-6). These included bronchiectasis (Thomson et al, 1961; Poggi et al, 1971); pulmonary tuberculosis (Pellet et al, 1964); mitral stenosis (Read et al, 1959; Heard et al, 1961); lung cancer, (Williams et al, 1960; Bader et al, 1961; Hany, 1967; Poggi et al, 1970); cancer of the stomach (Bader et al, 1961); cancer of the breast (Thomson et al, 1961); obesity (Thomson et al, 1961); mesothelioma (Thomson et al, 1961; Gracey et al, 1971); pleural effusion (Thomson et al, 1961; Gracey et al, 1971); lung resection and lobectomy (Pellet et al, 1964; Poggi et al, 1970). Other cases not reported in this table had hypertension (Thomson et al, 1961, patient A24) and coronary artery disease (Bader et al, 1965, subjects 12 and 13).

Incomplete data:

In 58 of the case reports reviewed, data was incomplete and they could not be classified (Tables 2-1, I-6). Many of these cases were reported before 1950. Others studied primarily to elucidate diffusion were usually found to have a lowered oxygen saturation.

Group studies:

A further 2669 subjects have been reported in epidemiologic studies with mean values or range being given (Tables 2-2, I-7). Subjects were usually grouped according to radiological changes (Wright, 1955; Gregoire et al, 1958; Scansetti et al, 1960; Teirstein et al, 1960; Kleinfeld et al, 1966b; Leathart, 1965; Smither, 1969; Regan et al, 1970; Harries, 1971; Jodoin et al, 1971; Woitowitz, 1971); by job and exposure (Ferris et al, 1971; Harries, 1971; Murphy et al, 1971); by age (Sluis-Cremer, 1970); by pulmonary function (Hunt, 1965; Bader et al, 1970); and also by clinical features based on exposure, questionnaire, radiology and pulmonary

TABLE 2-3 - SPECIFIC MECHANICS IN ASBESTOS WORKERS
(Details in Table I-8)

CRITERIA	STATIC COMPLIANCE		DYNAMIC COMPLIANCE		RESISTANCE					
					Inspiratory		Expiratory		Total	
	No. Subj.	L/cmH_2O	No. Subj.	L/cmH_2O	No. Subj.	cmH_2O/LPS	No. Subj.	cmH_2O/LPS	No. Subj.	cmH_2O/LPS
No small irregular opacities	28	.133 to .310	41	.090 to .662	23	2.0			46	1.0 to 10.0
With small irregular opacities	3	.130 to .313	56	.018 to .192	5	4.1 to 8.2	5	2.3 to 3.6	23	1.0 to 9.0
Without pleural Changes									11	3.0 ± 1.0
With pleural changes									11	3.5 ± 2.8
Miscellaneous	10	.055 to .100	46	.020 to .270	6	1.5 to 8.0	6	3.0 to 12.0	466	1.8 to 9.0

TABLE 2-2 - PULMONARY FUNCTION PROFILES IN ASBESTOS WORKERS: REPORTS OF GROUPS (Details in Appendix I, Table II-7)

REFERENCES		CASES		RESTRICTION		ALVEOLAR-CAPILLARY BLOCK	OBSTRUCTION	
First Author	Date	Total reported	Total classified	Definite	Probable		Definite	Probab
Stone	1940	148	13					
Wright	1955	57	57					
Grēgoire	1958	35	12					
Leathart	1960	23						
Scansetti	1960	34	34	14				
Teirstein	1960	10	10					
Eliseo	1964	28	24					
Hunt	1965	450	450	110				
Leathart	1965	78	78					
Schaaning	1965	11	11	11				
Thomson	1965	28	28					
Kleinfeld	1966a	56	56	56				
Gandevia	1967	41	41					
Ardalan	1968	22	18					
Smither	1969	53	32					
Bader	1970	598	598		172		29	7
Sluis-Cremer	1970	179	179					
Ferris	1971	185	185		185			
Jodoin	1971	24	24	24				
Harries	1971	369	369					
Murphy	1971	195	195		195			
Regan	1971	210	210		53		44	
Woitowitz	1971	22	22					
TOTAL		2847	2669	215	605	-	73	7

KERS: REPORTS OF GROUPS

ON	ALVEOLAR-CAPILLARY BLOCK	OBSTRUCTION		MIXED		INDERTERMINATE SYNDROME	NORMAL	INCOMPLETE DATA
able		Definite	Probable	Predominant Rest.	Obst.			
								13
						57		
					12			
								23
					12	8		
								10
								24
							340	
						78		
						28		
						41		
						18		
						32		
72		29	7				390	
							179	
35								
						369		
95								
53		44				104		
				11			11	
05	–	73	7	11	24	735	920	70

function (Bader et al, 1970). Results will, of course, depend on how the sample was chosen. Nevertheless, it is of interest that some groups have a restrictive profile (Scansetti et al, 1960, group 3; Gandevia, 1967; Jodoin et al, 1971, group 2) and others possibly have a restrictive profile, but some data are incomplete (Wright, 1955; Teirstein et al, 1960; Schaaning et al, 1965; Kleinfeld et al, 1966a; Jodoin et al, 1971, group 1; Woitowitz, 1971, group 1; Murphy et al, 1971; Ferris et al, 1971). Several groups have a mixed profile (Gregoire et al, 1958; Scansetti et al, 1960, groups 1 and 2; Thomson et al, 1965; Leathart, 1968; Harries, 1971). Certain groups seem to be within normal limits (Sluis-Cremer, 1970; Bader et al, 1970; Woitowitz, 1971, group 2). Finally, incomplete data do not permit any conclusion in some surveys (Stone, 1940; Eliseo et al, 1964; Leathart, 1965; Ardalan, 1968; Smither, 1969). In other words, the conclusions are in accord with those reached on the basis of analysis of individual case reports. It should also be noted that most individual and group reports refer to workers in the secondary industries; only those of Grégoire et al (1958) on workers in open chrysotile mines and those referred to by Sluis-Cremer (1970) on crocidolite miners, deal with exposures in the primary processing.

Specific mechanics:

To complete this review of the pulmonary function in asbestos workers, reference will be made to reports on lung mechanics (Tables 2-3, I-8). The range of values for static compliance was large and was not different in the presence or absence of small irregular opacities; lower values were found in the miscellaneous group. Dynamic compliance was on the whole lower in presence of small irregular opacities than in their presence or in the miscellaneous group. Different degrees of resistance were found in the different groups. Woitowitz (1971) and Jodoin et al (1971) found resistance significantly increased with higher dust exposure even in absence of radiological changes.

b) Profiles in Quebec asbestos workers:

Because the present study is concerned with Quebec workers, previous reports on this working population by Gregoire et al (1952) and Wright (1955) were reviewed. They described the respiratory function of 57 men who had had a long exposure in the mines of Quebec, and radiographic evidence of advanced asbestosis. They were found to have reduced lung volumes with relative preservation of ventilatory efficiency. Alveolo-arterial differences in oxygen pressure ($A\text{-}a_{O_2}$) were usually increased at rest, and always on exercise, indicating an impairment of gas exchange. This pattern differs little from that described elsewhere.

It should be pointed out that Quebec asbestos workers in the present study are unusual in that they are almost all engaged in primary industry whereas most other reports of the effects of exposure are in secondary industries. This difference in exposure has generally been considered of little importance. However, Wright (1969) underlines the differences between chrysotile and the five amphiboles, and suggests they may have different biological effects: "In view of the great variation of chemical "and physical properties, it is most unsafe to predict that the biologic "reactions of one variety of asbestos will be mimicked by another in terms "of either actual consequences or mechanisms. To interpret the biologic "action of asbestos, it is imperative that the character of exposure in "terms of concentrations, size and types of fibers be known. This sort "of data is scant or often inexistant at present with respect to exposure "of humans."

The different physical and chemical characteristics of chrysotile could perhaps explain why, in another study, Grégoire et al (1958) found a mixed obstructive profile in the 12 subjects they studied. Chrysotile is known to penetrate less deeply and be expelled faster (Timbrell et al, 1971). Moreover, Jodoin et al (1971) have demonstrated in chrysotile workers small airways changes which support the concept of a limited dust penetration. This thesis based on subjects working in chrysotile only can possibly help to demonstrate if differences in biological effects do indeed exist between the different types of asbestos.

c) Summary:

The general consensus of medical textbooks is that the pulmonary function of asbestosis is that associated with fibrosis i.e. the restrictive profile and/or alveolar-capillary block. The predominant features are small lung volumes, decreased diffusing capacity and increased A-a oxygen difference due to reduced surface area of the alveolar-capillary membrane, thickening of this membrane and/or $\dot{V}$-$\dot{Q}$ disturbance. The obstructive profile is considered to be coincidental.

Most of the published reports on the subject reach the same conclusions as those in the textbooks. However, a detailed analysis of 375 workers whose results are reported individually (Table 2-1) revealed a somewhat different picture. Thus, only 21.9% had a definite restrictive profile and 12.8% a possible restrictive profile, 10.9% had a definite obstructive and 7.2% a possible obstructive profile; 18.4% had a mixed profile, only 4.3% an alveolar-capillary block, while 2.9% had normal function and 6.1% associated diseases likely to have affected their lung function. Fifteen percent (15.3%) could not be classified because of incomplete data.

The data on 2669 workers reported as groups in epidemiological studies was less susceptible to this type of analysis by lung profile, both because of the choice of population, and because the results were less complete or impossible to classify.

It can therefore be concluded that restriction is often associated with asbestos exposure, but that normal and obstructive function profiles are also found in an important proportion of subjects.

3. RELATIONSHIP OF PULMONARY FUNCTION TO OTHER MEASUREMENTS OF HEALTH AND TO ASSOCIATED AGENTS

A brief reference to reports on the relationships between pulmonary function and other measurements of health i.e. symptoms, signs and chest radiography on one hand, and associated agents such as dust, effort and cigarettes on the other, will complete this review of the literature.

Clinical Findings and Pulmonary Function:

Wright (1955) and Bastenier et al (1955) concluded that symptoms and signs did not correlate closely with pulmonary function changes.

Leathart (1960) showed some relation of dyspnea and tachypnea to decreased dynamic compliance, but not to oxygen saturation. Bader et al (1961) and Kleinfeld et al (1966a) described a poor correlation between clinical and functional changes in their material. Nevertheless in another report on the same material (1966b) they note that those with dyspnea and lung crepitations had a significantly lower mean VC and TLC than those in whom these findings were absent. The D_L was also lower in the group with crepitations, but no relation could be established with clubbing. Pellet et al (1964) noted the following paradox: oxygen saturation on effort decreased in subjects with only dyspnea but not in subjects with dyspnea, cough and sputum.

By contrast, Williams et al (1960) found a significant relationship between the severity of dyspnea and grade of finger clubbing on the one hand, and the standardized ventilation, the dyspneic index (ratio of standardized ventilation to the maximum ventilatory capacity) and the reduction in D_L on the other hand. Bader et al (1965) stated that in half of their 17 cases, the progression of dyspnea on exertion correlated well with the decreased VC. Hunt (1965) noted a good correlation between lung function results and clinical findings in advanced cases. Harries (1971) suggested that there is a relationship between dyspnea and values for exercise ventilation, standardized ventilation and D_L. Murphy et al (1971) in a study of shipyard workers demonstrated a relation between dyspnea, rales and clubbing on the one hand and decreased VC on the other. These were also related to duration of exposure.

Radiological Changes and Pulmonary Function:

In 1955, Wright concluded that in asbestosis one may find "(1) "physiologic abnormality without definite roentgenologic abnormality, "(2) roentgenologic abnormality plus physiologic abnormality, and (3) "roentgenologic abnormalities without any physiologic abnormality."

As Wright suggested in his first proposition, Bastenier et al (1955), Amsler (1958) and Leathart (1960) suggested that physiological changes may precede radiological changes; the last author suggested that a low compliance and a decreased D_L with a history of asbestos exposure may suggest the diagnosis of asbestosis before any radiological change. Hunt (1965) also concluded that asbestosis can be detected by lung function before radiological changes. Bader et al (1970) showed that pulmonary function abnormalities appear much earlier (5 to 9 years exposure) than extensive radiographic changes, 2 and 3 (20 years of exposure). They do not comment on the relationship of pulmonary function changes and early radiologic changes.

By contrast, Roemheld et al (1940) and Gaffuri et al (1957) showed a relationship between loss of VC and the increase in radiological changes. Bader et al (1961) found in general a relationship between physiological abnormalities and radiological changes when these became definite (grade 1 and 2 +). Pellet et al (1964) found no significant pulmonary function abnormalities if the radiogram was normal, but some changes if it was not. Becklake et al (1970) on the same group of men reported in this thesis, found a significantly decreased VC and FVC with doubtful (0/1) radiological changes when compared to the men with normal radiogram (0/0). VC was also progressively reduced in relation with the increase in radiological changes, but $D_{LCO_{SB}}$ and $D_{LCO_{SS}}$ were only affected when radiologic change was marked. In men with no parenchymal changes (0/0), pleural changes were associated with minimal but significant reduction in RV, TLC, FEV_{75}, $FEV_1\%$ and $V_{A_{SB}}$. Similar small differences were seen with advancing parenchymal involvement (0/1-), but without reaching significant levels. In most measurements of lung volumes, flow rates and diffusion, values were consistently lower in the presence of pleural changes. Another point of interest was that the VC of workers with no parenchymal or pleural changes on the chest radiograph was slightly lower than the mean VC in many normal series. Harries (1971), in his study of shipyard workers, came to the same conclusions as Becklake et al.

Finally, Williams et al (1960) showed a significant correlation between reduction in diffusing capacity and radiological grade of mottling. Reduction of inspiratory capacity and TLC were also related, but less closely so, to radiological changes. Hunt (1965) found that at the more advanced stages, the lung function results correlated very well with radiological changes. Bader et al (1970) also stated that in men after 30 years of exposure, the prevalences of function and radiologic abnormalities were similar.

Dust Exposure and Pulmonary Function:

Wright (1955) commented that a gross correlation might be expected between the intensity and duration of exposure and physiological changes, but that some subjects do remain normal even with a prolonged and very intense exposure. Bader et al (1961) agreed with this point. They could find no correlation between the degree of functional impairment and the number of years of exposure to asbestos, and this was also true for intimacy of exposure. Kleinfeld et al (1966a) were also unable to demonstrate a relationship between the duration of exposure and functional changes.

However, more recent studies have generally supported such a correlation. Thus, in 1970, Bader et al, examining the relationship of VC and $FEV_1\%$ with exposure in 598 workers, showed a relation between the decrease of function with an increase in exposure after five years of exposure.

The results of Harries's survey (1971), using an independant assessment of lung function, also provide evidence of an association between the development of lung function abnormalities and the intensity of exposure but not the duration of exposure. Jodoin et al (1971) demonstrated that even before radiological changes, the intensity of exposure had an influence on respiratory function, as measured by increase in the static elastic recoil and the upstream resistance. The data reported in this thesis was also examined for such a relationship and it was found that IC and VC (or FVC) decreased with increasing dust both in non-smokers and smokers, and MMF and $FEV_1\%$ in high dust exposure (Becklake et al, 1972). In addition, in non-smokers, D_L dropped with increasing dust exposure.

Cigarettes and Pulmonary Function:

Although smoking is known to alter pulmonary function, its influence has been assessed only infrequently in asbestos workers. One of the first reports to do so was that Ferris et al (1971), who found a higher than expected prevalence of breathlessness in pipe coverers in general and especially in those who smoked more than 25 cigarettes per day. Likewise, VC and DCO_{SB} was lower in pipe coverers than in two other groups, but always lower in the smokers in the three categories. In the measurement of total resistance as well as the volume-flow curves, no difference was shown between smoking categories.

Jodoin et al (1971) studied 24 men in two categories of dust exposure and found more upstream resistance in the higher dust category. On the basis of the smoking history of their subjects, they concluded that the increase could not be attributed to smoking. On the other hand, Harries

(1971) found that VC and TLC, transfer factor and D_m were lower in smokers than in non-smokers in his groups. He made the comment that the smoking history is often not reliable, the subjects underestimating the number of cigarettes during their working time.

McDonald et al (1972) analysed the smoking habits of the subjects of the present study and found that smoking was related to cough and phlegm, but not to breathlessness. On the same material, Becklake et al (1972) showed that with increasing dust exposure VC and TLC decreased in both smokers and non-smokers, RV increased in smokers; there was also a greater decrease in MMF and $FEV_1\%$ in smokers than in non-smokers whereas DCO_{SS} on exercise dropped less in smokers than in non-smokers.

Summary:

In relating the clinical symptoms and signs with pulmonary function changes, dyspnea and rales seem to correlate well with changes in VC, exercise ventilation and transfer factor whereas clubbing and cyanosis show only a poor correlation with functional changes. In early asbestosis, the pulmonary function may be altered before the chest radiograph changes, but as the disease advances, changes in pulmonary function parallel changes in the radiograph. Lung function changes appear to relate to the intensity rather than the duration of asbestos exposures while volume (VC, TLC) and flow measurements (MMF, FEV_1) are lower and RV higher in smokers than non-smokers.

4. CONCLUSIONS

The review of the literature has shown that many reported cases of asbestosis could not be classified into pulmonary function profiles, data being incomplete or impossible to assess individually. However, in 375 cases reported in sufficient detail to be classified, 2.9% were normal even in the presence of radiological changes, about 35% had a restrictive profile, 18% an obstructive profile, 18% a mixed one and 4.3% a possible alveolar-capillary block; some 15% could not be classified or had other associated disease likely to have affected lung function.

In general, pulmonary function changes were related to dyspnea and crepitations, advanced radiological changes, intensity of exposure and smoking; the relationship was less evident with cyanosis and clubbing, normal or early abnormal radiological changes and duration of exposure.

3 - MATERIAL

1. SELECTION OF SUBJECTS FOR TESTING.

2. SUBJECTS TESTED AND RESULTS ANALYSED.

1. SELECTION OF SUBJECTS FOR TESTING:

The purpose of studying the current working population was to get information on the relationship of asbestos exposure to health. To this end, it was decided to draw a random sample, stratified for age, and weighted towards the older men, who it was thought would be most likely to show health effects of exposure because of their more lengthy exposure.

The subjects of the study were then chosen in the following way. A complete list of all the current workers in the eight constituent companies of the Quebec Asbestos Mining Association was made on 31 October 1966 and contained 6180 male employees. These are grouped in Table 3-1 according to their age in the employment records and to the company for which they worked. The companies are designated by letters. There are nine letters but only eight companies because the factory workers on one company, the largest, are separated from those in its mine and mill.

The selection of the group continued with the exclusion of one hundred and two men because they were under 21, and 37 because they were more than 65 years of age. From the 6,041 remaining, an age-stratified, random sample was selected by dividing them into five-year age groups, and sampling so far as possible in such a way that the ratio of subjects in each group as one proceeded from youngest to oldest was 4:5:6:7:8:9:10:11:12. Thus, for every four workers sampled from the age range 21-25 years, five were sampled from the age range 26-30, six from 31-35 and so on until 12 were included in the group 61-65. This ensured that the sample included a relatively higher proportion of older men with long exposure.

TABLE 3-1 - MEN EMPLOYED AS OF 31 OCTOBER 1966, CLASSIFIED BY AGE AND COMPANY AND MEN CALLED FOR PULMONARY FUNCTION TESTS IN 1967, 1968*

AGE Yrs	COMPANY									
	A	B✗	C	D	E	F	G	H	I	TOTAL
16-20	14	9	42	13	2	1	21	-	-	102
21-25	82	56	153	24	34	-	45	19	7	420
	(12)	(6)	(12)	(6)	(6)	-	(8)	(4)	(4)	(58)
26-30	73	22	128	30	46	5	103	29	3	439
	(15)	(7)	(15)	(7)	(7)	(5)	(10)	(5)	(3)	(74)
31-35	122	34	195	80	64	19	126	41	9	690
	(18)	(9)	(18)	(3)	(9)	(6)	(12)	(6)	(6)	(93)
36-40	309	28	289	76	59	23	114	32	25	955
	(21)	(11)	(21)	(11)	(11)	(7)	(14)	(7)	(7)	(110)
41-45	372	37	425	70	49	29	100	27	33	1142
	(24)	(12)	(24)	(12)	(12)	(8)	(16)	(8)	(8)	(124)
46-50	264	48	370	54	25	31	58	19	27	896
	(27)	(13)	(27)	(13)	(13)	(9)	(18)	(9)	(9)	(138)
51-55	226	33	294	37	29	24	35	6	8	692
	(30)	(15)	(30)	(15)	(15)	(10)	(20)	(6)	(8)	(149)
56-60	149	51	234	30	12	18	15	2	5	516
1967	(33)	(17)	(33)	(17)	(12)	(11)	(14)	(2)	(5)	(144)
1968										(120)
61-65	78	30	132	22	11	5	4	2	7	291
1967	(36)	(18)	(36)	(18)	(11)	(5)	(4)	(2)	(7)	(137)
1968										(121)
66 +	-	-	19	99	5	1	-	-	3	37
TOTAL	1689	348	2281	445	336	156	621	177	127	6180
1967	(216)	(108)	(216)	(108)	(96)	(61)	(116)	(49)	(57)	(1027)
1968										(241)

* Number of men called for test in brackets under the number of men employed.

✗ Factory.

The final aspect of the selection was to include in each age group subjects from all eight companies in such a way that comparison between them could be facilitated since the characteristics of asbestos does differ somewhat from mine to mine. The smaller companies were more fully represented than the larger ones by selecting the subjects in proportion to the square root of the total number of current male employees.

In theory, the random sample should have included 1,080 men but when actual names were being selected, only 1,027 were included (Table 3-1). For example, it was found that the actual age of some men differed from that listed in the company records and they were actually over 65. Also, in some companies there were not enough older men to complete the groups. Finally, when the factory workers of one company were separated from those of the mine and mill, there were not enough factory workers to fill all age groups.

An additional survey was considered necessary when it was found that only 71 (8%) of the original random sample had radiographic evidence of small irregular opacities and only eight of these were placed in categories 2/1 or greater. Therefore, a second field study was carried out in the summer of 1968 to increase the number of older men in the survey. To this end all men, aged 60-65 in 1968, and not previously tested in A, B, C, were invited to participate (Table 3-1).

2. SUBJECTS TESTED AND RESULTS ANALYSED

From this random sample of 1,027 men selected in 1966, 85 (8%) were

TABLE 3-2 - SAMPLE SELECTED, CALLED, TESTED AND ANALYSED

AGE	CURRENT EMPLOYEES	SUBJECTS CHOSEN^x FOR TESTS		SUBJECTS TESTED*		RESULTS ANALYSED	
		1967	1968	1967	1968	1967	1968
16-20	102	-	-	-	-	-	-
21-25	420	58	-	40	-	40	-
26-30	430	74	-	72	-	72	-
31-35	690	93	-	69	-	69	-
36-40	955	110	-	107	-	107	-
41-45	1142	124	-	105	-	103	-
46-50	896	138	-	136	-	136	-
51-55	692	149	-	118	-	118	-
56-60	516	144	120	128	33	128	28
61-65	291	137	121	105	151	97	135
66 +	37	-	-	5	-	2	-
TOTAL	6180	1027	241	885	184	871	163
		1268		1069		1034	

x classified as to age at the 1st of October 1966.

* classified as to age at the time of testing.

not available in 1967 when the testing was done because they had retired, were sick, had died or were not given an appointment (clerical error); a further 57 (6%) were unwilling to participate (Table 3-2). Finally, only 871 sets of tests were actually analysed because 14 of the subjects were unable to adequately perform all the tests required because they could not tolerate the mouthpiece, could not follow the technician's directives, or were too tired.

With regard to the 1968 group, 241 were selected from A, B, C industries but only 184 were examined, 38 (16%) not being available and 19 (8%) declining the invitation to participate (Table 3-2). Only the tests of 163 were actually analysed, as the other 21 subjects were unable to complete all the tests for the same reasons as mentioned for the first survey.

In summary, the total number selected, tested and analysed in both surveys is shown in Table 3-2. From the 6180 current employees in 1966, analysis of the results of pulmonary function tests on 1034 individuals will be included in this thesis.

4 - METHODS

1. GENERAL

2. PULMONARY FUNCTION

Laboratory
- Construction
- Calibration
- Personnel
- Tests

Recording of Data

Control of Quality and Validity of the Results

First Analysis of Results
- Predicted values
- Coding of Results and Classification into profiles

3. ASSOCIATED INFORMATION

Anthropology

Clinical data

Radiology

Dust exposure and effort

Smoking habits

4. STATISTICAL ANALYSIS

1. GENERAL

Although the present report is more concerned with the methods of collecting and analysing the pulmonary function data, this section includes a general description of the entire McGill survey of the Eastern Townships asbestos worker and his environment. Emphasis will be given on how information was obtained on the clinical aspects, dust exposure, anthropology and how the radiological classification of pulmonary abnormalities was done.

2. PULMONARY FUNCTION

Laboratory:

The apparatus for testing pulmonary function was designed and constructed for mobility. Within a few hours, it could be crated, moved and reassembled elsewhere despite the complexity of circuits and number of accessories. It was first assembled in Montreal in the winter of 1966-1967 and moved to Thetford Mines in April, 1967. In September, the laboratory was transferred to Asbestos and in November returned to Montreal. In June 1968, it was again installed in Asbestos, and the following month in Thetford Mines.

The equipment was initially tested and calibrated over a three month period in Montreal. When the laboratory was moved to Thetford Mines in April 1967, a complete re-testing of circuits was done by the engineer and technicians and the entire calibration was repeated. Each month, one full day was taken for further calibration procedures. In addition, daily cali-

TABLE 4-1 - PULMONARY FUNCTION TESTS LISTED IN THE SEQUENCE PERFORMED

TEST	CIRCUIT	METHOD
HbCO	Henderson Circuit	Rebreathing techniques, Henderson and Apthorp, 1960
FRC RV M%	Collins Helium Circuit* and Rustrak Recorder**	Closed-circuit helium Bates et al, 1962 Goldman and Becklake, 1954
VC FVC FEV MMF	Stead-Wells Spirometer*	Expiratory and inspiratory VC Forced vital capacity calculated from the best of 3 $FEV_{0.75}$ sec. $FEV_{1.0}$ sec.
$D_{CO_{SB}}$	Collins Box-balloon*	Single breath technique McGrath and Thompson, 1959
$D_{CO_{SS}}$ 1) rest 2) exercise: 200, and 400 or 600 KgM/min.	Pengelly-Bartlett circuit with analysis of expired gases (CO-O_2-CO_2)*** Elema-Schönander Ergometer	Steady-state technique End tidal sampling Bates et al, 1955 Six minutes of exercises Mostyn et al, 1963

* Warren E. Collins, Boston, Mass., U.S.A.

** R.O.R. Associates, 21 Polack Drive, Scarborough, Ontario, Canada.

*** Pengelly, D., Faculty of Medicine, Hamilton, Ontario, Canada.

bration procedures were carried out and recorded before the first subject in the morning and before the first in the afternoon. These readings were compared to the preceeding ones so that any deviation could be promptly investigated and corrected.

The personnel of the laboratory consisted of two research technicians who performed all the tests and the daily and monthly calibrations, an engineer who maintained the equipment, and three physicians who supervised the techniques, checked the calculations and were present during the exercise studies.

The tests were performed in the sequence given in Table 4-1. Standard techniques were used with the exception of the steady-state diffusing capacity at rest and on exercise, which is described in detail in Appendix II. Subjects were alternatively allocated to each technician during the survey, so that any inter-technician differences would not bias any one group studied.

Recording of Data:

The data on each subject was handled in the following manner to ensure the greatest possible accuracy. The technician who performed the subject's tests extracted raw data from her readings on the analyzers and entered them on the raw data sheet (Fig. 4-1). One of the three physicians checked the technician's work and completed the necessary calculations for the raw data sheet. The sequence of calculations and how they were done is to be found in Appendix II (Table II-1). Another physician, usually the author, rechecked completely this transfer of data and the calculations, and ensured

FIGURE 4-1 - DATA SHEET FOR THE COMPUTOR

McGill University, Depart. of Epidemiology and Experimental Medicine

Pulmonary Function Data Operators - please initial each cc.

Card No. 1

1	Case no.
7	Card no. 1
8	Surname
14	First name
20	Age yr.
22	Ht. ins.
26	Wt. lbs.
30	Day
32	Month
34	Year
36	PB
40	Temp. (room)
43	PW for temp. (room)
45	
	Questionnaire
50	Cough (yes to Q5)
51	Sputum (yes to Q10)
52	Chest illness (yes to Q21)
53	Breathlessness (0-3)
54	Other disease
55	No. cigs./day
58	Years of employment
61	X-ray
	Operators for
76	HBCO
77	Flowrates
78	FRC
79	Dco SB
80	Dco SS

Card No. 2

1	Case no.
7	Card no. 2
8	
12	
16	Temp. 1
19	PW for T 1
21	ERV 1
24	IC
27	VC (total)
30	FEV 0.75
33	FEV 1
36	FVC
39	MMF
42	
49	Temp. 2
52	PW for T 2
54	F - He % 1
58	F - He % 2
62	Temp. 3
65	Switch diff. ±
68	O_2 diff. ±
71	ERV 2
75	V_T 1
79	Breaths to 90%

Card No. 3

1	Case no.
7	Card no. 3
8	CO (rebreathe)
11	FI-He %
15	FI-CO-units
19	VI
23	Time 1 secs.
26	FA - He %
30	FA - CO units
36	FIO_2
40	Load kgm/10 - rest
42	Heart rate
45	FA_1CO units
47	FICO units
50	FECO units
53	FA_2CO units
56	V 1
61	V 2
66	Time min.
67	sec.
69	f
71	$FECO_2$ %
74	FEO_2 %
78	Total time min.

Card No. 4

1	Case no.
7	Card no. 4
8	Load kgm/10
10	Heart rate
13	FA_1CO units
15	FICO units
18	FECO units
21	V 1
26	V 2
31	Time min.
32	sec.
34	f
36	$FECO_2$ %
39	FEO_2 %
43	Total time min.
44	Load kgm/10
46	Heart rate
49	FA_1CO units
51	FICO units
54	FECO units
57	V 1
62	V 2
67	Time min.
68	sec.
70	f
73	$FECO_2$ %
76	FEO_2 %
80	Total time min.

TABLE 4-2 - FLOW-DIAGRAM OF DATA CALCULATION AND RECORDING

Step 1 -	Raw data sheet.	
Step 2 -	Raw data cards and listing	1st verification
Step 3 -	Calculation and print out of results	2nd verification
Step 4 -	Corrections of program and calculation	3rd verification
Step 5 -	New program for 2nd, 3rd and 4th phase.	
Step 6 -	Calculation and listing of all results Correction	4th verification

Step 7 - Data prepared for analysis for

a) statistician
- cards:
  1) Volumes and flows
  2) $D_{LCO_{SS}}$ rest, $D_{LCO_{SB}}$ technicians
  3) $D_{LCO_{SS}}$ exercise
  4) General data
- tape

b) Physiologist
- cards:
  1) General data, technicians
  2) Volumes, flows, (results)
  3) Volumes, flows, (predicted)
  4) $D_{LCO_{SB}}$ - (results and predicted)
  5) $D_{LCO_{SS}}$ rest (results and predicted)
  6) $D_{LCO_{SS}}$ 200 (results and predicted)
  7) $D_{LCO_{SS}}$ 400 or 600 (results and predicted)
  8) % predicted
- tape

Step 8 - Preparation of a 9nd card to facilitate analysis.

that the raw data sheet was correct in every detail. The values were then punched on four raw data cards to be processed on an IBM 360 computer using a program calculating the pulmonary function results. A print-out of the results were obtained from the computer, and after corrections, a print and a card output were produced for use in the statistical analysis. The flow diagram for the handling of the data prior to analysis is shown in Table 4-2.

Control of Quality and Validity of the Results:

Inter-observer differences were studied by repeated sequential measurements on two subjects. No significant difference was found between the results of the two technicians testing the same subject, nor between morning and afternoon testing (Table 4-3). From this it was concluded that neither inter-observer nor within-subject variation was likely to have been important in this study.

As the study conducted in two cities lasted several months, the influence of place, season, increasing experience of technicians and the state of the apparatus might all have contributed to the between-subject variation. An overall check of the laboratory quality was obtained by testing 31 men twice, once in Thetford Mines, once in Asbestos. The two sets of results were compared (Table 4-4). No significant difference was found in tests where cooperation was not required; a slight increase, significant at the 0.05 level was found in tests such as VC and those conducted during exercise where training could play a role (Fournier-Massey et al, 1970).

TABLE 4-3 – REPEAT PULMONARY FUNCTION MEASUREMENTS ON TWO SUBJECTS (BETWEEN MORNING AND AFTERNOON MEASUREMENTS) ANALYSED FOR INTER-OBSERVER AND WITHIN SUBJECT VARIATION **

	SUBJECT A.S.					SUBJECT R.K.				
TEST	no of trials	mean	within subject diff.	S.E.' of a single observation	inter-observer diff.	no of trials	mean	within subject diff.	S.E.' of a single observation	inter-observer diff.
VC L.	23	4.70	- 0.05	0.09	+ 0.01	15	5.99	- 0.05	0.15	- 0.13
FRC L.	23	2.46	- 0.10x	0.10	- 0.05	15	4.16	+ 0.06	0.16	+ 0.01
RV L.	23	0.81	- 0.02	0.10	- 0.04	15	1.66	+ 0.07	0.03	+ 0.00
TLC L.	23	5.63	- 0.02	0.12	- 0.01	15	7.82	+ 0.07	0.13	- 0.13
ME %	23	63.40	- 2.36	9.91	- 4.80	15	57.90	+ 2.34	7.37	+ 1.00
FEV$_{75}$ L.	23	3.73	- 0.04	0.09	+ 0.07	15	4.63	+ 0.05	0.11	+ 0.00
FEV$_1$ L.	23	4.08	- 0.02	0.09	+ 0.08	15	5.19	+ 0.05	0.11	+ 0.02
FVC L.	23	4.81	- 0.00	0.07	+ 0.04	15	6.13	- 0.04	0.13	+ 0.15
FEV$_1$ %	23	86.10	- 1.28	2.24	+ 1.76	15	86.00	- 0.90	2.36	- 0.22
MMF L/sec	23	4.20	+ 0.06	0.36	+ 0.11	15	5.18	+ 0.23	0.37	+ 0.26
$D_{LCO_{SB}}$ **	23	36.00	+ 5.78x	3.40	+ 1.68	15	41.50	+ 2.26	3.40	+ 5.22
K_{CO} cc/min	23	5.93	+ 0.94	0.54	+ 0.21	15	5.19	+ 0.12	0.61	+ 0.59
$D_{LCO_{SS}}$ rest	22	13.84	+ 0.30	1.62	+ 0.38					
200	22	20.13	+ 2.13	1.78	+ 1.40					
600	22	26.05	+ 2.75	1.95	+ 0.05					
Ext$_{CO}$ %										
rest %	22	39.60	- 1.15	2.78	+ 0.57					
200 KMm	22	41.50	- 0.39	2.19	+ 1.61					
600 KMm	22	33.90	+ 0.76	1.63	+ 1.04					
Heart min										
rest	22	84.20	+ 8.83	10.00	- 0.87					
200 KMm	22	97.60	+13.41	11.75	+ 3.12					
600 KMm	22	139.10	+ 6.25	9.88	+ 2.82					
$\dot{V}_E$ L/min										
rest	22	11.20	- 0.16	1.71	- 0.30					
200 KMm	22	16.50	+ 0.63	1.35	- 0.47					
600 KMm	22	33.80	- 0.64	2.80	- 1.59					
$\dot{V}_{O_2}$ L/min										
rest	22	0.31	+ 0.02	0.02	+ 0.04					
200 KMm	22	0.63	+ 0.03	0.03	- 0.02					
600 KMm	22	1.31	+ 0.06	0.06	- 0.05					

' S.E. Standard error

x P = 0.05

* Variance analysis

** ccCO/min/mm Hg

TABLE 4-4 - RESULTS OF 31 SUBJECTS TESTED AT THETFORD AND AT ASBESTOS

TEST		No. of Subjects	FIRST TEST Mean ± S.D.		CHANGE Mean ± S.D.	
VC	L.	31	3.99	0.71	+ 0.16	0.29*
FRC	L.	31	3.03	0.61	+ 0.02	0.25
RV	L.	31	1.64	0.36	- 0.06	0.26
TLC	L.	31	5.97	0.88	+ 0.08	0.23
ME	%	31	56.10	7.80	- 0.10	14.60
FEV_{75}	L.	31	3.27	0.55	+ 0.03	0.20
FVC	L.	31	4.35	0.81	+ 0.10	0.26
FEV_1	%	31	83.40	7.40	- 2.30	4.80*
MMF	L./sec.	31	4.02	1.18	- 0.14	0.60*
$D_{LCO_{SB}}$	ccCO/min/mmHg	30	34.00	8.70	- 0.90	4.80
K	ccCO/min	30	5.57	1.63	- 0.18	0.64
$V_{A_{SB}}$	L.	30	5.61	0.82	+ 0.03	0.42
$D_{LCO_{SS}}$	ccCO/min/mmHg					
	rest	30	13.70	3.80	- 0.30	2.90
	200 KMm	30	27.10	9.40	- 1.90	3.90*
	400 KMm	6	27.00	5.40	- 3.90	1.90*
	600 KMm	13	38.20	6.10	- 3.70	3.80*
Ext_{CO}	%					
	rest	30	43.00	6.00	0.00	5.00
	200 KMm	30	43.00	7.00	0.00	4.00
	400 KMm	6	33.00	4.00	- 1.00	3.00
	600 KMm	13	39.00	5.00	- 2.00	2.00
Heart	min					
	rest	30	81	1	- 3	9
	200 KMm	30	102	2	- 4	11
	400 KMm	6	121	6	- 1	7
	600 KMm	13	134	1	- 3	9
$\dot{V}_E$	L./min					
	rest	30	10.30	3.20	0.10	1.80
	200	30	18.20	5.30	- 1.30	3.20
	400	6	32.50	4.20	- 2.80	3.70
	600	13	35.40	3.70	- 1.00	2.40
$\dot{V}_{O_2}$	L./min					
	rest	30	0.26	0.70	0.00	0.30
	200 KMm	30	0.69	0.09	- 0.02	0.12
	400 KMm	6	1.04	0.12	- 0.05	0.10
	600 KMm	13	1.37	0.09	- 0.02	0.07

* $P < 0.01$ t-Test for paired values.

TABLE 4-5 - ASSIGNMENT OF CODES TO RESULTS OF THE FIVE TESTS USED TO CLASSIFY PULMONARY FUNCTION PROFILES

TEST	% OF PREDICTED VALUE	CODE
Volumes: RV and TLC	< 70	7
	70 - 79	8
	80 - 89	9
	90 - 110	10
	111 - 120	11
	121 - 130	12
	131 <	13
Flows: FEV75 and MMF	< 70	13
	70 - 79	12
	80 - 89	11
	90 - 110	10
	111 - 120	9
	121 - 130	8
	131 <	7
Flow-Volume: FEV$_1$%	< 84	13
	85 - 89	12
	90 - 94	11
	95 - 105	10
	106 - 110	9
	111 - 115	8
	116 >	7

First Analysis of Results:

In order to classify subjects according to their lung function profile, comparison with expected values was necessary. Those of Goldman and Becklake (1959) were used for the volumes; those of Needham (1954) and Bates et al (1962) for mixing efficiency; those of Cotes et al (1966) for flow rates; those of Cotes (1965) for $D_{LCO_{SB}}$; those of Bates (1962) for $D_{LCO_{SS}}$ and Donevan et al (1959) for that on exercise. The formula of these predicted values are found in Appendix II, Table II-2.

The second step was to classify each subject by his pulmonary function into restrictive, obstructive, a mixed or normal pulmonary function. The third step was to group subjects with similar results together.

The lung function profiles were determined from the following five measurements, each expressed as % expected: RV, TLC, FEV_{75}, MMF and $FEV_1\%$. Codes were assigned to each of these five tests (Table 4-5) in such a way that when added, a low score indicated a restrictive profile and a high score an obstructive one. The sum of the five codes gave scores ranging from 37 to 65 (Table 4-6).

Score 50 could be obtained by all five codes having a value of 10 (normal profile) or by a mathematical balance of codes under, equal to and over 10 (undifferentiated profile). Score 49 and under could result from all five codes ranging from 7 to 10 inclusively (restrictive profile) or codes ranging from 7 to 13 but predominantly under 10 (dominant restrictive profile). In the same fashion, scores 51 and over could result from codes for all tests lying between 10 and 13 (obstructive profile) or by the combination of codes from 7 to 13 with a predominance of codes over 10 (dominant

TABLE 4-6 - LUNG FUNCTION TYPES BASED ON SCORING SYSTEM

TESTS AND CODES	SCORES	PROFILES
All tests have code 10	50	NORMAL
Tests have codes 7 to 10 incl.	38-49	DEFINITE RESTRICTIVE
Tests have codes 10 to 13 incl.	51-65	DEFINITE OBSTRUCTIVE
Tests have codes 7 to 13 incl.		
equally divided below & above 10	50	UNDIFFERENTIATED
most tests under 10	40-49	DOMINANT RESTRICTIVE
most tests over 10	51-58	DOMINANT OBSTRUCTIVE

It was impossible to have the scores 35 to 37, because if volumes are decreased severely, flows usually drop, and the codes will then be under 10 for the volumes (small volumes) and over 10 for the flows (small flows) giving a mixed profile.

obstructive profile).

For example, a low score of 42 could result from the addition of five low codes (8, 8, 8, 8, 9) or three low, one normal and one high (7, 7, 7, 10, 11). The former would be classified as a definite restrictive profile and the latter as a dominant restrictive one. Likewise, the score 58 could be given by the addition of one 10 and four over 10 (11, 10, 13, 11, 13) or by the combination of one under 10, one 10 and three over 10 (9, 10, 13, 13, 13).

The results of the 1034 men were separated in this way in six profiles: normal or undifferentiated function, definite or dominant restriction, and definite or dominant obstruction.

3. ASSOCIATED INFORMATION

The following additional information was obtained on each subject:

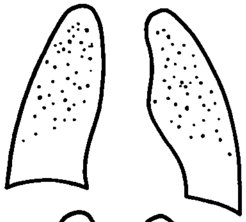
Anthropology:

Height, weight and arm span were measured when the subjects came for their pulmonary function tests.

FIGURE 4-2

U.I.C.C./CINCINNATI CLASSIFICATION OF RADIOGRAPHIC APPEARANCES OF PNEUMOCONIOSES

1



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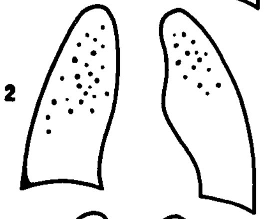

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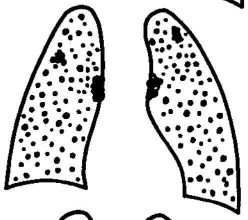

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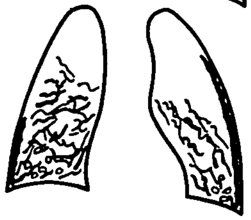
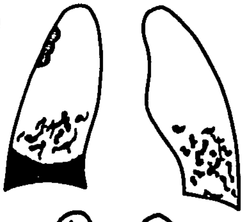
5

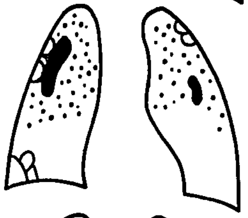


		ROUNDED SMALL OPACITIES				IRREGULAR SMALL OPACITIES				LARGE OPACITIES			PLEURAL THICKENING						PLEURAL CALCIFICATION						
Sketch Number	Quality	Type	Profusion	Zones R	Zones L	Type	Profusion	Zones R	Zones L	Type	Size	Costophrenic angle	Diffuse	Plaques	Grade	None	ILL DEFINED DIAPHRAGM	ILL DEFINED CARDIAC OUTLINE	Diaphragm	Wall	Other	Grade	None	Symbols	Comments
1		p	2/2	✓ ✓ ☐	✓ ✓ ☐		0/0	☐ ☐ ☐	☐ ☐ ☐		0	0				0	0	0					0	0	0
2		q	1/2	✓ ✓ ☐	✓ ☐ ☐		0/0	☐ ☐ ☐	☐ ☐ ☐		0	R				0	0	0					0	0	0
3		r	3/3	✓ ✓ ✓	✓ ✓ ✓		0/0	☐ ☐ ☐	☐ ☐ ☐		0	0				0	0	0					0	es ax	0
4			0/0	☐ ☐ ☐	☐ ☐ ☐	s	2/1	☐ ✓ ✓	☐ ☐ ✓		0	0				0	0	0	L R	L R	L R	3		cp	0
5			0/0	☐ ☐ ☐	☐ ☐ ☐	t	3/2	☐ ✓ ✓	☐ ✓ ✓		0	0	L R		3		0	0					0	ho	0
6			0/0	☐ ☐ ☐	☐ ☐ ☐	u	2/1	☐ ☐ ✓	☐ ☐ ✓		0	0		L	1		0	0					0	ca	ca = mesothelioma effusion
7		q	2/2	✓ ✓ ☐	✓ ✓ ☐		0/0	☐ ☐ ☐	☐ ☐ ☐	wd	B	0				0	0	0					0	bu	0
8			0/0	☐ ☐ ☐	☐ ☐ ☐	t	3/4	✓ ✓ ✓	✓ ✓ ✓	id	B	L R	L R		1		L R	3					0	0	0
9		r	1/0	✓ ✓ ☐	✓ ✓ ☐		0/0	☐ ☐ ☐	☐ ☐ ☐		0	L R				0	0	0					0	di tba cv	?silico-tuberculosis
10		p	2/1	✓ ✓ ☐	✓ ✓ ☐	s	2/3	✓ ✓ ✓	☐ ✓ ✓		0	0				0	0	0					0	ca k	0
	+ ± ± U/R	p q r	0/– 0/0 0/1 1/0 1/1 1/2 2/1 2/2 2/3 3/2 3/3 3/4	Check zones involved		s t u	0/– 0/0 0/1 1/0 1/1 1/2 2/1 2/2 2/3 3/2 3/3 3/4	Check zones involved		wd id	0 A B C	0 R L	R L		1 2 3	0 if none	0 R L	0 1 2 3	R L			1 2 3	0 if none	0 co es co ed cp tba	

6



7



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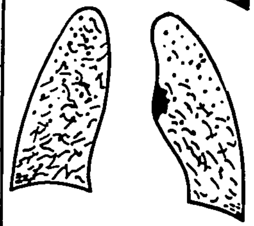


Clinical Data:

Each subject, who presented himself for pulmonary function testing, also answered a questionnaire in French or English. This was essentially a modified form of British Medical Research Council questionnaire (Fletcher, 1966, Appendix II). Questions 1 to 31, dealing with cough, phlegm, breathlessness, wheezing, effect of weather, nasal catarrh and history of chest illnesses were used without any modification.

The occupational history was recorded in greater detail and five questions were added on arthritic and rheumatic symptoms. These represent diseases which could influence the pulmonary function at rest and on exercise. Finally, questions were asked concerning trauma, pulmonary and pleural problems.

Radiology:

The most recent chest radiograph taken within the previous 12 months was assessed by an international panel of six readers: Dr. L.J. Bristol (U.S.A.), Dr. J.C. Gilson (U.K.), Dr. J.K. Sluis-Cremer (South Africa) and Drs. P. Cartier, T.R. Grainger and J.C. McDonald from Canada. The classification used has been described previously (Böhlig et al, 1970). It is based essentially on the presence and profusion of small opacities, round and/or irregular; it allows for comment on large opacities, pleural thickening, poorly defined diaphragm and /or cardiac border, and pleural calcification as illustrated in Figure 4-2. The profusion of the small opacities was graded by an expansion of the usual four point scale (0, 1, 2, 3) to a 12 point scale (0/-, 0/0, 0/1, 1/0, 1/1, 1/2, 2/1, 2/2, 2/3, 3/2, 3/3, 3/4) in the manner suggested by Liddell (1963). Each radiograph was allocated to a category according to the second highest score of the six readers.

Dust exposure and effort:

The influence of the working environment was assessed by developing indices based on the dust concentration and on the physical effort involved in any job, using a method developed by Gibbs and already reported in detail (Gibbs and Lachance, 1972).

The occupational history of each employee was obtained from the cardex of every company where he had worked. The cardex provided the date when he began and left each position and what he had done during that time.

Each of these positions was rated for dust exposure and physical effort involved. Dust measurements have been made in the Quebec Asbestos industry for many years. A dust sampling engineer was appointed by the Quebec Asbestos Mining Association about 1952, but some five years prior to this date, the same individual began to carry out a number of dust measurements in the industry while employed by the Quebec Government. All these figures were available, and were arranged as to year and job location. The dust concentration was classified into thirteen categories. The physical effort of each job was assessed by designing a scale for physical effort and physical application based on the number of pounds lifted per hour, and points were assigned for each job. For those positions whose title had become obsolete, a correlation was made with existing positions. For those positions which had disappeared, descriptions were obtained from personnel records and the older employees.

Three indices were calculated: one involving the dust exposure only, the two others the dust exposure and the physical effort required for each job. The dust index (Dust I) for each person was calculated by adding together the product of time spent in each job, in years or fraction of years, and the average estimated dust concentration in millions particles per cubic foot (MPPCF). For example, a man who worked for three years at 80 MPPCF, seven at 10 MPPCF and eight at 15 MPPCF would be assigned an index of 430 (240 + 70 + 120). This procedure implies that biological significance of a given dust index is essentially the same whatever the combination of years and dust concentrations. Though the method is commonly used because it gives a more quantitative evaluation than the number of years of work in the industry, the underlying assumption may not be wholly valid.

The accumulated dust exposure weighted for physical effort was also calculated in a similar fashion as the accumulated sum of the product of the physical factor (based on the number of pounds lifted per hour) and the accumulated dust exposure for each individual job. A third index took into account not only the rate of work, but also the duration of effort. In this thesis, the third index was preferred to the second one and will be referred ~~now~~ to as Dust II.

Smoking Habits:

From the Questionnaire mentioned previously (Fletcher, 1966), questions on smoking were adapted in a very minor way to the local idiom. Smoking histories were examined by a classification based on the number of cigarettes (or equivalent) currently smoked per day. Non-smokers were defined as those who never smoked as much as one cigarette a day for as long as one year.

As for the pulmonary function tests results, all data on the measurements of health and the associated factors were transferred on cards for subsequent analysis.

4. STATISTICAL ANALYSIS

Pulmonary function results were described by using the means and standard deviations of the means for groups of individuals divided on the basis of their lung function scores. Other measurements of health and associated factors were related to function by determining prevalence rates for different groups of individuals as defined above.

Principal component analysis was done in two steps: the first one includes 18 principal variables in which the five tests used to separate restrictive and obstructive profiles were included, and the second one where they were omitted, leaving 13 variables. By this technique, those factors, which apparently play a part in determining the pulmonary diseases, could in theory be separated into those which are important and independant and those which are less important. The initial set of correlated variables was treated by linear transformation to give a new set of uncorrelated components. Each component was then extracted in order of its contribution to the total variance of the original variables: the nature of the variability which remains can be ignored. The component score for each individual was then calculated as a weighted sum of the values of the original variables after they have been standardized by substracting the mean and dividing by the standard deviation. When the individual scores are plotted against the axis of the components, meaningful trends may emerge.

To evaluate the importance of each coding test in the definition of the profiles, a multivariate path or a dependance analysis was done. This type of analysis, which is an extension of the multiple regression coefficient analysis, defines the causal linkages of input variables (five coding tests, plus 13 other ones) over dependant variables (code) (Heise, 1969).

5 - RESULTS

1. GENERAL.

2. PULMONARY FUNCTION IN RELATION TO ASBESTOS EXPOSURE.
   Distribution of subjects by pulmonary function scores.
   Pulmonary function in the subgroups classified by profile.
   Pulmonary function profiles by decade.

3. ASSOCIATION OF PULMONARY FUNCTION PROFILES WITH QUESTIONNAIRE AND RADIOGRAPH.
   Questionnaire.
   Radiology.

4. PULMONARY FUNCTION PROFILES IN RELATION TO:
   Duration of work in the industry.
   Dust exposure - Dust I and Dust II.
   Cigarettes.
   Dust II and cigarettes.

5. PRINCIPAL COMPONENT ANALYSIS.
   Analysis with 18 variables including the five tests used to determine profiles.
   Analysis with 13 variables excluding the five tests used to determine profiles.

6. SUMMARY.

TABLE 5-1 - DISTRIBUTION OF SUBJECTS BY PULMONARY FUNCTION SCORE IN THE 1967 AND 1968 SURVEYS

	FUNCTION SCORES	DEFINITE PROFILES				DOMINANT PROFILES		
		1967	1968	Total		1967	1968	Total
	38	1	-	1	DOMINANT RESTRICTION			
	39	4	-	4				
RESTRICTION	40	9	2	11		1	-	1
	41	11	3	14				
	42	25	1	26				
	43	26	5	31		9	1	10
	44	33	1	34		11	1	12
	45	35	3	38		6	2	8
	46	43	4	47		11	1	12
	47	42	6	48		18	1	19
	48	37	6	43		20	5	25
	49	36	1	37		33	11	44
NOR-MAL	50	27	-	27	UN-DIFF.	47	10	57
	51	22	3	25	DOMINANT OBSTRUCTION	29	9	38
	52	27	3	30		26	6	32
	53	30	6	36		15	11	26
OBSTRUCTION	54	38	8	46		12	5	17
	55	31	7	38		13	1	14
	56	29	6	35		13	2	15
	57	13	5	18		7	1	8
	58	19	9	28		5	1	6
	59	21	2	23				
	60	7	4	11				
	61	9	2	11				
	62	10	4	14				
	63	6	3	9				
	64	2	-	2				
	65	2	-	2				
SUMMARY								
	38-49	302	32	334		109	22	131
	50	27	-	27		47	10	57
	51-65	265	63	328		121	36	157
TOTAL		594	95	689		277	68	345

1. GENERAL

Every worker examined had been exposed to asbestos; the results were analysed so that three major questions could be answered:

1) What is the prevalence of lung function profiles in these workers?
2) How are these profiles related to clinical or radiological findings?
3) In what way are dust and cigarettes responsible for the functional changes?

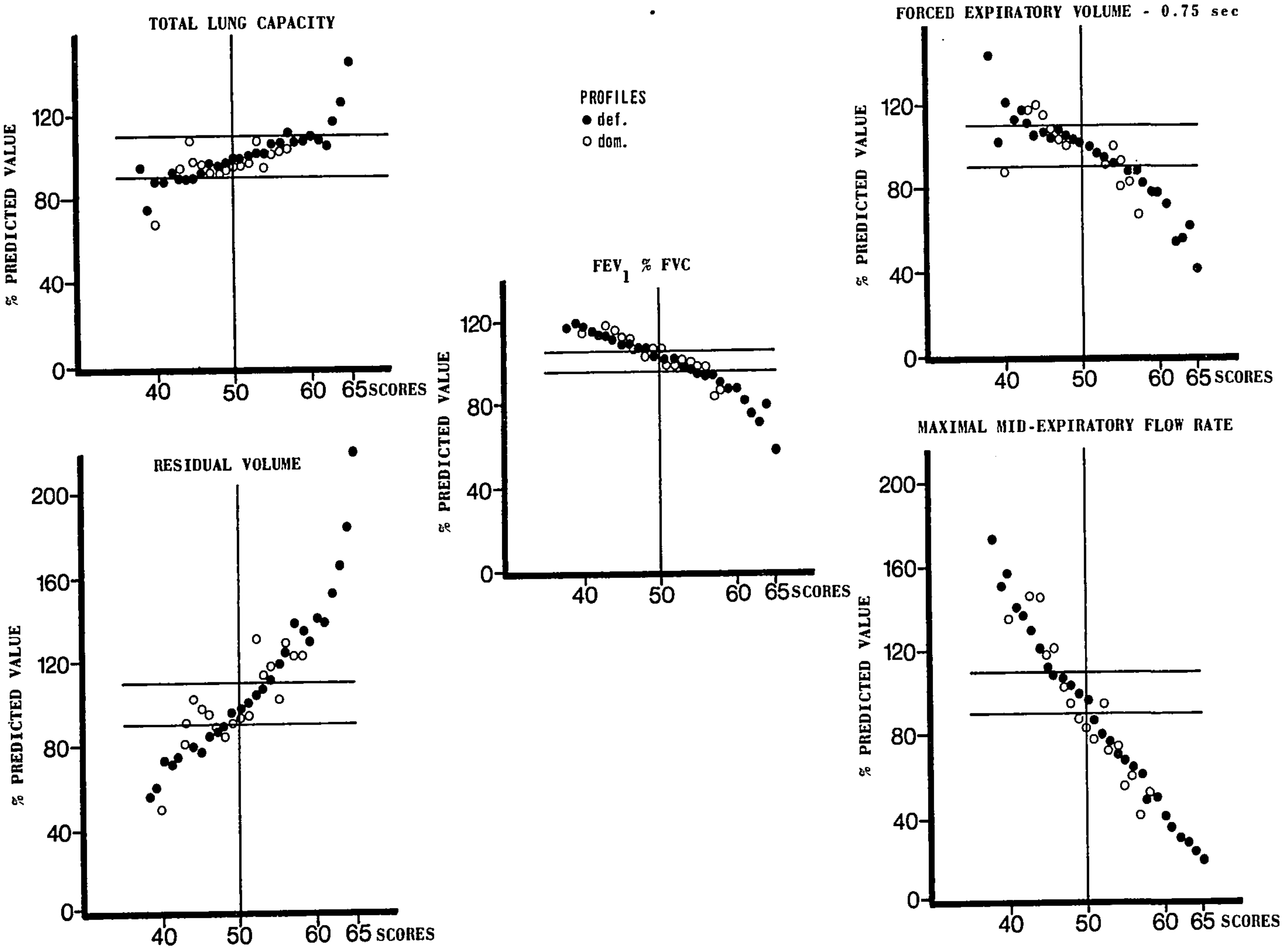
The answer to the first question was obtained by examining the distribution of pulmonary function scores in the workers tested, and analysing the results in terms of six main profiles. The second was answered by correlating these profiles with clinical symptoms and radiological findings, and the third one by assessing the influence of dust exposure, physical effort and smoking, which have been implicated in the pulmonary function alterations in asbestos workers.

2. PULMONARY FUNCTION IN RELATION TO ASBESTOS EXPOSURE:

Distribution of subjects by pulmonary function scores:

The distribution of subjects by pulmonary function scores (the score derived from RV, TLC, FEV_{75}, FEV_1 and MMF as indicated above) is shown in Table 5-1 (opposite page). A score of 50 (i.e. indicating

FIG. 5-1 - MEAN VALUES OF THE FIVE SCORING TESTS, EXPRESSED AS % PREDICTED VALUES IN THE - 1967-1968 SURVEYS



results + 10% of expected established the demarcation between the decreasing scores of the restrictive profile and the increasing scores of the obstructive one.

It will be seen that there are no men with scores indicating marked restriction (below 37), because if volumes were markedly reduced, flows were automatically decreased, and the subject would then be classified as having a dominant rather than a definite profile.

Only 27 subjects were found to have a score of 50 in the 1967 survey and no one in 1968. However, 302 and 32 subjects (in 1967 and 1968 respectively) had scores below 50, i.e. fell into the restrictive side, and 265 and 63 respectively scores above 50 in the obstructive area. In subjects who were classified as having dominant patterns, (47 subjects in 1967 and 10 in 1968) had a score of 50 (i.e. undifferentiated abnormal pattern), 109 and 22 respectively fell below 50 (dominant restrictive), and 121 and 36 above 50 in the range indicating a dominant obstructive pattern.

Figure 5-1 indicates the contribution of each test to the score and its relative importance in classifying the subjects, results of the 1967 and 1968 surveys being combined. In subjects classified as dominant, scores also fell in the same ranges but had a much greater standard deviation.

An analysis of dependance was performed to define what tests were more important in defining the codes, definite and dominant. The definite codes depend primarily on MMF (correlation coefficient - 0.545), less on RV, $FEV_1\%$ and FEV_{75} (0.441, -0.351 and - 0.320) respectively, and very little on TLC (0.086). The dominant codes were based more on RV (0.523), about equally on MMF and FEV_{75} (- 0.453 and - 0.450) and less on TLC and $FEV_1\%$ (0.276 and

TABLE 5-2 - CLASSIFICATION OF SUBJECTS ACCORDING TO PULMONARY FUNCTION SCORE

SCORES	PROFILES	SUBJECTS Number 1967	1968	1967-68	% Total	Age Standardized % of Total
38-44	RESTRICTIVE					
	Definite	109	12	121	11.7	12.8
	Dominant	21	2	23	2.2	2.1
45-55	"NORMAL"					
	Normal	367	47	414	40.0	44.3
	Undifferentiated	231	62	293	28.3	26.5
56-65	OBSTRUCTIVE					
	Definite	118	36	154	14.9	12.2
	Dominant	25	4	29	2.9	2.1
TOTAL	Definite	594	95	689	66.6	69.7
	Dominant	277	68	345	33.4	30.3
	TOTAL	871	163	1034	100.0	100.0

- 0.226).

The analysis of the 45 groups according to pulmonary function scores alone and with the measurements of health and associated factors would have been difficult from a practical point of view. Results were first examined with the subjects divided into 12 groups according to their lung function score (7 definite and 5 dominant profiles); to further simplify the analysis, sub-groups were then amalgamated, reducing the number to six profiles. As this did not seem to modify the conclusions, results are so reported here.

Table 5-2 lists the number of subjects in each profile, in both surveys, separately and combined. Three definite profiles are listed: restrictive, normal and obstructive; and three dominant ones: restrictive, undifferentiated and obstructive. More subjects were classified into the definite obstructive profile (118 and 36 in 1967 and 1968 respectively, or 14.9%), than in the definite restrictive profile (109 and 12 in 1967 and 1968 respectively, or 11.7%). Likewise, there were more with a dominant obstructive profile, (25 and 4 in 1967 and 1968, respectively, or 2.9%), than with a dominant restrictive profile (21 and 2 in 1967 and 1968 respectively, or 2.2%). A normal profile was found in 367 subjects in 1967 and 47 in 1968, or 40.0%. The undifferentiated abnormal profile was present in 231 subjects in 1967 and 62 in 1968 or 28.3%. Finally, more subjects with definite as opposed to dominant profiles were found in the 1967 survey than in the 1968, in the proportion of two-thirds to one-third respectively.

The selection of subjects had included progressively more in the older age groups (i.e. was age-stratified). In order to draw conclusions about

TABLE 5-3 - MEANS AND STANDARD DEVIATIONS OF PULMONARY FUNCTION RESULTS IN EACH DEFINITE AND DOMINANT PROFILE, COMBINED 1967-68 SURVEYS.

		NORMAL		UNDIFF. PROFILE		RESTRICTION				OBSTRUCTION			
						DEFINITE		DOMINANT		DEFINITE		DOMINANT	
		Mean±S.D.		Mean±S.D.		Mean±S.D.		Mean±S.D.		Mean±S.D.		Mean±S.D.	
No Subj		414		293		121		23		154		29	
Age	yrs	46.3	12.1	49.6	12.4	46.1	12.3	48.7	12.4	53.2	10.2	55.0	8.4
Ht	cm	169.1	6.7	167.3	6.4	169.8	5.6	169.2	6.8	166.8	6.1	168.7	7.3
Wt	kgs	73.2	11.3	70.7	11.9	78.1	11.4	74.1	10.4	69.7	11.6	71.8	10.5
Tests chosen for definition of profiles													
RV	% P	96.9	17.6	100.3	63.3	74.6	14.9	95.8	22.4	138.6	24.8	126.1	26.9
TLC	% P	98.3	8.3	96.6	16.5	90.0	10.3	99.5	18.5	109.3	11.1	100.3	22.3
FEV_{75}	% P	101.8	11.7	99.5	19.1	113.5	14.2	121.4	25.0	79.1	16.7	79.6	29.5
$FEV_1\%$	% P	103.2	6.3	102.9	7.4	113.1	5.0	115.0	5.0	87.3	10.4	90.7	12.6
MMF	% P	92.7	18.9	87.6	61.7	133.7	20.2	145.7	36.2	49.1	18.5	52.9	19.7
Other tests													
VC	% P	92.1	10.3	89.8	17.4	90.8	12.6	95.6	21.0	86.8	13.9	79.0	23.8
FRC	% P	90.5	16.7	90.8	20.4	74.7	15.2	90.7	21.5	112.8	16.7	103.6	19.9
FEV_1	%	79.8	5.2	79.0	5.8	87.4	3.8	88.5	4.8	66.6	8.1	68.8	9.5
ME	% P	95.0	22.2	94.8	22.8	100.8	26.5	101.0	23.1	83.4	24.5	95.3	24.0
FVC	L	4.0	0.8	3.7	0.9	3.0	0.8	4.0	1.0	3.4	0.8	3.2	1.1
No subj		179		131		48		9		86		13	
$D_{L}CO_{SB}$	*	30.0	7.7	25.3	6.6	28.4	6.3	27.6	7.2	25.6	7.1	25.4	7.1
K_{CO}	'	4.9	1.0	4.6	1.0	5.1	0.9	4.3	1.1	4.2	0.9	4.2	1.0
V_A	L	5.7	0.8	5.2	1.1	5.2	0.8	6.0	1.1	5.6	0.9	5.6	1.1
REST													
No subj		410		290		120		23		152		29	
$D_{L}CO_{SS}$	*	12.8	4.3	11.6	4.2	13.9	5.1	12.6	3.2	10.8	4.1	10.3	4.0
Ext_{CO}	%	42.3	5.9	40.7	6.5	42.5	6.5	42.9	7.9	39.0	7.7	38.7	6.3
$\dot{V}$	+	9.4	2.3	9.5	2.6	10.2	2.6	9.7	3.2	9.6	2.5	9.7	2.0
$\dot{V}O_2$	+	0.27	0.05	0.26	0.05	0.29	0.05	0.27	0.05	0.26	0.05	0.27	0.07
200KMm													
No subj		363		248		110		18		130		24	
$D_{L}CO_{SS}$	*	23.6	5.5	22.0	6.1	24.3	6.8	24.0	5.3	20.6	6.6	19.1	4.5
Ext_{CO}	%	40.4	5.3	38.8	6.0	40.7	5.7	41.6	5.2	37.0	6.6	36.2	5.8
$\dot{V}$	+	19.2	3.3	19.6	3.3	19.8	3.6	18.9	3.1	20.0	4.4	20.6	4.0
$\dot{V}O_2$	+	0.73	0.13	0.72	0.12	0.74	0.13	0.72	0.11	0.70	0.14	0.73	0.11
400KMm													
No subj		158		114		52		10		59		12	
$D_{L}CO_{SS}$	*	28.2	5.5	27.3	5.4	28.6	5.2	31.5	11.4	26.8	6.0	25.6	4.2
Ext_{CO}	%	35.9	4.5	35.1	4.8	36.1	4.5	39.2	4.9	33.9	5.8	34.4	4.1
$\dot{V}$	+	30.3	4.3	30.8	4.6	31.0	4.6	28.0	3.4	32.3	6.5	30.8	5.6
$\dot{V}O_2$	+	1.24	0.15	1.22	0.17	1.24	0.15	1.24	0.14	1.22	0.16	1.26	0.11
600KMm													
No subj		86		38		17		3		8		1	
$D_{L}CO_{SS}$	*	35.8	5.6	36.7	6.6	37.9	9.2	36.6	9.3	37.1	5.0	26.3	
Ext_{CO}	%	37.0	3.8	37.2	4.5	40.2	5.7	41.3	7.0	38.6	4.9	35.0	
$\dot{V}$	+	37.1	4.3	37.2	5.1	33.8	3.5	31.4	3.9	35.3	5.8	32.1	
$\dot{V}O_2$	+	1.63	0.22	1.64	0.17	1.65	0.17	1.59	0.08	1.64	0.14	1.03	

' - cc/min * - ccCO/min/mmHg + - L/min

the parent population of asbestos workers of the Eastern Townships the age-standardized prevalence of the different lung function profiles was calculated (Table 5-2); it can be seen that 12.8% of the subjects showed a profile of restriction and 12.2% one of obstruction. The prevalence of a normal profile was 44.3%, of undifferentiated abnormal function 26.5% and of the dominant restriction and obstruction, 21% each. Thus in this working population, the obstructive profile was observed as often as the restrictive one, and mixed syndromes were found in 30% of the cases.

Pulmonary Function in the subgroups classified by profile:

Mean values of physical characteristics and pulmonary function tests for subjects in the six profiles in the combined survey are given in Table 5-3. (The results of each survey separately and combined are included in Appendix III, Table III-1).

Mean age was slightly higher in the obstructive and dominant obstructive profiles compared to the others. By contrast, the subjects with restriction or dominant restriction were slightly taller and heavier than those in the other groups.

Measurements not used to define the function profiles merit comment. The subjects with a restrictive profile had the lowest values for FRC, whereas those with obstruction and dominant obstruction had the lowest VC, a lower K_{CO}, lower $DL_{CO_{SS}}$ and extraction factor at rest and on most levels of exercise. In general measurements in subjects with the dominant obstructive profile were more impaired than those in subjects with definite obstruction. Little difference between the profiles was found in ventilation and oxygen consumption.

TABLE 5-4 - PREVALENCE % IN EACH DECADE OF PULMONARY FUNCTION PROFILES

PREVALENCE OF PULMONARY FUNCTION PROFILES

DECADES	No. of SUBJECTS	NORMAL %	UNDIFFERENTIATED %	RESTRICTION		OBSTRUCTION	
				Definite	Dominant	Definite	Dominant
21-30	112	48	26	16	3	7	-
31-40	175	52	26	13	2	5	1
41-50	239	45	25	12	1	15	2
51-60	274	32	28	12	4	19	4
61 +	234	31	35	8	1	21	4

In summary, subjects were classified into one of six profiles of pulmonary function, three definite and three dominant. The profile of definite obstruction was more frequent than that of the definite restriction; one third of subjects had dominant profiles, most of them in the undifferentiated abnormal group. Subjects with the obstructive profile showed in general more abnormal lung function than those with restrictive profile, particularly in terms of VC, flows and D_L at rest and on exercise.

Pulmonary Function Profiles by Decade:

The prevalence % of subjects in each decade included in each pulmonary function profile is shown in Table 5-4. It can be seen that the prevalence of the restrictive profile decreased with age. Likewise, the prevalence of the normal profile decreased from the younger subjects to the older ones. By contrast, the obstructive profile increased in prevalence with age. The prevalence of the dominant restrictive was low and variable from decade to decade. There was a rather higher prevalence of subjects with undifferentiated abnormal profile which, if anything increased with age. Likewise, there was an increase in prevalence of the dominant obstructive pattern with age.

The mean values for pulmonary function tests for each decade in each profile are included in Tables III-2,3,4. These values shown graphically in Fig. 5-2 are those tests on which the classification into function profiles was based. MMF and $FEV_1\%$ in every decade separate restrictive, normal and obstructive profiles better than FEV_{75}, RV and TLC.

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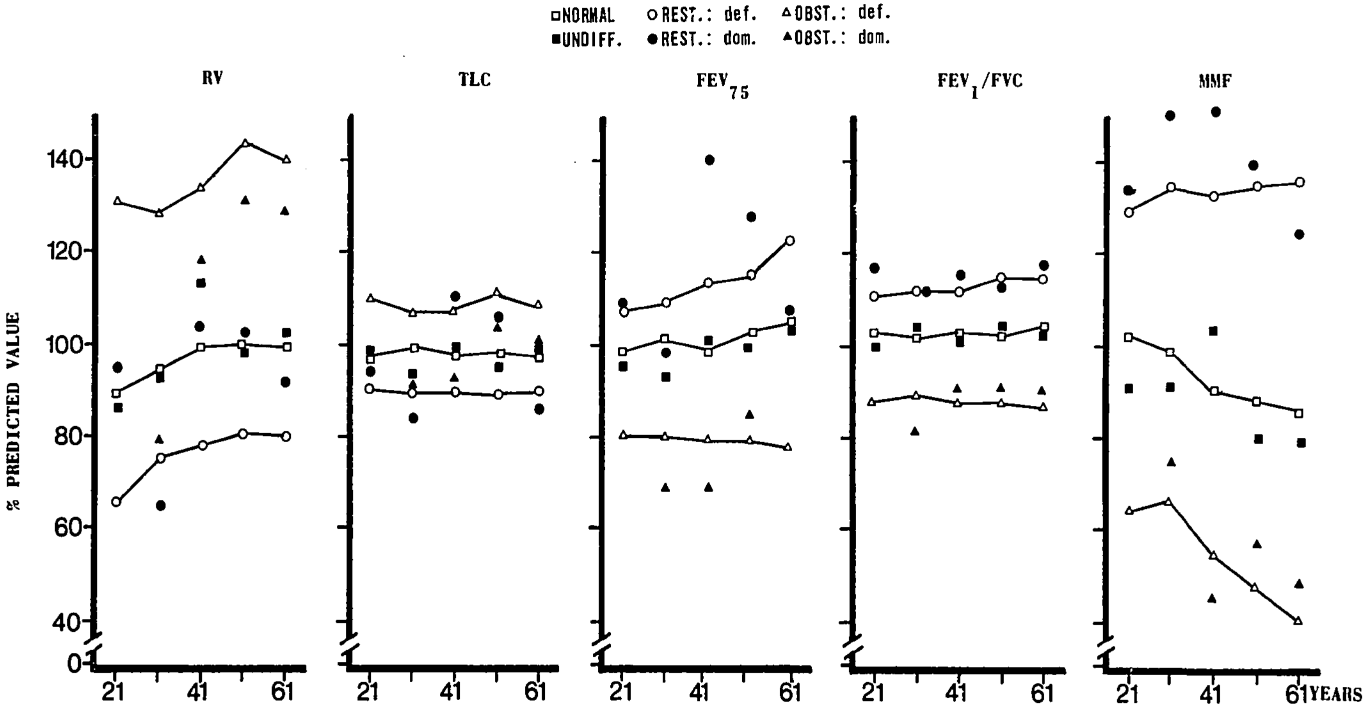
FIG. 5-2 - PULMONARY FUNCTION PROFILES: MEAN VALUES OF THE FIVE SCORING TESTS, EXPRESSED AS % PREDICTED VALUE PER DECADE.



In Fig. 5-3, are included the other principal measurements. It can be seen that VC tended to be lower in obstruction than restriction in every decade. FRC, which varied by more than 30% of expected values between obstruction and restriction at all decades, increased only slightly from 21-30 to decade 61-. Mixing efficiency was normal in restriction and decreased in obstruction. FEV_1% closely allied to the FEV_{75} which was used in classifying the profiles, was in consequence over 85% of FVC in restriction, less than 70% in the obstructive profile. There were less impressive differences of diffusing capacity between profiles, Thus, for $D_{L_{CO_{SB}}}$ the restrictive profile was associated with slightly lower values in the decades 31-40 and 41-50, and slightly higher ones in the other decades, while in the obstructive profile there were generally lower values for $D_{L_{CO_{SS}}}$, at rest and on exercise than in restriction.

In summary, when lung function profiles were examined by decade, the obstructive profile was found to increase and the restrictive profile to decrease in prevalence with age. In general, VC and D_L were lower in that profile compared to the others.

FIG. 5-3

- PULMONARY FUNCTION PROFILES: MEAN VALUES OF VOLUMES, FLOWS AND DIFFUSION TESTS, EXPRESSED AS % PREDICTED VALUES PER DECADE.

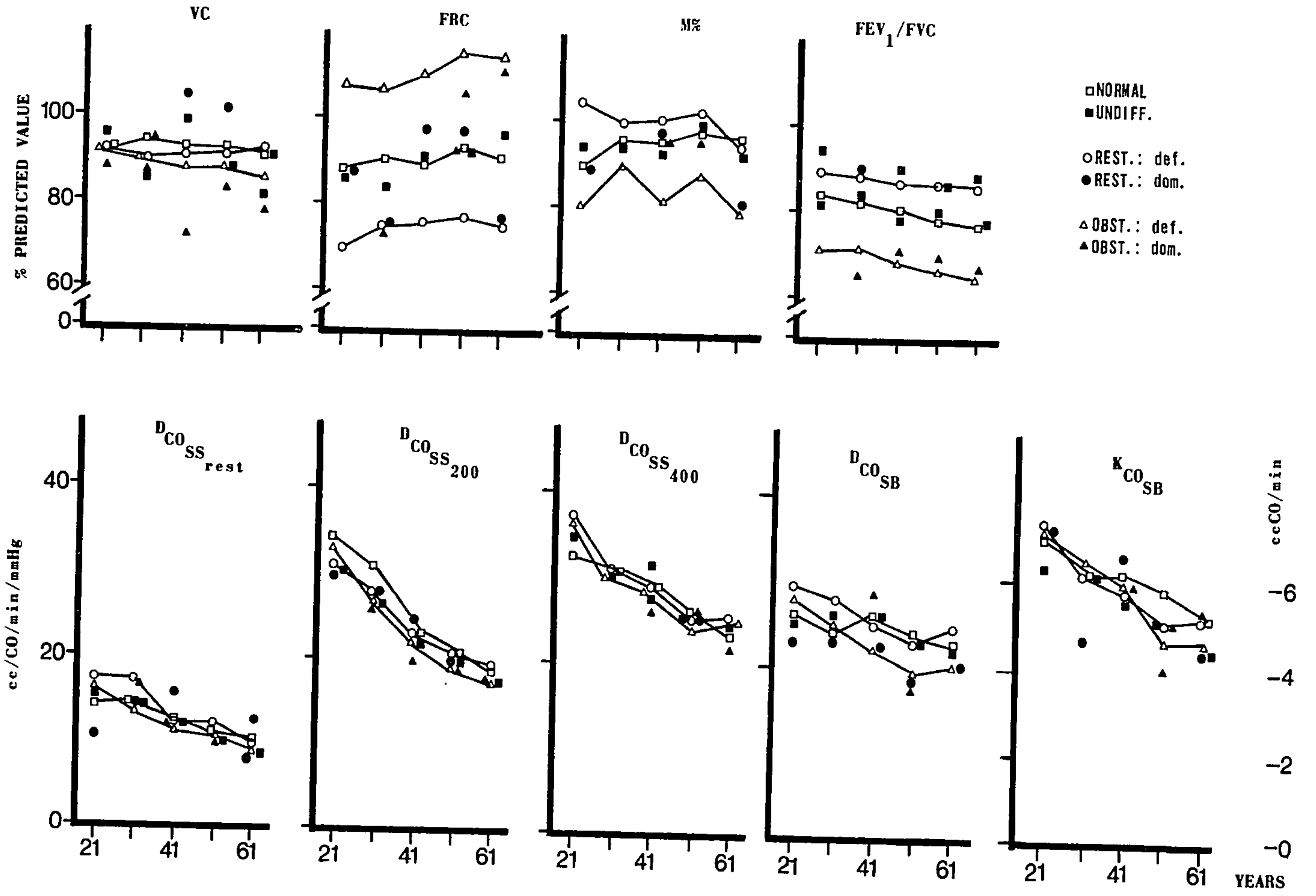


TABLE 5-5 - PREVALENCE % OF RESPIRATORY SYMPTOMS IN PULMONARY FUNCTION PROFILES WITHOUT AND WITH AGE STANDARDIZATION FOR TOTAL POPULATION

PULMONARY FUNCTION PROFILES	No. of SUBJECTS	COUGH 3 mo. %	PHLEGM 3 mo. %	COUGH & PHLEGM 3 mo. %	BREATHLESS-NESS (same age)[x] %	CHEST ILLNESS %
NORMAL	407	49 (48)	45	34 (33)	16 (14)	13
UNDIFFERENTIATED	286	56 (53)	45	35 (31)	26 (17)	13
RESTRICTION						
definite	120	36 (35)*	37	21 (20)	18 (16)	12
dominant	22	29 (14)	33	24 (10)	19 (7)	29
OBSTRUCTION						
definite	149	72 (79)	55	49 (44)	38 (22)	17
dominant	27	74 (47)	48	44 (25)	26 (39)	19

* ( ) Prevalence % age standardized for total population.

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3. ASSOCIATION OF PULMONARY FUNCTION WITH QUESTIONNAIRE AND RADIOGRAPH

The association of lung function profiles with other measures of health i.e. questionnaire and radiology, was then examined. Although examined for both surveys independently, only the conclusions for the combined results will be considered here.

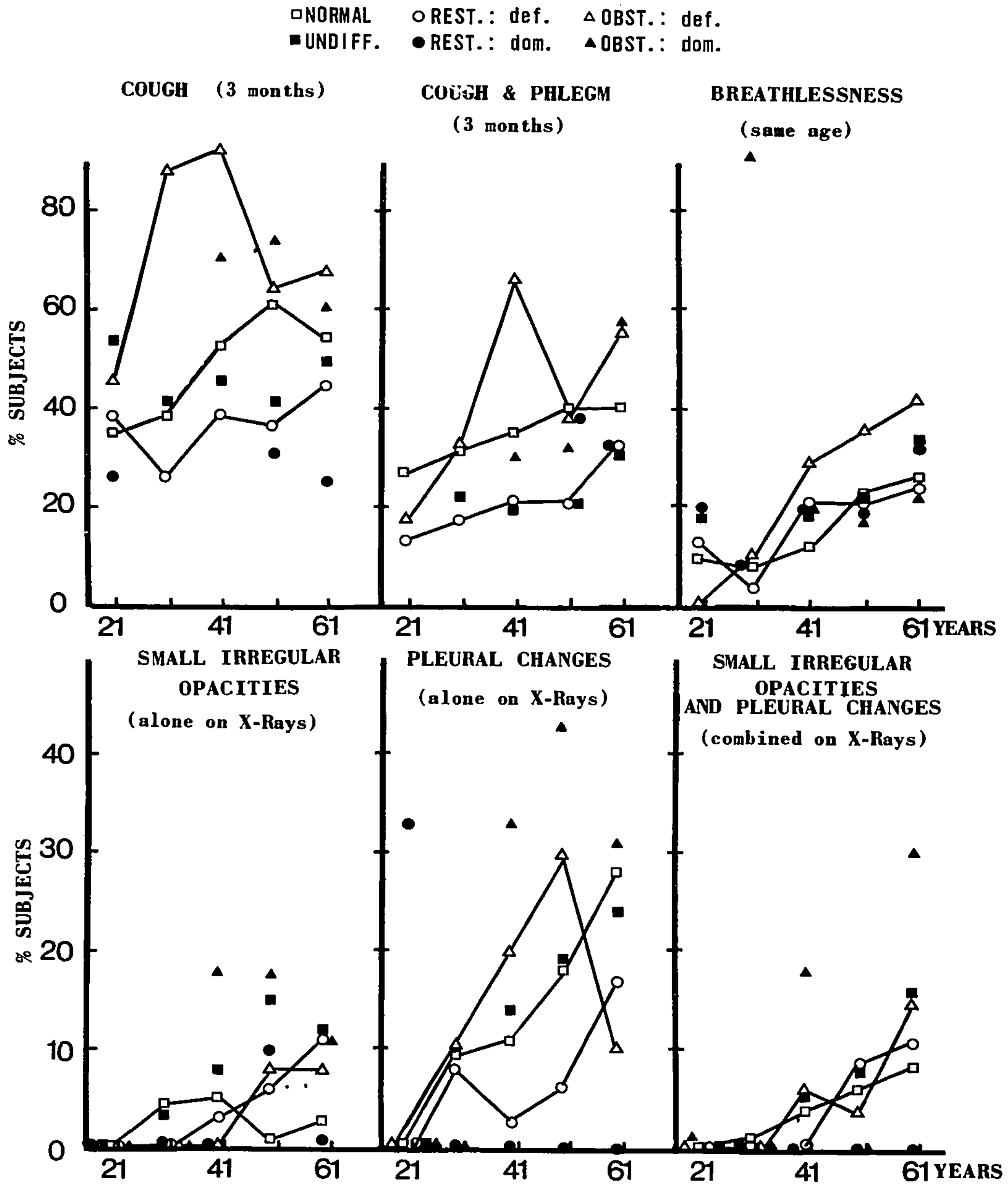
Questionnaire:

Some subjects who completed pulmonary function tests could not answer the questionnaire adequately, so results on only 1011 out of 1034 are analyzed in Table 5-5.

The prevalence of cough, phlegm and breathlessness was higher amongst those subjects showing definite or dominant obstructive profiles than in those with the restrictive profiles. The prevalence of chest illness was higher in the dominant restrictive group.

The selection of subjects could have influenced the prevalence of the symptomatology in the profiles and not reflect the exact state in the total population. When prevalence of symptoms was age-standardized for the total population (Table 5-5), the group with definite obstruction showed the highest prevalence for cough, while the group with dominant obstruction showed a prevalence similar to the normal. Cough and phlegm were also more frequent in the obstructive profile. For breathlessness, the dominant obstructive profile had a higher prevalence followed by the obstructive one. The undifferentiated, restrictive and normal profiles had about the same prevalence. So even after standardization, the obstructive profile had a

FIG. 5-4 RESPIRATORY SYMPTOMS AND RADIOLOGICAL CHANGES IN PULMONARY FUNCTION PROFILES, EXPRESSED AS % OF SUBJECTS PER DECADE.



higher prevalence of symptoms in its subjects than most of the other ones.

When prevalence of symptoms was considered by decade (Fig. 5-4, Table III-5), it was seen that for restriction, cough was similar in each decade, whereas in obstruction it increased abruptly from the decade 21-30 to the two following decades, and decreased slightly in the last two decades. The prevalence of phlegm increased with age in the three definite profiles particularly that of obstruction. Breathlessness also increased with age in the three definite profiles, obstruction having a higher prevalence except in the decade 21-30.

In the dominant profiles (Fig. 5-4) no trend was evident, perhaps because of the limited number of subjects with restriction and obstruction. The prevalence of cough, cough and phlegm and breathlessness was quite stable with increasing age except for an increase in the last decade.

In summary, the prevalence of symptoms increased with age in all the function profiles; in addition, there was in general a tendency towards a higher prevalence of symptoms in subjects with the definite obstructive profile.

Radiology:

The prevalence of radiological changes in subjects grouped according to pulmonary function profiles is shown in Table 5-6. The prevalence

TABLE 5-6 - PREVALENCE % OF RADIOLOGICAL CHANGES IN PULMONARY FUNCTION PROFILES, WITHOUT AND WITH AGE STANDARDIZATION FOR TOTAL POPULATION

PULMONARY FUNCTION PROFILES	NO OF SUBJ	NORMAL	DIFF. IRR. OPACITIES ALONE 1/0 + %	PLEURAL CHANGES ALONE %	DIFF. IRR. OPAC. AND PLEURAL CHANGES COMBINED %
NORMAL	414	80 (78)	3 (3)	14 (12)	3 (7)
UNDIFFERENTIATED	293	69 (78)	9 (6)	15 (12)	7 (4)
RESTRICTION					
definite	121	84 (89)*	4 (3)	7 (6)	5 (2)
dominant	23	92 (93)	4 (2)	4 (5)	-
OBSTRUCTION					
definite	154	69 (78)	5 (2)	19 (16)	7 (4)
dominant	29	38 (63)	14 (9)	31 (21)	17 (7)

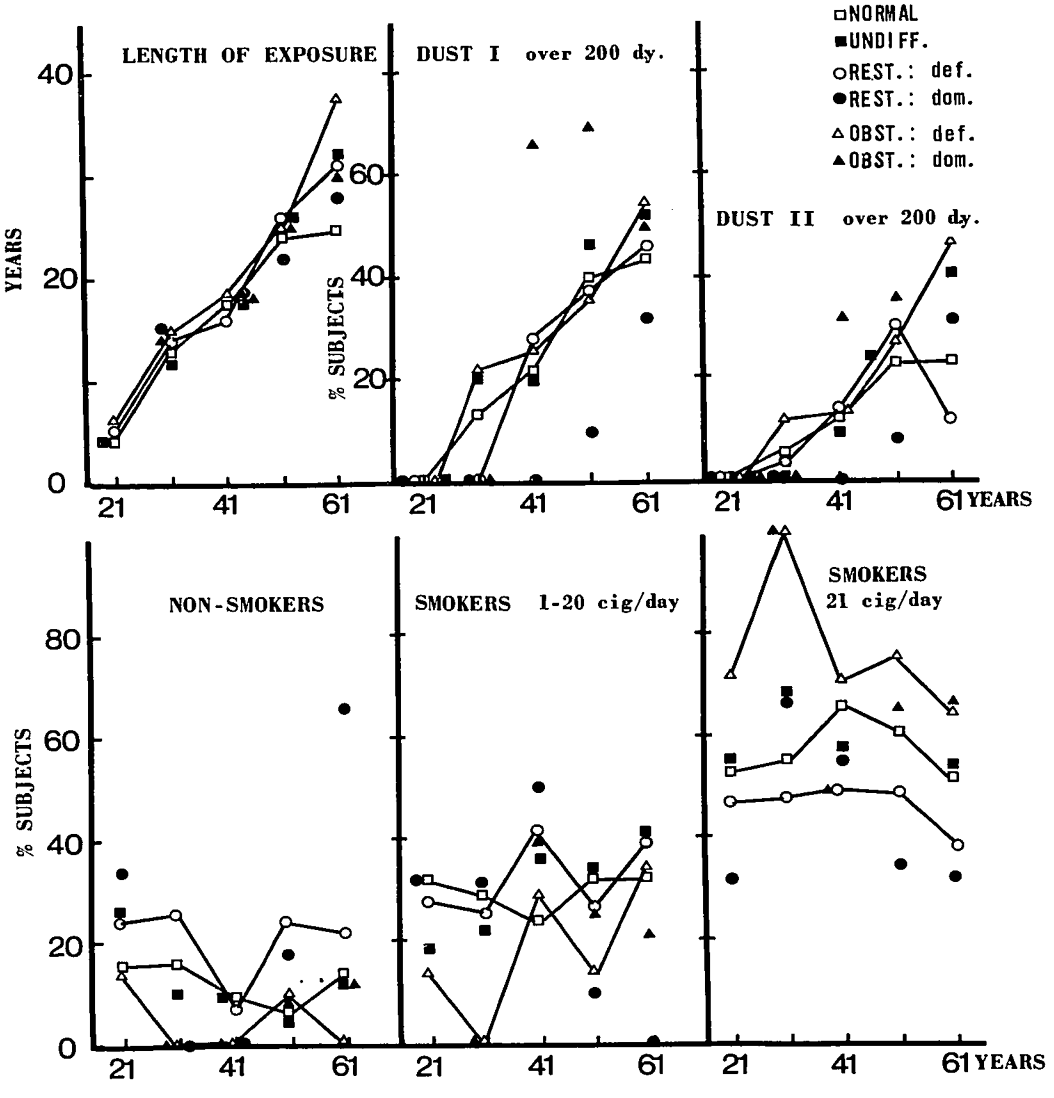
* ( ) Prevalence % age standardized for the total population.

of small irregular opacities was in general low; it was however higher in the dominant obstructive profile but similar in the subgroups with the restrictive and the obstructive profiles. However, a higher prevalence of pleural changes and also of combined radiological changes on the same radiograph was found in the obstructive profile groups. It was also evident that any of the six function profiles may be associated with a normal chest radiograph.

As discussed above, the prevalence of radiological changes in the profiles could have been influenced by the selection of subjects. When age-standardized for the total population (Table 5-6), the prevalence of small irregular opacities alone was greater in the undifferentiated and dominant obstructive profiles, the definite restriction having a slightly higher prevalence than the definite obstruction. The dominant and definite obstruction had more pleural changes alone. For the combined radiological changes on the same radiograph, the dominant obstruction and the normal profiles had the higher prevalence, the definite obstruction having more changes than the definite restriction.

As already mentioned, general conclusions about overall working population must also be related to age to define the progression of the abnormalities. Thus, the radiological changes by pulmonary function profiles were compared by decades (Fig. 5-4, Table III-6): an increasing prevalence was found with increasing age in each profile. More pleural changes were found in the normal, obstructive and undifferentiated profiles; small irregular opacities alone occured in about equal proportion in each profile group. There was also a tendency to a greater prevalence of radiological changes in subjects over 51 years.

FIG. 5-5 ASSOCIATION OF PULMONARY FUNCTION PROFILES WITH DUST EXPOSURE AND SMOKING EXPRESSED AS MEAN YEARS OF WORK AND % OF SUBJECTS PER DECADE.



In summary, the overall prevalence of radiological changes was greater in the subjects with obstruction than those with restriction or normal function. Radiological changes were found to increase with age in every subgroup.

4. PULMONARY FUNCTION PROFILES IN RELATION TO WORK, DUST AND CIGARETTES

In the hope of drawing some conclusions about association and, by inference etiology, two associated factors were specially studied in this survey: namely, work including dust exposure, and cigarette smoking, both factors known to influence pulmonary function. For reasons outlined above, the analysis was done by decades; however, analysis for the profiles without and with age adjustment for total population are shown for Dust Index I, II and smoking separately, and for Dust II and smoking combined (Tables III-7-8).

Duration of Work in the Industry

The mean years at work in each decade is essentially similar in each profile except in the 61 and over where the subjects with obstruction have had the longest work service (Fig. 5-5, Tables III-9-10).

Dust Exposure: Dust I and II

Two dust categories have been studied, below 200 dust-years and above. The value of 200 dust-years is equivalent to five million particles per cubic foot (5 MPPCF) for 40 years or its equivalent i.e. more dust in a shorter time or vice versa. Note that 5 MPPCF was the Threshold Limit Value of the American Hygiene Society, based on Dreessen's study (1938) until recently. New threshold levels based on the number of fibers per cc, were discussed and adopted in 1968 (Lane et al) but are not yet evaluated.

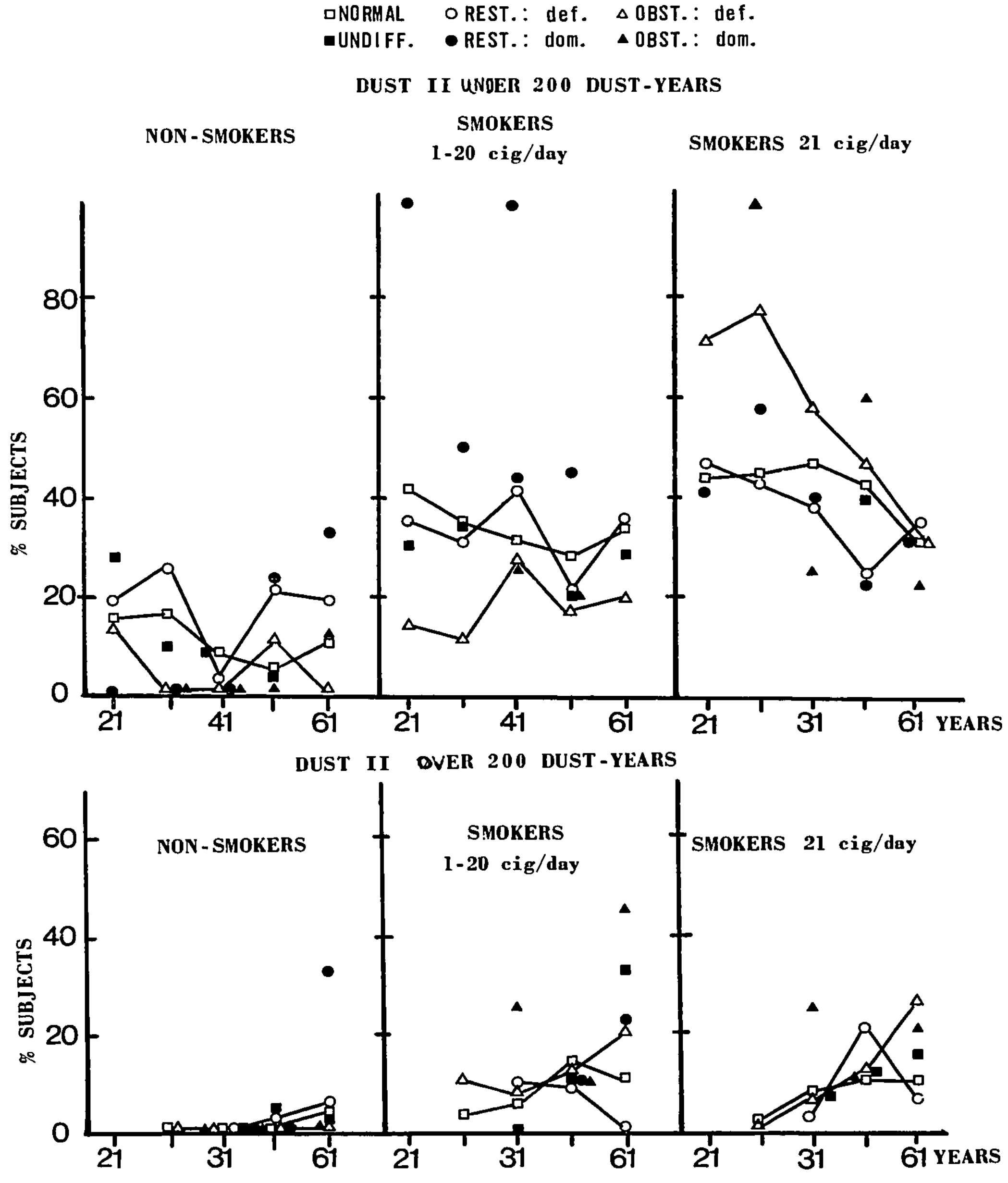
The prevalence of subjects with high dust exposure (Dust I 200 +) in each pulmonary function subgroup increased with age (Fig. 5-5; Table III-10), and tended to be slightly higher in the subgroups classified as undifferentiated abnormal function as well as in the obstructive and dominant obstructive subgroups.

In the index taking into account the physical effort (Dust II), the distribution of high dust indices in the pulmonary function subgroups was similar to that described above.

Cigarettes

Four categories of smokers were analyzed and the results can be found in Tables III-7-11. In Fig. 5-5 are illustrated results for non-smokers, smokers of 1-20 cigarettes daily, and smokers of more than 20 cigarettes daily. There were more non-smokers in the subgroups with dominant restriction and restriction, and less in the subgroups with obstructive, dominant obstructive and undifferentiated profiles, and a similar trend was found in the category of smoking 1 to 20 cigarettes per day. By contrast, the prevalence of heavy smokers (21 cigarettes or more per day) was lower in the subgroups showing a dominant restriction

FIG. 5-6 - ASSOCIATION OF PULMONARY FUNCTION PROFILES WITH DUST II COMBINED WITH SMOKING EXPRESSED AS % OF SUBJECTS PER DECADE.



and restriction, and the highest in subgroup with the definite obstruction. The prevalence of smoking patterns was surprisingly similar from one decade to another. Caution must be observed in interpreting this data because it cannot be standardized for age-differences between the subgroups with different lung function profiles.

Dust II and cigarettes

In an attempt to look at the interrelation of dust, effort (Dust II) and smoking in relation to function profiles, the data in Fig. 5-6 were broken down according to smoking habits. The prevalence of non-smokers was higher, and the prevalence of heavy smokers lower in the dominant restrictive and the restrictive profiles with less dust and physical application, whereas the prevalence of smokers is higher in the normal and undifferentiated profiles, the restrictive and obstructive ones having about the same prevalence.

But in the higher dust category, the prevalence of smokers is higher in the dominant obstructive and the obstructive profiles and lowest in the restrictive, dominant restrictive and normal profiles.

Caution must also be observed in interpreting these data for the reasons given above.

5. PRINCIPAL COMPONENT ANALYSIS

The many variables studied for this large group of men produced a wealth of data in which trends could be easily hidden. Furthermore,

TABLE 5-7 - RELATIVE POWER OF EIGHTEEN PULMONARY FUNCTION, CLINICAL RADIOLOGICAL AND ASSOCIATED VARIABLES TO EVALUATE LUNG DISEASE AND TO SEPARATE RESTRICTION FROM OBSTRUCTION IN 996 ASBESTOS WORKERS. (RELATIVE POWER OF VARIABLES ARE EXPRESSED IN STANDARDIZED WEIGHTINGS)

COMPONENT I (32.87% TV)* (Health - disease)			COMPONENT II (12.28% TV) (Restriction - obstruction)		COMPONENT III (7.78% TV) (Clinical picture - exposure)	
1o	FEV_{75}	$-.920^{x}$	RV	+.774	Phlegm	+.681
2o	VC	-.845	TLC	+.747	Cough	+.668
3o	MMF	-.794	FEV_1	-.658	Cig.	+.327
4o	Age	+.776	Ht	+.431	Dyspnea	+.268
5o	Dust I	+.665	MMF	-.359	Dust I	-.264
6o	$D_{LCO_{SS}}$	-.647	Cig.	+.328	Dust II	-.255
7o	Dust II	+.615	VC	+.308	Age	-.199
8o	Ht	-.571	SIO	-.175	$D_{LCO_{SS}}$	-.187
9o	TLC	-.566	Cough	+.173	RV	-.180
10o	Ext_{CO}	-.547	Phlegm	+.108	Ext_{CO}	-.174
11o	FEV_1	-.474	Age	+.102	FEV_{75}	+.085
12o	Dyspnea	+.429	$D_{LCO_{SS}}$	+.083	MMF	+.084
13o	PC	+.384	PC	-.072	SIO	+.083
14o	SIO	+.381	FEV_{75}	-.056	FEV_1	+.081
15o	RV	+.342	Dust I	-.040	TLC	-.059
16o	Cough	+.280	Ext_{CO}	-.039	VC	+.038
17o	Phlegm	+.187	Dust II	-.018	Ht	-.031
18o	Cig.	+.092	Dyspnea	+.012	PC	+.015

* TV : Total Variance

x Standardized weighting

it would seem reasonable that certain of the variables would prove more important than others in determining the results found. To clarify these points, principal component analysis was done.

Analysis with 18 variables including the five tests used to determine profiles

Nine hundred and ninety six (996) of the 1034 workers had data on all of the 18 variables selected for analysis (Table 5-7). The first three components so derived account for 52.9% of the total variance (TV) and the 15 remaining seem unworthy of further consideration. The Table 5-7 gives the standardized weightings in decreasing order of magnitude for components I, II and III.

The first component is probably concerned with differentiating health and disease of the respiratory system. The important variables in this differentiation are FEV_{75}, VC, MMF and D_{LCOSS} as well as age and dust exposure. Component II is probably concerned with differentiating restriction and obstruction, and RV, TLC, FEV_1 are primary responsible for this separation. Component III relates symptoms more to cigarettes than dust, even for dyspnea. In Fig. 5-7 in Part A, the plot of 996 individuals using the scores of component I on the horizontal axis and those of component II on the vertical axis, and in Part B, the scores of component I on the horizontal axis and those of component III on the vertical one. Each subject was identified by his pulmonary function profile. To simplify the figures, only the extreme boundaries of each profile were drawn. The variables were added on the basic graphs to show visually their relative importance in the determination of the components (reducing by 8 times the value of their correlation coefficient).

FIG. 5–7 PULMONARY FUNCTION PROFILES IN RELATION WITH COMPONENTS I, II and III.

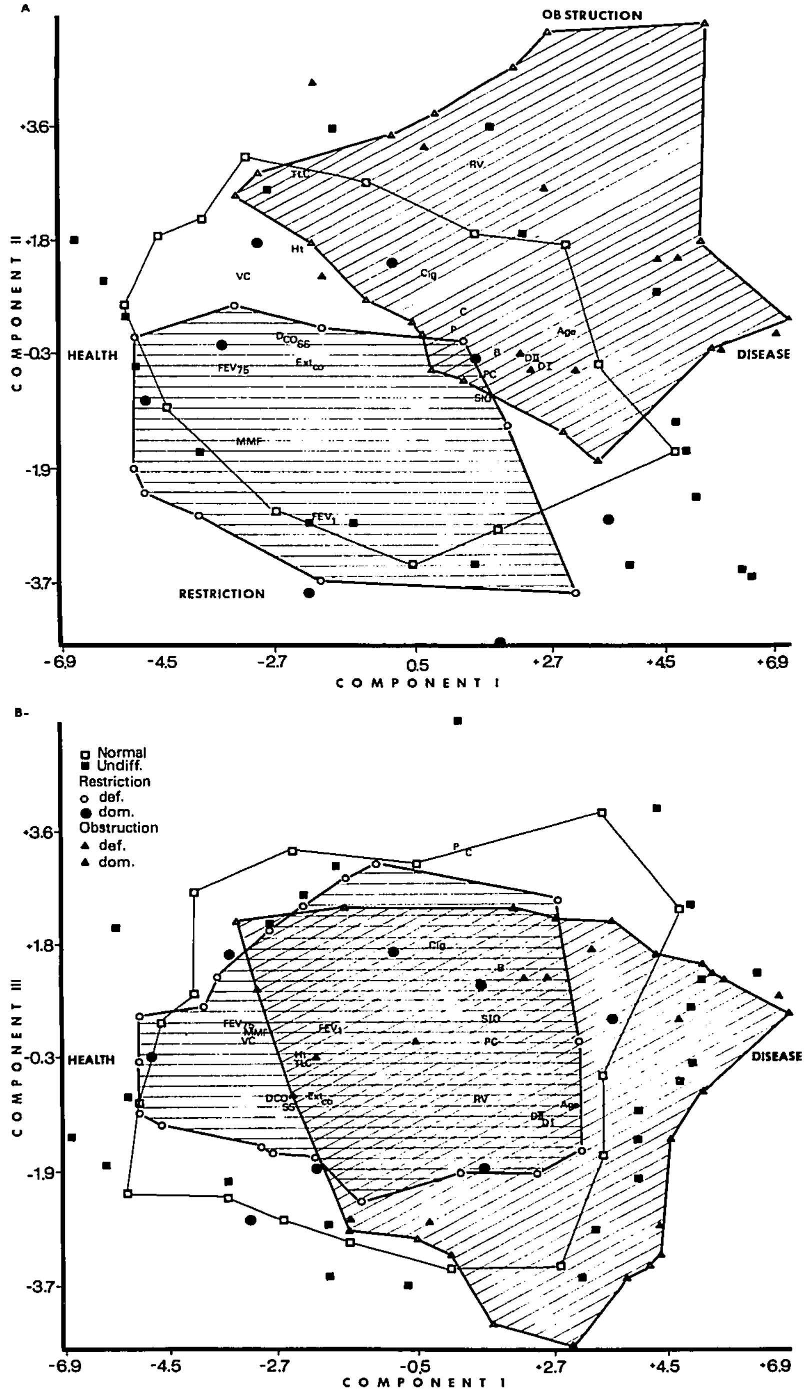


TABLE 5-8 – PRINCIPAL COMPONENT ANALYSIS BY DECADES TO ELIMINATE SELECTION BIAS IN COMPONENT I

COMPONENT I (Health – disease)

	21-30 yrs (109 subjects) (19.5% TV)		31-40 yrs (174 subjects) (19.7% TV)		41-50 yrs (224 subjects) (22.7% TV)		51-60 yrs (266 subjects) (21.7% TV)		61+ yrs (233 subjects) (25.6% TV)	
1o	FEV_{75}	-.877	TLC	+.891	FEV_{75}	-.887	FEV_{75}	+.870	FEV_{75}	+.847
2o	TLC	-.761	VC	+.866	VC	-.793	VC	+.795	VC	+.838
3o	VC	-.733	FEV_{75}	+.770	MMF	-.672	MMF	+.688	$D_{LCO_{SS}}$	+.652
4o	Ht	-.671	Ht	+.714	TLC	-.648	$D_{LCO_{SS}}$	+.573	TLC	+.636
5o	MMF	-.610	RV	+.514	Ht	-.586	Dust I	-.501	MMF	+.622
6o	Age	+.461	$D_{LCO_{SS}}$	+.483	$D_{LCO_{SS}}$	-.535	TLC	+.495	Dust I	-.559
7o	$D_{LCO_{SS}}$	-.385	MMF	+.343	Dust I	+.432	Dust II	-.479	Ht	+.549
8o	RV	-.373	Dust I	-.294	Ext_{CO}	-.410	Ht	+.467	Ext_{CO}	+.543
9o	Dyspnea	+.331	Ext_{CO}	+.274	Dust II	+.373	Ext_{CO}	+.461	Dust II	-.513
10o	Dust I	+.243	Dust II	-.262	$FEV_1\%$	-.365	$FEV_1\%$	+.379	SIO	-.453
11o	$FEV_1\%$	-.236	Age	+.150	PC	+.350	Cough	-.344	PC	-.369
12o	Dust II	+.198	$FEV_1\%$	-.131	Cough	+.335	Dyspnea	-.310	Dyspnea	-.348
13o	Cough	+.141	Dyspnea	-.077	Age	+.321	PC	-.242	Phlegm	-.348
14o	Cig.	+.100	PC	-.051	Dyspnea	+.319	Phlegm	-.239	Cough	-.308
15o	Phlegm	+.072	Phlegm	-.042	SIO	+.281	Age	-.198	FEV_1	+.306
16o	SIO	-.010	Cig.	-.031	Phlegm	+.157	SIO	-.180	RV	+.115
17o	Ext_{CO}	-.009	SIO	-.029	RV	-.051	Cig.	-.105	Age	-.101
18o	PC	-.005	Cough	-.027	Cig.	.000	RV	-.093	Cig.	-.050

The less exposed subjects with good functional, clinical and radiological findings are at the extreme left side of the X axis and the more exposed ones, with altered function and more clinical and radiological findings on the extreme right side. The restrictive profiles, definite (open circle) and dominant (closed circle) are in the lower left quadrant obstructive (definite, open triangle; dominant, closed triangle) are in the upper right one. Thus the Component I differentiated between health and small exposure on one hand and disease with heavier exposure on the other. The Component II distinguished the restriction from the obstruction. The Component III on part B of the figure related the importance of clinical findings, cough and sputum as well as dyspnea with smoking more than with dust. It was, however, less well defined than the first two components.

The FEV_{75}, VC, MMF and $D_{L_{CO_{SS}}}$ appeared to be the more important tests to differentiate between health and disease, whereas RV, TLC, FEV_1 and MMF determine restriction or obstruction. Phlegm and cough were related to smoking, and dyspnea to smoking and dust.

The age factor had a high weighting in Component I and is in fact related to most of the pulmonary function measurements. To evaluate if the first component was not simply an age axis, the principal component analysis was redone by decades. As shown in Table 5-8, the age variable which was fourth rank in the total study (Table 5-7), progressively lost importance from the first to the last decade. Thus, the Component I is not based only on age but more on the deterioration of the pulmonary function, reflecting the concept Health-Disease.

TABLE 5-9 - PRINCIPAL COMPONENT ANALYSIS EXCLUDING THE FIVE SCORING TESTS
(996 Subjects - 13 variables)

A - ANALYSIS ON THE TOTAL SURVEY

	COMPONENT I (31.38% TV) (Health-disease)		COMPONENT II (10.99% TV) (Clinical picture Pollution)		COMPONENT III (9.15% TV) (Pollution-Radiology)	
1o	VC	-.812	Cough	+.689	Dust II	+.594
2o	Age	+.749	Phlegm	+.682	Dust I	+.550
3o	Dust I	+.726	Cig.	+.471	$D_{L_{CO_{SS}}}$	+.409
4o	$D_{L_{CO_{SS}}}$	-.682	Dust I	-.249	Ht	+.318
5o	Dust II	+.680	Dyspnea	+.242	Ext_{CO}	+.314
6o	Ext_{CO}	-.610	Dust II	-.236	Cig.	+.245
7o	Ht	-.576	Age	-.156	PC	-.217
8o	Dyspnea	+.462	Ext_{CO}	-.137	Cough	+.138
9o	SIO	+.433	Ht	+.130	Phlegm	+.134
10o	PC	+.404	VC	+.122	VC	+.133
11o	Cough	+.296	$D_{L_{CO_{SS}}}$	-.116	SIO	-.067
12o	Phlegm	+.209	PC	-.049	Dyspnea	-.020
13o	Cig	+.078	SIO	-.016	Age	-.006

B - ANALYSIS BY DECADES

COMPONENT I (Health - disease)

	21-30 yrs (15.8% TV)		31-40 yrs (18.2% TV)		41-50 yrs (21.0% TV)		51-60 yrs (21.3% TV)		61+ yrs (25.7% TV)	
1o	Age	+.614	Dust I	+.712	VC	-.716	VC	+.692	VC	+.743
2o	VC	-.612	Dust II	+.693	$D_{L_{CO_{SS}}}$	-.638	$D_{L_{CO_{SS}}}$	+.668	$D_{L_{CO_{SS}}}$	+.685
3o	Ht	-.555	VC	-.583	Dust I	-.616	Dust I	-.610	Dust I	-.638
4o	Dust I	+.534	Ext_{CO}	-.495	Dust II	-.568	Dust 11	-.589	Ext_{CO}	+.637
5o	Dust II	+.459	Ht	-.492	Ext_{CO}	-.550	Ext_{CO}	+.568	Dust II	-.594
6o	$D_{L_{CO_{SS}}}$	+.374	$D_{L_{CO_{SS}}}$	-.472	Ht	-.544	Cough	-.439	Ht	+.527
7o	Cig.	+.344	Age	+.443	PC	-.350	Ht	+.426	SIO	-.512
8o	Dyspnea	+.298	Dyspnea	+.288	Dyspnea	-.336	Dyspnea	-.376	Dyspnea	-.417
9o	PC	+.229	Cig.	+.132	Age	-.295	Phlegm	-.336	PC	-.376
10o	Ext_{CO}	-.209	Cough	+.101	SIO	-.285	SIO	-.239	Phlegm	-.373
11o	SIO	-.172	Phlegm	+.098	Cough	-.278	PC	-.233	Cough	-.364
12o	Cough	+.150	PC	+.071	Phlegm	-.179	Age	-.232	Age	-.133
13o	Phlegm	-.054	SIO	+.031	Cig.	-.027	Cig.	-.076	Cig.	-.089

Analysis with 13 variables excluding the five tests used to determine profiles

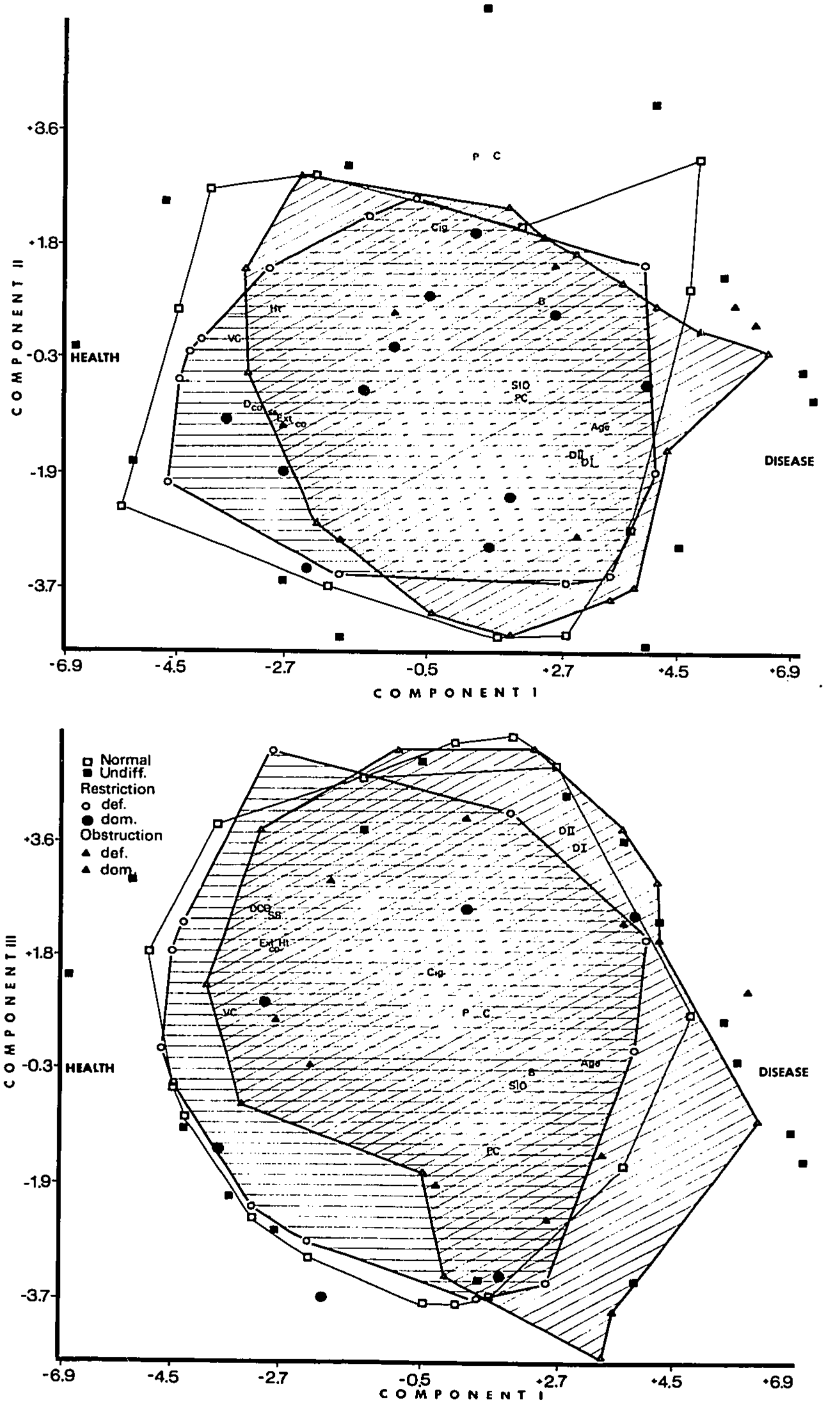
In an attempt to verify if the tests chosen for coding were really adequate to separate restriction from obstruction, a second analysis was done on the same subjects excluding the five tests used to define the lung function profiles.

The first three components account for 51.5% of the total variance. The other components were discarded after analysis because again they did not show a consistant trend.

The Table 5-9A gives the standardized weightings in decreasing order of magnitude for the Components I, II and III. Fig 5-8 plots the 996 individuals in the same way as the study with 18 variables. The Component II (restriction - obstruction) has disappeared as illustrated by the positions of the profiles on the figure. However, this Component II sorts out the usual clinical picture of obstruction having cough, phlegm and smoking with the higher weightings.

Again, as the age factor is important, the analysis by decade was completed (Table 5-9B). Age has now the highest weighting in the first decade, but loses rapidly its importance with increasing age. Pulmonary function tests and dust exposure continue to define this health-disease Component, radiological changes and clinical picture having less importance.

FIG. 5–8 PULMONARY FUNCTION PROFILES IN RELATION WITH COMPONENTS I, II and III, SCORING TESTS BEING OMITED



6. SUMMARY

The results of pulmonary function tests of a random group of asbestos and MMF), were divided into six pulmonary function profiles, three definite ones: restrictive, normal and obstructive; and three dominant ones: restrictive, undifferentiated abnormal function and obstructive. The principal component analysis supported the choice of the coding tests as appropriate for classifying subjects into lung function profiles. It also suggests that the conventional use of VC and D_{LCO} to separate restriction from obstruction may not be justified.

More subjects showed a definite (154) or dominant (29) obstructive profile compared to the restrictive (121) or dominant restrictive (23) profile. In the obstructive profile, the VC was lower, the FRC higher, the $D_{LCO_{SS}}$ at rest and on exercise lower than in the restrictive. In this group with obstruction, there is a greater prevalence of cough, cough and sputum, breathlessness and chest illness, and also of small irregular opacities and pleural changes alone or combined on the chest radiograph.

When results were analysed with the subjects divided by decades, the prevalence of restriction was higher in the younger decades and obstruction in the older men. The prevalence of symptoms increased with age and was more marked in those with the obstructive profiles compared to those with a restrictive one. The same trend was found for the radiological changes, except in the men 61 years old or more where a lower prevalence of small irregular opacities and pleural changes was found. In men with the undifferentiated abnormal profile and dominant obstructive profiles, there was a higher prevalence of radiological changes compared to the other patterns.

With regard to associated factors, men with the obstructive profile had had the same years of service, greater dust exposure, and also had worked in jobs demanding a greater level of effort. There were also more smokers in this group compared to the restrictive one.

The principal component analysis indicated that the restrictive group was younger than the obstructive one, even when the five coding tests were omitted. It also confirmed that the subjects with obstruction had lower VC, DL_{COSS}, more symptoms and radiological changes, higher dust exposure and cigarettes consumption. These findings suggest either a natural selection of the subjects, (the restrictive ones leaving the industry earlier than those with obstruction), or another form of pulmonary function disturbance caused by high dust and/or association of dust and cigarette smoke.

6 - DISCUSSION

1. PULMONARY FUNCTION PROFILES

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4. REVIEW ON PERTINENT PUBLISHED DATA ON PULMONARY FUNCTION PROFILES IN RELATION TO DUST EXPOSURE

    Harries (1971)

    Murphy (1971), Ferris et al (1971)

    Regan et al (1971)

    Muldoon and Turner-Warwick (1972)

1. PULMONARY FUNCTION PROFILES

General

In this study five pulmonary function tests have been used as the basis of a score by which the function of a population of asbestos exposed individuals has been classified into six profiles - normal, undifferentiated, definite and dominant restriction, definite and dominant obstruction (Table 5-2). In the population studied, 44.3% had a normal profile (i.e. all five tests within 20% of expected values), a further 26.5% had an undifferentiated profile. The definite and dominant restrictive profiles were shown in 12.8% and 2.1% respectively, while the values for the definite and dominant obstructive profiles were respectively 12.2% and 2.1%. Clearly, in this population, the functional change associated with exposure to asbestos was not exclusively that of a restrictive profile, but an obstructive profile was as common.

These findings, although in keeping with the present author's cases review (see Chap. 2), are nevertheless at variance with the conventional teaching of textbooks that asbestos exposure leads to a pulmonary disease characterised by fibrosis (i.e. asbestosis) and that the associated lung function profile is restrictive or one of alveolar-capillary block (Tepper and Radford, 1970).

Influence of methods on the study

In view of the importance of these findings, the conduct of the trial and the method of analysis must be carefully reviewed to determine if any factor might have influenced the distribution of subjects in the different profiles.

Sampling

Only current workers were selected, those retired or compensated being excluded. This, of course, would be expected to bias the sample towards those who remain well enough to work, but to what extent cannot be said. Within the currently working population, the sampling was weighted towards the older individuals. Thus, there were subjects awaiting compensation or near retirement giving a good picture of every stage of exposure. In addition, age standardization of the reported prevalence values was done. The results suggest that sampling had a negligeable influence in distribution of subjects into profiles (Table 5-2).

Function tests

The choice of function tests for the survey was made with a view to evaluating the health risk in relation to dust dosage (Becklake, 1972), and included the measurement of as many aspects of function as possible. Limiting factors were the time allowed for each subject, about 45 to 60 minutes, and the need that the tests be simple and without discomfort. Thus, measurements of compliance and blood gases were excluded.

The technical aspect of the survey has been already discussed and it was shown that very little intersubject variation could be attributed to apparatus, technicians, time in the day or change of season.

Predicted values

A control group of nonexposed individuals would have been useful for reference, but in practice, difficult to choose. Holt et al (1964) demonstrated how easy it is for animals in a room adjoining asbestos experimentation to become affected, and Murphy et al (1971) found 46% of their "control" group to have abnormal function. Because of these difficulties, results of most of the tests were related to expected (predicted values). This could theoretically introduce bias if they were consistently inappropriate to one subgroup and not to another e.g. to smokers, not to non-smokers.

For volumes and flows Becklake et al (1970) compared accepted predicted values in the literature with the means of the results of function studies in those present subjects without radiological change, and found general agreement. The VC and FVC were slightly lower but they did not contribute to the code for determining lung function profile. More important, the values for the flows were comparable except perhaps for MMF which was lower in this study. This test is used in the code and could thus have increased the number of subjects classified in the obstructive profile. However, pulmonary function changes can occur in the absence of radiological change, and Jodoin et al (1971) have suggested that asbestos affects the small airways at an early stage. Thus, the low MMF may reflect early changes in these radiologically normal subjects. In the absence of a control group, the use of predicted values for volumes and flows chosen in the analysis was considered acceptable.

With regard to the diffusing capacity, Fournier-Massey et al (1972) pointed out that the absolute values of $DL_{CO_{SS}}$ rest in a small group of French-Canadians did differ significantly from predicted values based on other ethnic groups. As the majority of the workers in the present study belong to this ethnic group, the use of predicted values could only have introduced a bias for this test in terms of absolute values, but not in terms of comparison of decades.

Nature of Classification

The definition of profiles was done using the results of five tests: RV and TLC which reflected the size of the lungs; FEV75 and MMF which reflected two anatomical levels of airway resistance, (the former being more dependant on the patency of large bronchi and to some extent of effort, the latter being less effort-dependant and more influenced by the state of the small airways); and finally $FEV_1\%$ which permits one to assess the interrelationship of volumes and flow. Five tests were used instead of three, as employed in the literature review, in the hope of achieving a more precise differentiation of the restrictive and obstructive profiles, and of delineating more accurately the mixed profiles.

It was of some interest to see to what extent this classification into three main function profiles, which is traditional practice amongst chest physicians, is in line with the findings in the essentially statistical principal component analysis. The principal component analysis of the present data, including the five coding tests (Fig. 5-7), clearly separated restriction from obstruction with the superposition of the dominant profiles on the definite ones. The normal and undifferentiated profiles were found between the obstructive and restrictive profiles with some overlapping, possibly due to large variation in the age of the selected subjects. Age and dust seem to be the elements which place the restrictive profile more on the left and the obstructive more on the right of the X axis. When the five tests are removed from the principal component analysis,

TABLE 6-1 – PREVALENCE % OF HIGHER, NORMAL AND LOWER THAN PREDICTED VALUES FOR THE TESTS USED TO CODE RESULTS OF 1034 ASBESTOS WORKERS INTO FUNCTION PROFILES

TESTS USED IN SCORES	REDUCED VALUE (79%≤) % subjects	NORMAL VALUE (80-120%) % subjects	INCREASED VALUE (121%≥) % subjects
RV	21	57	22
TLC	7	87	6
FEV_1/FVC	11	72	17
FEV_{75}	12	73	15
MMFR	40	46	14

restrictive and obstructive profiles overlap markedly (Fig. 5-8). This suggests that the tests used to develop the codes in this thesis were valid in separating restriction from obstruction.

Significance of the findings

The first point of interest is the low percentage of subjects with a normal profile (44.3%). Perhaps this can be explained, at least in part, by the selection of the subjects which was weighted towards the older age group (Table 5-4) since the prevalence of normal function profiles drops to about 30% in the last two decades. However, MMF was strictly within normal limits (± 20% predicted value) in only 46% of the subjects (Table 6-1) which is compatible with the possibility that many otherwise normal subjects have early changes in the small airways, either obstruction (40%) or restriction (14%), a finding in keeping with the study of Jodoin et al (1971) indicating that early disease manifested itself at that level. In addition, it must be remembered that this was a working population exposed to asbestos. The second and more important finding is that among those with abnormal profiles, obstruction is as frequent as restriction, and that one quarter of all subjects have a mixed restrictive and obstructive profile. Thus, asbestos exposure in these subjects, at least, appeared to be associated with any type of functional disturbance and not exclusively with the restrictive profile. This conclusion is furthermore in keeping with a detailed review of the literature (Tables 2-1 and 2-2) but does not accord with the generally stated conclusions of various investigators.

2. PULMONARY FUNCTION PROFILES IN RELATION TO OTHER HEALTH PARAMETERS

With this new concept of the pulmonary function changes following asbestos exposure a reexamination of the clinical and radiological parameters is indicated with a view to developing a more logical understanding of the syndrome of asbestosis and its natural history.

Pulmonary Function Profiles and Clinical Aspects

Most workers suggest that asbestosis is manifested clinically by dyspnea, with cough and phlegm being less frequently present (Wright, 1955; Leathart, 1960; Kleinfeld et al, 1966a; Tepper et al, 1970; Ferris et al, 1971). The present findings are in agreement. Thus, cough and phlegm were related to age and smoking habits, and perhaps also to dust exposure in non-smokers and light smokers (McDonald et al, 1972). By contrast, breathlessness on exercise was related to age and dust exposure but not to smoking.

As regards the different function profiles, the symptomatology was twice as frequent in those with obstruction compared to those with restriction, even when results were age standardized for total population (Table 5-5). In every decade, more cough, and more cough with phlegm was found in the subjects with profiles of obstruction and dominant obstruction (Fig. 5-4). Dyspnea was also found more frequently from 31 years of age onwards in these profiles. The higher prevalence of breathlessness in the dominant obstructive profile may reflect a restrictive component compounding the ventilation: perfusion inequality.

Contrary to expectation, the prevalence of symptoms was comparable in subjects with normal function and in those with the undifferentiated but abnormal function profile. This observation is in keeping with the possibility that current prediction values underestimate function in the manual worker, and that their "normal" values in fact represent a deterioration from previously "higher than normal" values. Moreover, even after symptoms developed , it is possible that the system of pulmonary defense could delay changes in pulmonary function by increasing clearance (see below).

Pulmonary Function Profiles and Radiological Changes

Exposure to asbestos may result in radiological changes in pleura as well as parenchyma (Böhlig et al, 1971) and these form a major basis for diagnosis and compensation.

The estimation of pulmonary function changes from pulmonary radiology has not proven very successful, and after asbestos exposure functional changes may occur earlier than radiological ones (Thomson et al, 1965; Leathart 1968; Bader et al, 1971; Becklake et al, 1970). However advanced radiological changes appear to relate better to pulmonary function changes than early ones (Bader et al, 1971).

In this study, the normal profile was associated with a prevalence of radiological change in 14 to 39% depending on the decade (Table III-6). Of those with abnormal profiles 30 to 100% had normal radiographs.

The discrepancy between radiology and function is not too surprising if one considers that the former measures what will be important enough at parenchymal level to be seen on the radiograph, whereas the second technique reflects the sum of functional disturbances of the thorax, the bronchial tree, the parenchyma as well as of the pulmonary and bronchial circulation and sometimes the heart.

When both functional and radiological changes are present, it is expected that these will be primarily of the restrictive type (Tepper et al, 1970). But in this survey, of the 12.8% and 2.1% with definite and dominant restriction respectively, only those with radiological changes would have had the fully developed clinical picture of asbestosis, i.e. under 10% or 15 subjects. On the other hand, in the subjects with definite and dominant obstruction, (12.2 and 2.1%, respectively) some 25% or 45 subjects had radiological changes, and in those with the undifferentiated profile (26.3%) 22% or 90 subjects. Thus, this survey has shown that many cases with asbestos induced biological effects would have been missed if the criteria used were radiological changes associated with a purely restrictive functional profile.

An interesting point was the higher prevalence of pleural changes in the obstructive and normal function profiles, leading to a possible explanation of the development of the functional changes. Normally the thorax and the parenchyma have opposing forces, the first tending to expand and the second to retract. These opposing forces equilibrate at the end of a normal expiration.

This point of equilibration can vary, for example, heavy workers have greater VC and TLC. It may also be different in disease. Usually, when fibrosis occurs in the parenchyma, contraction occurs increasing the lung recoil. If the thoracic cage and diaphragm are free, they will then follow the shrinking lung and a restrictive profile is found. However, if pleural thickening and calcification come early, as demonstrated in this survey (Table III-6), the thoracic walls or/and the diaphragm might resist the increased recoil of the parenchyma, and compensatory or irregular emphysema may develop. Functionally, these pathological changes could result in normal, undifferentiated or obstructive profiles depending on the initial pathology.

3. PULMONARY FUNCTION PROFILES IN RELATION TO DUST, EFFORT AND SMOKING

Pulmonary function Profiles in relation to Dust Exposure

There have been a number of studies of an epidemiologic nature having as their objective an evaluation of the health risks of asbestos exposure in relation to dust dosage (Bader et al, 1960, 1970; Harries, 1971; Ferris et al, 1971; Murphy et al, 1971; Becklake et al, 1972). In terms of pulmonary function, this has usually been done for individual function measurements. Thus three studies (Harries, 1971; Woitowitz, 1972; and one based on the present material, Becklake et al, 1972) have led to the conclusion that a dust-dose relationship exists in terms of VC or IC, but not in respect of gas exchange measurements. In a fourth study (Bader et al, 1970), a dust-dose relationship to function impairment was found; this was considered to be present when VC was less than 75% predicted and FEV_1 less than 70% of VC.

Definition of dust exposure has always been a problem: years of exposure, as used by Bader et al (1970) takes no account of exposure differences between jobs. Exposure estimated from current or principal job over the period of exposure, as used by Harries (1971) does not allow for changes in jobs or improvements in industrial hygiene. An index based on accumulated dust-time calculations, as used here, and by

TABLE 6-2 - PREVALENCE % OF SUBJECTS IN EACH PULMONARY FUNCTION PROFILE FOR DUST I AND DUST II CATEGORIES
(age standardized for the total population)

DUST I	NO.OF SUBJ	NORMAL	UNDIFF.	RESTRICTIVE		OBSTRUCTIVE	
				Definite	Dominant	Definite	Dominant
		%	%	%	%	%	%
> 10	91	52.8	27.0	12.4	2.2	5.6	-
10-100	453	43.7	25.6	13.8	2.9	12.5	2.0
100-200	158	38.3	30.5	10.4	2.6	17.5	0.7
200-400	133	39.7	27.8	13.5	-	11.1	7.9
400-800	109	30.6	32.4	4.6	2.8	25.0	4.6
800-	67	23.8	36.5	11.1	-	23.8	4.8
DUST II							
> 10	248	47.6	26.4	10.5	2.4	8.5	0.4
10-100	418	43.8	25.6	10.8	2.6	14.8	2.4
100-200	150	31.7	34.4	14.2	1.4	14.9	3.4
200-400	114	32.3	26.6	11.4	1.9	20.0	7.6
400-800	62	26.2	39.3	8.2	-	19.7	6.6
800-	19	22.2	33.3	-	5.6	38.9	-

Woitowitz (1972) does not examine the influence of exposure patterns and dust storage in the lung; thus a given index may be the consequence of a heavy remote exposure with little thereafter, or a continuous prolonged exposure to the present, or any combination of these.

In the present study of a quite stable population, the mean number of years of work was similar in each profile except in the 61- decade where the subjects with obstruction had worked longer (Fig. 5-6). However, high dust exposure had already occurred by the 31-40 decade; and there was a greater prevalence of heavy dust exposure in the dominant restrictive, the obstructive and in the undifferentiated profiles groups. The same trend was noted when dust exposure was expressed by an index which took physical application into account i.e. the level of exercise applied to the number of hours when it was done.

In an attempt to facilitate comparison with previous reports, prevalence of function profiles in dust categories was calculated (Table 6-2). Prevalence of normal function profiles diminished as Dust I and Dust II indices increased; restrictive profiles stayed almost stable. Undifferentiated abnormal function profile increased slightly with high dust years whereas the obstructive profiles attain almost a four fold increase in prevalence. It thus seems that for same years of work, high dust and heavy effort lead to a higher prevalence of undifferentiated and obstructive function profiles than of restrictive ones.

The pulmonary effects of asbestos dust (both in terms of fibrosis and small airway disease) are generally thought to be related to the amount of dust retained in the lung i.e. dust exposure less dust clearance. A small change in the balance between these two processes will, in the course of time, result in very considerable differences in dust retention. All the indices cited above consider only exposure, and indeed there are at present no practical ways to measure long term clearance in man. However, there is enough experimental work, some of which will be discussed in more detail later to indicate that penetration on the one hand, and clearance rates on the other, can be markedly influenced by factors such as depth and frequency of breathing, and by ciliary reaction and small airway narrowing which may occur in response to dust and cigarette smoke.

Pulmonary Function Profiles in Relation to Smoking

Smoking is known to be related to chronic bronchitis (Ferris, 1968; Bates et al, 1971) and to produce pulmonary function changes such as a drop in FEV_{75} (Wilson et al, 1960; Read et al, 1961; Zamel et al, 1963; Dawson, 1966) in VC and RV (Whitfield et al, 1951) and in D_{LCO} (Martt, 1962; Rankin et al, 1965; Krumholz et al, 1964). In asbestos workers, some studies have suggested that smoking is the primary factor accounting for cough, phlegm, increased RV and decreased flows. (Harries, 1971; Becklake et al, 1972; Ferris, 1971).

As expected, most subjects with obstruction in this survey are smokers of 21 cigarettes or more per day (Fig. 5-7); by contrast, more non-smokers and light smokers were found in the restrictive and dominant restrictive profiles. Age standardization for total population (Table III-7) did not modify significantly these findings except by diminishing appreciably the calculated prevalence of non-smokers in the dominant restriction group.

The principal component analysis related dust and smoking to cough and sputum, whereas dust was also related to dyspnea and both to the obstructive profiles. McDonald et al (1972) had also shown the relationship between symptoms and these associated factors.

Pulmonary Function in Relation to Dust Exposure Combined with Smoking

Although light dust alone was related more often to the restrictive profile, light and heavy dust associated with light or heavy smoking led to an obstructive profile (Fig. 5-8). It is difficult to reach any conclusion on the dominant groups because they are relatively small.

When age standardization for the total population was done (Table III-8), light dust alone or with light smoking was associated with an increase in the prevalence of the normal and restrictive profile whereas light dust and heavy smoking with an increase in the prevalence of obstruction. Heavy dust without smoking was too rare to be analyzed, but heavy dust with light or heavy smoking appeared to cause more obstruction.

It seems then that dust can affect different levels of the respiratory system, depending on the quantity of dust alone or whether it is associated with smoking; this would modify the laws of penetration, deposition and clearance in the airways, essential parts in the defense system of the lungs.

Theoretical Analysis of the Depth of Penetration, Deposition and Clearance of Particles and Fibers as Important Factors in the Development of Pulmonary Function Profiles

The respiratory system is well designed to provide the O_2 and eliminate the CO_2 necessary for aerobic metabolism of the body. It may be considered as five major functional parts: the gas pump and its control, the airways, the gas exchanger, the pulmonary circulation and its pump the heart, and finally the blood. The system as a whole adapts itself to multiple exogenous and endogenous stresses. The airways, with their properties of handling gas and foreign material, are the front line of defense and probably constitute the major host factor in the development of the pulmonary function profiles. A review of these properties may facilitate understanding of the effects of dust and smoking.

The airways were considered as a complicated system of tubes conducting gases to and from the gas exchanger during which time laminar and turbulent flows contributed to resistance. Recently, this concept has been modified in two ways. Firstly, air probably flows only to the 10th generation of bronchi and diffuses from that point on to the alveoli (Wilson et al, 1970). In other words, the mechanism of gas transport changes at the point of zero differential pressure, and movement of molecules proceeds no longer by differences in pressure but by differences in concentration. With increased ventilation, this zero point moves more and more towards the periphery as V_T approaches VC.

Secondly, the anatomical configuration of the bronchi, in which they split into daughters of smaller calibre results in a system of non-uniform tubing. Turbulent flow probably occurs at high respiratory rates, although the transformation from linear to turbulent flow is progressive. The flow regime can usually be described as laminar but distorted in type (Jaeger et al, 1970; Sudlow et al, 1971). From this dynamic concept of gas movement follows the conclusion that the depth of penetration of particles or fibers into the airways, their deposition and their clearance must be variable.

Besides variability in the host factor, a second major factor affecting the penetration, deposition and retention of foreign material is the behaviour by the particles themselves both in the normal bronchial tree, and in one altered by smoking. Finally, chrysotile asbestos is a fiber with important and distinct physical as well as chemical characteristics.

Penetration of particles appears to be largely dependent upon their size. Those larger than 5.0 microns do not penetrate very deeply and are removed by the defensive mucociliary blanket and cough (Gernez-Rieux et al, 1961). Particles under 0.5 microns probably enter the acini only to be carried out to the atmosphere again, and it is particles of a rather limited range of sizes only that reach and remain in the distal conducting tubes and acini. Should hyperventilation occur, such particles probably reach the smaller airways. The size of the particles also plays a role in their deposition. In a study of regional <u>deposition</u> of inhaled aerosols in normal man, Lippman et al (1971) found that particles bigger than 2 microns were deposited in the larger airways by impaction, whereas smaller ones sedimented on the mucus escalator of small sized airways. Their deposition varied greatly from subject to subject, but each individual has a characteristic size vs deposition relationship, possibly due to individual properties of the airways.

Deposition may also be influenced by the breathing rate (Dennis, 1971), for example, the increased respiratory rate of exercise augments the percentage of deposition. Variations in deposition could then be due to different breathing patterns.

Inhalation rate has also a marked effect on the clearance which is faster at faster inhalation rates, possibly because shorter time of exposure does not permit sedimentation (Camner et al, 1971), so less deposition.

A more complicated situation arises when the host is a smoker. Lippman et al (1971) demonstrated that tracheobronchial deposition of particles 1 to 5 microns was very much greater in smokers than in non-smokers but less than in bronchitic patients. Moreover, Sanchis et al (1971) stressed the importance of ventilation distribution differences in smokers as well as non-smokers because these differences can modify not only the depth of particles deposition but also the clearance . In fact, Camner et al (1971) have shown that clearance is faster if subjects have an acute exposure to tobacco smoke which seems first to stimulate mucociliary transport and later inhibit it if the dose increases beyond a certain limit.

Albert et al (1971) have paid a particular attention to this point, trying to establish the sequence of changes produced by smoking. They found that the average clearance time for smokers was increased only at the 90-100% level of bronchial deposition, and non-smokers differed little from this, whereas significantly increased clearance time was found in bronchitics. The paradoxical finding of abnormal clearance patterns without substantial differences in bronchial clearance time between smokers and non-smokers can be explained by (1) the wide inter-subject variability in clearance regardless of smoking habits, (2) differences in individual susceptibility to the effects of smoking and (3) the predominance of smoking effects in the trachea and the upper bronchi where clearance impairment has relatively little effect on total clearance times.

Trying to explain the pathogenesis of bronchitis, Albert et al (1971) divided the effect of smoking into three stages. In Stage 1, the early effects of smoking are reversible and include a) increased mucus production which tends to accelerate lower bronchial clearance, b) bronchial constriction which tends to increase bronchial deposition and shifts particle deposition to the more proximal parts of the bronchial tree, causing an apparent acceleration of the overall lung clearance, c) a ciliostatic effect which is greater in the trachea and larger bronchi than in the smaller ones, slowing upper bronchial clearance. In Stage 2, there is moderately advanced cigarette smoking injury, or mild chronic bronchitis resulting in excess mucus production combined with upper airways damage to the ciliated mucosa, and in stasis and refluxing of mucus into the large airways and increased coughing. At this stage, cigarettes have an expectorant action facilitating clearance. In Stage 3, with the severe chronic bronchitis associated with exertional dyspnea, the changes described in Stage 2 increase in severity and extend into the smaller airways, producing airflow obstruction. So the combined effect of smoking and dust exposure could favor a higher retention of particles at the level of the bronchial tree.

How do these findings help in interpreting the observations in this thesis? Do these events apply to asbestos? The workers in this survey were exposed mainly to particles of rock and to fibers although other substances do occur. When asbestos is deposited, are the specific characteristics of chrysotile asbestos important in any subsequent tissue effects?

Asbestos is composed of fibers whose size varies from over 100 microns to that where they can be seen only by electron microscope. Gibbs (1971) commented that the longer the chrysotile fiber, the more curved it is. However, the weathering factor which increases the harshness of the fiber tends to make it less curved.

The important factor in *penetration* of fibers is the diameter whereas fiber length is a major one in *retention* as shown by Timbrell et al (1971). So the wide range of *lengths* and possibly the curved *configuration* of chrysotile which will increase the sedimentation and the impaction on the walls, make it likely that *deposition* of the fibers occurs more in the airways than in the alveoli, whereas *penetration*, a *diameter* dependant phenomen, will allow some fibers to reach alveoli as well as pleura. It must not be forgotten that chrysotile is also the only type of asbestos which has an electric charge and that this might favor the clustering of fibers.

At the deposition site, the high cytotoxicity of chrysotile (Robock et al, 1971) could perhaps produce an inflammatory reaction of the bronchiolar wall and prevent a deeper penetration of the other fibers.

In the light of this review of the laws of penetration, deposition and clearance or retention of fibers and the effect of smoking, an attempt will be made to answer the question: to what extent can they *explain* the development of the different *lung function profiles*?

Some subjects have a normal pulmonary profile. Perhaps in these individuals, rate of deposition and clearance of foreign substances is adequate to defend them against such pollutants. In addition, the cross-sectional nature of the study must be born in mind, i.e. tests were done at one moment of the subjects' existence and results compared to predicted values. Many of these subjects were heavy physical workers who might have had unusually large VCs, small RVs and accelerated flows and when exposure to asbestos modified their function their results could fall within normal limits when they were tested. Only a longitudinal study could show the progression of their pulmonary function to one or other profile.

The restrictive profile is probably related, at least in part, to straight harsh dust entering normal airways and settling at the terminal bronchioles and in the acini, and in due course causing a fine fibrosis. This fibrosis is the basis of the restrictive syndrome and/or alveolar-capillary block. Dust exposure while exercising would be expected to result in increased tidal air and more uniform distribution of particles and the resultant fibrosis might be more uniform and severe. In the present survey, a restrictive profile was more frequent in the first three decades, i.e. in those subjects with lower dust exposure and little or no smoking, and also in non-smokers with high dust concentration.

Many factors may have interreacted to cause the obstructive profile. Increasing age with its associated decrease elasticity, and hence elastic recoil and bronchial support, could favor the development of obstructive syndrome in the older worker, and in this study the prevalence of obstruction did indeed increase with age.

Turning now to the influence of the particles themselves on the development of the obstructive syndrome, it seems reasonable to conclude that as the concentration of fibers in the inspired air rises, more would impact in the major bronchi and more would sediment in the small airways, leading to an increased prevalence of bronchitis with attendant bronchial obstruction. Such obstruction could limit the penetration of the fibers into the airways, and at the same time, accentuate the bronchitis and bronchiolitis. In the presence of yet another irritant substance, such as cigarette smoke, which also leads to bronchitis, asbestos dust might not penetrate so deeply (blocked by the mucus secretation and the spasm) and hence its influence might be more evident at the level of the large and small bronchi than the alveolar level.

Chrysotile, the only type of asbestos mined in Quebec, could by virtue of its physical characteristics perhaps also predispose to obstruction. Thus its curly configuration when fibers 30 microns and more are oriented parallel to the axis of the airways, makes impaction in bigger bronchioles more likely.

It is evident that many of the possible factors operative in the development of the obstructive syndrome could be interrelated, for example, the relationship of dust exposure and effort to the age of the worker. The dust exposure levels have changed considerably since the beginning of the century in the asbestos industry of the Eastern Townships. Thus, older subjects have had a greater dust exposure, possibly to longer fibers and under conditions of heavier physical work than the subjects who started in 1950. Such older men have possibly smoked fewer cigarettes or at least started at an older age than current younger workers. These temporal changes may well have influenced the age prevalence of the different lung function profiles; thus there was more obstruction in the last three decades, but no great differences in total number of years worked were observed between the obstruction and the restrictive profiles.

Mixed pulmonary function profiles are present in at least 30% of the workers in this survey. The dominant profiles (both restrictive and obstructive) appeared to be uninfluenced by age, but since numbers were few conclusions should remain guarded. Age did appear to related more to the undifferentiated abnormal function which was found to increase with age. As in the obstruction, the changes in concentrations of dust throughout the years, the fact that many of these workers were doing heavy work not only in the industry but on their farms, and the fact that their smoking habits may have started at an older age, could have lead to this mixed undifferentiated function profile which reflects perhaps the equilibrium between the restrictive and obstructive forces.

In conclusion, differences in the function profiles which individuals develop in relation to dust exposure may well be related to individual differences in the clearance characteristics of airways and of parenchyma, individual differences in the penetration and deposition of chrysotile and dust, and the associated effects of effort and smoking on these processes. In theory, at least, different combinations of these factors could result in normal restrictive, obstructive and mixed pulmonary function profiles.

4. REVIEW OF PERTINENT PUBLISHED DATA ON LUNG FUNCTION PROFILES IN RELATION TO ASBESTOS EXPOSURE.

Various aspects of the data in the present study have appeared in different presentations and publications: lung function and radiological appearance (McDonald et al, 1968; Becklake et al, 1969, 1970); lung function and dust (Becklake et al, 1972); lung function and respiratory symptoms (Fournier-

Massey et al, 1970); respiratory symptoms and dust (McDonald et al, 1972); and dust concentrations (Gibbs et al, 1972). As these have included data from similar investigations for comparison purposes, only points directly related to pulmonary function profiles will be reviewed in this last part of the discussion.

Harries (1971)

The first study that falls into this category is that of Harries (1971). A basic difference is the type of exposure - his study, also cross-sectional in nature, was conducted in a secondary industry on workers involved in the shipbuilding and refitting whereas the present survey was concerned with workers in the primary industry i.e. asbestos getting and milling.

He reported that 74% of his 369 workers had normal lung function, about 9% with restricted TLC, 7% with a transfer defect alone, 4% with diminished T_L and TLC combined, only 3% with obstruction and 5% with doubtful function defects. Although it is difficult to compare Harries' categories with the profiles of this series, it would seem that those working in the primary industry have more functional changes than those in the secondary one and that, in addition, more obstruction is to be found i.e. 14% as opposed to 3%. About the same amount of restriction was found in the two series.

As in the present studies, normal radiographs could be present in any of his lung function categories. In contrast to the present results, where parenchymal changes were present in every profile subgroup, he did not find any in his obstructive categories. Our findings showed the prevalence of parenchymal changes in the obstructive group to be comparable with that in the restrictive group.

Light dust exposure in Harries' series did not alter function very much (82.5% fell in the normal category), but heavy exposure led to 54% abnormal function mostly characterised by a restricted transfer factor and/or a reduced TLC. In the present series, heavy exposure alone or with effort led to more obstructive or undifferentiated profiles.

Although he did not specifically examine the relation of smoking to lung function categories, an examination of the mean results of the tests in each of his smoking categories reveals that T_L and FEV_1% are decreased in the heavy smoking group suggesting obstruction. The same trend was found in the present study.

A few other interesting findings in his study that correlate well with the present one are:

a) the longer exposure, the higher RV (corrected for age and height)

b) the FEV_1/FVC % is also lower in the men with heavy exposure

c) RV is higher when pleural changes are present in radiological categories 0/0, 0/1, and 2 and slightly lower in category 1, whereas FEV_1/FVC % is lower in every category.

Murphy et al (1971), Ferris et al (1971)

Murphy et al (1971) and Ferris et al (1971) also compared shipyard workers directly exposed to asbestos with a reference group less exposed to asbestos. Pulmonary function tests (Murphy et al, 1971) included FVC and its components, FEV_1/FVC %, Peak Flow, $D_{LCO_{SB}}$ and $D_{LCO_{SS}}$ exercise, airways resistance, ventilation, CO_2 tension and V_D. Since the individual results were not available, a direct comparison with the profiles of the present study is not possible. However, they found the same frequency of obstructive disease by physiological evidence in both the exposed and the control groups, but the former had more important obstruction. The two groups also had the same proportion of clinical chronic obstructive respiratory disease, though the pipe coverers had more symptoms. The two groups, matched for age, duration of work in the industry and smoking habits, differed in the severity of chronic obstructive respiratory disease, perhaps an effect of superimposed dust exposure in pipe coverers. These results were confirmed by Ferris et al (1971) who compared these pipe coverers to groups of pipe-fitters and welders exposed only intermittantly to asbestos.

Regan et al (1971)

Turning now to the study of Regan et al (1971), her subjects are similar to those in the present study in that they also manipulated raw asbestos. Though these workers did not define primarily the function profiles, interesting conclusions can be found in their principal component analysis. Exposure, in terms of number of years since the first exposition to asbestos, was relatively important in differentiating health from disease, but smoking was not. They also report the surprising finding that exposure and smoking have also a very low power in the differentiation between "asbestosis" and obstructive disease, and in fact, these variables are located in the obstructive side of the second component (obstruction - asbestosis); this observation perhaps confirms the suggestion that asbestos exposure can lead equally to obstruction as well as to restriction, or in fact to any functional profile.

Muldoon et al (1972)

The last paper to be considered is that of Muldoon and Turner-Warwick (1972), a report on 60 male and female subjects referred to the Pneumoconiosis Board, who were divided on the basis of specific conductance and TLC into four groups which correspond to the following profiles of this study: normal, undifferentiated, restriction and obstruction. With the workers in their series being referred for compensation, it is not surprising to find only 16% falling into the normal category (as compared to 44.3% in the present study). The other profiles were as follows: 4.0% undifferentiated (26.5% in this series), 42.7% restriction (14.9%) and finally 17.3% obstruction (14.3%). Unlike the present series where the obstructive profile had a higher prevalence of cough and sputum, no significant difference was found between their groups possibly because they have more advanced disease.

Eighty-five (85%) of the entire group had radiological changes which was considerably higher than in the present series. The normal, restrictive and obstructive groups had about the same percentage of pleural and parenchymal changes, (83%, 88% and 85% respectively) but the obstructive group had the highest prevalence of parenchymal changes (77% as opposed to 67% and 69% for the normal and restrictive groups respectively) and the restrictive group the highest prevalence for pleural changes (19% as opposed to 8% for the other two groups). However, the parenchymal changes were less extensive in their obstructive group probably because hyperinflation is more advanced. These findings further confirm the conclusions of the present study that radiological asbestosis may be associated with any type of profile even obstruction.

As in the present study duration of exposure played little part in the differentiation of the profiles. Unlike this present series, no significant difference could be demonstrated in smoking habits between the groups.

In summary, the conclusions of the present study were compared to four recent investigations; only that of Regan dealt with the primary industry. All of these studies support the present one in concluding that asbestos exposure can lead to more than one type of pulmonary function profile. Furthermore, the obstructive syndrome is as frequent as the restrictive in those working in the primary industry, and although sometimes reported as less frequent in the secondary industry, it is still much more important than previously thought.

There is good agreement that the radiological changes parallel the alteration in pulmonary function only in the advanced stages of the diseases. However, no agreement was found on the frequency of parenchymal changes in the different profiles. In both the present study and that of Muldoon et al (1972), they were more frequent in the obstructive profile.

Clinical symptoms were more common in the obstructive syndrome in the present survey, less so in the other investigations. With regard to the influence of dust concentration and duration of exposure, effort and amount of smoking, little agreement was found on their relationship to function profiles. These factors were associated with increases in the prevalence of obstruction in the present study whereas perhaps only smoking appeared to be important in other studies.

7. CONCLUSIONS

One thousand and thirty-four (1034) chrysotile asbestos workers, selected from 21 to 65 years of age in the Eastern Township Industry in Quebec, were studied by questionnaire, radiograph and pulmonary function tests at rest and on exercise. Their industrial history was given in terms of years of work, years of dust exposure alone and corrected for physical effort.

The analysis of the results was based on the definition of six (6) pulmonary function profiles: normal and undifferentiated abnormal function, definite and dominant restriction, and definite and dominant obstruction. The overall prevalence, age standardized, of these profiles in the working population was respectively 44.3% and 26.5%, 12.2 and 2.1, and 12.8 and 2.2%

Cough, sputum and dyspnea were associated more frequently with the obstructive profiles, but present also in the normal, undifferentiated and restrictive ones.

There was a comparable prevalence of normal radiographs in all of the profile groups; likewise the prevalence of small irregular opacities and pleural changes was similar in all groups; the restrictive profiles had a lower prevalence of changes compared to the normal, obstructive and undifferentiated ones.

For a comparable number of years at work in the asbestos industry, more dust exposure, and more dust exposure and effort were found in the undifferentiated and obstructive profiles. A greater proportion of non-smokers had a restrictive profile while most of the subjects with obstruction were heavy smokers. Non-smokers having a light dust exposure had proportionately more restriction, whereas association of heavy dust exposure and smoking led to more obstruction.

The laws of penetration, deposition and clearance of particles and fibers, the physical and chemical properties of chrysotile, and the dynamic concept of the respiratory system provide some explanation for the differences in response to chrysotile exposure and for the finding of not only restrictive pulmonary function profiles but of normal, undifferentiated and, more surprising, obstructive profiles.

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9 - APPENDICES

APPENDIX I: REVIEW OF THE LITERATURE

TABLE I - 1 — REVIEW OF THE RESTRICTIVE SYNDROME IN ASBESTOS WORKERS

Author	year	Subj. no.		PULMONARY FUNCTION																	ANTHROPOLOGY					QUESTIONN.					EXPOSURE		RADIOLOGY			ECG
				f	$\dot{V}$	VC		RV		TLC		RV/	MBC		FEV_1	DLCO		Sat O_2		$\dot{V}/\dot{Q}$	Sex	Age	Ht	Wt	BSA	C	P	B	Cy	Cr	Work	Dust	SIO	PC	SIO	
				R	E	L	%	L	%	L	%	TLC	L/m	%	%	*	%	R	L	R		Yrs	cm	Kg	m^2						Yrs				PC	
RESTRICTIVE (n = 82)																																				
Bastenier et al	1953	1		6.3	40		44		69		49	30		93				90			F	47	148	47		+	-	+	-	+	11	+	+			
Bastenier & al	1955	5		4.8	20		64		81		68	29		42	76					7.5	F	49	158	88		+		+			20	+			+	
Caffuri & al	1957	12				2.3	79	1.3	84	4.1	81	31	65		76							55	163	72	1.78								2			
		15				3.5	97	0.9	58	4.4	85	21	74		71							55	170	68									2			
		21				2.6	79	1.3	86	4.1	82	32	72		84							52	173	68									2			
		22				1.6	51	0.7	54	2.3	52	31	34		71							50	159	56											3	
		23				2.0	52	0.9	85	2.9	60	31	44		92							47	159	71											3	
		24				2.0	51	1.3	78	3.3	60	40	48		82							53	167	78											3	
		29				2.0	53	1.1	89	3.1	62	34	46		78							48	170	63											3	
Read & al (Williams & al, 1960)	1959	I 1			55	2.0		1.4		3.4		41	60		80	9.9	39			3.1	F	57						4		++	14		10			N
		2		7.0	30	1.3		1.2		2.4		48	38		84	9.8	39			17.1	F	56						3		++	3.5		12			R
		4		4.5	40	1.6		1.4		2.9		47	49		60	10.3	41			17.8	F	52						3		++	15		4			N
		5		7.7	36	3.8		1.1		4.9		22	105		78	13.8	47			4.0	M	53						0			11		5			
		6				1.8		1.5		3.3		46	53		75	11.2	68			9.9	M	50						4		4	18		8			L
		8		8.5	35	2.9		1.5		4.4		35	88		86	15.7	53			5.1	M	47						2		+	25		2			N
		9			32	2.9		1.6		4.5		35	95		86	13.1	58			6.9	M	48						2		++	10		5			
		10			30	1.5		1.3		2.8		46	51		86	13.8	60			7.5	M	44						2		++	11		6			N
		12			35	2.8		1.9		4.6		41	73		71	16.8	66			9.1	M	41						1		+	11		6			H
		11			42	1.8		1.4		3.2		44	46		70	13.1	63			20.5	F	37						2		+	3		4			M
		13		14.0		1.7		1.2		3.0		42	49		76	17.2	72			12.0	F	51						3		+	13		6			L
		II 4		19.0	78	1.9		2.2		4.2		54	58		86	9.3	38			7.2	M	55						4		+	16		4			
Williams & al	1960	I 1		11.0	30	2.1		1.4		3.5		41	71		88	11.6				8.7	M	50						3		++	16		6			
		11			48	2.8		2.0		4.8		42	87		85	19.6					M	60						3		++	18		10			N
		31			37	2.6		1.1		3.6		30	54		77	21.4	79				M	43						1		+	14		2			
		38		7.8	47	3.3		1.4		4.7		30	91		81	18.2					M	39						3		0	22		4			
Heard & al	1961	6					51		37		84	47		74	74	12.6					M	47						1			32		+			
Bader & al	1961	1		↓	↑		56		87		56	34		100		9.0(SS)		90	71			48				o		++			14	+++			+++	
		2		↑	↑↑		65		74		73	25		113				93	78			43				+		++			12	++++			+++	
Rubino & al	1961	3				3.0	79	1.2		4.2		29		60	74	31.5		90				41			1.80								2			
		4				2.9	85	1.7		4.6		37		80	76	22.2		87				59			1.49								2			
		5				1.7	48	1.0		2.7		37		55	79			86				58			1.80								3			
Thomson & al	1961	A 2					85		67		79	26			86		83				M	50	165	44		-	-	1	-	+	9		+			
		A 3					52		66		57	36			84		46				F	60	152	65		-	-	2	+	↔	3.5				+	
		A 5					75		73		74	30			83		62				F	50	152	68		+		3	-	+	13		+			
		A 8					91		87		90	30			79		90				M	60	173	84		-	+	2	+	+	17				+	
		A 16					86		66		79	25			80		57				M	50	175	76		+	-	1	±	±	26		+			
		A 32					61		66		66	24			84		52				M	45	170	70		-	+	2	-	+-	25		+			
Bellinelli & al	1963			↑	↑		44		45		45	32			73			95	86		M	50	161	55		+	±	+	+	+	30				+	
Bjure & al	1964	10	44	7.5	19	3.1	54	1.7		4.8		36			87	21.2		88×	96	1.4		33	173											+		
		12	30	13.1	23	3.4	78	1.3		4.7		28			78	15.0		104×	83×	2.3		49	168												+	
		13	36	6.5	26	3.4	89	1.7		5.1		33			86	11.5		93×	94×			47	168												+	
		14	25	7.7	31	2.9	70	1.8		4.7		38			79			96×	96×			46	164												+	
De Rosa & al	1964	I 1				3.7	70	1.5		5.2		29		65	84							40									10		1			
		2				3.2	86	1.8		5.0		36		64	73							27									8		1			
		3				3.0	85	1.4		4.4		32		60	73							28									8		1			
		4				3.8	91	1.4		5.2		26		87	89							27									5		1			
		5				3.7	84	1.4		4.1		34		74	85							31									15		1			
		7				3.4	90	1.5		4.9		31		85	88							40									8		1			
		8				3.5	90	1.6		5.1		31		74	82							43									8		1			
		12				3.4	88	1.2		4.6		26		77	85							35									11		1			
		13				3.6	89	1.6		5.2		31		75	83							38									14		1			
		14				3.0	88	1.5		4.5		33		61	82							38									9		1			
		15				3.6	96	1.4		5.0		28		86	77							33									7		1			
		17				3.4	88	1.6		5.0		32		75	88							41									8		1			
		19				3.9	93	1.5		5.4		28		72	82							37									3		1			
		20				3.5	84	1.6		5.1		31		73	85							35									7		1			
		24				3.3	86	1.7		5.0		34		59	87							34									8		1			
		25				3.5	76	1.5		5.0		30		68	78							44									15		1			
		26				3.0	75	1.6		4.6		35		70	86							38									9		1			
		27				3.2	65	1.8		4.0		45		51	77							48									13		1			
		29				3.4	69	1.6		4.0		40		55	76							37									4		1			
		II 2				3.0	88	1.5		4.5		33		74	80							55									9		2			
		4				2.9	57	1.3		3.2		40		49	89							41									10		2			
		5				2.9	78	2.0		4.9		40		62	79							49									24		2			
		7				3.9	73	1.5		5.4		27		69	82							55									15		2			
		8				3.0	78	1.4		4.4		31		66	83							34									16		2			
		9				2.9	73	1.8		4.7		38		54	89							33									9		2			
		10				4.0	105	2.0		6.0		33		96	90							45									14		2			
		11				2.8	85	1.4		4.2		33		71	81							40									14		2			
		13				3.0	85	1.4		4.4		31		64	73							52									16		2			
Pellet & al	1964	190				2.6	87	1.5	83	4.3	86	34			75			95	90		M	62				+		+					+			
		206				1.2	42	1.1	87	2.3	56	42			72			90	65		F	48														
Kleinfeld & al	1966b	1					69		71		69	34			71	27.3						45				+	+	-			23					N
		4					66		46		56	43			77	20.7						72				+		-		-	54				2	N
		8					38		89		68	49			89	19.9						57				-		+		-	14				2	N
		11					54		67		55	38			87	13.3						47				+	-	+		+	22		+++			N
		16					87		75		81	29			82	24.2						40				+	+	-		-	18		++			
		17					43		77		59	60			82	9.2						68				+		+		+	46		2			N
		19					49		63		50	43			76	18.3						54				-		-		-	32		+			N
		20					76		87		69	34			78	19.9						53				+	-	-		-	37		++			
Poggi	1970	3				2.3		1.0		3.2		30	60		71	13.0		76								+	+	+	+		30				1	

* ccCO/min/mmHg × P_{O_2}

TABLE I - 2 - REVIEW OF PROBABLE RESTRICTIVE SYNDROME IN ASBESTOS WORKERS

Author	year	Subj. no.	PULMONARY FUNCTION																		ANTHROPOLOGY					QUESTIONN.					EXPOSURE		RADIOLOGY			ECG
			f	V̇ R	V̇ E	VC L	VC %	RV L	RV %	TLC L	TLC %	RV/ TLC	MBC L/m	MBC %	FEV1 %	DLCO *	DLCO %	Sat O2 R	Sat O2 E	V̇/Q̇	Sex	Age yrs	Ht cm	Wt Kg	BSA M2	C	P	B	Cy	Cr	Work yrs	Dust	SIO	PC	SIO PC	
RESTRICTIVE - RV or TLC NORMAL (no = 16)																																				
Bader & al	1961	6		↑	↑		77		104		81	31		120		10.0		93	89			67				+-		+-			11	++	+-			
		12		↑	-		65		100		73	33		101				95	95			63				0		0			13	+	+			
		15		↓	N		81		94		77	28		118				96	95			38				++		0			4	+++-	0			
		16		N	↑↑		82		100		86	28		99				95	96			54				+-		+			8	++++	+++			
Heard & al	1961	5					45		97		69	49		62	82	18.0					M	45				+		2			2				+	
Thomson & al	1961	A 4					53		102		65	37			79		65				M	45	160	52	1.53	+	+	2	+	+	12		+			
		A 11					79		107		88	38			70		65				F	50	152	56	1.51	-	-	1		+	12		±			
		A 12					73		101		79	30			86		24				M	45	152	57	1.53	+	-	2		++	8				+++	
		A 14					75		97		80	29			72		68				M	40	168	61	1.70	-	-	-		+	12		+			
		A 15					62		93		72	39			77		60				M	60	168	53	1.60	+	-	-		+	17		+		++	
		A 21					83		103		89	35			77		59				F	60	168	59	1.69	+	+	2		++	13					
		A 25					68		105		78	39			75		91				M	50	183	66	1.87	-	+	-		-	13					
Kleinfeld & al	1966b	3					92		90		89	46			85	19.3						64				-		-		-	40					N
		5					62		93		74	50			93	16.9						54				+		+		-	20		++			N
		7					72		102		74	36			82	21.7						41				+	-			-	18		+-			
Hany & al	1967	7				3.7	70	2.1		5.8	95	36			70			94	94			41	171	70		+		+		-	6				+	
RESTRICTIVE - INCOMPLETE DATA (no = 32)																																				
Gernez-Rieux & al	1954	1	23	10.5	12	1.8	56	2.1		3.9		54	72					97	86		M	49						2			19					
		3	19	16.0		2.1	40	1.4		3.5		40	-					95	85		F	44						1			13					
Caffuri & al	1957	28				2.8	81	0.3	20	3.1	63	10	-		-							50	174	61									3			
Bjure & al	1964	8	40	6.9			63								73	15.2		98		2.7		50	168												+	
Sartorelli	1964	4					71					38			76	24.0		97			M	60											1			
		5					78					28			88	18.1		97			M	44											1			
		12					61					41			85	10.2		97			M	56											2			
		14					72					42			80	7.2		95			M	52											2			
		16					59					55			73	6.7		96			M	65											3			
Vaerenberg & al	1964	1					37					25	43		73	6.0																				
		2					100					22	65		74	10.0																				
		3					40					-	31		76																					
		4					64					32	54		88	8.0																				
		5					79					25	49		73	7.5																				
		6					91					20	54		73	6.0																				
		9					53					36	31		82	5.5																				
		10					63					30	34		71	8.0																				
		11					69					34	54		81	7.5																				
Vecchione & al	1964	AG					76					37		54	78	17.8						37									4		1			
		PV					78					30		60	83	14.0						40									7		2			
		MC					80					57		55	78	12.7						55									11		2			
		RF					80					33		79	78	21.8						34									9		2			
		FH					79					34		51	83	19.1						34									16		2			
		DVG					71					53		74	82	13.1						42									11		2			
		PC					50					56		69	81	11.3						58									15		2			
		AC					78					44		66	79	18.5						49									24		2			
		CV					69					34		72	76	27.5						44									15		1			
		BV					86					34		59	87	22.3						41									9		1			
		BP					65					45		71	77	20.1						51									11		1			
		MD					90					31		60	82	18.8						41									6		1			
		CC					88					30		38	82	24.5						37									3		1			
		DNV					79					32		62	79	15.1						55									15		2			

* ccCO/min/mmHg

TABLE I - 3 - REVIEW OF THE ALVEOLAR-CAPILLARY BLOCK SYNDROME IN ASBESTOS WORKERS

Author	year	Subj. no.	PULMONARY FUNCTION																		ANTHROPOLOGY					QUESTIONN.					EXPOSURE		RADIOLOGY			ECG
			f	V̇ R	V̇ E	VC L	VC %	RV L	RV %	TLC L	TLC %	RV/ TLC	MBC L/m	MBC %	FEV1 %	DLCO *	DLCO %	Sat O2 R	Sat O2 E	V̇/Q̇	Sex	Age yrs	Ht cm	Wt Kg	BSA M2	C	P	B	Cy	Cr	Work yrs	Dust	SIO	PC	SIO PC	
(no = 16)																																				
Read & al (Williams & al,	1959 1960)	II 5 (# 8)		7.0	39	3.2		2.1		5.3		39	87		72	10.2	39			2.9	M	45						3		++	9		7			L
Williams & al	1960	27		11.0	37	3.2		2.0		5.1		39	86		74	24.4	72		↓		M	52						1		+	10		-			
Bader & al	1961	4		4.5	14		88		109		93	29		131				93	86			66				-	-	-			10	+++			+++	
		5		4.5	14		117		142		120	29		120				95	88			42				+		++			13	++	+			
		8		4.1	13		97		94		96	24		88				96	91			46				+		+			24	++++	+			
		9		4.4	14		98		91		96	23		88				97	92			36				+-		-			13	+++			++	
		10		4.9	15		90		115		96	29		106				95	92			51				+		+			6	+++			+-	
		14		3.3	15		124		124		125	25		86				95	95			37				0		+			7	+++			+--	
Thomson et al	1961	A 7					108		79		101	18			77		83				M	45	168	42	1.94	-	-	-			11		-			
		A 17					99		97		98	23			71		56				M	45	173	57	1.69	+	+	2		++	9				++	
		A 20					105		93		103	21			77		59				M	45	170	79	1.91	-	-	-		±	11		-			
		A 29					99		93		97	30			72		77				M	55	170	85	2.01	-	-	-		-	16		-			
		A 37					116		115		116	30			71		83				M	65	168	49	1.56	+	+	1	-	+	11		2			
		A 38					112		118		114	32			76		59				M	50	173	59	1.71	+	+	1	-	+	34		+			
Pellet & al	1965	203				3.6	100	1.5	100	5.1	100	29			82			97	92		M	53											+			
Kleinfeld & al	1966b	12					93		98		88	32			79	20.4						45				-		-		-	18		++			

* ccCO/min/mmHg

TABLE I - 4 - REVIEW OF THE OBSTRUCTIVE SYNDROME IN ASBESTOS WORKERS

Author	year	Subj. no.	PULMONARY FUNCTION																		ANTHROPOLOGY					QUESTIONN.					EXPOSURE		RADIOLOGY			ECG
			f	$\dot{V}$		VC		RV		TLC		RV/	MBC		FEV$_1$	D$_{LCO}$		Sat O$_2$		$\dot{V}/\dot{Q}$	Sex	Age	Ht	Wt	BSA	C	P	B	Cy	Cr	Work	Dust	SIO	PC	SIO PC	
				R	E	L	%	L	%	L	%	TLC	L/m	%	%	*	%	R	%			yrs	cm	Kg	M^2						yrs					
OBSTRUCTIVE (no = 41)																																				
Bastenier & al	1955	6	37	7.1			70		202		102	48	62		64			92			M	58	175	81	1.97										+	
		7	41		27		53		207		94	53	66		66			91			M	61	164	70	1.77										+	
Caffuri & al	1957	1				3.9	109	1.6	103	5.5	103	33	79		68							57	171	65	1.76								1			
		5				3.9	112	3.6	236	7.5	150	48	70		59							56	168	65	1.74								1			
		9				4.0	105	1.7	100	5.7	104	29	50		66							52	176	73	1.88								1			
		10				2.0	59	2.9	272	4.9	110	59	35		59							47	163	50	1.52								2			
		14				2.5	72	2.3	155	4.8	95	48	31		52							61	163	65	1.70								2			
		26				3.0	88	1.4	96	4.4	91	32	58		65							62	165	61	1.67								3			
Sartorelli	1957	1	24	10.8	47		76		131		93	42			65			94	84			57						3			7					
Read & al	1959	II 1			49	1.6		2.9		4.5		65	25		36	↙				18.6	M	59						5		++	14		14			R
(Williams & al,	1960)	3			40	1.5		2.5		4.0		62	36		67	8.7	35			18.2	M	46						4		++	22		13			R
		6			46	3.2		1.9		5.1		37	75		46	12.4	43			7.6	M	45						2		+-	12		11			
		7		7.5	34	3.6		2.8		6.5		43	92		69	12.8	53			4.3	M	54						3		++	24		4			N
		9		10.8	31	2.8		2.7		5.5		49	72		66	18.4	67			3.6	M	54						2		++	32		6			N
Williams & al	1960	20		7.0	36	3.0		1.7		4.7		36	58		55	21.6					M	59						2		++	8		1			(R)
		22		9.7	31	3.8		2.1		5.9		35	95		64	22.8	74				M	45						0		+	16					
		26		10.0	29	4.0		2.4		5.8		42	81		58	21.3	73				M	41						0		+	21					
		28		11.5	35	3.5		1.7		5.1		33	73		62	29.5	100				M	48						0		-	23					
		29		9.5	30	2.7		2.6		5.2		49	56		66	19.2	69		↙		M	48						1		+	15					
		30		13.3	39	3.3		2.7		6.0		46	50		53	21.0	79				M	53						3			27		3			
		40			42	2.5		2.7		5.2		52	35		46	18.8					M	65						2		+	4		–			
Rubino & al	1961	1				4.3	103	2.3		6.3		36		71	60	25.6						43			1.64								1			
Thomson & al	1961	A 18					113		172		127	32			62	24.3	85				M	40	183	65	1.86	+	+	1	–	±	6					
		A 19					104		161		115	32			69	23.9	85				M	45	183	74	1.95	–	–	–	–	–	16					
		A 26				3.4	92	1.9	115	5.2	99				54	18.8	80				M	50	170		1.72											
		A 39					74		133		92	44			55	17.8	85				M	50	168	59	1.68	+	+	–	–	+	30					
Bjure & al	1964	7	36	11.7		4.5	91	2.0		6.5		32			66	11.8		92	94		M	51	172											+		
		11	28	9.5	25	3.9	87	2.7		6.6		42			58	9.4		98			M	48	180												+	
De Rosa & al	1964	I 10				3.2	85	1.6		4.8		33		30	32							44									17		1			
		21				3.7	95	1.5		5.2		28		73	70							32									2		1			
		22				3.4	85	1.6		5.0		32		60	64							49									12		1			
		28				1.2	72	2.8		4.0		70		40	53							51									11		1			
		II 1				2.6	72	2.9		5.7		51		52	63							54									10				2	
Pallet & al	1964	235				1.3	74	2.2	228	3.5	130	63			20						F	60														
		311				2.1	66	3.0	200	5.1	110	53			55						M	55											+			
		187		4.9		3.1	86	1.5	150	4.6	100	32			32			93	95		M	39											+			
		273				1.8	69	2.0	124	3.8	90	51			43			97	98		F	53											+			
		604				4.1	104	1.4	108	5.5	100	25			71			97	97		M	35											–			
		634				3.6	93	1.8	146	5.4	100	33			66						M	39														
		586				4.6	113	2.2	159	6.8	120	31			65			98	97		M	43											–			
Kleinfeld & al	1966	15					101		118		107	42			64	13.1						52				+	–				15				+	
OBSTRUCTIVE - INCOMPLETE DATA (no = 27)																																				
Cernez-Rieux & al	1954	2	16	18.0	36	2.8	78	2.8		5.9		47	78					93	86		M	45						1			15					
Caffuri & al	1957	17				3.1	67	2.0	179	5.1	90	40										33	174	74	1.89								2			
		18				2.1	57	1.5	127	3.6	91	33										42	165	76	1.84								2			
Bader & al	1961	13		5.8	9		107		121		112	27		87				98	95			67				–	–	–			11	++++			+++	
Sartorelli	1964	2					82					28			61	20.2		90			M	55											1			
		3					69					39			59	19.5		97			M	49											1			
		6					61					34			50	25.4		97			M	51											1			
		8					72					53			37	22.1		94			M	49											2			
		9					61					37			59	20.5		96			M	59											2			
		10					70					47			57	21.4		98			M	67											2			
		11					75					40			55	10.6		94			M	59											2			
		13					49					39			50	12.0		97			M	27											2			
		15					59					35			62	14.0		97			M	37											3			
		17					41					54			47	9.1		91			M	59											3			
		18					44					49			37	8.2		88			M	69											3			
Vaerenberg & al	1964	7					66					43	44		60	7.5		95	90																	
		8					59					25	54		69	8.0																				
Vecchione & al	1964	CR					85					32		66	64	28.1						34									8		1			
		ED					91					33		68	60	18.3						43									14		2			
Poggi & al	1970	2			2.3								56			17.0												+			11		?			
		4					66	↗					↙													+	+	+	+	+	37		1			
		5					89	↗					↙															+			11		?			
		6					82	↗					↙															+			12		?			
		7					76	↗								↙										+	+	+			20				1	
		8					57	↗					↙			4.0												+		+	20		1			
		9	↗				90	↗																				+			32		?			
		10					N	↗							↙													+			22		?			

* ccCO/min/mmHg

TABLE I - 5 - REVIEW OF MIXED SYNDROME IN ASBESTOS WORKERS

Author	year	Subj. no.	PULMONARY FUNCTION																		ANTHROPOLOGY					QUESTIONN.					EXPOSURE		RADIOLOGY			ECG
			f	$\dot{V}$		VC		RV		TLC		RV/	MBC		FEV$_1$	DL$_{CO}$		Sat O$_2$		$\dot{V}/\dot{Q}$	Sex	Age	Ht	Wt	BSA	C	P	B	Cy	Cr	Work	Dust	SIO	PC	SIC PC	
				R	E	L	%	L	%	L	%	TLC	L/m	%	%	*	%	R	E			yrs	cm	Kg	M^2						yrs					
MIXED - PREDOMINANTLY RESTRICTIVE (no = 43)																																				
Bastenier & al	1955	3		6.6			50		120		67	50	52		87			99			F	55	164	73	1.70										+	
		4		6.2	11		59		160		84	47	39		71			91			F	57	164	64	1.70										+	
		8	42	5.4			48		145		74	52	38		63			94			F	53	162	73	1.79										-	
		9	40	6.8	22		62		181		92	49	42		77			90			F	52	156	54	1.52										+	
Caffuri & al	1957	16				3.1	95	2.1	62	5.2	85	22	54		55							51	167	54	1.61								2			
1		27				2.8	61	1.7	118	4.5	75	37				53	(55)					49	179	91	2.12								3			
Marks & al	1957	I 9		4.2			76		137		92	35		69	90	13.3	(9)	94			M	48			1.79	+		++			13		+			
Read & al	1959	I 7		6.8	39	2.4		2.1		4.5		47	62		72	11.9	49			9.8	M	59														
		II 2	43	7.3		1.5		2.3		3.8		60	67		63	6.4	30			39.9	M	46						4		+-	12		12			R
Bader & al	1961	11		5.1	14		68		131		92	35		81				93	94			48				+		++			13	+++			++	
		17		4.0	9		70		115		64	41		133				95	96			54				+		+			8	++++			++	
Heard & al	1961	3					41		111		65	62		31	67	8.7	35	85			M	46				+		4			12		+			
Thomson & al	1961	A 10					133		68		95	22			51		97				M	60	163	63	1.71	+	+	2	-	+	10		+			
		A 13					80		145		95	37			72		66				M	35	163	55	1.62	+	+	2	-	+	18		-			
		A 22					100		84		95	27			58		83				M	55	168	66	1.76	+	+	2	-	++	19		2			
		A 24					74		105		84	39			67		79				M	50	168	70	1.80	+	+	-		+	15					
		A 27					74		109		82	31			68		98				M	45	168	64	1.73	-	-	-		±	15					
		A 30					80		105		87	37			57		68				M	60	183	72	1.94	+	-	3		+	12		+			
		A 31					63		86		68	29			68		37				F	40	152	77	1.74	-	+	2	-	++	15		+			
		A 34					78		64		73	17			64		88				M	55	168	63	1.71	+	+	1	-	+	6		+			
		A 36					65		92		73	38			34		66				M	50	175	63	1.72	+	++	1		+	23				++	
De Rosa & al	1964	I 15				4.0	101	1.3		5.3		25		75	75							46									8		1			
		II 6				2.6	66	2.0		4.6		43		53	76							58									15				2	
Pallet & al	1964	129				3.2	94	1.4	82	4.6	90	30			40						M	59														
		216				2.1	79	1.4	80	3.5	80	34			49						F	56														
		232				2.3	92	1.5	87	3.8	90	39			47						F	60														
		195				1.9	54	1.5	93	3.4	66	45			61			92	92		M	62														
		201				1.5	50	2.4	175	3.9	90	62			85			96	98		F	71											-			
		208				1.3	76	0.8	99	2.1	83	35			69			89	87		F	45											+			
		217				1.3	40	1.7	94	3.0	60	57			40			89	88		M	66											+			
		222				2.0	55	1.9	108	3.9	72	48			48			91	89		M	53											±			
		451				2.5	70	0.9	77	3.4	80	27			60			91	92		M	50														
Kleinfeld & al	1966b	2					68		65		71	56			65	8.3						77				-		+		+	55				3	N
		6					71		130		81	41			85	41.4						39				-		-		-	18		1			N
		9					71		107		85	44			65	19.6						40				-		-		-	15				1	
		10					76		103		79	43			62	17.6						57				-		-		+	35				3	
		14					94		114		89	36			87	24.4						52				-		-		-	25				1	
		18					66		82		71	48			68	13.0						63				-		+		+	38		1			N
		21					45		86		60	58			58	11.6						61				-		+		+	36		3			
Hany & al	1967	2				1.4	77	0.6		2.0	38	39		35				89	84			56	163	59		+		+		+	14		+			
		3				1.4	70	0.7		2.1	39	33		30				89	77			46	170	76		+	+	+	+	++	10				+	R
		5				3.5	75	1.5		5.0	75	30		64				94	96			39	179	77		+				+	8				+	R
Poggi & al	1970	1		3.6		1.0		3.0		4.0		75						88								+	+	+	+	+	26				2	
		14				1.2		2.2		3.4		65	22		50											+		+			31		2			
MIXED - PREDOMINANTLY OBSTRUCTIVE (no = 25)																																				
Bastenier & al	1955	2		3.7	22		76		209		110	48	47		70						F	56	155	56	1.54										+	
Caffuri & al	1957	2				4.8	107	1.8	153	6.6	117	26	110		77							33	176	71	1.86								1			
		3				5.0	112	2.0	143	7.0	120	29	105		69							44	174	88	2.03								1			
		4				4.6	58	1.9	154	6.5	110	29	125		90							29	174	73	1.83								1			
		6				3.6	97	2.2	197	5.8	121	35	83		76							48	176	55	1.67								1			
		7				4.4	111	2.3	186	6.7	129	34	115		87							46	172	68	1.80								1			
		8				4.3	94	1.8	153	6.1	106	29	115		89							28	176	66	1.62								1			
		11				2.9	98	2.9	215	5.8	135	50	67		76							56	155	51	1.48								2			
		13				3.2	95	2.8	187	6.0	124	46	78		82							55	171	57	1.66								2			
		19				2.7	61	2.6	201	5.3	94	49	56		70							49	154	97	1.95								2			
		25				1.6	47	2.1	140	3.7	70	61	25		50							59	154	71	1.70								3			
Williams & al	1960	35			45	2.5		2.0		4.5		44	63		68	15.7						36						3		+	17		1			
Bader & al	1961	3					53		171		76	44		81				95	83			35				++		++			11	+++			+++	
		7		6.0	17		71		162		112	35		113				94	90	8		62				++		++			10	++	+			
Heard & al	1961	2					51		118		87	51		25	36			85			M	59				+		5			12		+			
		4					45		111		107	62		88	69	12.8	53				M	54				+		3	+	+	14		+			
Thomson & al	1961	A 1					72		146		89	38			65		64				F	40	168	42	1.45	+	+	1	-	+	4		+			
		A 33					74		137		87	34			69		49				M	45	173	69	1.83	-	-	1	-	++	16		+			
		A 35					85		95		88	33			68		92				M	60	168	67	1.77	+	+	1	-	+	13		+			
Bjure & al	1964	9	28	9.0		4.0	74	3.0		7.0		43			82	17.3		97				40	188												+	
De Rosa & al	1964	II 12				3.3	68	1.7		5.0		34		53	58							42									12		2			
Pallet & al	1964	271					96		124		130	28			76						F	48														
Kleinfeld & al	1966	13					42		140		71	67			68	30.5						63				+	-	2			35				++	
Hany & al	1967	6				4.1	59	1.6		5.7	96	28		68				95	96			46	173	70				+		-	6		+			
		8				4.4	59	1.9		6.3	75	39		46				91	87			59	160	60		+		+		++	30				+	

* ccCO/min/mmHg

TABLE I - 6 - REVIEW OF MISCELLANEOUS PULMONARY FUNCTION IN ASBESTOS WORKERS

Author	year	Subj. no.	PULMONARY FUNCTION																		ANTHROPOLOGY					QUESTIONN.					EXPOSURE		RADIOLOGY			[illegible] or A.D.
			f	V̇		VC		RV		TLC		RV/	MBC		FEV$_1$	D$_{LCO}$		Sat O$_2$		V̇/Q̇	Sex	Age	Ht	Wt	BSA	C	P	B	Cy	Cr	Work	Dust	SIO	PC	SIO	x
				R	E	L	%	L	%	L	%	TLC	L/m	%	%	*	%	R	E			yrs	cm	Kg	M^2						yrs				PC	
NORMAL (no = 11)																																				
Gaffuri & al	1957	20				3.7	89	1.4	109	5.1	94	27	85		76							49	178	71	1.89								2			
Read & al	1959	I 3		10.0	42	3.5		2.4		5.9		40	91		72	9.4	40			7.1	M	64						2		++	11		5			N
(Williams & al,	1960)																																			
Williams & al	1960	23		10.0	34	4.0		1.8		5.8		32	109		75	26.4																				
		25		8.7	28	3.0		2.0		5.0		40	82		74	22.1																				
Rubino & al	1961	2				2.9	91	1.8		4.7		38		94	71	37.0		94				60			1.54								1			
De Rosa	1964	I 6				4.6	112	2.0		6.6		30		91	76							35									9		1			
		9				3.3	92	1.5		4.8		31		73	72							45									14		1			
		11				4.8	110	2.0		6.8		29		88	78							38									5		1			
		16				4.4	110	2.1		6.5		32		88	86							41									9		1			
		23				3.0	85	1.5		4.5		33		60	73							50									15		1			
		II 3				5.0	108	2.0		7.0		28		90	73							.33									8		2			
ASSOCIATED DISEASES (no = 23)																																				
Read & al	1959	II 8		9.8	59	1.9		3.6		5.5		66		46		14.4	56			11.8	M	52						5		++	21		9			MS
(Williams & al,	1960)																																			
Williams & al	1960	36				2.2		2.1		4.3		49	72		82	18.0					M	45						2		+	2		2			CaL
		37		11.4	40	2.9		1.4		4.3		33	69		73	12.1					M	63						3		++	19		12			CaL
		39				2.9		2.6		5.4		47	84		74	12.6					M	47						1		+	21		-			Me
Heard & al	1961	1					43		65		52	46		48	75	11.2					M	50				+		4			18				+	MSCa
Thomson & al	1961	A 6					67		63		66	29			79		40				F	50	152	64		-	+	3	-	+	15				+	CaB
		A 9					63		59		59	25			83		61				M	50	168	57		-	-	2	-	++	16					Brc
		A 23					104		82		97	26			72		80				M	50	170	98		-	-	-	-	+	9		-			O
		X̄ 25					55		132		88	35			54		57				M	40	168	54	1.61	-	+	3	-	+	7					PE
Pellet & al	1964	[illegible]				2.2	63	3.0	244	5.2	110	57			34			96	96		M	53														Tb
		450				0.9	31								60			94			F	49											+			Tb
		497				2.4	62	1.7	125	4.1	120	42			77			96	94		M	54											-			TbLR
		517				3.1	91	1.7	117	4.8	100	35			77						M	47														Tb
		561				5.3	121	2.2	167	7.5	130	29			78			98	98		M.	34											-			Tb
Bader & al	1965	4					72							141				91	80		M	66						0							3	CaS
		5					63							92				94	82		M	42						2							1	CaLR
		6					66							89				-	-		M	67						2							2	CaL
Hany & al	1967	1					70			4.3	85		84	65	74			95	93			48	172	92				+		++			+			CaL
		4					60			2.9	49		36	28	60			95	94			55	174	72				+		++			+			Tb
Poggi & al	1970	12		↑		2.0		1.1		3.1		35					47											+			10		+	(+)		Lo
		13																										+			31					Ca
		17					87		↑					↓		15.0												+			20		+	+		Brc
Cracey et al	1971	1				3.1	63	3.2	109	6.3	80	50	65.	39	73	14.0	44				M	44														PEMe
INCOMPLETE DATA (no - 57)																																				
Wood	1929	1				1.6															M	59				+		+	+		7	+++			+	
Roemheld	1940	1	26	11.7		1.4							27								M	67	157	67		+	-	+	+		11				3	
		2	26	12.4		0.8							16								F	62	148	63		+		+			10				3	
		3	23	8.1		1.6							51								M	62	174	71		+		+	+		15				3	
		4	27	10.8	18	1.0							37								M	60	168	64		+		+			22				3	
		5	22	6.1	12	1.2							27								F	49	153	54		+		+			19				2/3	
		6	17	10.2	60	2.0							47								M	54	162	75		+		+	+		14				2/3	
		7	28	8.4		1.1							28								M	52	162	48		+		+	+		10				2/3	
		8	29	16.8		1.0							29								F	40	158	81		+		+			13				2/3	
		9	18	10.8		1.4							38								F	51	160	78		+		+	+	+	10				2/3	
		10	30	6.3	20	1.2							44								M	53	116	70		+		+			10				2/3	
		11	18	5.4	60	1.7							72								F	46	163	77		+		+	+		15				2	
		12	23	8.1	64	1.9							57								F	57	159	79		+		+	+	+	18				2	
		13	20	10.5	52	1.4							32								F	39	160	[illegible]		+		+	+	+	11				2	
		14	24	5.4	40	1.1							21								F	64	154	59		+		+	+	+	13				2	
		15	11	6.6		1.8							43								F	30	160	61		+		+	+		8				1/2	
		17	15	4.1	76	2.4							67								M	36	162	67		+		+	+		7				1	
		18	18	4.1	40	1.9							47								F	40	163	67		+		+	+		12				1	
Gaffuri & al	1957	30				1.8	66															53	155	43	1.36											
Leathart	1960	1	39			1.8							41			6.8		95		1.0	M	65			1.65			5					3			
		2	33			1.6							40			4.9		94		0.7	M	65			1.53			3.5					2			
		3	40			2.6							56			7.3		90		0.8	M	60			1.62			3.5					2			
		4				1.4							33			4.4		84		0.8	M	54			1.93			4					2			
		5	25			1.6							57			10.8		92		1.0	M	54			1.49			4					2			
		6	27			1.9							33			10.4		90		0.8	M	53			1.45			3					1			
		7	29			2.2							64			8.7		94		0.8	M	53			1.75			3					2			
		8	34			2.2							62			7.7		94		0.8	M	51			1.55			3					2			
		9	26			1.6							33			5.3		92		0.7	F	52			1.56			3					3			
		10	31			1.7							23			8.1		89		0.9	F	48			1.40			3					2			
		11	11			3.2							72			36.4		90		0.9	M	64			1.90						22					
		12	19			2.0							84			10.3		91		0.8	M	63			1.95						36					
		13	24			2.3							76			12.9		96		0.8	M	62			1.85						45					
		14	30			3.4							115			12.9				0.8	M	52			1.85						18					
		15	16			2.7							116			14.7				0.8	M	49			1.98						23					
		16	26			3.2							96			18.4				0.7	M	48			1.80						4					
		17	21			3.5							134			15.9				0.8	M	46			1.64						29					
		18	18			3.8							106			6.9				0.7	M	46			1.77						12					
		19	28			2.9							89			11.9				1.0	M	44			1.67						30					
		20	7			4.5							124			15.3					M	39			1.50						9					
		21	20			3.7							104			13.0				1.0	M	35			1.62						1					
Pellet & al	1964	299				1.8	91											97	98		F	56											+			
		426				1.3	52								63						F															
		555					97								70						F	40														
Sartorelli	1964	1					91					27			70		38	93			M	44											1			
Bader & al	1965	1					43							85				93				48						2					3			
		2					34							62				87	65			43						3					4			R
		3					37							65				92	84			35						3					3			
		7					56							79				95	91			62						4					1			
		8					81							77				94	92			46						1					1			
		9					70							79				97	91			36						0					2			
		10					81							89				94	94			51						1					2			
		12					74							83				96	94			63						0					1			
		13					82							81								67						0					3			
		15					72							73				96	92			38						0					C/1			
Poggi & al	1970	11						↑								16.0										+		+			31		3			
		15					↓						↓			↓	↓											+			11					
		16					91	↓								12.2												+			29		+			
Smyth & al	1971					↓		↓					↓				↓				M	63				+		+			6					

x Code: Brc: Bronchiectasis; Ca: Cancer; CaB: Breast Cancer; CaL: Lung Cancer; CaS: Stomach Cancer; Lo: Lobectomy; LR: Lung Resection; Me: Mesothelioma; MS: Mitral Stenosis; O: Obesity; PE: Pleural Effusion; Tb: Tuberculosis.

* ccCO/min/mmHg

TABLE I - 7 - REVIEW OF GROUP FUNCTION STUDIES IN ASBESTOS WORKERS

Author	year	No. Subj.	PULMONARY FUNCTION																		ANTHROPOLOGY					QUESTIONN.					EXPOSURE		RADIOLOGY		
			f	$\dot{V}$		VC		RV		TLC		RV/	MBC		FEV_1	D_{LCO}		Sat	O_2	V/Q	Sex	Age	Ht	Wt	BSA	C	P	B	Cy	Cr	Work	Dust	SIO	PC	SIO
				R	E	L	%	L	%	L	%	TLC	L/M	%	%	*	%	R	E			yrs	cm	Kg	M^2						yrs				PC
GROUP STUDIES (no = 2069)																																			
Stone	1940	13					50to 75														M												3		
Wright	1955	57	↑	↑	↑↑					↓		N	↓					↓	↓		M														
Gregoire & al	1958	12		6.7	20		70		138		88	37		65			Ext_{CO}	94	92		M														
Leathart	1960	12				1.9							52			8.0	26																-		
		11				3.2							102			15.3	38																0		
Scansetti & al	1960	8					54to 108				73to 121	29to 60		41to 106							M	40to 60					+				5to 16		1		
		12					43to 90				59to 130	21to 59		39to 85							6M 6F	33to 73				+	+				7to 27		2		
		14					40to 70				44to 82	32to 46		37to 76							6M 8F	45to 72				+	+				15to 32		3		
Tairstein & al	1960	10					50to 90							82to 124							M														
Eliseo & al	1964	17		9.0	48																	28to 52									2to 17		1		
		7		9.4	42																	34to 55									6to 15		2		
Hunt	1965	340	N			N		N		N					N	N					M	<20to >60									1to 50				
		74				N↓		N↓		N						↓																			
		36				↓		↓		↓																									
Leathart	1965	31					50to 123									11.0to 32.6					M					-	-	-	-	-			0	0	
		41					30to 110									3.8to 17.8										+	+	+	+	+			+		
		6					75to 125									8.0to 37.3										-	-	-	-	-					+
Schaaning & al	1965	11				2.9 ±.4		1.9		4.6 ±.8		38 ±4	97 ±27		70 ±7						M	52to 70									1to 36				
Thomson & al	1965	19				2.0 to 3.7						25to 44			22to 82	7.5to 19.0						52	168								14		1(8) 2(9) 3(2)		
		9				3.0 td 3.9						30to 48			40to 75	14.0to 21.5						51	174								14		0(6) 1(3)		
Kleinfeld & al	1966a	56					81 ±2		97 ±4		83 ±2	112^{x} ±2			77 ±1	24.0 ±1.0						32to 77				(18)		(9)		(11)	14+		1(2) 2(9) 3(2)		
		20					88 ±2		105 ±7		89 ±2	112^{x} ±6			76 ±2	27.0 ±2.0						37to 69				(5)		(2)		(3)	18to 40		0		
		16					71 ±4		96 ±1		75 ±4	123^{x} ±5			75 ±3	21.0 ±2						39to 63				(8)		(4)		(5)	18to 38		+		
Candevia	1967	12		36	36 ±8	3.8 ±.7									79 ±12							50 ±9				(9)	(9)				15to 7				
		29			29 ±3	4.4 ±.6									75 ±10							41 ±9				(19)	(19)				9 ±9				
Ardalan	1968	18																N(8)N(8) A(10)F(3)				51													
Smither	1969	10									13	10to 50+						60to 100			M	38to 72					++++			(35)	5to 39		(25)(21)		
		14																			F	32to 60									1to 24				
Bader & al	1970	598				↓									N						M	<20to >70									0-4 (26) 5-9 (60) 10-19(271) 20-29(83) 30-39(112) 40- (46)		0-1(498) 2-3 (45)(37)(8)		
	R	172				↓									N																				
	O	29				↓									↓																				
	M	7				↓									↓																				
	N	390				N									N																				
Sluis-Cramer	1970	64					N									N					M	20to 29											0	0	0
		68					N									N					M	30to 39											0	0	0
		41					81to 126									N					M	40to 49											0	0	0
		6					N									N					M	50to 59											0	0	0
Ferris & al	1971	61				3.8									78	21.8					M	50	171	82									1 (12) 2+(10)		
		63				3.8									77	23.2 "					M	50	172	85									1 (7) 2+(4)		
		61				4.0									76	23.5 "					M	50	170	77									1 (1) 2+(5)		
Harries	1971	369		13 to58		1.6to 6.4		0.6to 4.4		3.0to 8.8		12 to 63			28to 97	8.6to 48.0					M	18to 70	135to 198								1to 47		(13)(193)(16)		
	Spr.	50		27 to53		1.7to 5.1		1.0to 4.3		3.0to 7.4		21to 62			40to 88	9.0to 41.0					M	38to 70	154to 185			(15)	(18)	(13)		(20)	1to 47		(4)(16)(8)		
	Lag.	98		21 to58		1.8to 6.3		0.6to 3.8		3.8to 8.0		12to 60			57to 97	9.6to 44.0					M	19to 65	150to 192			(27)	(27)	(14)		(13)	1to 36		(3)(27)(5)		
	St.	45		23 to50		2.2to .2		0.9to 3.4		3.6to 8.8		17to 56			40to 90	16.0to 45.0					M	18to 65	152 185			(3)	(3)	(1)		(2)	1to 32		(4)(6)(2)		
	Int.	176		13 to55		1.6to 6.4		0.7to 4.4		3.4to 8.6		12to 64			29to 95	9.0to 48.0					M	19to 69	135to 198			(33)	(33)	(11)		(17)	1to 47		(2)(54)(3)		
Joloin & al	1971	11				4.4	99	1.8	89	6.3	98	29	128	105	78	32.0 SB	18.0 SS				M	43	172	83		(3)	(2)	(5)		(1)	13	33	0	0	0
		13				4.1	95	1.5	76	6.0	94	25	128	105	81	32.0 "	17.0 "				M	43	171	82		(1	3	5)		(0)	21	161	0	0	0
Murphy & al	1971	101				3.9	93								72						M	42	175	76		(25)	(19)	(28)		(23)	17	+++	1(31) 2(9) 3(4)		
		94				4.3	103								84						M	41	176	79		(9)	(23)	(23)		(5)	17	+	1(19) 2(2)		
Regan & al	1971	210				4.2						35				24.5						44	169												
Woitowitz	1971	11				3.3		2.3		5.6		41			79				80		M	63	169	77							18		11)		
		11				3.4		2.6		5.9		43			72				76		M	63	169	70							33				(11)

* ccCO/min/mmHg   ( ): Number of subjects   x % predicted value   ( ) no of subjects

TABLE I-8 - REVIEW OF SPECIFIC MECHANICS IN ASBESTOS WORKERS (exposed as range or mean and standard deviation).

FIRST AUTHOR	YEAR	NO. SUBJ. SEX	OTHER CRITERIA	C_{st} L/cmH2O	Cdyn L/cmH2O	RESISTANCE insp.	exp. cmH2O/LPS	total
Small irregular opacities - absence								
Leathart	1960	10			.115 -.662			
Leathart	1965	31M			.090 -.290			
Gandevia	1967	5M		.133 -.310				
Woitowitz	1970	27M						1.0 -10.0
		19F						1.5 - 6.5
Jodoin	1971	12	< 110Dy.	.245 ±.020		2.1 ±0.2		
		11	> 110Dy.	.157 ±.010		1.9 ±0.2		
Small irregular opacities - presence								
Leathart	1969	10			.025 -.064			
Rubins	1961	5			.055 -.148	4.1 -8.2	2.3 -3.6	
			hypervent.		.032 -.105			
Leathart	1965	41M		.130 -.313				
Woitowitz	1970	16M						1.8 - 9.0
		7F						1.0 - 8.5
Pleural changes - absence								
Woitowitz	1971	11						3.0 ± 1.0
Pleural changes - presence								
Woitowitz	1971	11						3.5 ± 2.8
Miscellaneous								
Leathart	1960	6			⇓			
Teirstein	1960	10M			.023 -.095			
Vaerenberg	1964	10	6M - 4F	.055 -.100				
Bader	1965	21M			.020 -.270			
Hany	1967	6M			.030 -.170	1.5-8.0	3.0-12.0	
Ardelan	1968	9			.058 ±.026			
Woitowitz	1970	46M	<40yr W<1yr					2.1
		65M	<10					2.3
		41M	>10					2.2*
		31M	>40 <1yr					3.1
		61M	<10					2.4
		70M	≥10					2.8*
		23F	<40 <1yr					1.9
		33F	<10					2.7
		16F	>10					2.7*
		13F	>40 <1					2.5
		38F	<10					3.5
		28F	>10					3.4*
		21	FEV_1/FVC78					5.4(1.8-9.0)
		10	" 75					4.7(1.8-7.5)

* $P < 0.05$

APPENDIX II : METHODS

PULMONARY FUNCTION LABORATORY

The laboratory contained the following pulmonary function equipment: a Collins closed helium circuit modified for recording mixing efficiency and measuring $D_{LCO_{SS}}$; a Stead Wells spirometer; a HbCO circuit; a $D_{LCO_{SS}}$ circuit with a recorder, an O_2 and CO_2 analyser trolley; two current stabilizers; and a balance with height scale; chemicals, disposable items and test gases were purchased in one lot.

Disposable plastic mouthpieces were used at rest and on exercise for obvious reasons in such a large survey. They have been shown to be the equivalent of reusable mouthpieces (Fournier-Massey and Massey, 1971). However, for the expiratory flow-rates the Collins 1¼" cardboard ones were chosen.

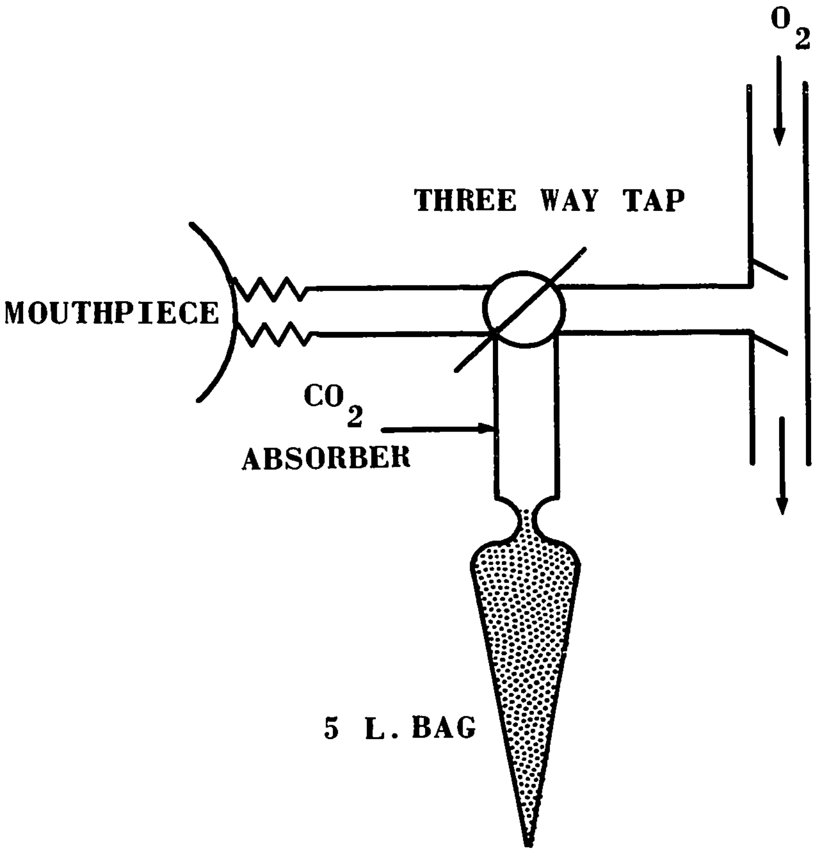
Measurements

The following measurements were made in this sequence:

1) HbCO was measured by the Henderson and Apthorp technique (1960). Each seated subject, connected to the circuit by a disposable mouthpiece, washed the nitrogen from his lungs by breathing 100% O_2 from a simple open circuit (Fig. II - 1) for three minutes. At the end of this time, he was instructed to take a maximum inspiration and hold his breath. A three-way tap was then turned and he exhaled through a CO_2 absorber, previously washed out with O_2, into an empty bag and re-breathed from this bag for a further three minutes.

At the end of the second three minutes, the patient was asked to expire fully into the same bag and then the tap was closed.

FIGURE II-1-CIRCUIT FOR MEASURING CARBOXYHEMOGLOBIN



The contents of the bag were analysed for CO using an infra-red meter, and for O_2. The initial HbCO% was then calculated using Dahlstrom's (1955) equation:

$$HbCO\% = \frac{M \times 100 \times P_{CO}}{P_{O_2} + (M \times P_{CO})}$$

where M = 231 and P_{CO} and P_{O_2} are the partial pressures of CO and O_2 in the equilibrated bag. The O_2 content of the gas (F_{O_2}) in the equilibrated bag which the subject rebreathed was assumed to be 92% as suggested by Henderson & Apthorp (1960). Being done at the onset of the experiment, this correction was applied to the $D_{L_{CO_{SB}}}$.

Backpressure of CO for the resting D_{CO} measurement was calculated from the recorded uptake of CO up to the midpoint of the measurement i.e. three minutes from the start of the test which last six minutes.

CO uptake during resting D_{CO} = $\dot{V}$ $(F_{I_{CO}} - F_{E_{CO}})$ x time

where $\dot{V}$ - minute ventilation

$F_{I_{CO}}$ - inspired CO fractional conc.

$F_{E_{CO}}$ - expired CO fractional conc.

CO Hb after 3 minutes breathing = (CO uptake)/2)/1.34

S_{CO} (% Hb combined with CO) = CO Hb/Total Hb

= CO Hb/(Wt. in Kgs x 1.01%)

= CO Hb/(Wt. in Kgs x .0101)

$$V_D = V_T \frac{(F_{E_{CO}} - F_{A_{CO}})}{(F_{I_{CO}} - F_{A_{CO}})}$$

$$F_{A_{O_2}} = \frac{F_{E_{O_2}} V_T - F_{I_{O_2}} V_D}{V_T - V_D}$$

$$\therefore P_{A_{O_2}} = P_B - 47) F_{A_{O_2}}$$

1. Beckman Oxygen Analyser. Beckman Instruments, Montreal, Quebec.

and it is assumed $P_{A_{O2}}$ $= P_{aO2}$

$P_{C'CO}$ at end of resting $= \frac{P_{A_{O2}} \times S_{CO}}{210 \times (100-S_{CO})}$

This value for $P_{A_{CO}}$ was subtracted from the denominator of the equation for D_{CO}.

The calculation for the back pressure of CO for exercise D_{CO} is as follows:

CO uptake during the exercise D_{CO} $= \dot{V} (F_{I_{CO}} - F_{E_{CO}}) \times \text{time}$

CO Hb $= \text{CO uptake during rest} + \frac{(\text{CO uptake})}{2}/1.34$

S_{CO} = CO Hb/(Wt in Kgs x .0101)

If we assume $P_{A_{O2}}$ on exercise = 100 mm Hg

then $P_{C'CO} = \frac{100 \times S_{CO}}{210 \times (100-S_{CO})}$

2) The FRC was measured using a Collins[1] nine liter Closed Helium Circuit modified to enable an index of mixing efficiency to be calculated at the same time.

The circuit consisted of a nine liter spirometer with an electrically driven kymograph, an external CO_2 absorption canister and a blower, all mounted on a two-shelf trolley. The blower circulated gas in the circuit at approximately 60 liters/min. The three-way tap at the mouthpiece enabled the subject to breathe either to the room or into the circuit. The central core of the spirometer was sealed off to reduce circuit dead space. From

1. W.E. Collins, Boston, Mass., U.S.A.

the main circuit, a by-pass line carried gas across the katharometer at about 100 cc/min. The readings of the katharometer were recorded on a Rustrak[1] recorder with the speed so chosen as to be able to superimpose its recording paper on that of the Collins paper. A three-way stopcock permitted He to be introduced in the circuit and a two-way stopcock served the same function for O_2. A thermometer was mounted in the tubing just beyond the spirometer. A counterweight was placed on the bell to balance it when the blower was working. The dead space of the circuit was 3.5 L.

The katharometer was always left on but the blower was started only 15 minutes before the first subject. The circuit was rinsed with room air by raising and lowering the bell several times and one liter of air was left in the bell. The test voltage to the katharometer was adjusted. The katharometer was then set to read zero, and 200 cc of O_2 and 700 cc of He were added to the circuit, producing an indicator reading of about 13%. The initial temperature was read. The same switch started the kymograph and the recorder.

The seated patient, breathing through a disposable mouthpiece, was then switched into the circuit at the end of a quiet expiration, and asked to breathe normally. When the concentration of He was stable between his lungs and the circuit, he was asked to empty his lungs completely and after to continue to breathe normally for one more minute. This last procedure was to ensure that complete equilibrium was attained. The switch was then closed, the subject disconnected, but the kymograph left running for another minute to verify the absence of leaks on the circuit.

[1] Rustrak, Manchester, N.H., U.S.A.

3) The VC was then measured on a Stead-Wells spirometer. The standing subject,using a plastic 3/4" disposable mouthpiece, breathed normally into the O_2 filled spirometer equipped with a CO_2 absorbent canister. After two or three minutes, when the baseline was steady, he performed a maximal inspiration followed by a maximal expiration, breathed quietly for one minute, and then performed a maximal expiration followed by a maximal inspiration.

The plastic mouthpiece was replaced by the cardboard 1¼" disposable Collins mouthpiece, the by-pass valve was turned and three forced vital capacities were done.

4) The subject then performed a $D_{L_{CO_{SB}}}$ on the modified Collins Helium circuit.

A 30 liter bag-box unit was connected to the spirometer by corrugated tubing and a five-way valve. Air containing about 0.3% CO and 10% He was put in the bag in the morning after three rinses. The initial F_I was measured before the first subject in the morning and in the afternoon. If the $F_{I_{CO}}$ and $F_{I_{He}}$ were different from expected values, the bag was emptied, rinsed and refilled and/or circuit checked. The He was analysed on the katharometer[1] and CO on an infra-red analyser[2]. Sodalime and Drierite were put on the sampling line to protect the analysers from CO_2 and humidity.

The subject was attached to the circuit through a disposable plastic mouthpiece. While breathing room air through a three-way valve, he was

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1. Katharometer, W.E. Collins, Boston, Mass., U.S.A.
2. CO analyser, Beckman Instruments, Montreal, Quebec.

instructed to do a maximal expiration and to hold his breath. At that point the valve was turned to permit a maximal inspiration of the bag mixture and the kymograph automatically started at the speed 32 mm/sec.. The subject then took a maximal inspiration, held it for 10 seconds during which the valve was turned to the expiratory line, and then slowly performed a maximal expiration into the box. When about 750 ml. entered the expiratory line, the valve was turned to collect about 1000 ml. in a 1 liter rubber bag attached to the five-way tap. The valve was then turned back to the expiratory line to record the end of the expiration. The subject was detached from the circuit and the expiratory sample analysed in the same way as the inspiratory sample.

5) The subject then performed a $D_{LCO_{SS}}$ at rest and at two levels of exercise on a Pengelly-Bartlett[1] circuit which consists of two trolleys, the first one or the diffusion circuit equipped with a dry gas meter, a pneumatic damping system, a sampling circuit and a CO analyser; the second one, or analyser-recorder circuit, with O_2 and CO_2 analyser and Weelco recorder. The gas was delivered through a high flow, low resistance Elder demand valve directly from the tank.

<u>Diffusion circuit</u> (Fig. II-2)

Inspired volume was measured using a Parkinson and Cowan dry gas meter, type CD 4, with a pointer resolution of 36 degrees/L.. This had been connected to a Sanborn bellows to provide a form of flow change integration first suggested by McKerrow (1953). The improvement in dynamic behavior of the volume measurement system provided by this technique increases the accuracy of the volume measurement, and reduces the total effective airflow resistance.

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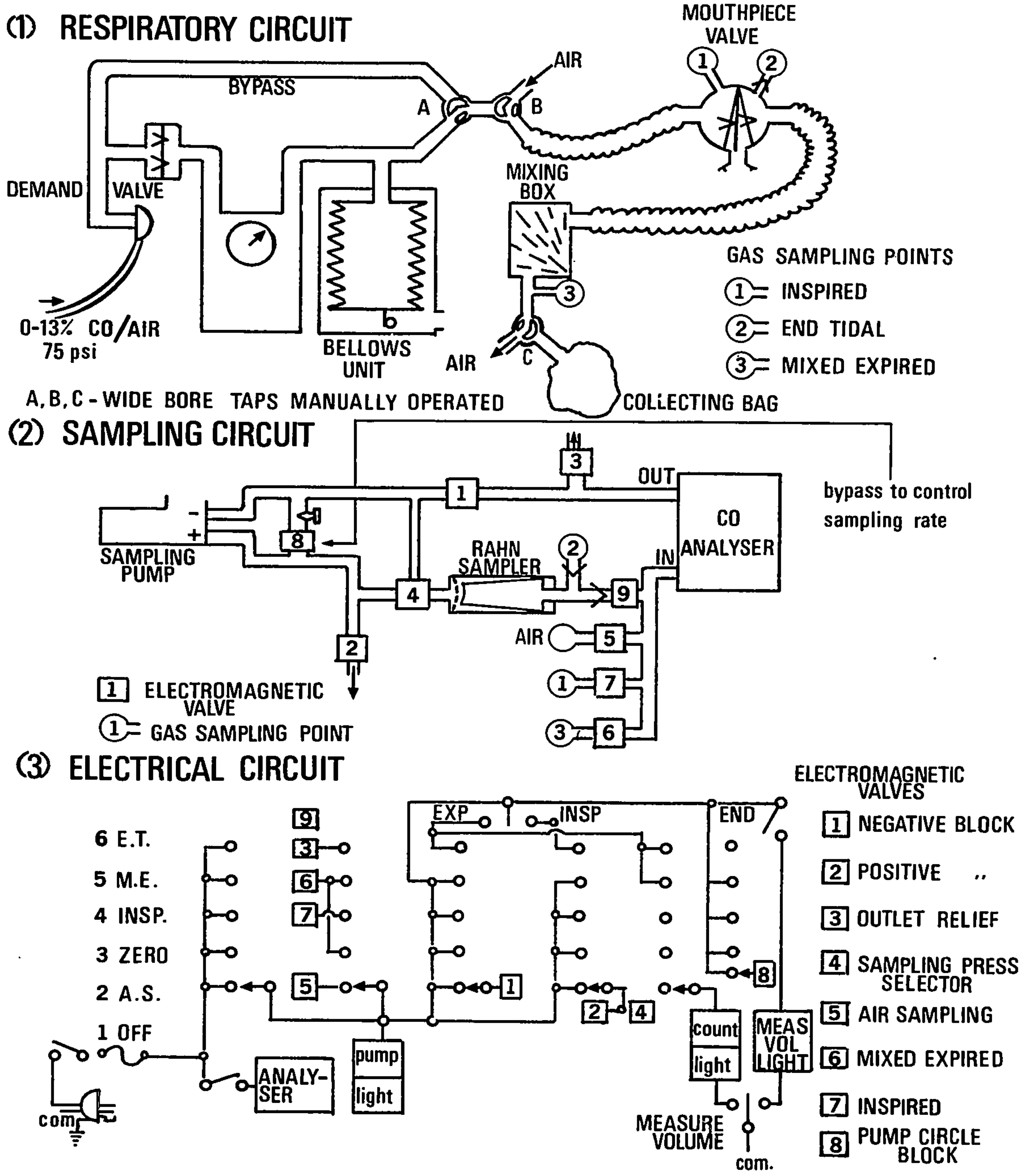
[1] Pengelly, D., School of Medicine, Hamilton, Ont., Canada.

FIG. II - 2 -

COMBINATION RESTING-EXERCISE CO DIFFUSION CIRCUIT



Because of the unidirectional gas flow through the inspired system, an average negative pressure is created within the system during steady ventilation which is less than the negative pressure peaks that would otherwise be produced without the "damping" effect of the bellows. This negative pressure increases from zero at the start of a run to some constant value at the end of a run with the result that the bellows become somewhat compressed and the circuit volume of the measurement system is different from that at the start by the amount the bellows is compressed.

To overcome this difficulty, a spring return system aided the return of the bellows to the static position by applying a practically uniform small force over the full range of the bellows travel. At the static or end position of the bellows, a switch was activated, which causes the green "end" light to be illuminated on the control panel. Thus volume readings taken when this light was illuminated would not suffer from inaccuracy due to bellows compression.

Since the bellows oscillated at the respiratory frequency, a velocity/force transducer has been incorporated in the spring return mechanism which activates a switch when the respiratory cycle reverses phase. This switch activates an electromagnetic digital VeederRoot counter which was energised only when ventilation was being measured. The counter could be reset to zero.

Respiratory valves used were the 120 degree valve made by H.W. Creager modified with an aluminium core which had the lowest resistance in all positions. All piping was either 3.1 cm. dia. copper or 3.2 cm. dia. flexible plastic, wire reinforced. This plastic tubing has a resistance of 0.2 $cmH_2O/L/sec/metre$. The plastic mouthpiece valve had an effective dead space of

20-30 ml. owing to the divider in the central portion, and had an inspiratory and expiratory resistance of 0.35 $cmH_2O/L/sec$.

It has been found experimentally that a baffle-plate type of mixing box was a most effective method of integrating the fluctuations in F_E within tidal excursions. Tests on this box at tidal volumes of 0.3 L to 3.0 L show that it would perform this function adequately at rest and on exercise. It was preferred to the propeller type because of its simplicity.

In order to produce a constant volume of end-tidal sample per cycle, a modified Rahn-Otis sampler has been used. Driving pressure for the sample container was produced by the sampling pump and switched by electromagnetic valves controlled from the respiration counter switch. This has the advantage of a sufficiently large constant-volume sample without the added cost and complication of an electronic time-delay unit.

The respiratory circuit contained only three respiratory valves, labelled A, B, C. (Fig. II-2). Valve A allowed the selection of unmeasured (for volume) inspired test gas or alternatively test gas which has passed through the volume measurement system. Valve B allowed the inspired gas to the subject to be either from room (ambient) air or from the test gas (60 lbs/pi^2) supply. Valve C allowed the mixed expired gas to exhaust to ambient, or to a collection bag attached to one outlet of the valves.

The sampling system (Fig. II-2) was controlled by electromagnetic valves. These were actuated by a manually operated program selector, which either activated them directly, or through an automatic system for end tidal sampling. There were six positions of the selector:

1. Off: the whole sampling system was inactivated.
2. Air Sampling - ambient air was admitted to the inlet manifold of the analyser through Valve 5, which was energised (open). Valves 2, 4 and 1 were energised, opening the pump outlet to ambient, connecting the sampler to negative pressure and allowing negative pressure to be applied to the analyser outlet.
3. Zero (CO_2 correction) - mixed expired air was admitted to the inlet manifold through Valve 6. Valves 2, 4 and 1 were energised, as they were in all positions except 1 and 6.
4. Inspired - inspired gas was sampled from the inspired side of the mouthpiece valve. Valve 7 was energised.
5. Mixed expired - same as position 3.
6. End Tidal - Valve 3 was opened, allowing the analyser to exhaust to ambient. During expiration Valve 1 was opened, allowing the pump to suck from Valve 3 and ambient. Valve 2 was closed, and all available positive pressure was diverted through Valve 4 to empty the sampler through its one-way valve to the inlet manifold. During inspiration, Valve 1 was closed, and negative pressure was diverted through Valve 4. The pump exhausted through Valve 2. Valve 3 remained open. The sampler sucked through its one-way valve from the expiratory side of the mouthpiece valve.

The respiratory counter could be used in positions 5 and 6 of the selector. It was automatically activated upon rotation of manual tap A to the volume measurement position, and re-activated when in the other position. The counter light was energised with the counter during expiration.

The "measure volume" light was energised in positions 2 through 6 when the "end" switch was operated at the limit of bellows descent.

This system was completed by a recorder-analyser circuit on a second trolley and consisted of one O_2[1] and CO_2[1] analysers, and a Wheelco[2] recorder. A pump with a circulation of some 150 ml/min. drew inspired, expired and alveolar samples through the two analysers where the O_2 and CO_2 were directly measured. The volume, CO_2, CO, and O_2 concentrations were recorded on the Weelco four-point recorder.

Diffusion Test:

The test at rest or on exercise lasted six minutes.

The seated subject was connected to the circuit and during the first minute, while he was breathing ambient air, the minute volume and the content of CO, O_2 and CO_2 in the expired air was recorded. The subject then breathed a .13% CO mixture in air for three minutes and the inspired CO was recorded.

During the fifth and the sixth minutes, the subject was switched into the volume measuring circuit and the F_{ECO} and F_{ACO} were recorded. The pulse was counted during the last minute.

The subject was disconnected from the circuit at the end of the sixth minute. The volume reading was taken only when the rubber bellow was completely down as indicated by a green light on the central line. Respirations

1. Beckman, Instruments, Montreal, Canada.
2. Barber Coleman, Montreal, Canada.

were read on the counter. The technicians subtracted one from this number, one respiration being counted when the valve was turned on.

The subject then exercised on a bicycle ergometer at 200 KMm. The procedure was the same as at rest except that F_A was not measured.

A second exercise was done at 600 KMm for the subjects between 20 and 40 years of age, and 400 KMm for the subjects over 40 years. If the pulse on the first exercise was over 120 beats per minute, the second exercise was cancelled. This was based on Holmgren's evidence that the maximal stroke volume (and probably maximal D_{CO} is obtained when the heart beats at 120/min. (1965).

CALCULATIONS

The calculations were done in the following sequence: from the Stead-Wells spirometer tracings ERV and IC were calculated and transferred to the raw data sheet where the addition of the two values gave VC.

The highest of the 3 FVCs was then chosen. A correction was done to determine the starting point for the calculations and a perpendicular line was placed between the upper and lower horizontal lines delineating the height of the FVC. (Kory et al, 1961). From this line, the FEV_{75}, FEV_1 and MMF 25-75 were found, either by using the mask especially prepared for this or by a simple ruler, and the values were entered on the raw data sheet. This section was completed by adding the circuit temperature and the water vapour pressure for that temperature.

The next step in calculations was the FRC. The initial and the final temperature and helium concentrations having been recorded during the performance of the test itself, the switch difference, the oxygen difference and the ERV were calculated. The Rustrak paper its recording of the decrease in helium concentration during the test was attached to the Collins paper and directly aligned with the ventilation tracing. From this tracing, 90% of the decline in helium concentration and the number of breaths to achieve it were calculated. The tidal air was estimated by putting two parallel lines at the inspiratory and expiratory limits of the first 10 or 15 breaths.

The $D_{L_{CO_{SB}}}$ was recorded on the same chart paper as that of the helium test. The IV was calculated from the point where the subject was turned into the circuit to the highest point where he started to hold his breath. The time in seconds was calculated from the point delineating half the inspiration time to the point delineating 2/3 of the expiratory time in the bag. These values were transferred to the raw data sheet.

The three $D_{L_{CO_{SS}}}$, rest and exercise, were then calculated. First the volume was checked on the paper recording and then values for CO_2 and O_2 were calculated for the last minute of the test. If the six or seven points were not strictly in line, a mean of the slope was taken. The values of $F_{I_{CO}}$, $F_{E_{CO}}$ and $F_{A_{CO}}$ recorded on the Wheelco paper were compared with those read by the technicians. In those very few cases where six points of the alveolar CO were not in a stable line, a mean was substituted for the value read on the analyser.

Calculations were done by computer and program for the IBM 360-50 using Fortran language is listed in Table II-1. The formulae used for predicting normal (i.e. expected) values are listed in Table II-2.

TABLE II - 1 - COMPUTOR PROGRAM FOR PULMONARY FUNCTION CALCULATIONS

```
2ND  PUNCH RUN 1  OCT NOV                      FORTRAN SOURCE LIST                03/03/68
    ISN         SOURCE STATEMENT

       0 $IBFTC PULMFN
          C------------------------------------------------------------------------------
          C                                                                      ---PULM0010
          C                                                                         PULM0011
          C          MODIFIED DECK  -  VALID FOR AFTER MAY 1, 1967                  PULM0012
          C             CALIBRATION CURVE FOR OCT AND NOV INSERTED                  PULM0015
          C       PULM0238C  CHANGED TO READ GO TO 420                              PULM0016
          C-------------------------------------------------------------------------PULM0017
       1          LOGICAL ZERO(3)                                                ---PULM0020
       2          DATA ZERO / 3* .FALSE. /                                          PULM0050
       3          DIMENSION CARDD(13)                                               PULM0060
       4          DIMENSION NOWDAT(2)                                               PULM0100
       5          ASSIGN 660 TO L                                                   PULM0110
       6           CALL EOF(5,L)                                                    PULM0112
       7          READ(5,5000) CARDD                                                PULM0114
      10     5000 FORMAT(13A6)                                                      PULM0120
      11          CALL GETDAY(NOWDAT)                                               PULM0130
      12          CALL GETIME(NOWTIM)                                               PULM0140
      13          IPAGE = 0                                                         PULM0150
      14       10 LINE=0                                                            PULM0155
      15          WRITE(6,5002) CARDD                                               PULM0160
      16     5002 FORMAT(1H ,13A6)                                                  PULM0170
      17          IPAGE = IPAGE + 1                                                 PULM0180
      20          WRITE(6,5004) NOWDAT,NOWTIM,IPAGE                                 PULM0185
      21     5004 FORMAT ( 76H1PULMONARY FUNCTION STUDIES - QAMA SURVEY OF THE EASTEPULM0190
                 1RN TOWNSHIPS OF QUEBEC , 20X,2A6,5X,A6,6X,4HPAGE,I3)              PULM0200
      22          N = 0                                                             PULM0210
      23          PRINT 5006                                                        PULM0220
      24     5006 FORMAT(124H    NO.   NAME          AGE      VC   FRC    RV  TLC  MX     PULM0230
                 1   FEV1  FVC FEV1   MMF          DIFFUSING CAPACITY AT REST AND EXERCIPULM0250
                 2SE      /                                                         PULM0260
                 3      132H             HT    WT                                   PULM0270
                 4            -FVC           SB-R  K    VASB  SS- EXT PACO   VCO  RATE VE   PULM0280
                 5VO2   VT            / 9X,4HDATE,66X,4HLCAD,4X,6H(PDCO),5H (VC) //)      PULM0290
      25       20 READ 5008, MNC1,MCARD1,NAMES,NAMEC,AGE,HT,WT,MDY,MMTH,MYR,PB,TEMP,PULM0390
                 1PW, C1, C2, C3, C4, C5, C6, SERV    ,XRAY,U1,U2,U3,U4,U5          PULM0400
      35     5008CFORMAT (A6,I1,2A6,F2.0,2F4.1,3I2,F4.1,F3.1,F2.0, 5X, 5I1, I3,     PULM0430
                 1 F3.1,I1,14X,5I1)                                                 PULM0440
      36        . READ 5010, MNC2,MCARD2, T1, PW1, ERV1, VIC, VC, FEV75, FEV1, FVC, PULM0450
                 1  XMMF,T2, PW2, FHE1, FHE2, T3, SWD, O2D, ERV2, VT1, BR90         PULM0460
      41     5010CFORMAT ( A6, I1, 8X, F3.1, F2.0, 3F3.2, 4F3.2, 7X, F3.1, F2.0,    PULM0470
                 12F4.2, F3.1, 2F3.2, F4.3, F4.3, F2.0 )                            PULM0480
      42          HT        =  HT * 2.54                                            PULM0490
      43          WT        =   WT * 0.4536                                         PULM0500
      44          PFEVVC    =   ( PFEV1 / PFVC ) * 100.                             PULM0510
      45          PVC      .= 0.064*HT - 0.031*AGE - 5.335                          PULM0520
      46          PFRC       =0.051 * HT - 5.18                                     PULM0530
      47          PTLC      = 0.094*HT  -0.015*AGE- 9.167                           PULM0540
      50          PRV       = PTLC - PVC                                            PULM0550
      51          PFEV75    = ((31.2 -1.78*AGE + 1.065* HT) * 0.88) / 40.           PULM0560
      52          PFEV1     =   0.035 * HT  - 0.033*AGE  - 1.12                     PULM0570
      53          PFVC      =.0508 * HT  - 0.032 * AGE - 3.02                       PULM0580
      54          PFVCP     =  65.35 - 0.169 * AGE                                  PULM0590
      55          PMMF      = 2.016 - 0.041*AGE + 0.02 * HT                         PULM0600
      56          MXP       =  65. - ( AGE - 30.) /2.                               PULM0610
      57          MEXIP     = 82.085 - 0.341 * AGE - 0.322 * HT/ 2.54                PULM0620
      60          PDCOSB    = 0.457 * HT  - 0.299* AGE  - 38.1                       PULM0640
      61          PK        =  - 0.038 * AGE     +  5.78                             PULM0650
      62          CRT1      =  310. / ( 273. + T1)                                   PULM0660
      63          CRT2      =  (273. + T2) / ( 273. + T3)                            PULM0670
      64          CRP1      = ( PB  - PW1 ) / ( PB - 47.)                            PULM0680
      65          CRPT1     =  CRP1 * CRT1                                           PULM0690
      66          FEV75     = FEV75 * CRPT1                                          PULM0870
      67          FEV1      =  FEV1 * CRPT1                                          PULM0880
      70          FVC       =  FVC * CRPT1                                           PULM0890
      71          XMMF      = XMMF * CRPT1                                           PULM0900
      72          MFEV1P    =  ( FEV1 /FVC) * 100.                                   PULM0910
      73          MFVCP     = PFVCP                                                  PULM0920
```

```
      ERV      = ERV1 * CRPT1 * 0.9948                                   PULM0700
      VIC      =  VIC * CRPT1 * 0.9948                                   PULM0710
      VC       =  ERV + VIC                                              PULM0720
      IF(FHE1.EQ.0.) GO TO 63
   60 FRC      =  (( 5.4 * ( FHE1  - FHE2 * CRT2 )  +02D* FHE2* CRT2 )/  PULM0760
     1FHE2 )  + SWD  - 0.03                                              PULM0770
      ERV2     =  ERV2 * 0.9926                                          PULM0780
      FRC      = FRC * CRPT1
      RV       =  FRC - ERV2 * CRPT1                                     PULM0800
      IF(VC.NE.0.) GO TO 51
      TLC=0.
      GO TO 61
   51 IF(FVC.GT.VC) GO TO 52
      TLC=RV+VC
      GO TO 61
   52 TLC=RV+FVC
   61 VT1      = VT1 * 0.9926
      Q        =  ( FRC / ( FRC + VT1*CRPT1)) *  ((5.3 - VT1*CRPT1 )/5.3)PULM0830
      W        =  ALOG 10 (Q)                                            PULM0840
      PBR90    =  -1. / W                                                PULM0850
      IF(BR90.NE.0.) GO TO 62
      MX=0
      GO TO 64
   62 MX       = P2R90 / ( BR90 - 1. ) * 125.
      GO TO 64
   63 FRC=0.0
      RV=0.00
      TLC=0.00
      MX=0.00
   64 MAGE=AGE
      MHT      = HT                                                      PULM0940
      PRINT 5012, MNO1, NAMES, MAGE,              PVC,PFRC,PRV,PTLC,     PULM0960
     1 MXP,     PFEV75,           PFEV1,     PFVC,      MFVCP,     PMMF, PULM0970
     2  PDCOSB,    PK,     MEXTP
 5012 FORMAT ( 2A7, I6, F6.2, 3F5.2    , I4, F9.2,  F6.2,    F5.2,      I5,PULM1010
     1  F5.2,  F6.1,  F5.2,  I14)
      N = N+1                                                            PULM1040
C*************************                                               PULM1100
      DIMENSION      LOAD(3), RATE(3),   FAICO(3), FICO(3),   FECO(3),   PULM1110
     1    V1(3),      V2(3),      F(3),      TMN(3),     TSC(3),    FECO2(3),  PULM1120
     2    FEO2(3),   VENT(3),   TTMN(3),               TIME(3),   TTIME(3),  PULM1130
     3    VSTPD(3), VBTPS(3), VO2(3),     VCC(3),     MEXT(3),  VT(3),     PULM1140
     4    FMIN(3),   VD(3),      DCOSS(3), XPACO(3), YPACO(3), XPCCO(3),  PULM1150
     5    MBTPS(3), MRATE(3) , PDCOE(3)                                  PULM1160
     6,PVO2(3), PDCOSS(3)   , XLOAD(3)
      READ 5014,  MNO3,          MCARD3,    FCOHB,     FIHE,      FICOSB,    PULM1190
     1      VI,          TIME1,       FAHE,       FACOSB ,   FIO2,            PULM1200
     2       LOAD(1), RATE(1),  FAICO(1), FICO(1),   FECO(1),   FA2CO,     PULM1210
     3      V1(1),      V2(1),                   TMN(1),     TSC(1),     F(1)   ,   PULM1220
     4      FECO2(1), FEO2(1),   TTMN(1)                                 PULM1230
 5014OFORMAT  (     A6,  I1,          F3.1,                F4.2,      F4.1,      PULM1260
     1   F4.3,       F3.1,        F4.2,       F3.1,  3X,  F4.2,             PULM1270
     2   I2,  F3.0,F2.1,          3F3.1,      2F5.2,      F1.0,       F2.0,    F2.CPULM1280
     3,  F3.2,        F4.2,        F1.0     )                            PULM1290
      READ  5016,     MNO4,       MCARD4,                                PULM1310
     1       LOAD(2), RATE(2),  FAICO(2), FICO(2),   FECO(2),   V1(2),     PULM1320
     2      V2(2),      TMN(2),     TSC(2),     F(2),         FECO2(2), FEO2(2),  PULM1330
     3      TTMN(2),                                                     PULM1340
     4       LOAD(3), RATE(3),  FAICO(3), FICO(3),   FECO(3),              PULM1350
     5      V1(3),      V2(3),                   TMN(3),     TSC(3),     F(3),      PULM1360
     6      FECO2(3), FEO2(3),   TTMN(3)                                 PULM1370
 5016 FORMAT ( A6, I1, I2,     F3.0,        F2.1,        2F3.1,      2F5.2, F1.0, PULM1390
     1   2F2.0,      F3.2,        F4.2,        F1.0,        I2,           F3.0,   F2.1,PULM1400
     2   2F3.1,      2F5.2,       F1.0,        F2.0,F3.0,F3.2,        F4.2,   F1.0)PULM1410
      DO 140 NLOG=1,3                                                    PULM1420
  140 ZERO(NLOG) = .FALSE.                                               PULM1430
      CSTPD    = ( 273. / ( 273. + T1    ) ) * ( ( PB  -PW1) / 760.)     PULM1460
      I=0                                                                PULM1470
      FIO2  =  FIO2  / 100.
      DO 320     J=1,3                                                   PULM1480
      I = I + 1                                                          PULM1490
      LOAD(I)=      LOAD(I) * 10                                         PULM1500
      TIME(I)       = TMN(I) + TSC(I)/60.                                PULM1510
```

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170        VENT(I)        =    (V2(I) - V1(I))   / TIME(I)
171        FMIN(I)        =     F(I) / TIME(I)                          PULM1520
172        VSTPD(I)       =     VENT(I)  * CSTPD                        PULM1530
173        VBTPS(I)       =     VENT(I) * CRPT1                         PULM1590
174        VT(I)          =   VBTPS(I) / FMIN(I)                        PULM1610
175        IF  ( FEC2(I) . EQ.  0.0 ) GO TO 149                         PULM1620
200        FECO2(I)       =    FECO2(I) / 100.
201        FEO2(I)        =  FEO2(I) / 100.                             PULM1640
202        VO2(I)   = VSTPD(I) * FIO2 - VSTPD(I) * (( 1.0 -FIO2) / ( 1. -  PULM1650
          2 FECO2(I) - FEO2(I) )) * FEO2(I)
203        GO TO 150
204    149 VO2(I)         =  0.0
205    150 XLOAD(I)       =   LOAD(I)
     C 149 XLOAD(I)       =  LOAD(I)
     C     IF ( LOAD(I) . EQ. 0 ) GO TO 190
206        PVO2(I)        =  0.410  +  0.0023 * XLOAD(I)
207        GO TO 200
210    190 PVO2(I)   =  0.00
211    200 CONTINUE
212        IF ( FICO(I) .LT. 5.00 ) ZERO(I) = .TRUE.                    PULM1840
215        IF ( FICO(I) .GE. 61.8 .AND. FICO(I). LT. 100.0 ) GO TO 220
220        IF ( FICO(I) .GE.42.3  .AND. FICO(I). LT. 61.80 ) GO TO 230
223        IF ( FICO(I) .GE.0.00  .AND. FICO(I). LT. 42.30 ) GO TO 240
226    220 FICO(I)        =  (FICO(I) - 9.0 )  *  0.0001581
          1  /10.
227        GO TO 260
230    230 FICO(I)        =  ( FICO(I)  - 4.0  )   *  0.0001538
          1  /10.
231        GO TO 260
232    240 FICO(I)        =    FICO(I)      *  0.0001395
          1  /10.
233    260 FECO(I) = FECO(I) - FAICO(I)
234        IF ( FECO(I) .LT. 5.000) ZERO(I) = .TRUE.                    PULM2020
237        IF ( FECO(I) .GE. 61.8 .AND. FECO(I). LT. 100.0 ) GO TO 270
242        IF ( FECO(I) .GE.42.3  .AND. FECO(I). LT. 61.80 ) GO TO 280
245        IF ( FECO(I) .GE.0.00  .AND. FECO(I). LT. 42.30 ) GO TO 290
250    270 FECO(I)        =  (FECO(I) - 9.0 )  *  0.0001581
          1  /10.
251        GO TO 310
252    280 FECO(I)        =  ( FECO(I)  - 4.0  )   *  0.0001538
          1  /10.
253        GO TO 310
254    290 FECO(I)        =    FECO(I)      *  0.0001395
          1  /10.
255    310 MEXT(I)        =  ( (FICO(I) -FECO(I) ) / FICO(I) )  * 100.  PULM2140
256      . MRATE(I)       =   RATE(I)                                   PULM2150
257    320 CONTINUE                                                     PULM2200
261        FA2CO          =  FA2CO - FAICO (1)                          PULM2210
262        IF ( FA2CO .LT. 15.00) ZERO(1) = .TRUE.
265        IF (FA2CO      .GE. 61.8 .AND. FA2CO  . LT. 100.0 ) GO TO 330
270        IF ( FA2CO     .GE.42.3  .AND. FA2CO  . LT. 61.80 ) GO TO 340
273        IF ( FA2CO     .GE.0.00  .AND. FA2CO  . LT. 42.30 ) GO TO 350
276    330 FA2CO          =  (FA2CO   - 9.0 )  *  0.0001581
          1  /10.
277        GO TO 370
300    340 FA2CO          =  (   FA2CO   -   4.0   )  * 0.0001538
          1  /10.
301        GO TO 370
302    350 FA2CO          =    FA2CO    *  0.0001395
          1  /10.
303    370 CONTINUE
304        IF ( FACOSB .EQ. 0. ) GO TO 420                              PULM2340
307        IF ( FACOSB   .GE. 61.8 .AND. FACOSB . LT. 100.0 ) GO TO 380 PULM2380
312        IF ( FACOSB   .GE.42.3  .AND. FACOSB . LT. 61.80 ) GO TO 390
315        IF ( FACOSB   .GE.0.00  .AND. FACOSB . LT. 42.30 ) GO TO 400
320    380 FACOSB         =  (FACOSB  - 9.0 )  *  0.0001581
          1  /10.
321        GO TO 420
322    390 FACOSB         =  ( FACOSB   - 4.0   )   *  0.0001538
          1  /10.
323        GO TO 420
324    400 FACOSB         =    FACOSB       *  0.0001395
          1  /10.
```

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      C                                                                         PULM2550
      C       DIFFUSING CAPACITY - SINGLE BREATH                                PULM2560
      C                                                                         PULM2570
 325    420 COHBSB         =  FCOHB   * 0.0001395
           1  /10.
 326    450 FVCO           =    COHBSB   * 100.  / 92.                          PULM2640

 327        IF(FACOSB.NE.0.) GO TO 470                                          PULM2650
 332    460 CONTINUE                                                            PULM2660
 333        DCOSB=0.                                                            PULM2670
 334        SBK=0.                                                              PULM2680
 335        VASB1=0.                                                            PULM2690
 336        VISB=0.                                                             PULM2700
 337        GO TO 510                                                           PULM2710
 340    470 CONTINUE                                                            PULM2720
 341        IF ( VI . GE. 1.5) GO TO 480                                        PULM2730
 344        VDSB           = 0.125 + 0.08* VI                                   PULM2740
 345        GO TO 490                                                           PULM2750
 346    480 VDSB      =          0.15 + 0.06 * VI                               PULM2760
 347    490 FAHE           =   FAHE * 0.95                                      PULM2770
 350        FACOSB = FACOSB * 0.95
 351        VI=VI*0.9926                                                        PULM2780
 352        VISB=VI*CRPT1                                                       PULM2790
 353    500 VASB      = ( VI * CRPT1  - 0.07  -VDSB)     * FIHE /FAHE           PULM2810
 354        VASB1=VASB+VDSB                                                     PULM2820
 355        VASB      =  VASB * 0.8606  * ( (PB   - 47. ) / 760. )              PULM2840
 356        FICOSB=(FICOSB-9.0) * 0.0001581/10.
 357        FOCO           = (FICOSB * FAHE / FIHE )  -  FVCO                   PULM2890
 360        SBK      =   ( 60. / TIME1) * ALOG ( FOCO /(FACOSB   -   FVCO ) )   PULM2900
 361        DCOSB    =    ( VASB * 1000.   * SBK   ) / ( PB  - 47. )            PULM2920
 362    510 PRINT 5018, MHT,  WT, VC, FRC, RV, TLC, MX, FEV75, FEV1, FVC,       PULM2980
          2 MFEV1P,XMMF            ,DCOSB,SBK,VASB1 ,VISB                       PULM2990
 363   5018 FORMAT ( I11, F6.1, F11.2, 3F5.2, I4, F9.2, F6.2, F5.2, I5, F5.2   PULM3040
          1    ,F6.1,F5.2,F5.2,2H (,F4.2,1H) )                                  PULM3050
      C                                                                         PULM3120
      C        DIFFUSING CAPACITY AT REST                                       PULM3130
      C                                                                         PULM3140
 364        I = 1                                                               PULM3150
 365        XVCO     =VSTPD(I)*FICO(I) - (VSTPD(I) -(0.2*VO2(I)))*FECO(I)       PULM3160
 366        VCO(I)   = XVCO * 1000.                                             PULM3170
 367        COHB     =   ( ( 210. * 100. * COHBSB) / ( 0.92 + 210. * COHBSB ))  PULM3210
          1 * 0.0101 * WT  *10.                                                 PULM3220
 370        COHB1 = (VCO(I)*TTHN(I))/1.34                                       PULM3240
      C      COHB1 = COHB GMS AT START                                          PULM3250
      C      COHB1 = COHB INCREASE DURING DCO AT REST                           PULM3260
      C      COHB2 = COHB HALFWAY THRU                                          PULM3270
      C      COHB3 = COHB SATURATION PER CENT  HALFWAY THRU                     PULM3280
 371        COHB2= COHB+COHB1/2.                                                PULM3300
 372        COHB3 = COHB2 /(0.0101 * WT*10.   )                                 PULM3320
 373        FCCO3 = ( ( 100. / ( PB- 47. ) ) * COHB3 ) /                        PULM3330
          1       ( 210. * ( 100. - COHB3) )                                    PULM3340
 374        XPCCO(I)= FCCO3 * (PB - 47.)                                        PULM3350
 375        XPACO(I) = (FAZCO * ( PB - 47. ) ) - XPCCO(I)                       PULM3360
 376        DCOSS(I)= VCO(I) / XPACO(I)                                         PULM3400
 377        PDCOSS(I) = ((13.05 - 0.279 * AGE + 0.185 * ( HT / 2.54 ))
          1    * 273. / 310. )
 400        IF ( .NOT. ZERO(I) ) GO TO 520                                      PULM3410
 403        VCO(I)=0.0                                                          PULM3415
 404        XPACO(I)=0.0                                                        PULM3420
 405        DCOSS(I)=0.0                                                        PULM3425
 406        MEXT(I)    =  0
 407        PDCOSS(I) = 0.0

 410    520 CONTINUE                                                            PULM3430
      C                                                                         PULM3440
      C       DIFFUSING CAPACITY ON EFFORT - STEADY STATE                       PULM3450
      C                                                                         PULM3460
 411        DO 640  J=1,2                                                       PULM3470
 412        I = I + 1                                                           PULM3480
 413        IF ( LOAD(I) .NE. 0 ) GO TO 570                                     PULM3490
 416        DCOSS(I)       = 0.                                                 PULM3500
 417        MEXT(I)        =0                                                   PULM3510
 420        VCO(I)         = 0.                                                 PULM3520
 421        XPACO(I)       = 0.                                                 PULM3530
 422        MRATE(I)       = 0                                                  PULM3540
 423        MBTPS(I)       = 0                                                  PULM3550
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      VO2(I)        = 0.
      VT(I)         =0.                                              PULM3560
      VD(I)         = 0.                                             PULM3570
      PDCOSS(I) = 0.0                                                PULM3580
      GO TO 630
  570 IF ( FICO(I) . EQ . 0. ) GO TO 623                             PULM3590
  575 IF(VT(I) .GE.  1.5 ) GO TO 580                                 PULM3591
      VD(I)    = 0.125 + 0.08 * VT(I) + 0.07                         PULM3592
      GO TO 590                                                      PULM3610
  580 VD(I)    = 0.15 + 0.06 * VT(I) + 0.07                          PULM3620
  590 VCO(I)   = VSTPD(I) * ( FICO(I) - FECO(I)) * 1000.             PULM3630
      YPACO(I)=(( VT(I) * FECO(I) - VD(I) * FICO(I))/ (VT(I) -VD(I)))PULM3640
     1 * ( PB - 47. )                                                PULM3650
      IF( J.EQ.2) GO TO 610                                          PULM3660
      COHBE1 = ( VCO(I) * TTMN(I) ) / 1.34                           PULM3670
      COHBE2 = COHB + COHB1 + COHBE1 / 2.                            PULM3680
      COHBE3 = COHBE2 / ( 0.0101 * WT * 10. )                        PULM3690
      FCCOE3 = ( ( 100. / ( PB - 47. ) ) * COHBE3 ) /                PULM3700
     1      ( 210. * ( 100. - COHBE3 ) )                             PULM3710
      XPCCO(I) = FCCOE3 * ( PB - 47. )                               PULM3720
      XPACO(I) = YPACO(I) - XPCCO(I)                                 PULM3730
      GO TO 620                                                      PULM3740
  610 COEE1 = (VCO(I) * TTMN(I) ) / 1.34                             PULM3750
      COEE2= COHB + COHB1 + COHBE1 + COEE1 / 2.                      PULM3760
      COEE3 = COEE2 / ( 0.0101 * WT * 10. )                          PULM3770
      FCOEE3 = ( ( 100. / ( PB - 47. ) ) * COEE3 ) /                 PULM3760
     1      ( 210. * ( 100. - COEE3 ) )                              PULM3790
      XPCCO(I)= FCOEE3 * ( PB - 47. )                                PULM3800
      XPACO(I) = YPACO(I) - XPCCO(I)                                 PULM3810
  620 DCOSS(I)      = VCO(I) / ( XPACO(I) )                          PULM3820
  621 PDCOSS(I) = 35.0 - 0.497 * AGE + 9.946 * PVO2(I)               PULM3890
      IF ( .NOT. ZERO(I) ) GO TO 625
  623 VCO(I)=0.0                                                     PULM3892
      XPACO(I)=0.0                                                   PULM3894
      DCOSS(I)=0.0                                                   PULM3896
      MEXT (I) = 0                                                   PULM3897
      PDCOSS(I) = 0.0
  625 CONTINUE
  630 CONTINUE                                                       PULM3898
      IF(J.EQ.1) GO TO 640                                           PULM3900
      WRITE(6,5020) MDY,MNTH,MYR,                                    PULM3940
     1   ( LOAD(L), PDCOSS(L), DCOSS(L), MEXT(L), XPACO(L), VCO(L),  PULM3950
     2    MRATE(L),
     1    VBTPS(L), VO2(L), VT(L), L=1,1)
 5020 FORMAT(7X,3I3,I67,                                             PULM3970
     2      4X,1H(,F4.1,1H),F5.1,
     2                               I4,F5.2,F6.2,I4,F5.1,F5.2,F5.2)
      WRITE(6,5022) SERV,XRAY,Q6,                                    PULM3980
     1   ( LOAD(L), PDCOSS(L), DCOSS(L), MEXT(L), XPACO(L), VCO(L),  PULM4000
     2    MRATE(L),
     1    VBTPS(L), VO2(L), VT(L), L=2,2)
 5022 FORMAT(F12.1,I2,I3,                                            PULM4020
     1   I66,4X,1H(,F4.1,1H),F5.1,                                   PULM4030
     2                               I4,F5.2,F6.2,I4,F5.1,F5.2,F5.2)
      WRITE(6,5024)                                                  PULM4040
     1   ( LOAD(L), PDCOSS(L), DCOSS(L), MEXT(L), XPACO(L), VCO(L),  PULM4060
     2    MRATE(L),
     1    VBTPS(L), VO2(L), VT(L), L=3,3)
 5024 FORMAT(I83,                                                    PULM4080
     1      4X,1H(,F4.1,1H),F5.1,
     2                          I4,F5.2,F6.2,I4,F5.1,F5.2,F5.2)
  640 CONTINUE                                                       PULM4130
      WRITE(6,5026)                                                  PULM4140
 5026 FORMAT(1H )                                                    PULM4150
      IF ( (MNO1.EQ.MNO2) .AND. (MNO1.EQ.MNO3) .AND. (MNO1.EQ.MNO4)  PULM4160
     1 .AND. (MCARD1.EQ.1) .AND. (MCARD2.EQ.2) .AND. (MCARD3.EQ.3)   PULM4161
     2  .AND. (MCARD4.EQ.4) ) GO TO 650                              PULM4162
      WRITE(6,5028) MNO1,MCARD1,MNO2,MCARD2,MNO3,MCARD3,MNO4,MCARD4  PULM4163
 5028 FORMAT( 10X, 35HIDENTIFICATION OR SEQUENCE ERROR  -    ,       PULM4164
     1      3X,A6,I5, 3 ( /48X,A6,I5 ) )                             PULM4165
      GO TO 10                                                       PULM4166
  650 CONTINUE                                                       PULM4167
      LINE=LINE+1                                                    PULM4168
      IF(LINE.EQ.9 ) GO TO 10                                        PULM4170
      GO TO 20                                                       PULM4180
  660 WRITE(6,5002) CARDD                                            PULM4190
      STOP                                                           PULM4195
      END                                                            PULM4220
                                                                     PULM4230
```

TABLE II-2 - REGRESSION EQUATIONS FOR PREDICTED VALUES OF PULMONARY FUNCTION IN MEN

Ht	cm	=	Ht (inches) x 2.54
Wt	Kgs	=	Wt (lbs) x 0.4536
FEV_1/FVC	%	=	$(PFEV_1/PFVC)$ x 100
VC	L.	=	0.064 Ht - 0.031 Age - 5.335
FRC	L.	=	0.051 Ht - 5.18
TLC	L.	=	0.094 Ht - 0.015 Age - 9.167
RV	L.	=	TLC - VC
FEV_{75}	L/min	=	((31.2 - 1.78 Age + 1.065 Ht) x 0.88) /40
FEV_1	L.	=	0.035 Ht - 0.033 Age - 1.12
FVC	L.	=	0.508 Ht - 0.032 Age - 3.02
FVCP		=	85.35 - 0.169 Age
MMF	L/sec	=	2.018 - 0.041 Age + 0.02 Ht
ME	%	=	65 - (Age - 30) /2
$D_{LCO_{SB}}$	*	=	0.457 Ht - 0.299 Age - 38.1
K_{CO}	ccCO/min	=	-0.038 Age + 5.78
$D_{LCO_{SS}}$rest	*	=	((18.05 - 0.279 Age + 0.185 (Ht'/2.54)) 273/310
Ext_{CO}	%	=	82.085 - 0.341 Age - 0.322 (Ht'/2.54)
$D_{LCO_{SS}}$exercise	*	=	35.0 - 0.497 Age + 9.946 $\dot{V}_{O_2}$
$\dot{V}_{O_2}$	L/min	=	0.410 + 0.0023 x load in KMm

* ccCO/min/mmHg

' inches.

QUEBEC ASBESTOS STUDY - QUESTIONNAIRE

NO. DE L'ETUDE: ☐☐☐☐☐

	jour	mois	année
Date de l'entrevue	☐	☐	☐
Date de naissance	☐	☐	☐

NOM ....
(Nom de famille)

....
(Prénoms)

Sexe M ☐ F ☐

Grandeur *(à $\frac{1}{4}$ pouce moins)* ☐☐☐ /4

	F.	A.	Autres
Langue maternelle	☐	☐	☐

Envergure *(à $\frac{1}{4}$ pouce moins)* ☐☐☐ /4

Nom de l'enquêteur ....

Pesanteur *(à $\frac{1}{4}$ livre)* ☐☐☐☐ /4

Posez chaque question tel que redigée. Inscrivez un X dans la case correspondante après chaque question. Dans le doute inscrivez 'NON'.

INTRODUCTION Je vais vous poser quelques questions principalement sur votre thorax. Veuillez s'il vous plaît attendre que j'aie posé la question complète. J'aimerais que vous répondiez par 'OUI' ou par 'NON' toutes les fois que ce sera possible.

TOUX

1. A n'importe quel moment de votre réveil jusqu'à ce que vous sortiez, habituellement toussez-vous deux fois ou plus l'hiver? ☐ Oui ☐ Non
Tenez compte de la toux en fumant la première cigarette, ou lors de la première sortie. Excluez le nettoyage de gorge ou une simple toux.

3. Toussez-vous habituellement pendant la journée - ou la nuit - en hiver? ☐ Oui ☐ Non
Ne pas tenir compte d'une toux occasionelle.
Si 'Non' aux questions 1 et 3 passez à la question 6.
Si 'Oui' à 1 ou 3:

5. Toussez-vous comme ça presque tous les jours (toutes les nuits*) pendant trois mois ou plus chaque année? ☐ Oui ☐ Non ☐ N.A.

* *Pour les sujets qui travaillent la nuit.*

SECRETIONS PULMONAIRES

6. A n'importe quel moment de votre réveil jusqu'à ce que vous sortiez, avez-vous habituellement des crachats qui viennent des bronches l'hiver? ☐ Oui ☐ Non

Tenez compte des sécrétions qui viennent des bronches seulement. Comptez les sécrétions en fumant la première cigarette ou lors de la première sortie. Comptez les sécrétions avalées.

8. En hiver, le jour ou la nuit avez-vous habituellement des crachats? ☐ Oui ☐ Non

Acceptez deux ou plus.

Si 'Non' aux questions 6 et 8 passez à la question 12a.

Si 'Oui' à 6 ou 8:

10. Pendant trois mois ou plus chaque année continuez-vous à avoir ces crachats presque tous les jours (les nuits*)? ☐ Oui ☐ Non ☐ N.A.

* *Pour les sujets qui travaillent la nuit.*

12a. Pendant les trois dernières années, y a-t-il eu une période au cours de laquelle vous avez souffert d'une toux et des crachats, (plus que d'habitude*) qui ont durés trois semaines ou plus? Non ☐

Si 'Non' à la question 12a passez à la question 13.

Si 'Oui' à la question 12a:

* *Pour les sujets qui ont habituellement des sécrétions.*

12b/c Avez-vous eu plus d'une telle période?

Oui - une fois ☐

Oui - deux fois ou plus ☐

13. Avez-vous déjà craché du sang? Non ☐

Si 'Non' à la question 13 passez à la question 14a.

Si 'Oui' à la question 13.

13a. Est-ce que c'était au cours de l'année dernière?

Oui - l'année dernière ☐

Oui - mais non l'année dernière ☐

DIFFICULTE DE LA RESPIRATION

14a. Avez-vous de la difficulté à respirer quand vous vous dépêchez sur un terrain plat ou quand vous marchez sur une pente légère?

Incapacité* ☐

Non - a. ☐

Si 'Non' à la question 14a passez à la question 15a.

Si 'Oui' à la question 14a:

14b. Avez-vous de la difficulté à respirer quand vous marchez avec d'autres personnes de votre âge sur un terrain plat? Non - b. ☐

Si 'Non' à la question 14b passez à la question 15a.

Si 'Oui' à la question 14b:

14c. Etes-vous obligé de vous arrêter pour prendre votre respiration quand vous marchez d'un pas régulier sur un terrain plat?

Non - c. ☐

Oui - c. ☐

* *Incapacité de marcher causées pour toutes autres raisons sauf celles du coeur et des poumons.*

Page 3

RESPIRATION SIFFLANTE

15a. Est-ce que vous observez un sifflement ou une sibilance dans votre thorax? Non ☐

Si 'Non' à la question 15a passez à la question 16.A
Si 'Oui' à la question 15a.

15b. Est-ce que ce sifflement ou cette sibilance survient presque tous les jours - toutes les nuits?

Oui, mais pas presque tous les jours (les nuits) ☐

Oui, presque tous les jours (les nuits) ☐

16a. Avez-vous déjà eu la respiration coupée en même temps qu'un sifflement? Non ☐

Si 'Non' à la question 16a passez à la question 17.
Si 'Oui' à la question 16a:

16b. Votre respiration est-elle absolument normale entre les attaques?

Non ☐

Oui ☐

CONDITIONS ATMOSPHERIQUES

17. Les conditions atmosphériques affectent-elles votre thorax? Non ☐

Inscrivez 'Oui' seulement si le mauvais temps affecte régulièrement le thorax.

Si 'Non' à la question 17 passez à la question 18.
Si 'Oui' à la question 17:

17a. Les conditions atmosphériques vous coupent-elles le souffle?

Oui ☐

Non ☐

17b. Spécifiez quelles conditions atmosphériques, e.g. la brume, l'humidité, le froid, la chaleur, autres ....

CATARRHE

18. Avez-vous le nez bouché ou le catarrhe, ou des sécrétions habituellement l'hiver? ☐ Oui ☐ Non

19. Cela vous arrive-t-il l'été? ☐ Oui ☐ Non

Si 'Non' aux questions 18 et 19 passez à la question 21.
Si 'Oui' à la question 18 ou 19:

20. Est-ce que cela vous arrive presque tous les jours, pendant trois mois ou plus, par année? ☐ Oui ☐ Non ☐ N.A.

MALADIES DU THORAX

21. Durant les trois dernières années avez-vous eu des maladies du thorax qui vous ont empêché de remplir votre travail régulier pendant une semaine ou plus? Non ☐

Si 'Non' à la question 21 passez à la question 22.
Si 'Oui' à la question 21:

21a. Au cours d'une de ces maladies avez-vous eu plus de crachats que d'habitude? Non ☐

Si 'Non' à la question 21a passez à la question 22.
Si 'Oui' à la question 21a:

21b. Combien de maladies de ce genre avez-vous eues au cours des trois dernières années?
1 maladie ☐
2 ou plus maladies ☐

AVEZ VOUS DEJA EU:

22. Un traumatisme, un accident ou une opération au thorax? .... ☐*
....

23. Maladie de coeur/angine/douleurs à la poitrine causées par un effort? .... ☐*
....

24 Bronchite? .... ☐**
....

25. Pneumonie? .... ☐**
....

26. Pleurésie? .... ☐**
....

27. Tuberculose pulmonaire? .... ☐*
....
....

28. L'asthme bronchique? .... ☐*
....
....
....

29. Emphysème? .... ☐*
....

30. Bronchectasie? .... ☐*
....

31. D'autres troubles pulmonaires? ☐**
....

*** Code: 0-non; 1-une fois; 2-2 fois; .... 9-9 fois ou plus.*
** Code 0-non; 1-oui.*
Donnez les renseignements pertinents après chaque réponse affirmative.

INTRODUCTION Je vais maintenant vous poser quelques questions d'ordre général.

INCAPACITE

33a. Avez-vous déjà souffert des douleurs dans les articulations? ☐ Oui ☐ Non

33b. Au réveil ressentez-vous des raideurs ou des courbatures dans les muscles ou les articulations? ☐ Oui ☐ Non

Si 'Oui' à la question 33b:

Est-ce que votre condition change à mesure que la journée progresse? ☐ Non ☐ Mieux ☐ Pire

33c. Avez-vous déja eu les articulations enflées? (Excepté les cas d'enflure provenant de blessures ou d'accidents.) ☐ Oui ☐ Non

33d. Avez-vous déjà souffert d'arthrite, de rhumatisme ou d'autres maladies de ce genre? ☐ Oui ☐ Non

34. Avez-vous de la difficulté à mouvoir vos membres et/ou votre corps? ☐ Oui ☐ Non

<u>FUMER</u>

35a. Avez-vous déjà fumé? ☐ Oui ☐ Non

Si 'Non' à la question 35a passez à la question 38.

35b. Fumez-vous maintenant? ☐ Oui ☐ Non

Si 'Non' à la question 35b passez à la question 35c.

A quel âge avez-vous commencé à fumer régulièrement? .... (âge)

Combien de cigarettes fumez-vous habituellement? Jour de travail ....

Fin de semaine ....

Combien de tabac à pipe fumez-vous habituellement par semaine? .... livres / onces / paquets

Combien de cigares fumez-vous habituellement par semaine?
Spécifiez gros (G) ou petit (P) ....
Passez à la question 38.

35c. Avez-vous jamais fumé une seule cigarette ou plus par jour (ou un once de tabac ou plus par mois) pendant un an? ☐ Oui ☐ Non

Si 'Non' à la question 35c passez à la question 38.
Si 'Oui' à la question 35c.

A quel âge avez-vous commencé à fumer régulièrement? .... (âge)

A quel âge avez-vous cessé de fumer la dernière fois? .... (âge)

Option: Est-ce que c'était au cours du mois passé? ☐ Oui ☐ Non

Combien de cigarettes fumiez-vous par jour quand vous avez cessé?

Jour de travail ....

Fin de semaine ....

Combien de tabac à pipe fumiez-vous par semaine quand vous avez cessé? .... livres / onces / paquets

Combien de cigares fumiez-vous par semaine quand vous avez cessé?
Spécifiez gros (G) ou petit (P)

....

EMPLOI

38. Par quelle compagnie d'amiante êtes-vous employé? ....

....

39. Depuis combien de temps êtes-vous à l'emploi de cette compagnie? .... années

40. Pour quelles autres compagnies d'amiante avez-vous travaillé? Aucune ☐

	Dates
....	....
....	....
....	....
....	....
....	....

41. Avez-vous déjà travaillé ailleurs? ☐ Oui ☐ Non

Si 'Non' à la question 41 terminez l'entrevue.

			Dates
42. Avez-vous déjà travaillé dans une mine de charbon?	☐ Oui	☐ Non	....
dans une mine d'or?	☐ Oui	☐ Non	....
dans une mine de cuivre?	☐ Oui	☐ Non	....
dans quelqu'autres compagnies minières?	☐ Oui	☐ Non	....

Si 'Oui' spécifiez ....

avec des gaz irritants ou des émanations chimiques?	☐ Oui	☐ Non	....

Si 'Oui' spécifiez ....

quelqu'autres emplois ou il y avait de la poussière?	☐ Oui	☐ Non	....

Si 'Oui' spécifiez ....

QUEBEC ASBESTOS STUDY - QUESTIONNAIRE

SURVEY NUMBER ☐☐☐☐☐☐

	day	month	year
Date of interview	☐	☐	☐
Date of birth	☐	☐	☐

NAME ....
(Surname)

....
(First name)

Sex M ___ F ___

Standing height (in) *(to the ¼in. below)* ☐☐☐ /4

Mother tongue Fr ☐ E ☐ O ☐

Span (in) *(to the ¼in. below)* ☐☐☐ /4

Weight (lbs) *(to the ¼lb.)* ☐☐☐☐ /4

NAME OF INTERVIEWER ....

Use the actual wording of each question. Put X in appropriate square after each question. When in doubt record 'NO'.

PREAMBLE I am going to ask you some questions, mainly about your chest. I should like you to answer 'YES' or 'NO' whenever possible.

COUGH

1. Do you usually cough first thing in the morning (on getting up*) in the winter? ☐ Yes ☐ No
Count a cough with first smoke or on first going out of doors. Exclude clearing throat or a single cough.

3. Do you usually cough during the day - or at night - in the winter? ☐ Yes ☐ No
Ignore an occasional cough.
If 'No' to both questions 1 and 3, go to question 6.
If 'Yes' to either question 1 or 3:

5. Do you cough like this on most days (or nights*) for as much as three months each year? ☐ Yes ☐ No ☐ N.A.

PHLEGM

6. Do you usually bring up any phlegm from your chest first thing in the morning (on getting up*) in the winter? ☐ Yes ☐ No
Count phlegm with the first smoke or on first going out of doors. Exclude phlegm from the nose. Count swallowed phlegm.

8. Do you usually bring up any phlegm from your chest during the day - or at night - in the winter? ☐ Yes ☐ No
Accept twice or more.
If 'No' to both question 6 and 8, go to question 12a.
If 'Yes' to either question 6 or 8:

* *For subjects who work by night.*

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10. Do you bring up phlegm like this on most days (or nights*) for as much as three months each year? *(* For subjects who work by night)* ☐ Yes ☐ No ☐ N.A.

12a. In the past three years have you had a period of (increased*) cough and phlegm lasting for three weeks or more?
If 'No' to question 12a, go to question 13.
If 'Yes' to question 12a:

No ☐
Yes - 1 period ☐

12b/c. Have you had more than one such period?
** For subjects who usually have phlegm.*

Yes - 2 or more periods ☐

13. Have you ever coughed up blood?
If 'No' to question 13, go to question 14a.
If 'Yes' to question 13:

No ☐
Yes - in past year ☐

13a. Was this in the past year?

Yes - not in past year ☐

BREATHLESSNESS

14a. Are you troubled by shortness of breath when hurrying on level ground or walking up a slight hill?
If 'No' to question 14a, go to question 15a.

If 'Yes' to question 14a:

Disabled* ☐
No - a. ☐

14b. Do you get short of breath walking with other people of your own age on level ground?
If 'No' to question 14b, go to question 15a.
If 'Yes' to question 14b:

No - b. ☐

14c. Do you have to stop for breath when walking at your own pace on level ground?
** Disabled from walking by any conditions other then heart or lung disease.*

No - c. ☐
Yes - c. ☐

WHEEZING

15a. Does your chest ever sound wheezing or whistling?
If 'No' to question 15a, go to question 16a.
If 'Yes' to question 15a:

No ☐
Yes, but not most days (or nights) ☐

15b. Do you get this most days - or nights?

Yes, most days (or nights) ☐

16a. Have you ever had attacks of shortness of breath with wheezing?
If 'No' to question 16a, go to question 17.
If 'Yes' to question 16a:

No attacks ☐

16b. Is/was your breathing absolutely normal between attacks?

No ☐
Yes ☐

WEATHER

17. Does the weather affect your chest?
Only record 'Yes' if adverse weather definitely and regularly causes chest symptoms.
If 'No' to question 17, go to question 18.
If 'Yes' to question 17:

No ☐

17a. Does the weather make you short of breath?

Yes ☐
No ☐

17b. Specify type of weather, e.g. fog, damp, cold, heat, other.................

NASAL CATARRH

18 Do you usually have a stuffy nose or catarrh at the back of your nose in the winter? ☐ Yes ☐ No

19. Do you have this in the summer? ☐ Yes ☐ No

If 'No' to both questions 18 and 19, go to question 21.
If 'Yes' to either question 18 or 19:

20. Do you have this on most days for as much as three months each year? ☐ Yes ☐ No ☐ N.A.

CHEST ILLNESSES

21. During the past three years have you had any chest illness which has kept you from your usual activities for as much as a week? No ☐

If 'No' to question 21, go to question 22.
If 'Yes' to question 21:

21a. Did you bring up more phlegm than usual in any of these illnesses? No ☐

If 'No' to question 21a, go to question 22.
If 'Yes' to question 21a:

21b. How many illnesses like this have you had in the past three years?

1 illness ☐
2 or more illnesses ☐

HAVE YOU EVER HAD:

22. An injury or operation affecting your chest? .... ☐*
....
23. Heart trouble/angina/chest pain on exertion? .... ☐*
....
24. Bronchitis? ....
.... ☐**
25. Pneumonia? ....
.... ☐**
26. Pleurisy? ....
.... ☐**
27. Pulmonary tuberculosis? ....
.... ☐*
....
28. Bronchial asthma? ....
.... ☐*
....
29. Emphysema? ....
.... ☐*
30. Bronchiectasis?..................
.... ☐*
31. Other chest trouble? ....
.... ☐**

** Code: 0-no; 1-once; 2-twice ... 9-nine or more times.
* Code 0-no; 1-yes.
give relevant details after each positive answer.

PREAMBLE I am now going to ask you a few more general questions.

DISABILITY

33a. Have you ever had pain in any joint? ☐ Yes ☐ No

33b. Do you usually wake up with stiffness or aching in your joints or muscles? ☐ Yes ☐ No

If 'Yes' to 33b:

Does your condition change as the day progresses? ☐ No ☐ Better ☐ Worse

33c. Have you ever had swelling of any joints, other than as the result of an injury? ☐ Yes ☐ No

33d. Have you ever had arthritis or rheumatism or another disease of that type? ☐ Yes ☐ No

34. Have you any difficulty in moving your body and/or limbs fully? ☐ Yes ☐ No

TOBACCO SMOKING

35a. Have you ever smoked? ☐ Yes ☐ No
If 'No' to question 35a, go to question 38.

35b. Do you smoke now? ☐ Yes ☐ No
If 'No' to question 35b, go to question 35c.

How old were you when you started smoking regularly? .... (age)

How many cigarettes do you usually smoke per working day? ....
on weekends? ....

How much pipe tobacco do you usually smoke per week? .... pounds / ounces / pkts

How many cigars do you usually smoke per week? ....
Specify large (L) or small (S).
Go to question 38.

35c. Have you ever smoked as much as one cigarette a day (or one ounce of tobacco a month) for as long as a year? ☐ Yes ☐ No
If 'No' to question 35c, go to question 38.
If 'Yes' to question 35c:

How old were you when you started smoking regularly? .... (age)

How old were you when you last gave up smoking? .... (age)

Optional: Was this within the last month? ☐ Yes ☐ No

How many cigarettes per day were you smoking before you gave up?

.... at weekends .... per working day

How much pipe tobacco were you smoking per week before you gave up? .... pounds / ounces / pkts

How many cigars per week were you smoking before you gave up? ....
Specify large (L) or small (S).

APPENDIX III: RESULTS

TABLE III-I - MEANS AND STANDARD DEVIATIONS OF PULMONARY FUNCTION TESTS FOR THE INDIVIDUAL AND COMBINED SURVEYS

		1967		1968		1967-68	
		Mean ±	S.D.	Mean ±	S.D.	Mean ±	S.D.
No.subjects		871		163		1034	
Age	yrs	46.1	11.6	62.0	1.4	48.6	12.2
Height	cm	168.9	6.5	164.9	6.4	168.3	6.7
Weight	kgs	73.1	11.5	69.2	12.2	72.5	11.7
Tests chosen for profile definition:							
RV	% P	101.9	43.6	105.9	25.3	102.6	41.3
TLC	% P	98.5	13.4	98.9	14.3	98.6	13.5
FEV_{75}	% P	98.8	18.8	99.5	21.1	98.9	19.1
FEV_1%FVC	% P	102.3	10.4	99.5	10.9	101.8	10.5
MMF	% P	92.4	45.3	74.6	32.5	89.6	44.0
Other tests:							
VC	% P	90.5	14.2	88.7	15.2	90.2	14.4
FRC	% P	102.1	38.4	96.4	20.0	101.2	28.3
FEV_1	% FVC	79.1	8.3	74.3	8.2	78.4	8.4
ME	% P	94.9	23.7	89.3	23.6	94.1	23.8
FVC	L	3.9	0.9	3.1	0.7	3.8	0.9
No.subjects		308		159		467	
$D_{LCO_{SB}}$	*	29.0	7.9	24.6	5.4	27.5	7.4
K_{CO}	cc/min	4.7	1.1	4.5	0.8	4.6	1.0
$\dot{V}_A$	L	5.6	0.9	5.1	1.0	5.5	0.9
REST							
No.subjects		865		159		1024	
$D_{LCO_{SS}}$	*	12.7	4.5	9.6	2.7	12.2	4.3
Ext_{CO}	%	42.0	6.4	37.2	6.4	41.3	6.6
$\dot{V}$	L/min	9.6	2.5	9.4	2.4	9.5	2.5
$\dot{V}_{O_2}$	L/min	0.27	0.05	0.26	0.05	0.27	0.05
200KMm							
No.subjects		766		128		894	
$D_{LCO_{SS}}$	*	23.5	6.1	17.8	3.7	22.7	6.1
Ext_{CO}	%	40.0	5.8	35.9	5.3	39.4	5.9
$\dot{V}$	L/min	19.6	3.6	19.1	3.0	19.5	3.5
$\dot{V}_{O_2}$	L/min	0.73	0.13	0.71	0.08	0.72	0.13
400KMm							
No.subjects		368		37		405	
$D_{LCO_{SS}}$	*	28.2	5.7	23.4	4.0	27.8	5.7
Ext_{CO}	%	35.9	4.6	31.4	5.0	35.4	4.8
$\dot{V}$	L/min	30.5	4.8	33.3	5.1	30.8	4.9
$\dot{V}_{O_2}$	L/min	1.22	0.16	1.31	0.10	1.23	0.16
600KMm							
No.subjects		153		-		153	
$D_{LCO_{SS}}$	*	36.3	6.4			36.3	6.4
Ext_{CO}	%	37.5	4.4			37.5	4.4
$\dot{V}$	L/min	36.5	4.6			36.5	4.6
$\dot{V}_{O_2}$	L/min	1.63	0.20			1.63	0.20

* ccCO/min/mmHg

TABLE III-2 - MEANS AND STANDARD DEVIATIONS OF PULMONARY FUNCTION TESTS IN NORMAL AND GROUPED IN DECADES

						NORMAL							
		21-30 yrs		31-40 yrs		41-50 yrs		51-60 yrs		61+ yrs		21-30 yrs	
		Mean ±	S.D.	Mean ±	S.D.	Mean ±	S.D.	Mean ±	S.D.	Mean ±	S.D.	Mean ±	S.I.
# subj.		54		93		106		89		72		29	
Age	yrs	26.3	2.7	36.4	2.7	46.0	2.6	55.7	2.9	62.6	1.3	26.1	2.5
Ht	cm	172.4	4.8	170.8	6.7	169.3	6.9	167.7	6.2	165.8	6.0	171.6	6.2
Wt	Kgs	72.2	9.3	72.9	10.3	75.2	12.0	72.8	11.4	71.6	12.5	73.5	11.1
Tests chosen for profile definition:													
RV	% P	89.8	17.5	94.4	20.4	98.4	15.6	100.2	17.5	99.5	14.9	85.9	23.0
TLC	% P	97.5	7.9	99.4	9.1	98.3	8.6	98.5	8.0	97.3	7.8	97.7	11.6
FEV_{75}	% P	99.3	9.2	101.4	9.3	99.5	13.0	103.3	11.5	105.9	13.0	95.5	13.6
FEV_1%	% P	103.5	5.8	102.9	6.0	102.8	6.6	103.4	6.6	103.9	6.5	99.7	8.9
MMF	% P	102.3	15.1	99.6	16.1	90.8	18.6	89.0	18.0	85.6	21.6	90.9	21.9
Other tests:													
VC	% P	91.8	10.5	93.9	10.3	91.9	10.9	91.9	9.4	90.8	10.2	95.2	10.4
FRC	% P	87.7	13.6	90.3	14.3	89.3	13.5	92.7	14.0	91.1	15.1	85.9	15.1
FEV_1	%FVC	83.5	4.7	81.2	4.8	79.5	5.0	78.3	5.0	77.4	5.0	81.1	6.5
ME	% P	89.4	22.0	95.6	20.5	95.6	23.4	97.1	21.9	94.9	22.9	93.8	16.5
FVC	L	4.9	0.5	4.5	0.5	4.0	0.6	3.6	0.5	3.2	0.5	5.0	0.7
# subj.		17		35		37		40		50		6	
$D_{LCO_{SB}}$	*	35.3	6.5	31.9	7.1	31.8	9.9	29.4	7.8	25.9	3.9	31.7	7.2
K_{CO}	'	5.2	0.7	4.9	0.7	5.2	1.3	4.8	1.2	4.5	0.6	5.0	1.1
$\dot{V}_A$	L	6.3	0.6	6.0	0.8	5.6	0.7	5.7	0.6	5.3	0.7	5.9	1.4
REST													
# subj.		54		93		105		89		69		29	
$D_{LCO_{SB}}$	*	14.5	3.7	14.3	5.4	13.0	4.0	11.6	3.7	10.6	2.7	15.6	6.2
Ext_{CO}	%	44.4	5.5	43.7	5.5	42.4	5.9	41.2	6.1	40.2	6.8	44.7	5.7
$\dot{V}$	+	9.2	3.1	9.2	2.0	9.6	2.1	9.4	2.1	9.1	2.4	11.0	4.8
$\dot{V}_{O_2}$	+	0.28	0.06	0.28	0.05	0.28	0.05	0.26	0.05	0.26	0.05	0.29	0.07
200KMmin													
# subj.		52		90		88		78		55		29	
$D_{LCO_{SS}}$	*	29.5	4.9	26.1	3.9	23.0	4.9	20.9	4.3	18.8	3.7	30.1	5.3
Ext_{CO}	%	44.5	4.0	43.3	4.0	39.7	5.0	37.9	4.6	36.7	4.9	43.8	5.6
$\dot{V}$	+	18.6	2.9	18.4	2.7	19.4	3.2	20.2	3.6	19.6	3.8	20.2	4.9
$\dot{V}_{O_2}$	+	0.73	0.12	0.70	0.14	0.72	0.12	0.74	0.13	0.74	0.13	0.74	0.11
400KMmin													
# subj.		6		32		65		38		17		8	
$D_{LCO_{SS}}$	*	32.7	3.9	30.7	4.5	28.9	5.8	26.4	4.5	23.4	4.1	34.9	5.9
Ext_{CO}	%	37.8	5.1	37.6	4.1	36.3	4.4	35.1	4.3	32.5	3.5	38.9	5.0
$\dot{V}$	+	31.1	6.1	29.9	4.5	30.3	3.8	30.2	4.4	31.2	5.3	30.1	4.5
$\dot{V}_{O_2}$	+	1.28	0.11	1.22	0.18	1.23	0.15	1.24	0.12	1.26	0.20	1.19	0.30
600KMmin													
# subj.		42		44		-		-		-		15	
$D_{LCO_{SS}}$	*	38.0	5.4	33.7	4.8							39.5	7.4
Ext_{CO}	%	38.0	3.9	36.0	3.5							37.4	4.8
$\dot{V}$	+	36.7	4.0	37.5	4.5							38.6	5.7
$\dot{V}_{O_2}$	+	1.67	0.15	1.59	0.27							1.68	0.10

* ccCO/min/mmHg + L/min ' cc/min

UNCTION TESTS IN NORMAL AND UNDIFFERENTAITED PROFILES SUBJECTS

		UNDIFFERENTIATED									
61+ yrs		21-30 yrs		31-40 yrs		41-50 yrs		51-60 yrs		61+ yrs	
Mean ±	S.D.	Mean ±	S.D.	Mean ±	S.D.	Mean ±	S.D.	Mean ±	S.D.	Mean ±	S.D.
72		29		46		59		76		82	
62.6	1.3	26.1	2.5	35.7	2.7	45.4	2.8	56.5	3.2	62.5	1.3
165.8	6.0	171.6	6.2	170.0	5.8	168.2	5.4	167.2	5.8	163.5	6.2
71.6	12.5	73.5	11.1	73.1	11.3	70.4	10.7	72.1	11.0	67.4	13.7
99.5	14.9	85.9	23.0	93.5	25.0	113.7	32.0	98.0	23.3	101.8	25.8
97.3	7.8	97.7	11.6	92.8	15.4	99.2	15.7	94.9	17.7	98.1	17.9
105.9	13.0	95.5	13.6	92.7	16.9	100.0	16.4	100.1	20.5	103.9	21.2
103.9	6.5	99.7	8.9	103.5	8.0	101.2	5.9	104.2	7.5	103.9	7.1
85.6	21.6	90.9	21.9	91.3	26.2	103.5	28.6	80.5	24.5	79.6	21.2
90.8	10.2	95.2	10.4	86.0	15.5	92.8	16.8	87.3	18.7	90.3	19.0
91.1	15.1	85.9	15.1	83.3	18.7	90.5	20.3	91.8	20.5	96.1	21.6
77.4	5.0	81.1	6.5	82.0	6.2	78.5	4.5	78.4	5.8	77.5	5.3
94.9	22.9	93.8	16.5	94.2	20.3	92.8	19.0	99.0	21.9	92.8	28.5
3.2	0.5	5.0	0.7	4.1	0.8	4.1	0.8	3.4	0.8	3.0	0.7
50		6		11		21		33		60	
25.9	3.9	31.7	7.2	32.1	3.9	28.4	6.0	25.5	6.5	22.3	5.5
4.5	0.6	5.0	1.1	5.2	0.8	4.5	0.8	4.6	1.3	4.4	0.9
5.3	0.7	5.9	1.4	5.8	0.7	5.9	1.0	5.2	1.0	4.7	1.0
69		29		46		58		76		81	
10.6	2.7	15.6	6.2	14.3	3.7	12.2	3.7	10.5	3.0	9.1	2.6
40.2	6.8	44.7	5.7	44.2	5.8	42.0	5.9	40.0	4.9	36.8	6.7
9.1	2.4	11.0	4.8	9.8	2.8	9.4	1.9	9.0	1.8	9.2	2.1
0.26	0.05	0.29	0.07	0.28	0.05	0.27	0.05	0.25	0.04	0.25	0.05
55		29		46		53		65		56	
18.8	3.7	30.1	5.3	26.4	5.8	21.8	4.1	19.7	4.0	17.4	3.8
36.7	4.9	43.8	5.6	42.6	5.1	39.3	4.3	37.0	4.6	34.9	6.0
19.6	3.8	20.2	4.9	18.6	2.6	19.6	2.4	20.1	2.9	19.9	3.8
0.74	0.13	0.74	0.11	0.73	0.12	0.72	0.12	0.73	0.11	0.70	0.12
17		8		13		38		35		20	
23.4	4.1	34.9	5.9	31.1	5.8	27.3	4.7	25.5	4.6	24.6	3.5
32.5	3.5	38.9	5.0	37.6	3.3	36.1	4.5	33.9	3.9	32.3	5.4
31.2	5.3	30.1	4.5	29.1	3.1	29.5	4.4	31.2	3.0	33.7	6.4
1.26	0.20	1.19	0.30	1.23	0.10	1.22	0.16	1.20	0.15	1.25	0.19
-		15		23		-		-		-	
		39.5	7.4	35.1	5.6						
		37.4	4.8	37.0	4.3						
		38.6	5.7	36.3	4.5						
		1.68	0.10	1.61	0.20						

TABLE III-3 - MEANS AND STANDARD DEVIATIONS OF PULMONARY FUNCTION TESTS IN RESTRICT

DEFINITE RESTRICTION

		21-30 yrs		31-40 yrs		41-50 yrs		51-60 yrs		61+ yrs		21-30 yr	
		Mean ±	S.D.	Mean ±	S.D.	Mean ±	S.D.	Mean ±	S.D.	Mean ±	S.D.	Mean ±	S.
# subj.		18		24		28		33		17		3	
Age	yrs	26.6	2.7	36.5	2.6	45.0	3.2	56.0	2.8	62.8	1.4	26.3	3
Ht	cm	172.0	6.3	171.3	4.2	171.5	4.6	168.5	5.8	164.9	4.7	172.5	7
Wt	Kgs	78.7	13.0	78.0	8.9	77.5	12.6	80.1	10.8	74.7	12.0	70.5	6
Tests chosen for profile definition:													
RV	% P	65.6	14.8	75.5	15.2	78.0	14.6	80.6	12.2	80.0	16.1	95.3	34
TLC	% P	90.5	9.8	89.9	9.0	90.3	10.3	89.5	11.2	90.4	11.7	94.3	18
FEV_{75}	% P	107.5	10.4	109.1	10.4	112.7	12.9	115.5	15.5	123.1	17.2	109.0	18
FEV_1%	% P	110.8	3.7	112.2	3.4	112.0	5.8	115.0	4.8	115.1	5.2	117.0	4
MMF	% P	128.8	12.2	135.0	16.1	132.8	22.0	135.0	20.1	135.8	29.1	134.3	15
Other tests:													
VC	% P	91.8	13.6	89.3	11.0	90.4	12.1	90.9	13.4	92.2	14.2	87.7	15
FRC	% P	69.5	13.5	74.4	16.8	75.6	15.0	76.8	15.3	75.2	15.5	87.3	33
FEV_1	% FVC	89.4	3.3	88.6	2.7	87.0	4.6	86.9	3.4	85.7	3.9	94.3	3
ME	% P	104.7	32.4	99.7	21.1	101.0	33.5	102.4	25.1	94.5	15.7	89.7	11
FVC	L	4.8	0.5	4.3	0.6	4.1	0.7	3.5	0.6	3.2	0.5	4.7	1
# subj.		5		7		10		11		15		1	
$D_{L}CO_{SB}$	*	36.9	9.4	31.0	4.7	29.0	4.7	25.6	5.2	26.1	4.8	36.3	
K_{CO}	'	5.9	1.6	5.6	0.9	5.0	0.7	4.6	0.8	4.9	0.7	4.6	
$\dot{V}_A$	L	5.8	0.6	5.2	0.9	5.4	0.7	5.1	0.9	4.9	0.7	7.3	
REST													
# subj.		18		24		28		33		17		3	
$D_{L}CO_{SS}$	*	17.4	4.6	17.4	6.9	12.6	3.7	12.4	3.4	10.2	2.8	11.1	
Ext_{CO}	%	46.4	5.9	44.6	6.7	41.6	5.5	41.8	6.0	38.3	6.8	38.0	
$\dot{V}$	+	10.4	2.4	11.7	3.4	9.9	2.3	9.6	2.2	9.6	1.9	9.3	
$\dot{V}_{O_2}$	+	0.31	0.06	0.31	0.06	0.27	0.05	0.27	0.05	0.27	0.02	0.27	0
200KMmin													
# subj.		18		24		25		28		15		3	
$D_{L}CO_{SS}$	*	30.9	5.6	28.1	7.0	22.9	5.2	20.7	4.4	19.4	4.5	29.9	
Ext_{CO}	%	44.9	5.7	43.9	5.7	39.8	4.1	38.2	4.1	36.5	5.3	44.0	
$\dot{V}$	+	20.3	3.9	19.0	4.9	19.4	3.0	20.2	2.7	20.5	3.0	18.3	
$\dot{V}_{O_2}$	+	0.79	0.16	0.75	0.10	0.68	0.16	0.74	0.13	0.78	0.09	0.75	0
400KMmin													
# subj.		3		10		19		16		3		1	
$D_{L}CO_{SS}$	*	37.1	4.0	31.0	3.8	28.9	5.2	25.6	3.9	25.1	3.6	35.6	
Ext_{CO}	%	41.3	6.1	38.5	4.6	36.1	4.2	34.4	3.1	32.0	3.6	41.0	
$\dot{V}$	+	28.4	6.2	30.0	6.5	31.1	4.3	31.2	3.4	34.4	3.8	27.9	
$\dot{V}_{O_2}$	+	1.17	0.16	1.21	0.18	1.25	0.13	1.23	0.16	1.40	0.08	1.18	
600KMmin													
# subj.		8		9		-		-		-		1	
$D_{L}CO_{SS}$	*	38.7	8.2	37.2	10.5							38.7	
Ext_{CO}	%	40.5	4.2	39.9	7.0							42.0	
$\dot{V}$	+	34.1	3.0	33.5	4.1							30.3	
$\dot{V}_{O_2}$	+	1.70	0.11	1.60	0.21							1.51	

* ccCO/min/mmHg + L/min ' cc/min

NCTION TESTS IN RESTRICTIVE PROFILES, SUBJECTS GROUPED IN DECADES

		DOMINANT RESTRICTION									
61+ yrs		21-30 yrs		31-40 yrs		41-50 yrs		51-60 yrs		61+ yrs	
Mean ± S.D.		Mean ± S.D.		Mean ± S.D.		Mean ± S.D.		Mean ± S.D.		Mean ± S.D.	
17		3		3		3		11		3	
62.8	1.4	26.3	3.1	35.3	4.0	45.3	3.8	55.5	3.2	62.7	2.1
164.9	4.7	172.5	7.9	167.5	4.8	171.2	2.2	168.0	7.3	170.3	10.9
74.7	12.0	70.5	6.1	78.9	10.9	64.7	6.3	73.4	10.5	85.1	7.5
80.0	16.1	95.3	34.2	65.0	18.7	104.3	9.5	103.2	17.7	91.7	21.7
90.4	11.7	94.3	18.9	84.0	25.2	110.7	3.5	105.6	15.8	86.3	21.6
123.1	17.2	109.0	18.4	98.7	22.9	140.7	10.1	129.5	22.7	108.0	33.8
115.1	5.2	117.0	4.4	112.3	5.5	115.7	4.0	114.2	5.5	118.0	4.4
135.8	29.1	134.3	15.0	164.3	86.1	182.3	15.6	139.5	22.8	124.7	17.2
92.2	14.2	87.7	15.7	87.0	26.4	105.3	12.3	101.4	22.7	81.3	18.8
75.2	15.5	87.3	33.2	75.6	27.0	98.0	14.7	97.5	18.5	77.0	19.2
85.7	3.9	94.3	3.8	89.0	2.9	90.0	3.6	86.5	4.6	88.0	3.6
94.5	15.7	89.7	11.9	138.3	21.1	96.7	27.5	100.6	13.1	80.7	27.2
3.2	0.5	4.7	1.1	3.8	0.9	4.8	0.4	3.9	0.8	3.0	1.5
15		1		1		2		3		2	
26.1	4.8	36.3		23.6		33.5	10.5	25.6	5.6	22.3	2.6
4.9	0.7	4.6		4.7		5.2	2.3	3.7	0.4	4.1	1.1
4.9	0.7	7.3		4.6		6.1	0.7	6.3	0.7	5.3	2.0
17		3		3		3		11		3	
10.2	2.8	11.1	2.5	14.8	0.9	16.1	2.4	11.4	2.9	13.1	4.5
38.3	6.8	38.0	8.9	52.7	5.0	47.7	10.4	40.1	4.5	43.7	10.4
9.6	1.9	9.3	0.3	7.7	1.0	11.9	7.9	9.4	2.5	10.9	2.0
0.27	0.02	0.27	0.02	0.27	0.01	0.31	0.08	0.26	0.05	0.30	0.05
15		3		3		3		9		-	
19.4	4.5	29.9	8.1	28.3	4.1	24.7	1.7	20.3	1.6		
36.5	5.3	44.0	7.8	46.7	5.5	44.3	3.8	38.2	2.0		
20.5	3.0	18.3	3.9	18.2	2.5	17.5	3.5	19.9	3.1		
0.78	0.09	0.75	0.10	0.73	0.12	0.76	0.13	0.68	0.11		
3		1		-		2		6		-	
25.1	3.6	35.6				31.9	4.3	25.6	0.7		
32.0	3.6	41.0				43.5	2.1	35.8	1.0		
34.4	3.8	27.9				23.4	1.7	30.2	1.9		
1.40	0.08	1.18				1.26	0.13	1.29	0.11		
-		1		2		-		-		-	
		38.7		35.5	12.9						
		42.0		41.0	9.9						
		30.3		31.9	5.4						
		1.51		1.63	0.06						

TABLE III-4 - MEANS AND STANDARD DEVIATIONS OF PULMONARY FUNCTION TESTS IN OBSTRUCTI E PRC

		DEFINITE OBSTRUCTION											
		21-30 yrs		31-40 yrs		41-50 yrs		51-60 yrs		61+ yrs		21-30 yrs	31-
		Mean ±	S.D.	Mean ±	S.D.	Mean ±	S.D.	Mean ±	S.D.	Mean ±	S.D.	Mean ± S.D	Mea
# subj.		8		9		35		53		50		-	
Age	yrs	27.3	2.1	35.5	2.3	45.8	2.7	56.2	3.0	62.7	1.4		32
Ht	cm	170.3	7.4	168.7	6.9	168.6	5.2	166.1	5.6	165.3	6.5		177
Wt	kgs	67.5	11.4	68.7	7.3	69.3	12.8	70.2	12.3	70.0	11.0		95
Tests chosen for profile definition:													
RV	% P	130.9	41.2	128.2	9.4	133.8	25.0	143.7	24.8	139.7	22.7		79
TLC	% P	110.1	11.5	107.3	8.1	107.4	11.1	111.6	11.9	108.5	10.5		91
FEV$_{75}$	% P	80.9	10.5	80.5	14.2	79.5	16.0	79.2	18.0	78.2	17.3		69
FEV$_1$%	% P	87.6	9.5	89.7	5.6	87.4	10.3	87.6	12.1	86.4	9.4		82
MMF	% P	64.3	15.9	66.9	12.0	55.1	17.7	47.8	18.3	40.9	15.9		75
Other tests:													
VC	% P	91.6	14.4	89.9	10.7	87.6	14.0	87.9	14.4	85.6	13.6		94
FRC	% P	107.6	18.7	106.8	15.5	109.9	16.4	115.3	17.7	114.2	15.6		73
FEV$_1$	% FVC	70.5	7.6	71.1	4.5	68.0	8.0	66.3	9.0	64.4	7.1		65
ME	% P	79.8	26.2	90.3	24.3	81.5	26.6	87.8	25.9	79.4	21.1		125
FVC	L	4.9	0.9	4.3	0.8	3.8	0.7	3.2	0.6	2.9	0.6		4
# subj.		5		7		9		28		37		-	
$D_{LCO_{SB}}$	*	36.6	2.5	32.8	4.8	30.3	7.4	23.6	5.8	23.1	6.9		
K_{CO}	'	5.6	0.5	5.0	0.5	4.5	0.8	3.9	0.8	4.1	0.9		
$\dot{V}_A$	L	6.2	0.9	6.1	1.2	6.2	0.7	5.6	0.9	5.2	0.8		
REST													
# subj.		8		9		34		52		49		-	
$D_{LCO_{SS}}$	*	16.7	6.8	14.0	3.4	11.4	3.4	10.8	4.1	9.0	2.5		16.
Ext$_{CO}$	%	45.6	4.5	47.6	4.3	39.6	8.2	39.4	7.7	35.4	6.1		42.
$\dot{V}$	+	10.9	4.1	8.4	1.1	9.9	2.9	9.1	1.9	9.9	2.6		10.
$\dot{V}_{O_2}$	+	0.32	0.10	0.27	0.04	0.26	0.05	0.24	0.05	0.26	0.04		
200KMmin													
# subj.		8		8		33		40		41		-	
$D_{LCO_{SS}}$	*	33.1	5.2	26.8	5.4	21.9	6.4	19.0	5.6	17.5	4.0		23.
Ext$_{CO}$	%	45.3	6.3	43.6	4.9	37.7	6.8	36.1	6.4	34.4	4.8		41.
$\dot{V}$	+	21.5	10.1	18.3	2.9	19.8	3.4	20.0	4.2	20.2	3.8		19.
$\dot{V}_{O_2}$	+	0.71	0.22	0.77	0.10	0.66	0.12	0.71	0.16	0.71	0.12		0.4
400KMmin													
# subj.		2		2		23		20		12		-	
$D_{LCO_{SS}}$	*	36.7	3.1	30.3	3.8	28.9	4.8	24.1	4.7	24.9	7.4		
Ext$_{CO}$	%	40.0	5.7	36.5	7.8	35.3	5.3	32.8	4.7	31.5	7.5		
$\dot{V}$	+	29.5	4.5	31.2	7.8	32.0	7.5	31.6	5.0	34.7	7.0		
$\dot{V}_{O_2}$	+	0.90	0.0	1.24	0.04	1.20	0.13	1.24	0.17	1.26	0.17		
600KMmin													
# subj.		3		5		-		-		-		-	
$D_{LCO_{SS}}$	*	36.1	4.9	37.7	5.6								26.
Ext$_{CO}$	%	39.0	7.2	38.4	4.0								35.
$\dot{V}$	+	33.8	7.7	36.2	5.2								32.
$\dot{V}_{O_2}$	+	1.51	0.10	1.71	0.10								1.0

* ccCO/min/mmHg + L/min ' cc/min.

ON TESTS IN OBSTRUCTIVE PROFILES, SUBJECTS GROUPED IN DECADES.

DOMINANT OBSTRUCTIVE

yrs		21-30 yrs		31-40 yrs		41-50 yrs		51-60 yrs		61+ yrs	
±	S.D.	Mean ±	S.D	Mean ±	S.D.	Mean ±	S.D.	Mean ±	S.D.	Mean ±	S.D.
50		–		1		6		12		10	
.7	1.4			32.0		44.5	1.9	55.8	3.7	62.6	1.3
.3	6.5			177.8		165.3	4.0	169.9	8.4	168.3	7.2
.0	11.0			95.5		72.0	5.6	70.6	9.2	70.8	12.5
.7	22.7			79.0		118.2	26.4	131.3	27.1	129.2	24.9
.5	10.5			91.0		92.3	17.0	104.8	23.7	100.7	25.0
2	17.3			69.0		69.2	21.6	85.7	29.9	79.6	35.0
4	9.4			82.0		91.3	13.0	91.6	12.7	90.1	13.8
9	15.9			75.0		46.0	17.4	57.7	21.1	49.2	19.1
6	13.6			94.0		71.8	25.0	82.8	23.2	77.3	25.9
2	15.6			73.0		91.7	6.1	105.8	19.9	111.1	21.3
4	7.1			65.0		71.0	10.0	69.3	9.6	67.1	10.3
4	21.1			125.0		95.5	22.6	95.2	27.6	92.4	21.7
9	0.6			4.9		3.1	1.2	3.4	1.1	2.9	1.1
7		–		–		2		4		7	
1	6.9					29.8	9.5	20.2	4.8	27.0	6.9
1	0.9					5.7	1.1	3.5	0.2	4.2	0.9
2	0.8					4.8	0.6	5.3	1.3	5.9	1.0
9		–		1		6		12		10	
0	2.5			16.8		12.2	5.7	10.1	2.2	8.8	4.0
4	6.1			42.0		41.0	10.1	38.9	5.6	36.8	4.4
9	2.6			10.6		10.1	2.1	9.9	1.7	9.2	2.6
5	0.04			–		0.31	0.07	0.27	0.04	0.25	0.09
1		–		1		6		11		6	
5	4.0			23.6		19.9	6.9	19.2	3.5	17.6	3.6
4	4.8			41.0		36.7	9.4	35.5	4.7	36.0	4.2
2	3.8			19.9		20.3	5.0	21.8	4.3	18.7	2.2
1	0.12			0.45		0.75	0.14	0.76	0.08	0.71	0.07
2		–		–		4		6		2	
	7.4					26.0	3.0	26.6	5.0	22.0	3.0
	7.5					37.3	3.4	34.2	3.3	29.5	3.5
	7.0					26.9	2.3	32.4	6.7	33.8	2.1
	0.17					1.17	0.02	1.30	0.11	1.27	0.04
		–		1		–		–		–	
				26.3							
				35.0							
				32.1							
				1.03							

TABLE III-5 - PREVALENCE % OF RESPIRATORY SYMPTOMS IN PULMONARY FUNCTION PROFILES, SUBJECTS GROUPED BY DECADES

PULMONARY FUNCTION PROFILE	DECADES yrs	No. Subj.	COUGH 3 months	PHLEGM 3 months	COUGH & PHLEGM 3 months	BREATH-LESSNESS same age	CHEST ILLNESS
NORMAL							
	21-30	54	35	35	26	10	6
	31-40	93	38	45	31	9	8
	41-50	102	52	41	34	12	15
	51-60	87	61	58	39	22	16
	61+	71	54	52	40	27	18
UNDIFFER.							
	21-30	28	61	46	36	18	4
	31-40	45	49	40	31	7	11
	41-50	59	53	39	28	19	14
	51-60	72	49	44	30	22	15
	61+	82	68	49	41	34	15
RESTRICTION definite							
	21-30	17	38	19	13	13	0
	31-40	23	26	48	17	4	9
	41-50	29	38	34	21	21	17
	51-60	33	36	39	21	21	15
	61+	18	44	39	33	28	17
dominant							
	21-30	3	33	0	0	0	0
	31-40	3	0	33	0	0	33
	41-50	2	0	0	0	0	0
	51-60	11	40	50	40	20	30
	61+	3	33	33	33	67	67
OBSTRUCTION definite							
	21-30	7	50	17	17	0	0
	31-40	9	89	33	33	11	11
	41-50	35	91	69	66	29	26
	51-60	52	64	48	38	36	16
	61-	46	67	44	56	42	15
dominant							
	21-30	-	-	-	-	-	-
	31-40	1	0	0	0	100	0
	41-50	5	80	40	40	20	20
	51-60	12	83	50	42	17	8
	61+	9	67	56	56	33	22

TABLE III-6 - PREVALENCE % OF RADIOLOGICAL CHANGES IN PULMONARY FUNCTION PROFILES, SUBJECTS GROUPED BY DECADES.

PULMONARY FUNCTION PROFILES	DECADES yrs	No. Subj.	NORMAL	SMALL IRREGULAR OPAC. ALONE	PLEURAL CHANGES ALONE	SMALL IRREG. OPAC. & PLEURAL CHANGES COMBINED	TOTAL CHANGES
NORMAL							
	21-30	54	100	–	–	–	–
	31-40	93	86	4	10	–	14
	41-50	107	82	5	11	2	18
	51-60	89	73	1	20	6	27
	61+	72	61	3	28	8	39
UNDIFFER.							
	21-30	29	97	–	3	–	3
	31-40	47	87	2	11	–	13
	41-50	59	76	7	12	5	24
	51-60	76	62	13	17	7	37
	61+	82	50	13	22	15	50
RESTRICTION definite							
	21-30	18	100	–	–	–	–
	31-40	23	91	–	9	–	9
	41-50	29	94	3	3	–	6
	51-60	33	79	6	6	9	21
	61+	18	61	11	17	11	39
dominant							
	21-30	3	67	–	33	–	33
	31-40	3	100	–	–	–	–
	41-50	3	100	–	–	–	–
	51-60	11	91	9	–	–	9
	61+	3	100	–	–	–	–
OBSTRUCTION definite							
	21-30	8	100	–	–	–	–
	31-40	9	89	–	11	–	11
	41-50	35	74	–	20	6	26
	51-60	53	58	8	30	4	42
	61+	49	67	8	10	15	33
dominant							
	21-30	–	–	–	–	–	–
	31-40	1	100	–	–	–	–
	41-50	6	33	17	33	17	67
	51-60	12	42	16	42	–	58
	61+	10	30	10	30	30	70

TABLE III-7 - PREVALENCE OF MEN WITH DUST I > 200, DUST II > 200, AND SMOKING WITHOUT AND WITH STANDARDIZATION FOR TOTAL POPULATION. (Age standardization)

PULMONARY FUNCTION PROFILES	No. Subj.	DUST I	DUST II	SMOKING Cigarettes/day		
		200 dy. %	200 dy. %	0 %	1-20 %	21+ %
NORMAL	407	25 (21)*	14 (12)	12 (11)	30 (29)	58 (60)
UNDIFFER.	286	33 (23)	19 (10)	8 (10)	32 (29)	59 (61)
RESTRICTION						
definite	120	24 (20)	14 (12)	20 (19)	33 (33)	48 (48)
dominant	22	9 (3)	9 (3)	23 (12)	40 (36)	49 (41)
OBSTRUCTION						
definite	149	41 (25)	15 (28)	4 (4)	23 (16)	73 (80)
dominant	27	60 (39)	40 (21)	7 (3)	26 (23)	67 (75)

* ( ) Prevalence % standardized for total population.

TABLE III-8 - PREVALENCE % OF MEN WITH DUST II AND SMOKING IN EACH PROFILE, WITHOUT AND WITH STANDARDIZATION FOR TOTAL POPULATION. (Age standardization)

PULMONARY FUNCTION PROFILES	No. Subj.	DUST II					
		< 200 dy.			> 200 dy.		
		0 Cig/day %	1 - 20 Cig/day %	21 + Cig/day %	0 Cig/day %	1 - 20 Cig/day %	21+ Cig/day %
NORMAL	407	10 (11)*	33 (33)	43 (44)	1 (.5)	7 (6)	6 (6)
UNDIFFER.	286	7 (10)	33 (36)	41 (45)	1 (1)	9 (3)	9 (6)
RESTRICTION							
definite	120	18 (17)	33 (34)	36 (38)	2 (1)	6 (5)	6 (6)
dominant	22	19 (6)	50 (84)	13 (4)	6 (2)	12 (4)	-
OBSTRUCTION							
definite	149	6 (5)	19 (18)	48 (62)	-	14 (9)	13 (6)
dominant	27	4 (.5)	12 (12)	42 (49)	-	25 (13)	17 (12)

* ( ) Prevalence % standardized for total population.

TABLE III-9 - DECADE DISTRIBUTED FUNCTION PROFILES CORRELATED WITH DUST I AND DUST II - MEANS AND STANDARD DEVIATIONS

PULMONARY FUNCTION PROFILES	DECADES	No. Subj.	WORK		DUST I		DUST II	
	yrs		yrs Mean ±	S.D.	dy. Mean ±	S.D.	dy. Mean ±	S.D.
NORMAL	21-30	54	4.1	3.5	11	11	5	5
	31-40	93	12.9	5.7	96	161	59	119
	41-50	103	18.1	7.5	162	240	88	116
	51-60	90	24.3	8.1	274	348	173	277
	61+	72	30.1	8.8	328	474	220	422
UNDIFFER.	21-30	28	3.5	2.5	15	15	7	7
	31-40	46	11.8	6.3	87	117	38	45
	41-50	59	17.7	6.7	133	166	83	98
	51-60	75	25.1	10.2	296	355	162	245
	61+	81	31.5	8.8	530	704	315	524
RESTRICTION definite	21-30	17	5.1	2.8	18	13	5	5
	31-40	23	13.7	8.9	55	56	45	57
	41-50	29	16.3	7.0	162	242	103	143
	51-60	33	26.3	10.2	310	413	153	154
	61+	17	30.9	8.9	193	105	83	5
dominant	21-30	3	1.5	1.6	10	15	2	3
	31-40	3	15.0	4.4	75	46	42	44
	41-50	3	18.3	4.5	105	39	102	81
	51-60	11	22.3	14.4	161	238	162	245
	61+	3	28.3	9.6	261	267	363	441
OBSTRUCTION definite	21-30	8	5.5	3.1	28	40	10	11
	31-40	9	14.4	6.5	152	210	135	244
	41-50	35	18.4	7.5	183	224	105	166
	51-60	52	24.6	9.9	378	615	181	255
	61+	49	37.7	7.7	613	660	481	901
dominant	21-30	-	-		-		-	
	31-40	1	7.2		14		14	
	41-50	6	22.5	5.5	354	196	277	133
	51-60	12	25.2	9.7	318	280	179	220
	61+	9	31.1	9.8	354	487	228	251

TABLE III-10 - PREVALENCE % OF YEARS OF WORK WITH DUST I AND DUST II IN EACH PULMONARY FUNCTION PROFILE, SUBJECTS GROUPED BY DECADES.

PULMONARY FUNCTION	DECADES Yrs	No. Subj.	WORK Yrs				DUST INDEX Dust yrs		DUST INDEX II Dust yrs	
			0-1	1-10	10-30	30+	<200	>200	<200	>200
NORMAL										
	21-30	54	20	67	13	-	100	-	100	-
	31-40	93	1	31	68	-	87	13	95	5
	41-50	102	-	18	75	7	77	23	86	14
	57-60	89	-	2	71	27	60	40	76	24
	61+	72	-	-	53	47	57	43	76	24
UNDIFFER.										
	21-30	28	14	86	-	-	100	-	100	-
	31-40	48	2	38	60	-	81	19	100	-
	41-50	59	2	15	81	2	81	19	92	8
	51-60	76	1	12	57	30	57	43	76	24
	61+	81	-	-	42	58	46	54	59	41
RESTRICTION										
Definite										
	21-30	17	6	94	-	-	100	-	100	-
	31-40	23	-	39	57	4	100	-	96	4
	41-50	29	-	17	83	-	72	28	86	14
	51-60	33	-	12	52	36	61	39	70	30
	61+	17	-	-	41	59	53	47	88	12
Dominant										
	21-30	3	67	33	-	-	100	-	100	-
	31-40	3	-	-	100	-	100	-	100	-
	41-50	3	-	-	100	-	100	-	100	-
	51-60	11	-	9	73	18	91	9	91	9
	61+	3	-	-	33	67	67	33	67	33
OBSTRUCTION										
Definite										
	21-30	8	-	88	12	-	100	-	100	-
	31-40	9	-	22	78	-	78	22	89	11
	41-50	35	-	11	83	6	74	26	86	14
	51-60	52	-	4	67	29	63	37	73	27
	61+	49	-	2	33	65	35	65	53	47
Dominant										
	21-30	-	-	-	-	-	-	-	-	-
	31-40	1	-	100	-	-	100	-	100	-
	41-50	6	-	-	83	17	33	67	67	33
	51-60	13	-	8	46	46	31	69	62	38
	61+	10	-	-	50	50	50	50	50	50

TABLE III-11 - PREVALENCE % OF SMOKERS IN EACH PULMONARY FUNCTION PROFILE BY DECADE.

PULMONARY FUNCTION PROFILES	DECADES yrs	No. Subj.	SMOKERS					EX-SMOKERS			
			0	1-10	11-20	21+	Total	1-10	11-20	21+	Total
NORMAL	21-30	54	15	4	28	53	85	2	2	7	11
	31-40	93	16	7	22	55	84	1	2	6	9
	41-50	102	9	6	18	67	91	2	1	6	9
	51-60	87	6	10	23	61	94	2	2	9	13
	61+	71	14	14	21	51	86	8	3	15	26
	Total	407	12	8	22	58	88	3	2	9	14
UNDIFFER.	21-30	28	25	4	14	57	75	-	-	-	-
	31-40	45	9	7	15	69	91	-	2	9	11
	41-50	59	8	12	24	56	92	3	2	10	15
	51-60	72	4	8	25	63	96	1	-	18	19
	61+	82	5	16	24	55	95	-	4	7	11
	Total	286	8	10	22	59	92	1	2	10	13
RESTRICTION											
Definite	21-30	17	24	24	4	47	76	-	-	18	18
	31-40	23	26	9	17	48	74	-	4	13	17
	41-50	29	7	14	28	51	93	3	3	14	20
	51-60	33	24	6	21	48	76	3	3	18	24
	61+	18	22	6	33	39	78	-	6	6	12
	Total	120	20	11	22	48	80	2	3	14	19
Dominant	21-30	3	33	33	-	34	100	-	-	-	-
	31-40	3	-	33	-	67	100	33	-	-	33
	41-50	2	-	50	-	50	100	-	-	-	-
	51-60	11	18	10	36	36	82	-	18	10	28
	61+	3	67	-	-	33	33	-	-	-	-
	Total	22	23	18	18	41	77	5	9	5	19
OBSTRUCTION											
Definite	21-30	7	14	-	14	72	86	-	-	-	-
	31-40	9	-	-	-	100	100	-	-	-	-
	41-50	35	-	3	26	71	100	-	-	6	6
	51-60	52	10	2	12	76	90	-	-	8	8
	61+	46	-	9	26	65	100	2	-	13	15
	Total	149	4	4	19	73	96	1	-	8	9
Dominant	21-30	-	-	-	-	-	-	-	-	-	-
	31-40	1	-	-	-	100	100	-	-	-	-
	41-50	5	-	20	20	60	100	20	-	20	40
	51-60	12	8	8	17	67	92	-	-	17	17
	61+	9	11	-	22	67	89	-	-	22	22
	Total	27	7	7	19	67	93	4	-	19	23
TOTAL		1011	11	9	21	59	89	2	2	10	14

TABLE III - 12 - ASSOCIATIONS BETWEEN ATMOSPHERIC POLLUTION (DUST, CIGARETTES) AND BIOLOGICAL PARAMETERS OF HEALTH (PULMONARY FUNCTION, X-RAYS AND SYMPTOMS)
SUBJECTS GROUPED BY DECADES

DECADES yrs	DUST II d.y.	CIG. /DAY	SUBJ. No	NORMAL								UNDIFFERENTIATED								RESTRICTIVE																OBSTRUCTIVE															
																				DEFINITE								DOMINANT								DEFINITE								DOMINANT							
					X-RAYS			SYMPTOMS					X-RAYS			SYMPTOMS					X-RAYS			SYMPTOMS					X-RAYS			SYMPTOMS					X-RAYS			SYMPTOMS					X-RAYS			SYMPTOMS			
				No	SIO	PC	SIO &PC	C	P	CP	Br	No	SIO	PC	SIO &PC	C	P	CP	Br	No	SIO	PC	SIO &PC	C	P	CP	Br	No	SIO	PC	SIO &PC	C	P	CP	Br	No	SIO	PC	SIO &PC	C	P	CP	Br	No	SIO	PC	SIO &PC	C	P	CP	Br
21-30	-200	0	20	8				1	3	1		8				3	3	2		3								-								1								-							
		1-10	10	3								2								4				2	1	1	1	1								-								-							
		11-20	29	19				6	6	3	1	7		2		6	4	3	2	2				1	1			-								1								-							
		21+	49	24				12	13	10	2	12				8	5	4	2	8				3	1			-								5				4	2	2	1	-							
	200+	0	-																																																
		1-10	-																																																
		11-20	-																																																
		21+	-																																																
31-40	-200	0	25	15		1		2	3	1	1	4								6		1		1	2	1		-								-								-							
		1-10	15	8		2			2			4		1		2				2								1					1			-								-							
		11-20	42	24	2	3		9	13	8	2	11		1		6	6	6	2	5		1		2	4	2		1								1				1	1	1		-							
		21+	86	41	1	2		21	19	16	5	27	1	2		14	12	9	1	10				3	5	1	1	-								7		1		6	2	2	1	1					1		
	200+	0	-	-								-								-								-								-								-							
		1-10	1	1		1						-								-								-								-								-							
		11-20	3	2	1			2	2	2		-								-								-								1								-							
		21+	2	2				1	1	1		-								-								-								-								-							
41-50	-200	0	15	8					1			5		1		2	2	2	2	2				1				-								-								-							
		1-10	26	6		1		2	1	1	2	13	2	2		2	4	2		3				1	2	1	1	1								3			2	3	2	2	2	-							
		11-20	55	25	1	3		13	10	8	2	14	2	1		8	5	3	4	9		1		3	3	1	2	-								6		1		6	4	4	2	1				1	1	1	1
		21+	103	48	3	5	2	31	21	19	8	24		2	2	12	9	8	5	11	1			5	4	4	2	-								19		3		18	12	12	5	1				1	1	1	
	200+	0	1	1							1	-								-								-								-								-							
		1-10	3	2					1			-								1								-								-								-							
		11-20	10	3				3	3	2		1	1			1				2					1		1	-								3				1	1	1		1		1		1			
		21+	16	8		2		6	3	5	1	4			1	2	2	2		1				1				-								2		1		2	2	2	1	1				1			
51-60	-200	0	21	4		1		2	2	2	1	2		2		1	1			7		1	1		1			2				1	1	1		6		2		2	3		2	-							
		1-10	23	11	1	2	1	6	3	3	1	5		2	1	2	2	2	2	3		1						1								2	1			1	1	1	1	1		1					1
		11-20	50	14	1	3		7	5	4	3	21	1	5	1	14	9	8	4	4	1			1	2	1	1	3					1			7		1		6	2	2	2	1	1			1			
		21+	109	38		9	1	26	20	18	6	31	6	4	2	10	11	6	7	8				4	2	1	1	2				1	1	1	1	24	3	8		16	12	11	6	6		1		4	3	2	1
	200+	0	3	-								2		1		1	1	1		1			1	1	1	1		-								-								-							
		1-10	9	6		1	1	5	3	2	2	1							1	2	1				1			-								-								-							
		11-20	21	6				4	5	4	3	6		1		4	2	2	2	1				1	1	1		1				1	1	1	1	6		2		4	3	3	2	1				1	1	1	
		21+	32	9		1	1	7	6	5	4	9	3		1	7	7	6		7			1	5	5	3	3	-								6		1	1	4	2	1	4	1		1		1	1	1	1
61+	-200	0	15	7		2		3	3	2	4	2	1			1	1	1	1	3								1							1	1	1							1							
		1-10	18	9		1	1	3	4	1	1	7		1	2	6	2	2	1	1			1	1				-								1			1	1	1	1	1	-							
		11-20	44	16		3	1	9	10	7	2	16	2	4	1	12	11	8	6	5		1		2	2	2	2	-								7				4	3	4	3	-							
		21+	70	23	1	9	3	14	14	13	7	26	2	4	1	16	9	7	7	6	1	2		4	3	3	1	-								13	1	1	1	10	10	9	7	2		1	1	2	2	2	
	200+	0	7	3		1		1	1	1		2				1	1	1	2	1	1							1							1	-								-							
		1-10	15	3		2	1	1			1	10	3	2	2	9	8	8	5	-								-								1				1	1	1		1	1						
		11-20	25	5		2		3	2	2	2	8	2	4	2	7	5	5	2	-								1				1	1	1		8		1	1	7	7	7	4	3		2		1			
		21+	33	7	1	1		6	4	4	4	12	1	4	3	6	4	3	5	1				1	1	1	1	-								11	1	2	5	5	5	4	3	2			2	2	2	2	2