

INCREMENTAL EXERCISE TESTING IN PLEUROPULMONARY DISEASE DUE TO INHALATION OF INORGANIC DUSTS: PHYSIOLOGIC DEAD SPACE AS THE MOST SENSITIVE INDICATOR

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INTRODUCTION

Evaluation of dyspnea, and of respiratory impairment and disability, is of great social and economic importance, let alone physiologic and clinical interest, in patients thought to have pulmonary and/or pleural fibrosis secondary to inhalation of inorganic dusts.¹⁻⁷ The relationship of abnormalities on exercise to those in standard pulmonary function tests (performed at rest) is controversial. Cotes² has recently concluded that "loss of exercise capacity cannot be predicted with acceptable accuracy from the 4 commonly used lung function indices (FVC, FEV₁, FEV₁/FVC, D_LCO_{SB}) alone or in combination."

We have correlated FVC and D_LCO_{SB} (henceforth further abbreviated as D_L) with a number of exercise variables (both invasive and non-invasive) in 43 patients undergoing maximal incremental exercise to evaluate likely pulmonary and/or pleural fibrosis due to inhalation of inorganic dusts (in 35 patients, the dust was asbestos). Our results indicate that an abnormal D_L predicts excessive dead space ventilation often present at rest, and conversely, that this abnormality of gas exchange is frequently present even when D_L is normal.

METHODS

Standard pulmonary function tests were performed according to the recommendations of the American Thoracic Society.^{8,9} Predicted values for spirometry were modified¹⁰ from an earlier publication of Morris¹¹ and for D_L CO_{SB} and TLC_{SB} were those separately established by this laboratory¹² for current smokers, ex-smokers and nonsmokers.

Incremental exercise testing was performed using a model 2000 Medical Graphics, Inc., breath-by-breath system which employs a pneumotachygraph to obtain expiratory flows and volumes, an infra-red CO₂ analyzer, and a zirconium fuel cell O₂ analyzer. Exercise was performed on a bicycle ergometer which increments 5 to 25 watts per minute. The patient sat quietly on the bicycle while adjusting to the nose clip, mouthpiece, ear oximeter (Hewlett-Packard model 47201 A), electrocardiographic leads and radial artery catheter. Measurements were then made sitting, during unloaded cycling, during incremental cycling and several

times following exercise. Exercise was terminated when the patient was unable to continue (usually limited by dyspnea) or if there were untoward changes in the electrocardiogram, blood pressure or O₂ saturation.

A microprocessor collected flow, F_ECO₂, and F_EO₂ data and computed O₂ consumption and CO₂ production for each breath. A separate computer (TEKTRONIX 4052 A) stored, analyzed and displayed data. Primary measurements included tidal volume, respiratory frequency, inspired and expired O₂ and CO₂ concentrations and heart rate (HR). These allow immediate calculation of such parameters as minute ventilation ($\dot{V}_E$), O₂ consumption ($\dot{V}O_2$), CO₂ production ($\dot{V}CO_2$), respiratory equivalent (R; $\dot{V}CO_2/\dot{V}O_2$), $\dot{V}_E/\dot{V}CO_2$, $\dot{V}_E/\dot{V}O_2$, O₂ pulse ($\dot{V}O_2/HR$) etc. Arterial blood was blood sampled every one to two minutes. Samples were stored in ice and analyzed immediately after the test on a Radiometer model ABL30. Entry of these results permits the system to calculate and print values for dead space ventilation (as a percentage of tidal volume, V_D/V_T) and alveolar-arterial differences for PO₂ (A-aDO₂) during all phases of the test.

Ventilatory response was evaluated as the slope of $\dot{V}_E$ vs. $\dot{V}O_2$ before ventilatory anaerobic threshold is reached; excessive values are ≥ 30 .¹³ Limit values for other tests are: FVC < 80% of predicted, FEV₁/FVC < 0.70 up to age 59 years and < 0.65 beyond age 59, D_L < 75% of predicted, $V_D/V_T \geq 0.35$ at rest and ≥ 0.25 on exercise ($\dot{V}O_2$ 1.0L)¹⁴ and A-a DO₂ 35 Torr during exercise.⁴

RESULTS

Of the 43 patients tested, 35 were studied because of occupational exposure to asbestos; several of these had normal chest radiographs and one-third had only pleural thickening. Of the remaining 8 patients, 6 were occupationally exposed to hard metal (half had normal chest radiographs) and 2 to beryllium (both had abnormal radiographs). D_L was not available on 4 patients. Dyspnea was equivocal in 9 patients, present in 29 and absent in 5. Because of the small number of patients without dyspnea, correlation with physiologic variables was not possible. It was noted that the 5 patients who did not complain of dyspnea had normal D_L (vs. 14 of the 26 with dyspnea) and 4 of the 5 had normal ventilatory responses (vs. 18 of 27 with dyspnea).

Mean values of the most important pulmonary function tests (FVC, D_L) and exercise variables ($\dot{V}E$ at $\dot{V}O_2$ 1.0L, V_D/V_T at $\dot{V}O_2$ 1.0L) and of V_D/V_T at rest are shown in Table I.

Table I

Mean Values of Pulmonary Function and Exercise Tests

Variable	Mean	SD
FVC (% pred)	80.2	18.2
D_L (% pred)	80.7	24.9
$\dot{V}E$ 1.0L (L/min)	30.2	9.73
V_D/V_T Rest ($\times 100$)	35.9	8.6
V_D/V_T 1.0L ($\times 100$)	28.8	9.9

Prevalence of Abnormal Test Results (Table II)

Of the patients studied, 18 (of 43) had a reduced FVC (42%), 15 (of 39) a reduced D_L (38%), 10 (of 41) increased ventilatory responses (24%) and 8 (of 41) an elevated A-a DO_2 (20%). The highest prevalence of abnormality was for V_D/V_T at rest and/or exercise (measured at a $\dot{V}O_2$ of 1.0L): 31 of 43 patients (72%). Of these 31, 19 were abnormal under both conditions, 5 at exercise only and 7 at rest only (4 of these did not have exercise values or did not reach a $\dot{V}O_2$ of 1.0L). Hence, 24 of 39 patients (62%) showed abnormal V_D/V_T at exercise and 26 of 43 (60%) did so at rest.

Correlations with D_L (Table III)

Of the 39 patients with D_L , 15 had abnormal values for this test (as stated above):

D_L (percent predicted) showed a moderate correlation with FVC ($r=0.315$, $P 0.05$) (Table III). Comparison of abnormal results for the two tests is shown in Table IV. 15 patients had abnormal values for FVC; 8 were abnormal for both tests, 17 normal for both, 7 abnormal only for D_L and 7 abnormal only for FVC.

D_L (percent predicted) correlated with V_D/V_T at rest ($r=-0.274$, $p < 0.1$) and more strongly on exercise ($r=-0.554$, $p 0.0005$) (Table III). Comparison of abnormal results for D_L and for V_D/V_T is shown in Table V. 27 patients had abnormal values for V_D/V_T ; 13 were abnormal for both, 10 normal for both, 14 abnormal for V_D/V_T alone and 2 abnormal for D_L alone. Thus, of the 15 patients with abnormal D_L , 13 (87%) had abnormal V_D/V_T yet 14 of the 24 (58%) with normal D_L still had abnormal V_D/V_T .

Only 8 patients had abnormal A-a DO_2 (Table VI); 6 were abnormal for both tests, 22 normal for both, 2 abnormal for A-a DO_2 alone and 8 abnormal for D_L alone. Of the 8 patients with abnormal A-a DO_2 , only 2 had a normal D_L .

Only 9 of the 39 patients had abnormal $\Delta \dot{V}E / \Delta \dot{V}O_2$ (Table VII); 5 of the 9 had abnormal D_L .

Correlations with FVC (Table III)

FVC (percent predicted) correlated with V_D/V_T both at rest ($r=-0.359$, $p 0.02$) and on exercise ($r=-0.436$, $p < 0.006$).

Correlations with Exercise $\dot{V}E$ (Table III)

Exercise $\dot{V}E$ (at a $\dot{V}O_2$ of 1.0 L² showed a weak correlation

Table II

Frequencies of Abnormal Test Results in 43 Patients with Suspect Pleuropulmonary Disease Due to Inorganic Dusts

FVC	42%	(18/43)
(FVC	38%)	(15/39)
D_L	38%	(15/39)
$\dot{V}O_2$ peak $< 75\%$ pred	28%	(12/43)
$\Delta \dot{V}E / \Delta \dot{V}O_2$	24%	(10/41)
A-a DO_2	20%	(8/41)
Resp. Rate > 50 /min		0
Resp. Rate > 40 /min	21%	(9/43)
V_D/V_T :		
Rest and/or 1.0L	72%	(31/43)
Rest	60%	(26/43)
1.0L	62%	(24/39)

Table III
Pearson Correlation Coefficients for Pulmonary Function and Exercise Tests

	$\dot{V}E$	FVC	D_L	V_D/V_T Rest	V_D/V_T 1.0L
$\dot{V}E$ 1.0L	1.00000	-0.22962	-0.41311*	0.38629*	0.48455*
FVC	-0.22962	1.00000	0.31537*	-0.36191*	-0.44035*
D_L	-0.41311*	0.31537*	1.00000	-0.27351	-0.55392*
V_D/V_T Rest	0.38629*	-0.36191*	-0.27351	1.00000	0.66262*
V_D/V_T 1.0L	0.48455*	-0.44035*	-0.55392*	0.66262	1.00000

* $p \leq 0.05$

Table IV
FVC vs. D_LCO_{SB}

	Abnormal FVC (15)	Normal FVC (24)
Abnormal D_L (15)	8	7
Normal D_L (24)	7	17
No D_L (4)	3	1

with FVC ($r = -0.230$, p 0.15), a strong correlation with D_L ($r = -0.413$, p 0.009) and strong correlations with V_D/V_T both at rest ($r = 0.386$, p 0.0115) and even more so on exercise ($r = 0.485$, p 0.0021).

$\dot{V}O_2$ Max

Of the 43 patients, 31 (72%) were able to reach a peak $\dot{V}O_2 \geq 75\%$ of predicted. The 12 who were not able were more likely to manifest other abnormalities, e.g.; 10 had abnormal V_D/V_T (vs. 20 of the 31 with normal $\dot{V}O_2$ max) and 8 had abnormal FVC (vs. 7 of the 31 with normal $\dot{V}O_2$ max). Of the 10 with decreased $\dot{V}O_2$ max who performed D_L , 6 had abnormal D_L (vs. 9 of the 29 with normal $\dot{V}O_2$ max). Nevertheless, 12 of the 18 patients with abnormal V_D/V_T

both at rest and on exercise were able to achieve a $\dot{V}O_2$ max $\geq 75\%$ of predicted.

Respiratory Pattern

No patient reached a respiratory rate > 50 min; 9 (21%) reached a rate between 41 and 50. Nine patients achieved a V_T/VC ratio ≥ 0.70 ; 6 of these 9 had normal FVC. The 2 patients whose V_T/VC exceeded 0.80 both had reduced FVC.

DISCUSSION AND CONCLUSIONS

Our goals were to assess (1) "invasive" variables requiring sampling of arterial blood and (2) the responses to incremental exercise both non-invasive ($\dot{V}E$, $\Delta \dot{V}E / \Delta \dot{V}O_2$, respira-

Table V
 V_D/V_T vs. D_LCO_{SB}

	Abnormal V_D/V_T (31)		Normal V_D/V_T at rest and at $\dot{V}O_2 = 1.0L$ (12)	
	At rest and at $\dot{V}O_2 = 1.0L$ (19)	At rest only* (7)	At $\dot{V}O_2 = 1.0L$ only (5)	
Abnormal D_L (15)	10	1	2	2
Normal D_L (24)	8	3	3	10
No D_L (4)	1	3	0	0

* Includes inability to reach $\dot{V}O_2 = 1.0L$ or no sample obtained.

Table VI
A-a DO_2 vs. D_LCO_{SB}

	Abnormal A-a DO_2 (8)	Normal A-a DO_2 (33)
Abnormal D_L (14)	6	8
Normal D_L (24)	2	22
No D_L (3)	0	3

tory rate and tidal volume) and invasive (V_D/V_T , A-a DO_2) compared with standard pulmonary function tests (FVC, D_L). Our patients demonstrated the full spectrum of disease from radiographically inapparent to minimal (1/0 irregular opacities and/or pleural thickening) to advanced diffuse pulmonary fibrosis. Most complained of dyspnea.

V_D/V_T was the most sensitive indicator of abnormality, being increased in 31 of 43 patients (72%), many of whom had normal FVC and/or D_L . The most useful comparison was with D_L ; 13 of the 15 patients with abnormal D_L had abnormal V_D/V_T . It may, therefore, be said that a decreased D_L predicts abnormal V_D/V_T and that measuring the latter

is then not required to detect disease. However, more than half the patients (58% or 14 of 24) with normal D_L still had abnormal V_D/V_T .

FVC was as likely to be abnormal as D_L (each was decreased in 15 of 39 patients who had both tests, or 38%). Abnormality of one was not very likely to predict abnormality of the other; roughly half the patients with an abnormal FVC had a normal D_L and vice-versa.

A-a DO_2 and ventilatory response during exercise were least likely to be abnormal (in 20% and 24%, respectively). Widening of the A-a DO_2 was associated with an abnormal D_L . No patient demonstrated a respiratory rate $> 50/\text{min}$.

Table VII
 $\Delta \dot{V}_E / \Delta \dot{V}O_2$ vs. D_L

	Abnormal $\dot{V}_E / \dot{V}O_2$ (10)	Normal $\Delta \dot{V}_E / \Delta \dot{V}O_2$ (31)
Abnormal D_L (15)	5	10
Normal D_L (24)	4	20
No D_L (2)	1	1

About three-quarters of the patients reached a $\dot{V}O_2 \geq 75\%$ of predicted maximum, demonstrating their motivation to perform. Many patients with manifest abnormalities achieved this level of work, e.g., two-thirds (12 of 18) of those with abnormal V_D/V_T both at rest and on exercise.

Of the 31 patients with abnormal V_D/V_T at rest or exercise, this was manifest in the majority (26 patients or 84%) at rest. It may thus be inferred that exercise is not usually necessary to demonstrate this derangement of gas exchange.

$\dot{V}_E$ at an exercise level corresponding to a $\dot{V}O_2$ of 1.0L/min has been advocated as a useful non-invasive measurement which additionally does not require maximal effort.² It was strongly correlated with D_L and with V_D/V_T both at rest and even more so at (the same level) exercise. An important consideration is whether anaerobic threshold (AT) has been reached before this level of exercise, which would increase $\dot{V}_E$ non-linearly; almost all our patients had a normal AT, beyond a $\dot{V}O_2$ of 1.0L.

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ROLE OF EXERCISE TESTS IN THE FUNCTIONAL EVALUATION OF SILICOTIC PATIENTS

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INTRODUCTION

Evaluation of labor capacity is frequently requested for patients with pneumoconioses. Spirometry and chest X-rays usually utilized in the diagnosis, have not been regarded as good predictors of pulmonary disability; and have poor correlation with the respiratory symptoms.^{3,8,9}

Among the methods utilized in the functional evaluation of pneumoconioses, the exercise tests have emerged as useful, for evaluating the cardiorespiratory abnormalities, not present at rest.^{1,2}

Although the exercise tests have been frequently utilized in the differential diagnosis of dyspnea,^{4,10,12,13} in occupational medicine, the studies are scattered and utilized diverse methodology, making difficult the comparison of the results.^{6,7,11}

Objectives

In this study, our purpose was to establish the role of the cardiorespiratory, metabolic and gas exchange analysis during exercise, in evaluating ceramic workers with the diagnosis of silicosis; and to correlate these findings with the degree of dyspnea, the radiological alterations and the pulmonary function tests at rest.

METHODS

Casualistic

We have studied forty three ceramic workers with the diagnosis of silicosis based on the occupational history of silica dust exposure and on the radiographic features. They were separated in three groups, based in the ILO Classification, 1980 (Table I).⁵

The characteristics of the patients, the silica dust and the smoking exposure were not significantly different when compared to the three groups. However, group III subjects, were older than the ones of Group I.

Protocol

The patients were first submitted to a clinical evaluation and thereafter tested for spirometry, flow-volume curves and arterial blood gases at rest.

Secondly, they went to an incremental exercise test on a cycloergometer to the maximum tolerance, for cardiovascular, ventilatory and metabolic evaluation (n = 40).

Finally, after 30 min. of resting, the patients were submitted to a submaximal test corresponding to 50% of the maximum tolerance, for the analysis of the cardiorespiratory and metabolic responses and the arterial blood gases.

Table I
Classification of the Silicotic Patients, According to the ILO Classification, 1980⁵

GROUP	OPACITIES/PROFUSION	n
I	Small Opac. (up to 3mm) 1/0 to 1/2	21
II	Small Opac. (up to 3mm) 2/1 to 3/3	13
III	Large opac. (A, B or C)	9

RESULTS AND COMMENTS

Dyspnea was the most frequent symptom, being reported by 26 (61%) of the patients, with similar distribution and intensity in the three groups (Figure 1). Cough, sputum production and bronchospasm, also had similar incidence among the patients.

The spirometry was altered in 14 subjects (33%), also with similar distribution in the groups I, II and III. There was no predominant pattern of respiratory impairment (obstructive or restrictive) and most patients had slight to moderate abnormalities (Figures 2 and 3).

In the analysis of flow-volume curves ($n = 41$), the $\dot{V}_{\max}$ 25% was the only variable that distinguished Group III from the other groups, being altered in 52% of subjects in Group I, 42% in Group II and 88% in Group III (Table III).

In the incremental exercise tests ($n = 40$), the patients of Group III had lower $\dot{V}O_{2\max}$ compared to Group I and II ($p < 0.05$ —Gr. I vs. Gr. III) (Table IV). The symptoms reported at the interruption of exercise were mostly dyspnea and leg pain, with similar distribution and intensity in the three groups. A value of $\dot{V}O_{2\max} < 70\%$ Pred., indicating some degree of functional limitation was found in 14 patients, however with different distribution in the three groups: 3 of them were from Group I (16%), 4 from Group II (31%) and 7 (88%) were from Group III ($p < 0.05$ —Group I + III vs. Group III) (Figure 4). This indicates an association between the more severe X-ray alterations and the lower working tolerance. However there were subjects of Group I, with reduced exercise capacity and conversely, subjects of Group III with normal exercise capacity (Figure 4).

No correlations were found between the exercise capacity

Table II
Characteristics of the Silicotic Patients

$\bar{X}$		AGE	Wt	Ht	Silica Dust	Smoking	
GR.	n	(yrs)	(kg)	(cm)	Exposition (yrs)	%	Pack/years
I	21	39.3	72.8	169	18.2	53	16.0
II	13	42.4	73.9	170	21.1	61	18.5
III	9	51.1*	65.4	165	22.6	33	29.0

* $p < 0.05$ - Gr. III > Gr. I. Kruskal-Wallis analysis of variance, and Dunn contrast test.

‡: percent of smokers in each group.

Table III
Flow-Volume Curve Variables in Silicotic Patients of the Three Groups

$\bar{X}$		$\dot{V}_{\max}$		$\dot{V}_{\max}$ 50%		$\dot{V}_{\max}$ 25%	
GR.	n	l/seg % Pred		l/seg % Pred		l/seg* % Pred*	
I	21	7.26	88	3.79	67	1.81	65
II	12	8.09	95	4.29	75	1.83	64
III	8	5.51	71	2.47	46	0.99	33

* $p < 0.05$ - I > III, II > III (l/seg); I > III (% Prev.)
Kruskal-Wallis analysis of variance, and Dunn contrast test.

Table IV
Maximal Exercise Test Variables, Obtained in the Patients of the Three Groups

GROUP	n	WORK LOAD* (watts)	$\dot{V}O_2\text{max}$ § (l/min)	% Pred §	FCmax bpm	% Pred
I	19	191	2.32	86.5	150	83
II	13	189	2.35	89.2	149	82
III	8	103	1.24	55.1	128	75

p < 0.05 - *Gr. I and II > III; § Gr. I > III. Kruskal-Wallis analysis of variance and Dunn contrast test.

of the patients and the clinical symptoms or the pulmonary function tests at rest.

The arterial blood gases at rest and during exercise were similar to the three groups; and the percentual frequency of hypoxemia and of decrease in PaO_2 < 5 mmHg (rest-exercise) was not significantly different when compared to the groups I, II and III. As the pulmonary function tests, the analysis of blood gases at rest and during exercise did not correlate with the exercise tolerance and the radiological changes of the patients (Figure 5).

Summarizing, the evaluation of the silicotic patients during an exercise test, revealed a certain number of incorrect prediction of working capacity, based on the resting data.

We concluded that the functional analysis during exercise can complete or modify the clinical, radiological and pulmonary function test analysis, in evaluating the impairment of patients with pneumoconioses.

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TIME DOMAIN SPIROGRAM INDICES OF SILICA EXPOSED WORKERS

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ABSTRACT

Time domain spirogram indices had been shown to be sensitive indicators of small airway function. The aim of this study is to assess the small airway function of 110 silica-exposed workers using these indices.

The workers were subdivided into high, moderate and low exposure groups, based on their occupational history. Their spiograms were digitized electronically and conventional indices as well as time domain indices (MTT—mean transit time, COVTT—coefficient of variation of transit time and IOSTT—index of skewness of transit time) were derived.

With adjustment for age, height and smoking status the FEV₁ and FVC did not differ significantly among the groups whereas all the time domain indices showed significant differences. FEF_{75%} and FEF_{75-85%} were also significantly lower in the high exposure group although the difference in FEF_{75%} in the moderate and high exposure groups was not statistically significant.

Separate analysis was performed for smokers and non-smokers, while excluding all those with FEV₁/FVC ratio of less than 0.75. Similar trend of greater small airways obstruction in the higher exposure groups was also seen. The most significant differences were seen with time domain indices, FEF_{75-85%} and FEF_{75%}.

This preliminary study supports the presence of small airway dysfunction among silica exposed workers. Furthermore, time domain spirogram indices appear to be more sensitive to small airway dysfunction.

INTRODUCTION

Airway resistance of the lungs can be partitioned into central and peripheral components. The peripheral component is composed of the resistance from airways of less than 2mm in internal diameter down to the gas exchange areas. This region is commonly termed as the small airways. Since small airways resistance contribute only 10–15% of total airway resistance, it is possible for a subject to have significant diffuse obstruction in the small airways while the total airway resistance are essentially normal.^{1,2} In normal individuals, maximum expiratory flow at large lung volumes like the peak flow and the forced expiratory volume in one second (FEV₁), depend mainly on flow in the larger airways whereas maximum flow at small lung volumes reflect predominantly the function of small airways.^{3,4,5}

Several spirometric indices especially flow rates at low lung volumes may reflect the status of small airways. These would include forced expiratory flow at 50% and 75% of forced vital capacity (FEF_{50%} and FEF_{75%}), forced expiratory flow between 25 and 75%, 75 and 85% of forced vital capacity (FEF_{25-75%}, FEF_{75-85%}).⁶⁻⁸ Time domain indices by using moments analysis of the volume time spirogram have also been shown to be sensitive indicators of small airways obstruction.^{4,9-15}

The mean transit time (MTT) is an index of the average rate of emptying of the vital capacity. It is influenced by all parts of the spirogram. Mathematically, this is the first moment about the origin (see appendix 1). The coefficient of variation of transit times (CoVTT), represents the amount of variation between the initial and the terminal slower portion of the VC. It is derived from the second moment about the mean. The index of skewness of transit times (IoSTT), is a measure of the 'slow finish' at the terminal end of the expiration. This is derived from the third moment about the mean. Some workers analyzed moments about the origin rather than moments about the mean.^{9-11,16} As an index of dispersion, these authors used the moment ratio (MR).

There had been few studies utilizing time domain indices to assess the small airways function of dust exposed workers. In this study we have applied the various spirometric indices as well as time domain indices on a group of granite quarry workers to evaluate their small airways function in relation to their dust exposure.

METHODS

Subjects

The volume-time spiograms of 132 currently employed granite quarry workers were selected. Each spirogram had

at least 3 satisfactory tracings. The tracing with the highest FVC was digitized using an electronic digitizer. The digitized data is stored into a micro-computer and volume-time as well as flow-volume curves are plotted on the computer screen for visual checking. Flow was calculated by least square regression using pairs of volume-time data in an interval of 0.05 seconds on either side of a given time point. This method of digitizing volume-time tracings had been shown to be an accurate and useful way of deriving volume-time and flow-volume indices from volume-time tracings.^{17,18} Early termination increases the error in indices at low lung volumes.⁶ Early truncation increases the variability of time domain indices.^{16,19} Hence only spiograms that had a flow rate of less than 0.05 l/s in the last 0.5 s were selected for further analysis.²⁰ Of the 132 spiograms, only 110 satisfy the above criteria. The FEV₁, FVC, FEF_{50%}, FEF_{75%}, FEF_{25-75%}, FEF_{75-85%}, MTT, CoVTT, IoSTT and MR were calculated.

Detailed information including age, height measurement, smoking habits and a lifetime history of occupational exposure to dust were recorded for each worker. The 110 workers were divided into three dust exposure groups based on occupational history and environmental assessment of personal dust exposure by job categories. The average quartz content in the respirable dust was 28%. The low exposure group comprised those who were in the administrative section all of their working life. The moderate exposure group consists of transport and maintenance workers. The high exposure group were those who were past or current drillers and crusher workers for most years of their working life. Recent full-sized chest radiographs taken of each worker had been read independently by three experienced readers according to the International Labour Organization Standard Classification of Radiographs of Pneumoconiosis. None of the 110 workers had radiological films with profusion of small opacities greater than 1/0.

Statistics

The data was processed on an IBM 3033 mainframe computer using statistical procedures from Statistical Analysis System (SAS). Adjustment for group differences in age, height and smoking was done using analysis of co-variance and separate analysis for smokers and non-smokers.

RESULTS

Description of Study Population

There were 50 non-smokers and 60 smokers in the study population. Non-smokers were younger (41.0 compared with 47.6 years for smokers). The mean height were similar (1.66 m for non-smokers and 1.64 m for smokers). 15 (25%) of the smokers have a FEV₁/FVC ratio of less than 0.75 whereas all the non-smokers have a ratio of greater than 0.75.

The mean age, height, duration of exposure as well as the proportion of smokers in the three exposure groups are significantly different (Table I). The high exposure group had the longest duration of employment while the low exposure group had the shortest. The high exposure group can therefore be expected to have the greatest dose of dust and the low exposure group, the lowest dose. Age and duration of employment was highly correlated ($r=0.78$ for non-smokers, $r=0.67$ for smokers).

Lung Function

With adjustment for age, height and smoking status the FEV₁ and FVC did not differ significantly among the groups whereas all the time domain indices showed significant differences (Table II). FEF_{75%} and FEF_{75-85%} were also significantly lower in the high exposure group although the difference in FEF_{75%} between the moderate and high exposure groups was not statistically significant.

Table I
General Characteristics of Study Population

	Exposure			p value
	Low	Moderate	High	
Number	26	39	45	
Age (years)	36.4	44.1	48.7	0.0001
Height (m)	1.67	1.64	1.63	0.0232
Duration of exposure (years)	7.9	13.2	15.9	0.0215
Smokers (%)	27	62	64	< 0.05

Table II
Age, Height and Smoking Status Adjusted Lung Function
Parameters of the Three Exposure Groups*

PARAMETER	EXPOSURE GROUPS			p VALUES		
	L	M	H	L vs M	L vs H	M vs H
FEV1 (l/s)	2.77 (0.08)	2.69 (0.06)	2.65 (0.06)	0.3868	0.2607	0.7078
FVC (l)	3.16 (0.09)	3.23 (0.07)	3.26 (0.07)	0.5359	0.4301	0.8042
FEF _{25-75%} (l/s)	3.40 (0.17)	3.09 (0.13)	2.86 (0.13)	0.1582	0.0188	0.1995
FEF _{75-85%} (l/s)	1.35 (0.08)	0.93 (0.06)	0.75 (0.06)	0.0001	0.0001	0.0283
FEF _{50%} (l/s)	3.98 (0.21)	3.86 (0.16)	3.61 (0.15)	0.6475	0.1722	0.2423
FEF _{75%} (l/s)	1.88 (0.10)	1.35 (0.08)	1.14 (0.07)	0.0001	0.0001	0.0572
MTT (s)	0.51 (0.03)	0.63 (0.02)	0.71 (0.02)	0.0019	0.0001	0.0202
CoVTT	1.00 (0.04)	1.22 (0.03)	1.45 (0.03)	0.0001	0.0001	0.0001
IoSTT	0.88 (0.26)	1.58 (0.20)	3.21 (0.19)	0.0367	0.0001	0.0001
MR	1.42 (0.03)	1.59 (0.02)	1.77 (0.02)	0.0001	0.0001	0.0001

* Adjusted for age, height and smoking status using analysis of covariance

() - standard error of adjusted means

Exposure groups :

L - Low exposure
M - Moderate exposure
H - High exposure

Separate analysis were performed for smokers and non-smokers, while excluding all those with FEV₁/FVC ratio of less than 0.75. Except for FEV₁ and FVC in the low exposure group, all the other parameters showed that the smokers have greater degree of airway obstruction than the

non-smokers (Tables III and IV). Similar trend of greater small airways obstruction in the higher exposure groups was also seen. The most significant differences were seen with time domain indices, FEF_{75-85%} and FEF_{75%}.

Table III
Age and Height Adjusted Lung Function Parameters of the Three Exposure Groups in Non-Smokers

PARAMETER	EXPOSURE GROUPS			P VALUES		
	L	M	H	L vs M	L vs H	M vs H
FEV1 (l/s)	2.81 (0.10)	2.93 (0.10)	2.79 (0.10)	0.4182	0.8522	0.3224
FVC (l)	3.15 (0.12)	3.38 (0.12)	3.32 (0.13)	0.1818	0.3347	0.7421
FEF _{25-75%} (l/s)	3.72 (0.20)	3.57 (0.22)	3.25 (0.22)	0.6301	0.1500	0.3062
FEF _{75-85%} (l/s)	1.49 (0.11)	1.19 (0.12)	0.87 (0.12)	0.0753	0.0007	0.0547
FEF _{50%} (l/s)	4.25 (0.25)	4.34 (0.26)	4.10 (0.27)	0.8192	0.7026	0.5356
FEF _{75%} (l/s)	2.11 (0.13)	1.65 (0.14)	1.28 (0.14)	0.0225	0.0002	0.0733
MTT (s)	0.46 (0.03)	0.56 (0.04)	0.63 (0.03)	0.0519	0.0022	0.1720
CoVTT	0.99 (0.04)	1.16 (0.05)	1.46 (0.05)	0.0135	0.0001	0.0001
IoSTT	0.51 (0.26)	1.15 (0.27)	2.44 (0.27)	0.1009	0.0001	0.0014
MR	1.42 (0.03)	1.54 (0.02)	1.78 (0.02)	0.0164	0.0001	0.0001

* Adjusted for age, height and smoking status using analysis of covariance

() - standard error of adjusted means

Exposure groups :

L - Low exposure

M - Moderate exposure

H - High exposure

Table IV
Age and Height Adjusted Lung Function Parameters of the Three Exposure Groups in Smokers

PARAMETER	EXPOSURE GROUPS			p VALUES		
	L	M	H	L vs M	L vs H	M vs H
FEV1 (l/s)	3.00 (0.12)	2.61 (0.07)	2.74 (0.08)	0.0076	0.0794	0.2213
FVC (l)	3.38 (0.13)	3.15 (0.08)	3.33 (0.08)	0.1318	0.7207	0.1311
FEF _{25-75%} (l/s)	3.47 (0.29)	3.04 (0.17)	2.96 (0.19)	0.2146	0.1563	0.7500
FEF _{75-85%} (l/s)	1.32 (0.13)	0.82 (0.08)	0.74 (0.08)	0.0017	0.0006	0.4923
FEF _{50%} (l/s)	4.22 (0.34)	3.91 (0.20)	3.64 (0.21)	0.4321	0.1658	0.3766
FEF _{75%} (l/s)	1.75 (0.18)	1.23 (0.10)	1.18 (0.11)	0.0161	0.0109	0.7266
MTT (s)	0.48 (0.05)	0.64 (0.03)	0.67 (0.03)	0.0074	0.0018	0.3912
CoVTT	1.04 (0.06)	1.29 (0.04)	1.51 (0.04)	0.0015	0.0001	0.0003
IoSTT	0.68 (0.46)	1.82 (0.27)	3.04 (0.29)	0.0381	0.0001	0.0041
MR	1.45 (0.05)	1.64 (0.03)	1.81 (0.03)	0.0024	0.0001	0.0002

* Adjusted for age, height and smoking status using analysis of covariance

() - standard error of adjusted means

Exposure groups :

L - Low exposure
M - Moderate exposure
H - High exposure

DISCUSSION

A few studies have reported evidence suggestive of small airways obstruction in occupationally exposed groups. In coal worker's pneumoconiosis without evidence of large airway obstruction, frequency dependence of compliance was demonstrated suggestive of small airways obstruction.²¹ Evidence of small airways abnormalities were also seen among asbestos exposed workers^{22,23} as well as mineral dust

exposure²⁴ and hard rock miners.²⁵ Among gold miners, those with silicosis had lower FEF_{25-75%} suggestive of small airways obstruction attributable to silica exposure.²⁶

Our present study suggests that small airway obstruction is present among silica exposed workers in the absence of radiological evidence of silicosis. There was also evidence of a trend of increasing small airways obstruction in higher dust exposure group. Wiles and Faure²⁷ demonstrated an

exposure-effect relationship between dust exposure and FEF_{25-75%}.

Smoking is known to affect both the larger and smaller airways.²⁸ As expected, smokers showed greater evidence of small airways obstruction even after excluding those with evidence of significant airway obstruction (FEV₁/FVC <0.75). The amount of cigarettes smoked (number of sticks per day × number of years smoked) was not significantly different in the three groups. Hence the trend of small airways obstruction in smokers is suggestive of the effect of silica exposure.

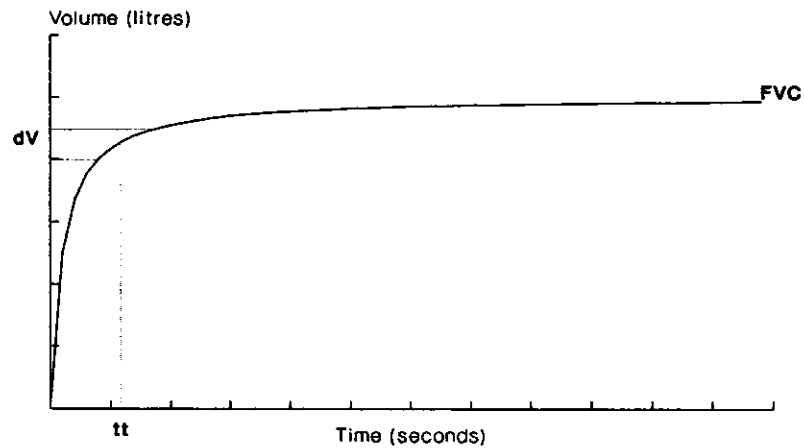
Our study also suggests that time domain indices are more sensitive to small airways obstruction. These indices give greater emphasis to the end of the forced expiratory manoeuvre and are hence more sensitive to events in the small airways.

The clinical and prognostic significance of early airways obstruction is still far from clear. Further studies would be required to evaluate its predictive value in identifying workers who will progress on to clinical airflow obstruction.

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APPENDIX I



$$M_1 \text{ (MTT)} = \frac{\sum dV \times tt}{FVC}$$

$$M_2 = \frac{\sum (dV \times tt)^2}{FVC}$$

$$MR = M_1/M_2$$

$$SDTT = \left[\frac{\sum (tt - M_1)^2 \times dV}{FVC} \right]^{1/2}$$

$$SKEWTT = \left[\frac{\sum (tt - M_1)^3 \times dV}{FVC} \right]^{1/3}$$

$$CoVTT = SDTT/MTT$$

$$IoSTT = SKEWTT/(SDTT)^{3/2}$$

M_n : N^{th} moment about the origin

SDTT : Standard deviation of transit times

SKEWTT : Skewness of transit times

LUNG FUNCTION IN SILICA EXPOSED WORKERS

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INTRODUCTION

In long term silica-exposed workers, the attribution of changes in lung function to a direct effect of dust exposure or to the development of silicosis has been the subject of considerable debate in the literature and occupational lung conferences. The topic remains to this date a controversial issue, particularly in view of a recent pathological study which documented the presence at autopsy of fibrotic lesions and silicotic nodules in men who had normal pre-mortem chest radiographs.⁷ Also, clinical studies⁴⁻⁶ in silica exposed workers documented on lung lavage that a subclinical quartz-induced alveolitis may be present in silica-exposed workers with normal chest radiograph.

In that regard, we have documented that CT scan does not identify more patients with minimal parenchymal disease, although it images the disease more clearly in several cases with significantly higher CT scan score of disease. Also we have clearly demonstrated that CT scan identifies significantly more coalescence and/or large opacities in 33% of patients who were thought to have simple silicosis on the plain chest radiograph. To further investigate the clinical significance of these CT scan observations, we expanded our studied population to 94 long-term silica-exposed workers who were examined concomitantly by standard clinical, radiographic and pulmonary function tests.

SUBJECTS AND METHODS

Silica Exposed Workers

The 94 workers of this study had worked in either the granite or foundry industries or gold mines of Quebec for an average of 29 ± 3 years (range 14–42 years). Ninety percent were either current or former cigarette smokers and they had smoked on the average 21 ± 5 pack-years. Eighty of the 94 were granite workers, 10 were foundry workers and 4 were gold miners.

Pulmonary Function Tests

The lung volumes, pressure-volume curves, flow-volume curves and diffusing capacities were measured according to standard methods¹ as previously applied in our laboratory.²

Chest Radiograph

Standard high-kilovoltage posteroanterior, lateral, and oblique films were obtained at maximal inspiration. The radiograph was graded by three observers according to the International Labour Organization (ILO) 1980 classification.⁸

CT Scan of the Thorax

Eighty CT examinations were performed on a General Electric Model 8800 scanner in Sherbrooke (Canadian General Electric, Co., Montréal, Quebec) and 14 were done on a Picker 600 scanner (Picker, New York, N.Y.). For each patient, at least 10 slices of 1-cm thickness were obtained with wide windows, and 10 with narrow windows, for adequate assessment of pulmonary, chest wall, and pleural changes. CT scans were obtained within 48–72 hr of the plain chest film.

Subsets of Workers Based on Diagnostic Criteria and CT Scan

The 94 silica exposed workers were divided into 4 categories on the bases of evidence of silicosis and the findings of CT scan of the thorax. Group 1 consisted of 21 workers who did not meet the diagnostic criteria for silicosis.

Group 2 consisted of 28 workers with simple silicosis on chest radiograph and CT scan of the thorax.

Group 3 consisted of 18 workers with simple silicosis on chest radiograph but with coalescence and/or conglomeration on CT scan of the thorax.

Group 4 consisted of 27 workers with complicated silicosis on chest radiograph and CT scan of the thorax.

Statistical Analysis

All results are expressed as the mean $\pm$ standard error of measurement. The data were tested by the Student t-test or Mann-Whitney U test for differences between groups, by the Wilcoxon matched-pairs signed-rank test for differences between radiologic methods, and by Spearman's correlation procedure when appropriate.^{9,10}

RESULTS

The lung volumes, compliance and change in vital capacity were within normal prediction in group 1. Subjects of group 2 had no significant change in lung volumes but lung compliance was significantly lower than that of group 1. In group 3, the silicotics with coalescence and/or large opacity on CT scan, we found significant reduction in vital capacity, lung compliance and an increased loss of vital capacity/year. The subjects of group 4 had lower total lung capacity, vital capacity, lung compliance and a significantly increased loss of vital capacity per year.

Diffusing capacity was normal in group 1 and decreased

gradually with increased disease severity. This was significant in groups 3 and 4. Exercise gas exchange parameters were also significantly reduced in groups 3 and 4. Group 2, patients with simple silicosis had gas exchange parameters between those without obvious disease, group 1, and patients with conglomerate disease, groups 3 and 4. These changes reached significance level for $\dot{V}_E/O_2$ ratio and exercise $\Delta(A-a)PO_2$.

In workers with radiographic silicosis, group 2, expiratory flow rates were lower than in group 1 and this reduction was more severe in groups 3 and 4, the workers with radiographic and/or CT scan coalescence/conglomeration. The lowest values were in group 4.

DISCUSSION

This study of lung function in long term silica exposed workers documents that the disease severity which is better defined radiographically by CT scan, is also reflected on lung function as restrictive changes. The disease severity also appears to be associated with excessive airflow limitation.

These data document that early coalescence/conglomeration in silicosis as seen often only on CT scan, is associated with worsened lung functions, a finding which strengthens our prior recommendation for the CT scan exam in radiographic simple silicosis.³ These data also support the

concept of a relationship of disease severity, loss of lung function and airflow limitation in silicosis.

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THE VALIDITY OF RADIOLOGICAL AND HISTOLOGICAL FINDINGS IN FORMER ASBESTOS WORKERS WITH LUNG CANCER

Die Validität der Röntgenologie und Histologie bei ehemals asbeststaubgefährdeten Beschäftigten mit Lungenkrebs

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Einleitung und Fragestellung:

Der Nachweis der fibrogenen Asbesteinwirkung als Asbestose der Lunge oder der Pleura ist seit 1943 bzw. 1988 die entscheidende Voraussetzung für die Anerkennung auch der krebserzeugenden Wirkung von Asbest [11,7]. Demnach müssen im Röntgen-Toraxbild eine Strukturvermehrung des Parenchyms von $\geq 1/1$ und/oder bestimmte ausgeprägte Veränderungen an der Pleura ($\geq 2a$) nach der ILO-Klassifikation [1,2,7,12] und/oder im histologischen Präparat des Lungengewebes eine Asbestose bzw. Minimalasbestose [12] für die Anerkennung einer Berufskrankheit in der Bundesrepublik Deutschland vorliegen. Wegen der erst kürzlich vorgenommenen Erweiterung des Begriffes "Asbestose" wurde in der Vergangenheit dem Pleura-Befund weder im Röntgenbild noch im histologischen Präparat genügend Bedeutung beigemessen. Unter dieser Einschränkung wurden Dignität und Validität der diagnostischen Verfahren bei Lungenkrebspatienten nach beruflicher Asbeststaub-Gefährdung untersucht.

Darüber hinaus stellt sich die Frage, insoweit die durch Asbest verursachte Fibrose weiterhin als pathogenetische Bedingung für den Lungenkrebs gelten kann?

Krankengut und Methodik

Es wurden 122 Patienten mit Lungenkrebs nach einer zurückliegenden, jeweils mehrjährigen bekannten Asbestfaserstaub-Gefährdung am Arbeitsplatz untersucht. Daz konnten u.a. das Alter bei Eintritt in die Gefährdung, die Expositionsdauer, nach grober Schätzung die kumulative Staubdosis sowie das Alter bei Diagnose bzw. Tod bestimmt werden. Dabei erfolgte die Unterscheidung nach Patienten *mit* und *ohne* Begleitasbestose sowie danach, ob sie in der Produktion oder im anwendenden Handwerk beschäftigt waren. Bei 76 Personen dieser Gruppe (62,3%) lag sowohl ein auswertbares Torax-Röntgenbild wie auch ein histopathologischer Befund vor. Eine Strukturvermehrung von $\geq 1/1$ im Röntgenbild [1,2] und der Nachweis einer histologischen Asbestose bzw. Minimalasbestose wurden als positiver Befund gewertet. Bei der Bestimmung der Validitätsmaße der Sensitivität und Spezifität wurde einmal die Röntgenologie und zum anderen die Histologie als abhängige Variable verwendet.

Ergebnisse

1. Krankengut

Tabelle I zeigt die verschiedenen Altersangaben. Auffallend dabei ist die Verschiebung von ca. 10 Jahren nach links bei den Personen *ohne* Begleitasbestose, die vorwiegend als Handwerker Asbeststaub ausgesetzt waren.

In Tabelle II sind die "Asbestose-Parameter" aufgezeigt. Bei weitgehend gleicher Gefährdungsdauer von 20 Jahren und gleichlanger Latenzzeit von etwa 26 Jahren findet sich der Hauptunterschied in der kumulativen Dosis. Die Personen, die *keine* Begleitasbestose entwickelt hatten, weisen im Median 70 Faser-jahre ($F \cdot 10^6/m^3 \cdot \text{Jahre}$) weniger auf als die Patienten *mit* Begleitasbestose.

Abb. 1 veranschaulicht in Teil A), daß selbst bei einer Dosis von unter 20 bzw. 50 Faserjahren noch histologisch erkennbare Fibrosen—hier meist Minimalasbestosen—auftreten. Im Teil B) erfolgt eine Unterscheidung nach den besonders gefährdenden Tätigkeiten. Unter den Anwendern ist nur in der Gruppe der Isolierer eine Fibrose gefunden worden.

2. Validitätsmaße

Röntgenbefunde des Torax

In Abbildung 2 ist die Bewertung des Röntgenbildes der histopathologischen Diagnose gegenübergestellt. Das Verhältnis von negativen zu fraglichen, bis hin zu eindeutig positiven Befunden korreliert demnach gut. Unter den Lungenkrebspatienten mit einer histologisch eindeutigen Asbestose weisen zu Lebzeiten im Röntgenbild 40% (6:15) keinen positiven Befund auf. Unter den Patienten mit Minimalasbestose zeigen weniger als 1/4 (3:13) eine röntgenologisch eindeutige Asbestose.

Histo-pathologische Diagnose

Die histo-pathologischen Befundberichte aus Autopsie, Operation oder Endoskopie wurden in 30 verschiedenen Prosekturen erstellt. Mitunter ergaben sich divergierende Aussagen zum Vorliegen oder Fehlen einer Pneumokoniose, wenn zwei Prosekturen zum gleichen Erkrankungsfall gehört wurden. Bei 44 der 76 hier besonders untersuchten Lungenkrebspatienten (58%) fand

Tabelle I

Altersangaben ab Eintritt in die Asbestfaserstaub-Gefährdung am Arbeitsplatz für 78 Lungenkrebspatienten, den Zeitpunkt der Diagnose Lungenkrebs sowie des Todes an Lungenkrebs in Abhängigkeit vom histologischen Nachweis einer Lungenasbestose. Entsprechende Angaben für 121 Lungenkrebspatienten in Abhängigkeit von den wichtigsten Tätigkeitsbereichen in der industriellen Herstellung und handwerklichen Anwendung von asbestprodukten.

LUNGENKREBS NACH ASBESTFASERSTAUB-GEFÄHRDUNG AM ARBEITSPLATZ: ALTERSANGABEN

	n	Median	Min. - Max.	n	Median	Min. - Max.	Median Diff.
Histologische Diagnose:	ASBESTOSE ODER MINIMAL-ASBESTOSE			KEINE ASBESTOSE			
Alter [Jahre] bei							
- Eintritt in die Gefährdung	28	32,0	14,0 - 53,0	50	23,0	14,0 - 52,0	+ 9,0
- Diagnose LUNGENKREBS	28	64,5	37,0 - 75,0	50	55,0	34,0 - 78,0	+ 9,5
- Tod (Stichtag)	28	66,0	38,0 - 76,0	50	56,0	36,0 - 79,0	+ 10,0
Tätigkeitsbereiche:	HERSTELLUNG			ANWENDUNG			
	VON ASBESTPRODUKTEN						
Alter [Jahre] bei							
- Eintritt in die Gefährdung	58	39,0	14,0 - 55,0	63	22,0	14,0 - 50,0	+ 17,0
- Diagnose LUNGENKREBS	58	64,0	34,0 - 80,0	64	54,5	36,0 - 78,0	+ 9,5
- Tod (Stichtag)	58	65,5	36,0 - 81,0	64	55,5	37,0 - 79,0	+ 10,0

zur Absicherung der histologischen Diagnose das lichtmikroskopische Zählergebnis von sogenannten "Asbestkörperchen" nach Lungengewebsveraschung Verwendung.

Validitätsmaße

In Tabelle III sind die Validitätsmaße für die geprüften diagnostischen Methoden gegenübergestellt. Unter A wurde der Röntgenbefund (R) als Variable und die Histologie (H) als gesichertes diagnostisches Verfahren eingesetzt.

Im Röntgenbild beträgt die Rate der falsch-negativen Diagnosen 57%, während die Rate der falsch-positiven lediglich 2% ausmacht. Im Röntgenbild werden jedoch nur 43%, d.h. nur fast die Hälfte der Patienten als eindeutige Asbestose-Kranke erkannt.

Unter B gilt die Histologie als abhängige Methode. Dabei zeigt sich eine hohe diagnostische Sensitivität. Die Rate

der falsch-positiven Diagnosen "Asbestose" liegt im Vergleich zum Röntgenbefund mit 25% jedoch relativ hoch. Die Rate der falsch-negativen Diagnosen beträgt knapp 8%.

Diskussion und Schlußfolgerungen

Als 1925 der Gesetzgeber das Recht für Arbeitsunfälle und Berufskrankheiten geschaffen hat, sollten den Arbeitnehmern, die einen beruflich verursachten Gesundheitsschaden erlitten hatten, als Ersatz für die verminderte Arbeitskraft eine Rente als Lohnersatz gezahlt werden. Mit diesem sozialen Gedanken sollte die moralische Verpflichtung des Arbeitgebers und der Gesellschaft umgesetzt werden, für beruflich verursachte Schäden aufzukommen und den Arbeiter und seine Familie vor wirtschaftlicher Not zu bewahren und dieses—wegen der Lohnersatzfunktion—möglichst zu seinen Lebzeiten.

Vor diesem Hintergrund und der Tatsache, daß die Überlebenszeit der Lungenkrebspatienten im Median 6 Monate beträgt [16] ist bei strenger Auslegung der Gesetze

Tabelle II

Kenngrößen der Asbestfaserstaub-Gefährdung am Arbeitsplatz für 78 Lungenkrebspatienten nach Unterteilung in Gruppen mit oder ohne histologisch nachgewiesene Lungenasbestose einschließlich Minimalasbestose.

**KENNGRÖSSEN DER ASBESTFASERSTAUB-GEFÄHRDUNG AM ARBEITSPLATZ
FÜR LUNGENKREBSPATIENTEN MIT HISTOLOGISCHEN DIAGNOSEN
(MEDIANWERTE)**

Dosisäquivalente	Mit Asbestose und Minimal- Asbestose (n = 28)	Ohne Asbestose (n = 50)	Diff.
Kumulative Dosis [10 ⁶ F/m ³ · Jahre]:	82,0	11,2	+ 70,8
Alter bei Eintritt in die Gefährdung [J.]:	32	23	+ 9
Gefährdungsdauer [J.]:	19,2	20,9	- 1,7
Latenzzeit (Tod bzw. Stichtag) [J.]:	27,2	26,8	+ 0,4

nicht gewollt, bis zum Tod des Erkrankten zu warten, um erst an der Leichenlunge festzustellen, ob der Beschäftigte zu Lebzeiten eine Berufskrankheit erlitten hatte.

Das bedeutet, daß sich die medizinische Untersuchung zur Frage, ob der Asbeststaub eine Fibrose verursacht hat, auf das Röntgenbild stützen muß. Invasive Eingriffe sind im Unfallrecht nicht duldungspflichtig.

Die Untersuchung der 122 Patienten mit Lungenkrebs nach einer erwiesenen, teilweise relativ geringen Asbeststaubgefährdung hat jedoch gezeigt, daß eine Begleitfibrose nur dann auftritt, wenn die kumulative Dosis einen bestimmten Schwellenwert, der nach BERRY und FINKELSTEIN zwischen 35 und 50 Faserjahren liegt [6], überschritten hat. Für die karzinogene Wirkung von Asbestfasern gibt es aber keinen Schwellenwert. Das läßt die Schlußfolgerung zu, daß die Fibrose pathogenetisch keine Bedingung für die Entstehung eines Tumors der Lunge darstellt, wie es am Beispiel des Mesothelioms nach Asbestgefährdung bekannt ist [4].

Wie die Validitätsmaße in Tabelle III und die Abbildung 1 zeigen, kann auch durch die Einführung der Begriffe "Minimalasbestose" oder "Pleura-Asbestose" diese Schlußfolgerung nicht verdrängt werden. Darüber hinaus gibt es weder in der Bundesrepublik noch international eine einheitliche Nomenklatur zur Grenzziehung, was eben noch eine Asbestose ist und wann eben keine Asbestose—trotz beruflicher Asbestgefährdung—mehr vorliegt. Die nach-

folgende Übersicht zeigt, in welchen Punkten eine einheitliche Normierung der Nomenklatur erforderlich erscheint:

**VORSCHLÄGE ZUR DEFINITION UND
DIAGNOSTIK DER "ASBESTOSE"**

1. Röntgenologische Diagnostik

- Lungenasbestose (Streuung $\geq 1/0$) und/oder
- Pleuraasbestose als diffuse Verdickung und/oder hyaline oder verkalkte Pleuraplaques.

2. Histologisch-pathologische Diagnostik

- Lungenasbestose nach Fibrosegrad^{a)} und/oder
- Pleuraasbestose als diffuse Verdickung und/oder hyaline oder verkalkte Pleuraplaques.

3. Faserstaubanalytische Diagnostik

- Anzahl der Asbestkörperchen^{a)} und/oder
- Anzahl der Asbestfasern^{a)}.

^{a)} Konventionen nach Prüfung der methodischen Zuverlässigkeitskriterien erforderlich.

Darüber hinaus gibt es keinen erkennbaren wissenschaftlich begründbaren Ansatz, wie ein Lungenkrebs nach beruflicher Asbeststaub-Gefährdung mit oder ohne Begleit-asbestose als asbestbedingt abgegrenzt werden kann. Demnach muß eine Konvention erarbeitet werden, unter welchen Randbedin-

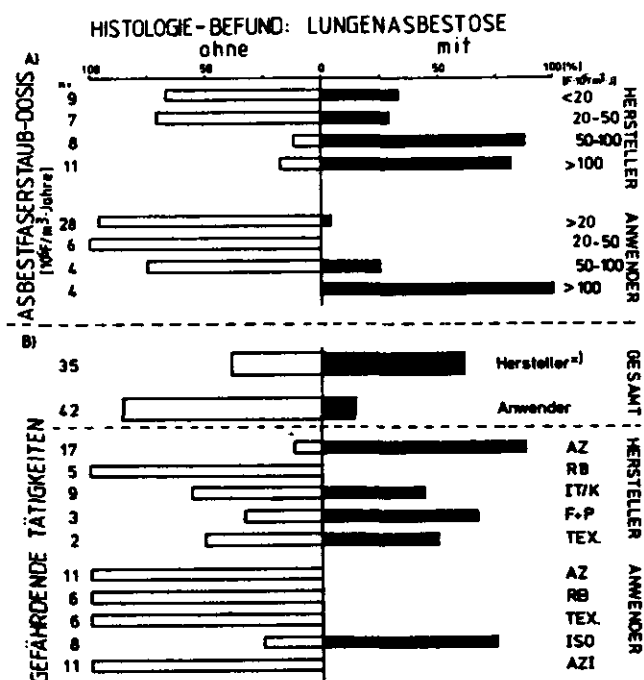


Abb. 1. Histologische Diagnose der Lungenasbestose (einschließlich Minimalasbestose) bei 77 Lungenkrebspatienten in Abhängigkeit von der über das Arbeitsleben kumuliert abgeschätzten Asbestfaserstaub-Dosis in 10⁶ Asbestfasern einer Länge über 5 µm prom³ Atemluft · Jahre (= Faserjahre), Teil A) bzw. B) unterteilt nach den wichtigsten industriellen Herstellungs- und handwerklichen Anwendungsbereichen von Asbestprodukten. Abk. der Tätigkeitsbereiche:

AZ = Asbestzement, F + P = Filter + Pappen, RB = Reibbeläge, IT/K = Gummi-Asbest u. Kunststoffe, Tex = Textilien, ISO = Isolierer, AZI = Asbest zum Isolieren

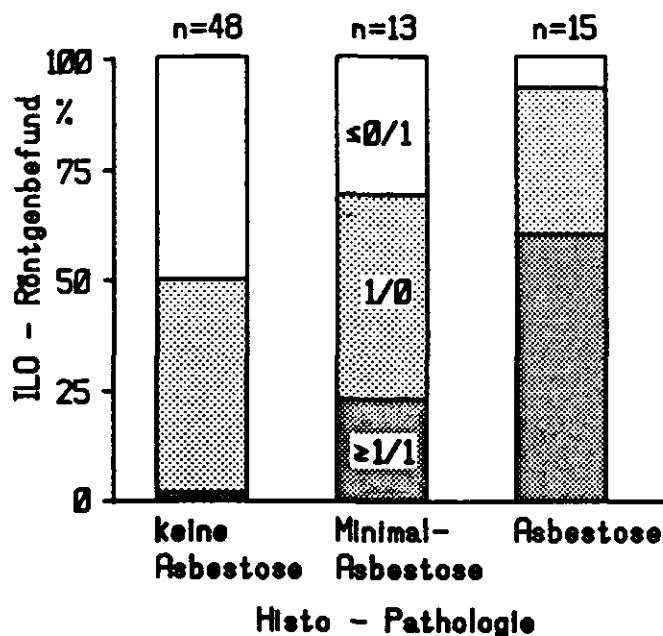


Abb. 2. Röntgenbefunde des Thorax im Hinblick auf eine Lungenasbestose in Abhängigkeit vom histopathologischen Befund bei 76 Patienten mit Lungenkrebs nach Asbestfaserstaub-Gefährdung am Arbeitsplatz.

Tabelle III

Vorschläge zur Definition und Diagnostik der Asbestose von Lunge und Pleura, einschließlich der Minimal-Asbestose und deren Faserstaub-analytischen Äquivalenten

Lungenkrebs nach Asbestfaserstaub-Gefährdung am Arbeitsplatz:
Validitätsmaße der röntgenologischen (R) und histologischen (H)
Diagnostik der Lungenasbestose¹⁾

	A) R : H		B) H : R	
	n	%	n	%
Sensitivität	12 : 28	42,9	12 : 13	92,3
Rate der Falsch-Negativen	16 : 28	57,1	1 : 13	7,7
Spezifität	47 : 48	97,9	47 : 63	74,6
Rate der Falsch-Positiven	1 : 48	2,1	16 : 63	25,4
Prädiktiver Wert des				
- positiven Testes	12 : 13	92,3	12 : 28	42,9
- negativen Testes	47 : 63	74,6	47 : 48	97,9

¹⁾ Positive Befunde:

- Histologie: Asbestose oder Minimal-Asbestose
- Röntgenstruktur: $\geq 1/1$ nach der ILO-Staublungenklassifikation

lungen—sei es die Dosis, sei es die Dauer der Gefährdung—ein derartiger Lungenkrebs als beruflich verursacht anerkannt werden soll.

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