# THE SINGLE BREATH DIFFUSING CAPACITY MEASUREMENT AS A PREDICTOR OF EXERCISE INDUCED OXYGEN DESATURATION IN PATIENTS WITH SILICOSIS

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The single breath diffusing capacity at rest is frequently found to be abnormal in patients with silicosis.[1-3] Little correlation exists between measurements of diffusing capacity by the steady state method and arterial oxygen tension.[4] Patients with conglomerate silicosis frequently show a reduced resting single breath diffusing capacity associated with exercise induced hypoxemia.[5] In patients with chronic obstructive pulmonary disease, a measurement of the resting single breath diffusing capacity greater than 55% of predicted has been shown to be specific in excluding desaturation on exercise.[6] In shipyard workers exposed to asbestos, a diffusing capacity below 70 percent of predicted was shown to be associated with abnormal arterial oxygen tension and gas exchange. Abnormalities in gas exchange on exercise were found also in some subjects with diffusing capacities greater than 70 percent of predicted.[7] We undertook the current study to determine the capacity of the single breath diffusing capacity measurement to predict exercise induced hypoxemia in patients with both simple and conglomerate silicosis.

## METHODS

We studied nine subjects with silicosis whose diagnosis was based on occupational history, and chest radiography. All subjects had chest roentgenograms showing simple or conglomerate disease. Each subject also had a measured arterial oxygen tension value greater than 55 mmHg at rest. All subjects undertook standard pulmonary function and exercise testing. The pulmonary function tests included flow rates, lung volumes and single breath diffusing capacity measurements using standard techniques. Progressive exercise testing was performed on a treadmill using standard incremental protocols. Indices monitored during exercise in all subjects included the electrocardiogram, workload, minute ventilation, breathing frequency, oxygen consumption ($VO_2$ ml/kg/min), carbon dioxide production ($VCO_2$ ml/kg/min). Oxygen and carbon dioxide levels were monitored using rapid response analyzers (Beckman OM-11 and Beckman LB-11). Arterial blood gases were measured both at rest and at peak exercise just before the termination of the exercise test using air blood gas analyzer (1L1303). Data analyzed at the breaking point of exercise were maximum heart rate, workload, maximum breathing frequency, maximum minute ventilation, maximum oxygen consumption ($VO_2$ max ml/kg/min); expired carbondioxide percent, and dead space/tidal volume $VD/_{VT}$ ratio.

Arterial samples were drawn from an indwelling radial artery cannula placed at rest. The samples were placed in ice and analyzed immediately. We examined whether an abnormal resting single breath diffusing capacity defined as equal to or less than 80 percent of predicted would predict in individual subjects altered gas exchange during exercise. A decrement in $PaO_2$ of greater than 5 torr on exercise and/or fall in oxygen saturation of 5 percent or greater was considered significant.

## RESULTS

Of the nine subjects, four had simple silicosis and five conglomerate silicosis. Their ages ranged 44 to 72 years. Five out of the nine subjects were smokers. All subjects performed a progressive incremental exercise test, and they achieved a mean workload of four METS. Two out of nine subjects had a normal resting single breath diffusing capacity (greater than 80 percent of predicted) and seven out of nine subjects had abnormal resting 80 single breath diffusing capacity (less than 80 percent of predicted). One of the two subjects with a normal resting single breath diffusing capacity had a decrement in arterial oxygen tension of 11 torr on exercise and seven out of the nine subjects with a resting single breath diffusing capacity less than 80 percent of predicted had decrements in arterial oxygen tension ranging from 5–20 torr on exercise. Three out of nine subjects with conglomerate silicosis had decrements in oxygen saturation of more than 5 percent on exercise. The alveolar-arterial oxygen difference increased on exercise in all seven subjects with abnormal resting single breath diffusing capacity measurements, by a mean value of 15.6 torr. Abnormalities in $VD/_{VT}$ ratio (defined as greater than 30 percent) were seen in all nine subjects on exercise. One of the nine subjects with a high resting $VD/_{VT}$ percent ratio of 51.8 had a decrement in $VD/_{VT}$ percent ratio to 37.8 on exercise.

The $VO_2$ max in all nine subjects ranged from 5.2 to 25.4 ml/Kg/min with a mean $VO_2$ max of 17.02 ml/Kg/min. The exercise test was terminated in all subjects by complaints of severe dyspnea.

## DISCUSSION

In early cases of silicosis, arterial blood oxygen desaturation is usually not present at rest,[5] however at high exercise loads a considerable proportion of silicosis patients show some degree of arterial blood desaturation.[6]

Table I
Anthropometric Characteristics of Patients

| | AA | AW | CL | LJ | KO | MS | KE | IH | RJ |
|---|---|---|---|---|---|---|---|---|---|
| Sex | M | M | M | M | M | M | M | M | M |
| Age (yrs) | 71 | 55 | 67 | 56 | 72 | 70 | 44 | 69 | 52 |
| Height (cm) | 169 | 179 | 175 | 170 | 170 | 171 | 175 | 177 | 173 |
| Weight (kg) | 76 | 86 | 69 | 98 | 67 | 74 | 113 | 80 | 70 |
| Smoker (S) Non Smoker (NS) | NS | S | S | NS | S | NS | S | S | NS |
| Smoker Pack Years | — | 30 | 75 | — | | — | 10 | 30 | — |
| Type of Occupational Exposure | | | | | | | | | |
| Exposure Years | 25 | 20 | 30 | 9 | 40 | 20 | 22 | 45 | 21 |

| | DLCO% PRED | $PaO_2$ REST mmHg | $PaO_2$ ex (mmHg) | $PaO_2$ mmHg |
|---|---|---|---|---|
| 1 | 56.0 | 82.0 | 64.0 | 18.0 |
| 2 | 72.0 | 86.0 | 77.0 | 9.0 |
| 3 | 44.0 | 67.0 | 60.0 | 7.0 |
| 4 | 80.0 | 85.0 | 72.0 | 13.0 |
| 5 | 100.0 | 73.0 | 73.0 | 0.0 |
| 6 | 56.0 | 73.0 | 60.0 | 13.9 |
| 7 | 90.0 | 93.0 | 82.0 | 11.0 |
| 8 | 75.0 | 64.0 | 59.0 | 5.0 |
| 9 | 55.0 | 93.0 | 82.0 | 11.0 |

| | FEV1/ FVC% | TLC% PRED | $VO_2MAX$ ml/Kg/min | $VD/V_T$% |
|---|---|---|---|---|
| 1 | 73.0 | 61.0 | 15.9 | 39.9 |
| 2 | 79.0 | 62.0 | 23.0 | 42.3 |
| 3 | 93.0 | 44.0 | 15.1 | 41.6 |
| 4 | 79.0 | 90.0 | 18.5 | 37.8 |
| 5 | 64.0 | 125.0 | 25.4 | 51.7 |
| 6 | 76.0 | 64.0 | 16.1 | 42.5 |
| 7 | 84.0 | 75.0 | 23.4 | 48.3 |
| 8 | 30.0 | 108.0 | 5.2 | 64.4 |
| 9 | 73.0 | 52.0 | 10.6 | 46.2 |

In a similar study performed in shipyard workers exposed to asbestos,[6] a diffusing capacity at rest of below 70 percent of predicted was usually associated with gas exchange abnormalities. However, in some subjects with diffusing capacities above 70 percent of predicted, $VD/_{VT}$ ratio, abnormal values for arterial oxygen tension and the alveolar-arterial difference in oxygen tension were found.

In our study three of the subjects with resting single breath diffusing capacity above 70 percent but below 80 percent of predicted had decrements in arterial oxygen tension in the range of 5–13 torr. One subject with single breath diffusing capacity of 90 percent of predicted had a decrement in arterial oxygen of 11 torr. Four subjects with single breath diffusing capacities below 70 percent of predicted had decrements in arterial oxygen on exercise in the range of 11 to 20 torr.

Abnormalities in gas exchange as shown by alveolar-arterial difference in oxygen and dead space/tidal volume ratio were seen in all our subjects during exercise. These abnormalities in gas exchange may be caused by increased perfusion to lung units without proportional increase in ventilation causing hypoxemia thus increasing the alveolar-arterial oxygen difference. Conversely the inability of perfusion to increase appropriately to the well ventilated lung units results in abnormally high dead space/tidal volume ratio and high arterial-end tidal difference in carbon dioxide. Our study revealed gas exchange abnormalities similar to those seen in subjects exposed to asbestos.[6] We also observed high dead space/tidal volume ratios on exercise which could not be predicted by resting single breath diffusing capacity measurements. Thus our results indicate that in seven of nine subjects with silicosis, resting single breath diffusing capacity equal to or less than 80 percent of predicted a decrement in arterial oxygen tension and/or oxygen saturation occurred with exercise.

In summary, in a small number of silicotic subjects, the single breath diffusing capacity measurement at rest appears to predict exercise induced decrements in arterial oxygen tension and/or oxygen saturation. Abnormalities in gas exchange as shown by increased alveolar-arterial oxygen difference and dead space/tidal volume ratios were seen in all subjects during exercise.

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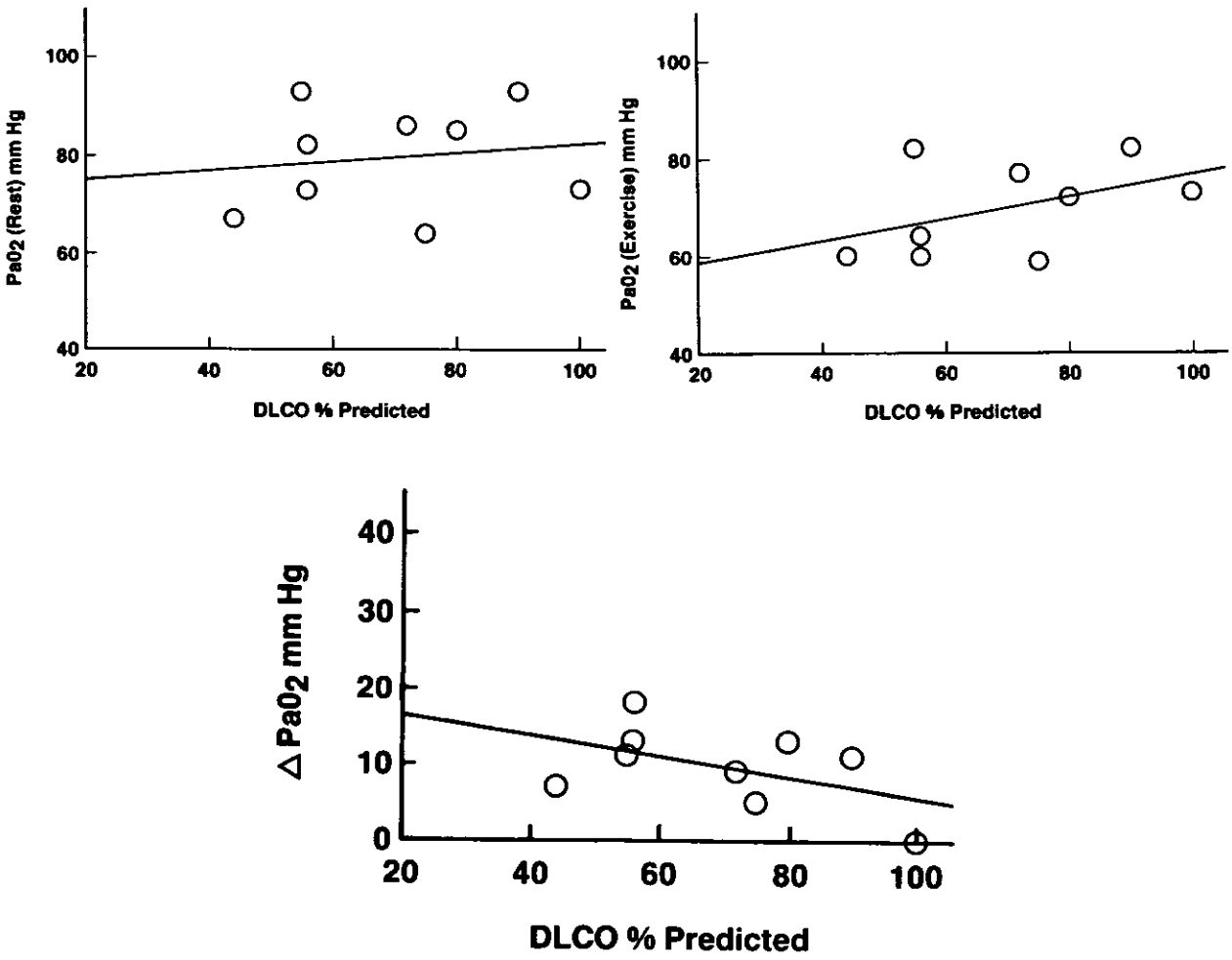

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# THE RELATIONSHIP BETWEEN ASBESTOS BODIES, SERUM IMMUNOGLOBULIN LEVELS AND X-RAY CHANGES IN ASBESTOS WORKERS

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Several authors have pointed to the imnmunological disorders which are the result of the fibrogenous effect of asbestos dust; this is a well-known phenomenon on which quite a few references exist.[1,4,5]

This is why we wanted to establish the possible relationship between the X-ray changes, the number of asbestos bodies and the level of serum immunoglobulins in a group of asbestos workers.

## MATERIAL AND METHODS

Out of 79 workers of the asbestos section in the factory for asbesto-cement products, 52 persons were studied. The examined workers were divided into three groups: Group 1 of the workers directly exposed to asbestos, with radiographic changes suggesting asbestosis, Group 2 of the workers also directly exposed to asbestos but without X-ray changes, and Group 3 of the workers who were not directly involved in the process of production. The lungs and the pleura of all the examined workers were x-rayed in PA projection. In all the studied workers the presence of asbestos bodies in the sputum was determined. The immunological status is concerned with the evaluation of the serum immunoglobulin levels (IgG,M,A) on RID plates.

For the evaluation of the results obtained adequate statistical methods $X^2$ test and Student t-test were applied.

## RESULTS AND DISCUSSION

In all the studied workers (fifty-two of them) the presence of asbestos bodies in the sputum was determined, on the native microscopic slide. Their number varied from 1 of 2 to over 20 within one field of vision. Most of them, as much as 36 of them had one to five asbestos bodies in a single (one) field of vision.

The statistical analysis pointed to the fact that there is no statistically significant difference between the groups with respect to the number of asbestos bodies in the sputum. Also, the statistical evaluation proved that there is no significant difference between the workers with radiographic (X-ray) changes suggesting asbestosis and those with normal radiographic findings (groups 2 and 3) with respect to the number of asbestos bodies.

This is an additional proof that the presence of asbestos bodies in the sputum is just a verification of a person' s exposure to asbestos.

As far as the immunological status is concerned, with the evaluation of the level of the three classes of immunoglobulins: IgG, IgM and IgA, we obtained the following results:

In Group 1 (11 workers) workers with radiographic changes suggesting asbestosis, with respect to the immunoglobulin type G in 10 persons the level of the serum IgG was above normal and in one worker it was within normal. On one worker only belonging to this group the level of IgM was higher, and also, in one worker only the level of IgA was lower.

In group 2, including workers directly exposed to asbestos, while without radiographic changes, that is 34 of them, in two persons higher level of IgG was determined, in one person the level of IgM was lower and in two workers the level of IgA was higher.

In Group 3, which included workers in the asbestos section of the factory who were not directly exposed to asbestos dust, the level of IgG in all workers was within normal, the level of IgM was lower in one worker, the level of IgA was higher in one worker, and in one worker the level of this type of immunoglobulin was lower.

In the process of the evaluation of the immunological status of the examined workers, the mean value of the three classes of serum immunoglobulins was calculated, as well as the significance of the differences in the mean values among individuals, previously selected, workers.

As part of the statistic evaluation of the obtained results, the significance of the differences in the mean values of particular classes of immunoglobulins were also determined in separate groups of workers.

The Student t-test showed a statistically significant difference in the mean values of IgG between Group 1 and Group 2, Group 2 and Group 3, and Group 1 and Group 3.

With respect to the M and A type of immunoglobulins, no statistically important difference in the mean values was determined either.

Since we have not noticed any significant deviations in the level of IgM and IgA, neither in the groups nor in the individuals, our research concerning the relationship among the number of asbestos bodies, radiographic changes suggesting pneumoconiosis and the immunological status has

been reduced to the relationship between asbestos bodies radiographic changes and the IgG type.

The $X^2$ test did not point to any statistically significant difference between workers with an increased level of IgG and those with normal or decreased level of this type of Ig in serum, all this of course with respect to the number of asbestos bodies.

This statistic evaluation indicated that there is a statistically important number of workers with radiographic changes im whom the level of IgG is increased, if compared to the number of workers without pneumoconiosis.

Numerous studies point to immunological disorders that are directly or indirectly connected with exposure to asbestos.[1,2]

Pernis in his research suggested that these immunological changes pointed to the fact that asbestosis, similar to silicosis included in its pathomechanisms immunological reactions as well.[4]

The slow destruction of macrophages can be suspected as a factor contributing to pneumofibrosis.[3] It is believed that the very same mechanism causes immunological disorders in persons exposed to asbestos.

## CONCLUSION

No connection between asbestos bodies in sputum, radiographic changes and the immunological status in the studied workers has been established. The obtained results indicated the statistically important increase in the level of IgG in Group 1, compared to Group 2, as well as to Group 3. There is a significantly larger number of workers with radiographic changes suggesting asbestosis, in whom the level of IgG is above normal.

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# CHANGES IN LUNG FUNCTION IN COAL-MINERS WITH AND WITHOUT CWP

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## ABSTRACT

Spirometry, body plethysmography, analysis of flow-volume curves and single-breath CO diffusing capacity measurements were made on 620 coalminers working in the same colliery. The coalminers were divided into groups according to X-ray categories of CWP, age, and underground working time. Smokers and nonsmokers were also compared.

All parameters of lung function were significantly different from the corresponding control values even in the non-pneumoconiotic group (439 miners). The greatest decrease found in the maximal expiratory flow at 25% of vital capacity (MEF-25%) and in the maximal midexpiratory flow (MMEF).

Differences from the corresponding control values in all measured parameters increased with age and underground working time. However, in the youngest age group (under 30 years) with a relatively short working time (under 5 years) only MEF-25% and MMEF values changed significantly indicating an early damage in the function of the peripheral airways.

Changes in lung function were more marked in pneumoconiotic miners. Though significant differences from predicted values were found in miners who never smoked, the changes in the lung function were found, however, markedly greater in the smokers.

No Paper provided.

# EFFECT OF ALVEOLAR LINING MATERIAL ON PARTICLE BINDING AND PHAGOCYTOSIS

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## ABSTRACT

Cellular mechanisms which mediate the particle-induced pulmonary fibrosis are not fully known. Alveolar macrophages actively phagocytize and clear the particulates from the alveolar surfaces. However, before macrophages encounter inhaled particles, the particles come in contact with the macromolecules of alveolar lining layer (ALL) which could alter their surface properties and consequent interactions with pulmonary cells. Since little is known about the role, the ALL components may have in interactions between inhaled particles and macrophages, we have initiated studies to understand this complex issue. Rat lung lavage was concentrated and centrifuged at 178000 × g for 1 hour to separate protein and lipid-rich fractions. The binding of particles (+vely charged carbonyl iron spheres and −vely charged glass beads; 4.5 mg/ml) to the macrophage monolayers ($2 \times 10^5$ cells) was studied scanning electron microscopy either by treating the cells with lavage fractions or by treating the particles with lavage components. When the cells were pre-treated with normal lavage (protein conc. 50 μg/ml), concentrated lavage (protein conc. 165 μg/ml), protein fraction (125 μg/ml) and lipid-rich fraction (phospholipid conc. 305 μg/ml), there was a significant reduction in particle binding. The concentrated lavage and protein fractions caused maximum inhibition which was concentration dependent. The effect was reversed by rinsing the cells with PBS prior to adding the particles. Pretreating the spheres with lavage fractions also caused significant reduction in particle binding which was not reversible. These fractions also blocked the phagocytosis of a significant number of particles. Thus, it is the interaction between particles and ALL components rather than an interaction between macrophages and the components which is responsible for decreased binding. The *in vitro* studies should be useful in understanding complex events may be occurring between particles and ALL on alveolar surfaces.

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# TOXICITY RISKS FROM BACTERIAL ENDOTOXIN INHALATION

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## INTRODUCTION

The effect of bacterial endotoxin on the lung is an important factor in shock following sepsis and adult respiratory distress syndrome (ARDS), wherein endotoxin or mediators stimulated by this ubiquitous substance reach the lung via peripheral circulation. Endotoxin is also important in causing pathophysiology to the lung when inhaled and thus represents a potential risk to workers subjected to certain types of environmental exposure.

It is known that inhalation of environmentally realistic concentrations of endotoxin causes a number of reactions, depending on dose, within 4–6 hrs. Among these are fever,[1] neutropenia followed by leukocytosis,[2] a decline in $FEV_1$.[1] endotoxin tolerance on subsequent challenge,[3,4] increased production of leukocytic enzymes in bronchial alveolar lavages,[5] significant decreases in lung volume due to changes in volume of the distal air space,[4] increased volume densities of neutrophils and platelets in pulmonary septal capillaries,[4] significant changes in pulmonary capillary endothelium, e.g., increased density of pinocytotic vesicles, cytoplasmic blebbing, and focal disruption,[4] increased pulmonary capillary permeability,[6] and possible septal infiltration of fluids and inflammatory cells.[6]

Also, there is evidence that prior insults to the lung render the lung subsequently more vulnerable to exposure to endotoxin. Such predisposing factors could be surgical manipulation, intubation, anesthesia,[7] hypoxia,[8,9] burns,[10] other effects induced by the endotoxin,[11] or even recent prior experience with endotoxin.[3] To supplement the knowledge of the known risks of workers exposed to inhalation of endotoxin, the purpose of this study is to determine if endotoxin inhalation may predispose workers to further pulmonary injury in an experimental model of ARDS.

## MATERIALS AND METHODS

Male hamsters, an experimental animal free of common pulmonary epizootics, were used throughout. Randomly divided groups were administered either standardized aerosols of purified *Enterobacter agglomerans* lipopolysaccharide as the source of endotoxin (5 hrs at 4 $\mu g/m^3$) or saline suspensions of *E. agglomerans* cells adjusted to an $O.D._{540}$ of 0.400 for 1 hr.[7] Control animals were given no aero- sol. Timing was commenced at the cessation of the aerosol. At appropriate intervals, the animals were anesthetized with barbiturates and subjected to bronchoalveolar lavage (BAL). Cells from lavages were tested for viability by trypan blue exclusion, counted, and analyzed differentially by cytocentrifugation and Wright-Giemsa staining. All cells proved to retain viability >95%.

## RESULTS

### Effect of Endotoxin Inhalation on Free Lung Cells

Twenty-two hamsters were randomly divided into control, 6, 24, and 48 hr post inhalation groups and subjected to either no aerosol (control) or the standard LPS inhalation challenge. Results from the lavages taken at the designated time intervals are depicted in Figure 1 and were statistically analyzed by the two-tailed T-test for independent variables (p was set at $<0.01$).

Inhaled endotoxin caused a marked increase in total free lung cells recovered by lavage, reaching a maximum at 24 hrs and returning to near normal by 48 hrs. PMNs began to increase proportionately within hours, reaching a maximum at 6 hrs whereas alveolar macrophages decreased proportionately and recovered slowly after that time. Although the total cell count had returned to near normal levels 48 hrs after aerosol exposure, the ratios of neutrophils and macrophages had not yet completely returned to normal values. Lymphocytes on the whole were unaffected except for the slight (not significant) rise at 24 hrs.

### Comparison of Inhaled Endotoxin vs. Inhaled Whole Bacteria

Next, pulmonary reactions were compared from animals challenged with aerosolized saline suspensions of endotoxin or whole *E. agglomerans* bacteria for 1 hr. Lavages were made at only one time point, at 6 hrs, the time for development of maximum microlesions. The results, statistically analyzed as previously, appear in Figure 2.

Inhalation of bacteria induced a significantly greater leukocyte infiltration into the lung. Most of this infiltrate consisted of alveolar macrophages and neutrophils. The ratio of alveolar macrophages was greater in the animals receiving whole cells, whereas the ratio of neutrophils was higher in the endotoxin-exposed animals.

### Effect of Combined Inhalation and Intravascular Contact with Whole Bacteria

Hamsters were given a standard aerosol of whole

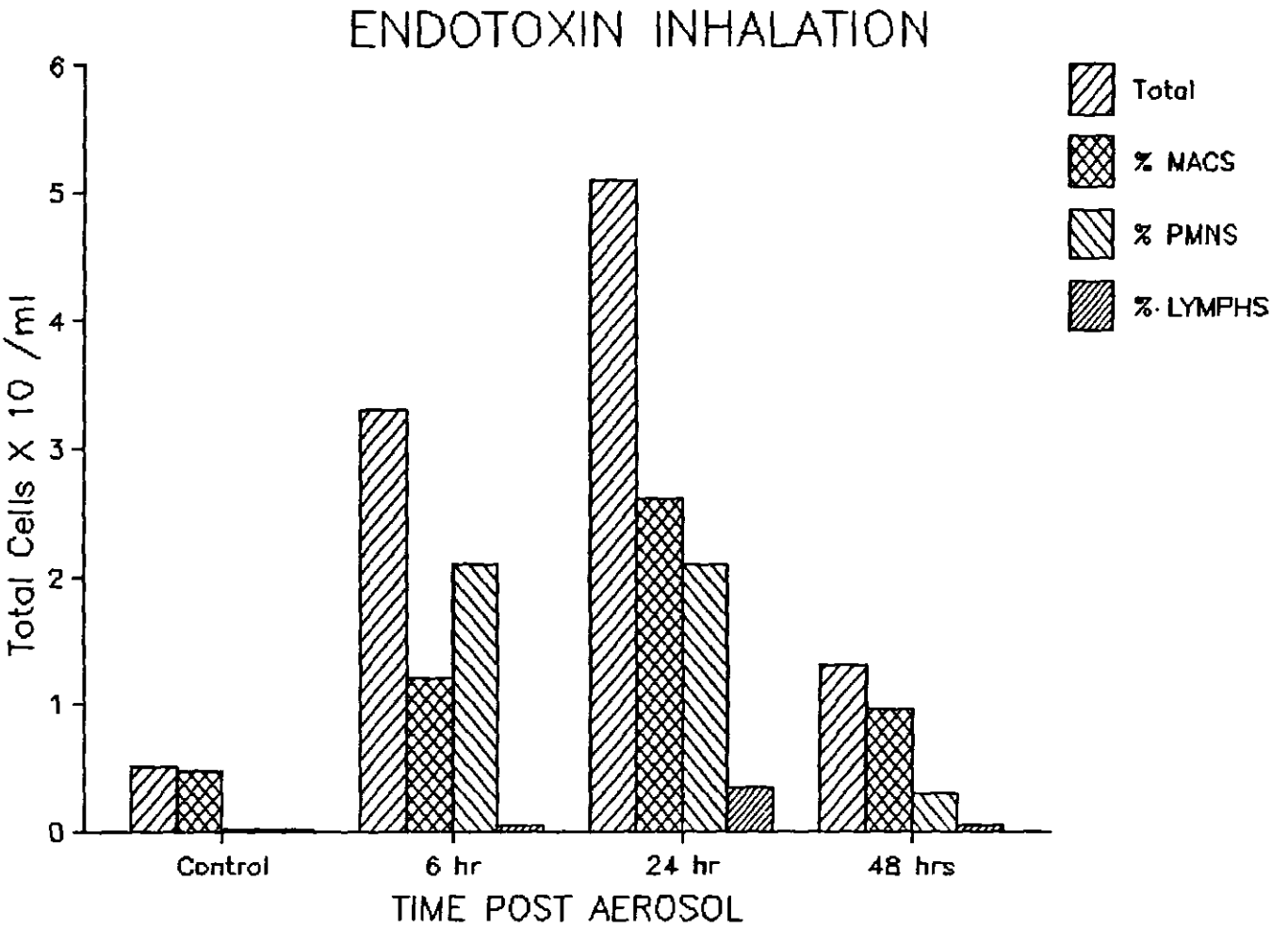


Figure 1. Free lung cell analysis of hamster bronchoalveolar lavages with time after endotoxin inhalation.

*E. agglomerans* cells for 30 min and allowed to rest for 6 hrs to maximally develop pulmonary microlesions.[4] One hour before this peak, the animals were anesthetized and intravascularly injected with 0.2 ml of the same suspension used for aerosolization. After 1 hr, the animals were killed and BAL made for free lung cell analyses. Since anesthesia[7] has been reported as one of the operative procedures that may predispose the ARDS condition and possibly enhances prior endotoxin exposure, controls included animals subjected to anesthesia with no intravascular injection. The data are presented in Table I. Two types of comparisons were statistically analyzed: one, where all treatment groups were compared with unexposed (normal) controls and the other where the complete regimen (aerosol, anesthesia, and I.V. bacteria) was compared with each of the other groups. The results giving the level of significance are shown in Table II.

Exposure to the complete regimen was characterized by a marked increase in erythrocytes and a relative decrease in the proportion of alveolar macrophages while the neutrophils proportionately increased. This could indicate possible pulmonary hemorrhage. The anesthetic, if anything lessened the effects of the bacterial aerosol, and seemed to contribute little on its own to the free lung cell reaction. The combined anesthetic and I.V. bacteria had no significant effect.

## DISCUSSION

Inhalation of either purified bacterial endotoxin or whole cells induces significant increases in total pulmonary leukocytes, due mostly to increases in alveolar macrophages and neutrophils. Inhalation of bacteria produced more pronounced reactions emphasizing a greater neutrophil response, whereas the reaction to inhaled endotoxin was lower and predominantly due to alveolar macrophages.

Since these PMNs are not seen in morphometric analysis of the alveoli, infiltration of the higher airways must be considered important.

If the lung were to receive a second insult during the time when the inflammatory response to the initial stimulus was highest, the lung might be in a more vulnerable position. When inhalation of Gram—bacteria was followed by an I.V. injection of similar cells, a large increase in erythrocytes, suggesting pulmonary hemorrhage accompanied by a relative decrease in the proportion of alveolar macrophages and a proportionate increase in neutrophils. Such changes were not

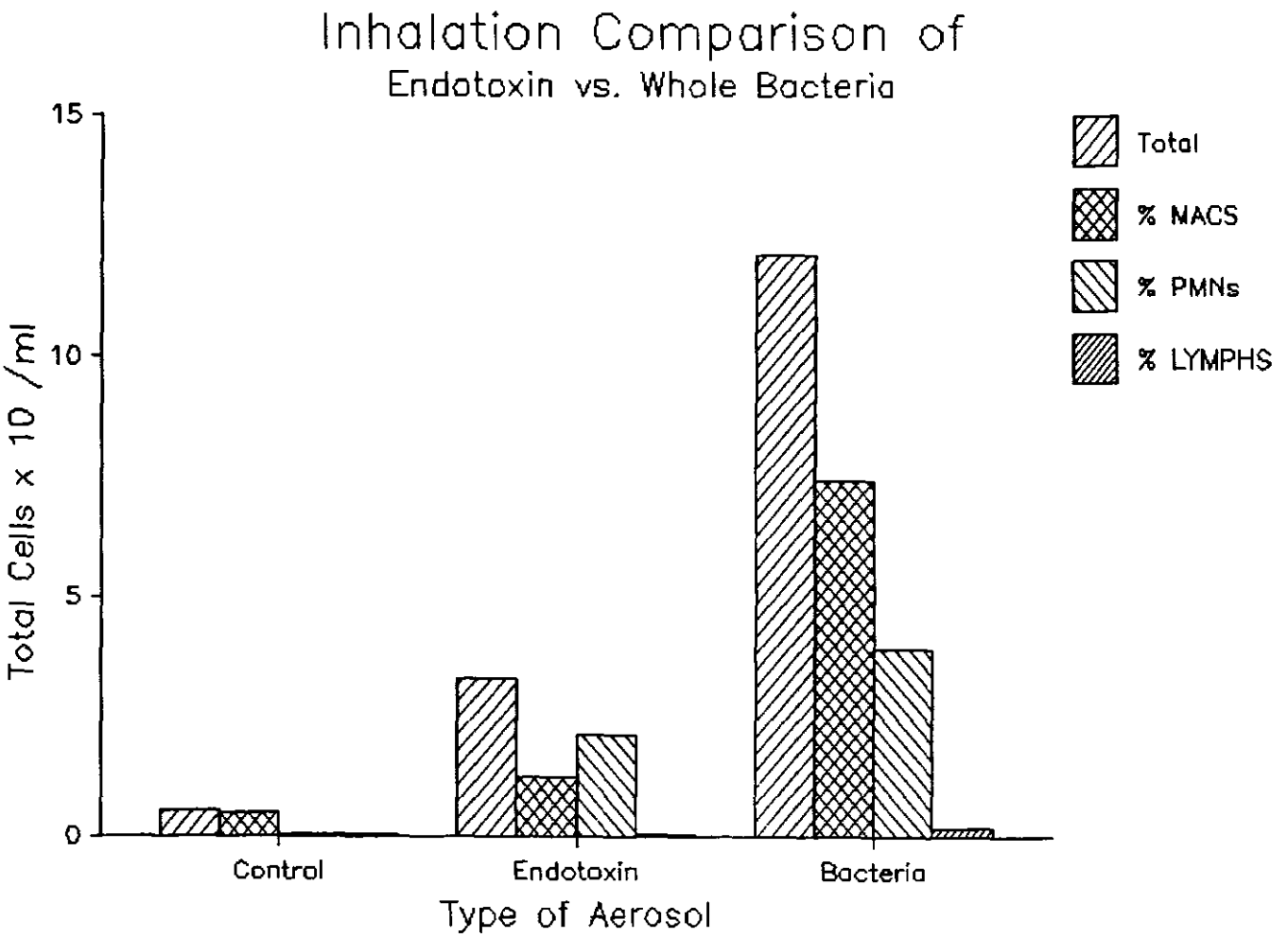


Figure 2. Comparison of free lung cell lavages taken 6 hrs after either inhalation to endotoxin or whole Gram negative bacteria.

due to intravenous bacteria alone, but were only significant when the bacteria were inhaled.

Taken together with the other known inflammatory effects of inhaled or endotoxin-containing bacteria, such inhalation in an occupational setting constitutes an increasingly recognized risk for workers.

Table I

Effect of Combined Pulmonary and Intravascular Exposure on Free Lung Cells

| | | Cells X $10^5$/ml | | | % Cell Content | | | |
|---|---|---|---|---|---|---|---|---|
| Type | n | Total | WBC | RBC | RBC | MO | PMN | Ly |
| Normal | 10 | 0.6±0.1 | 0.5±0.1 | 0.1±0.1 | 7.7±9.3 | 87.0±9.6 | 4.5±4.3 | 2.6±1.2 |
| Complete[1] | 5 | 8.5±3.5 | 1.8±0.6 | 6.7±3.5 | 31.4±9.6 | 36.0±9.9 | 31.7±8.1 | 0.3±0.3 |
| Bacteria + anesethesia | 8 | 6.8±1.0 | 2.5±1.1 | 3.2±1.7# | 2.6±0.8# | 92.0±2.6# | 3.5±2.3 | 2.0±1.2 |
| Bacteria aerosol only | 11 | 12.1±6.2 | 5.1±4.0 | 7.9±3.3* | 2.3±1.6* | 61.2±9.8 | 32.9±8.9 | 1.2±1.1 |
| Anesthes + IV Bacteria | 5 | 0.7±0.2 | 0.5±0.1 | 0.3±0.2 | 8.8±6.7 | 84.5±5.4 | 2.9±1.8 | 3.7±1.8 |

[1] Complete = bacterial aerosol, anesthesia, and I.V. bacteria

* n = 6

# n = 4

Table II

Statistical Analyses of Bronchopulmonary Lavages from Table II

| | | Cells X $10^5$ | | | % Cell Content | | | |
|---|---|---|---|---|---|---|---|---|
| Parameter | vs | Total | WBC | RBC | RBC | MO | PMN | Ly |
| Complete | Normal | .007 | .009 | .014 | .0005 | <.0001 | <.0001 | .0001 |
| Bact aer + anes | Normal | <.0001 | .001 | .04 | N.S. | N.S. | N.S. | N.S |
| Bact aer only | Normal | .0001 | .003 | .002 | N.S. | <.0001 | <.0001 | .01 |
| Anesthes + IV Bacteria | Normal | N.S. | N.S. | N.S. | N.S. | N.S. | N.S. | N.S. |
| Bact aer + anes | Complete | N.S. | N.S. | N.S. | .003 | .002 | .002 | .006 |
| Bact aer only | Complete | N.S. | .04 | N.S. | .003 | .0003 | N.S. | .04 |
| Anesthes + IV Bacteria | Complete | .008 | .01 | .015 | .003 | <.0001 | .002 | .02 |
| Bac aer only | Bact aer + Anes | .03 | N.S. | .03 | N.S. | <.0001 | <.0001 | .003 |

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# DESCRIPTION OF MEDICAL SERVICES RENDERED AT THE CHRISOTILA ASBESTOS MINE, WITH 1100 EMPLOYEES, IN THE STATE OF GOIÁS, BRAZIL

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## ABSTRACT

In order to have the conscientization, control and prevention of professional diseases, a Labour Medicine Service Center was created, with the following staff: 2 Labour Medicine physicians, 1 nurse, 1 Labour Medicine nurse attendant, 3 nurse attendants, 1 RX technician, 1 dentist, 1 secretary and 1 receptionist; and with the following equipment: a 500 mA RX equipment, an automatic processing machine, an audiometer, a spirometer and a complete dental office, all within a 250 $m^2$ area.

The specialized care for employees and their dependents (7000 persons) is done at the Company's hospital, which has 30 beds and a 60 people staff, including 8 physicians, 2 nurses, 3 dentists, amongst others.

The Labour Medicine program offers monthly conferences on the risks of ASBESTOS. The medical examinations are made upon admission, annually and upon transfers, promotions or dismissals of employees, as well as in dismissed or retired employees.

Taking into consideration the geographical localization of the Mine, 500 Km from a large populational center, the conscientization for safety and social stability is done to the workers in a multi-disciplinary work, jointly with the Social Security (Governmental entity), Technical Engineering, Labour Safety and Social Service Departments.

No Paper provided.

# HIGH-RESOLUTION COMPUTED TOMOGRAPHY OF PNEUMOCONIOSIS

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## INTRODUCTION

The usefulness of high-resolution computed tomography (HRCT) was evaluated in 37 cases of pneumoconiosis and diagnostic accuracy was compared with those of conventional chest radiography concerning profusion, shape and size according to the ILO (1980) classification of radiographs of pneumoconiosis.

## MATERIALS AND METHODS

37 patients of pneumoconiosis were all men with 39 to 86 years of age (mean 60.9±9.6). Except for 2 cases, they had history of cigarette smoking, and their smoking indices were 0 to 1980, with mean 655.8±398.0.

They had histories of occupational exposure to inorganic dusts in 17 of coalminers, 4 of tunnel drivers, 4 of coal and tunnel workers, 2 of welders and 2 had history of exposure to asbestos. Eight patients had history of exposure to miscellaneous dusts such as iron ore, zinc ore, silica brick, oven construction and their combination. Their radiographic findings were classified according to the ILO classification (1980).

The CT examination consisted of a series of high resolution 2mm thick sections scanned with a Siemens somatom II. A Siemens high resolution algorithm stressing the region of high spatial frequency with zooming model was used. The scanning was performed in 10 seconds, at 125kVp, 460mAs. The pixel size was 0.5mm with a magnification factor of 4.0. Six sections were scanned routinely from the level of the sternal notch caudad at 3cm intervals, grossly imaging the upper, middle, and lower lung fields (Figure 1). All scans were made in suspended moderate inspiration. No intravenous contrast materials was used. All images were observed and photographed with the window of 2024 Hounsfied units (HU) and the level of –600 HU, and additional settings were also used as needed.

Nodular and irregular opacities were graded according to the shape and size and profusion. Emphysema was evaluated separately according to their distribution (subpleural or parenchymal) and avascular area was graded to 4 classes as 1) (0–25%), 2) (26–50%), 3) (51–75), 4) (76–100%) respectively. Each conventional radiogram and CT was evaluated by 3 radiologists and 2 pulmonary specialists independently.

Dyspnea was graded to 1–5 according to Hugh-Jones criteria. Pulmonary function tests were performed using SRL M 100B,and FRC was measured by $N_2$ washout method and $DL_{co}$ was measured by breath holding method (Forster). Arterial blood gas was obtained under air breathing by brachial artery puncture and analyzed using automatic blood gas analyzer IL813.

## RESULTS

37 patients in the study were classified into 10 of category 1, 13 of category 2, 6 of category 3, and 8 of category 4 by plain chest X-P (Table I).

17 cases of coal workers pneumoconiosis were classified into 3 of category 1, 7 of category 2, 2 of category 3 and 5 of category 4. HRCT examination revealed marked parenchymal (central) emphysema from 50 to 100% of our criteria and nodular opacities was so attenuated that they were assessed as 0/1 p. All three cases showed marked obstructive ventilatory disturbance with 42 to 59% of $FEV_{1.0}$%. As compared with category 1 of coal workers pneumoconiosis, 7 of category 2 revealed milder emphysema score of 25% except for one case of 75%. Profusion of nodular opacities in HRCT are generally lower than conventional chest X-P in this group except for two cases which are complicated by tuberculosis. Among category 3, profusion of small opacities by HRCT was also lower than that of conventional X-P. Among category 4, evaluation of small opacities were very difficult because of destruction of intra-thoracic structure and emphysema.

3 of 4 tunnel drivers revealed dense nodular opacities higher than category 2 in conventional X-P and they are all graded as category 3 by HRCT. Three of four tunnel and coal workers also revealed marked nodular opacities by X-P and CT.

As a whole, except for category 4 and asbestos cases, 23 of 31 cases showed lower profusion score in CT than in conventional X-P. This may reflect the effect of summation in postero-anterior projection of plain X-P compared with the horizontal thin slice in CT. Subpleural curvilinear opacities were observed in three cases of coal workers pneumoconiosis and one case of asbestosis.

Two cases of asbestosis showed marked irregular opacities in the middle and lower lung field in plain X-P. One of them

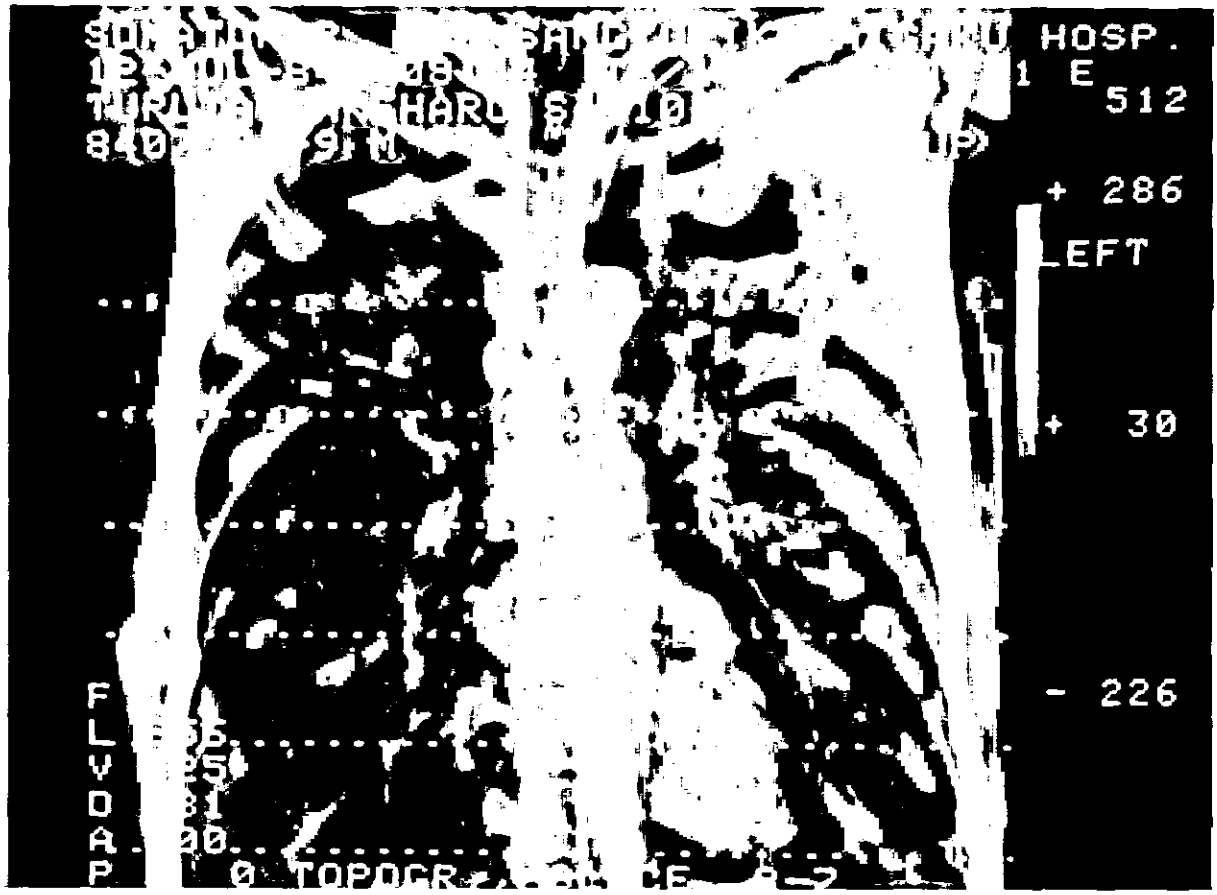


Figure 1. Tomogram showing the levels of the six routine sections.

also revealed calcified pleural plaques along the crura of the bilateral diaphragm. CT revealed more clearly the calcified plaques along the thoracic wall with varying thickness. Another case showed intense irregular opacities with honey comb appearance. The CT scan demonstrated marked interstitial changes with subpleural curvilinear opacities which could not be demonstrated by plain X-P. In the upper lung field, CT also revealed marked emphysematous changes which may explain the marked obstructive ventilatory disturbance (VC 116% of predicted, $FEV_{1.0\%}$ 55%). Dyspnea score was 2.5 ± 1.0. No clear correlation was found between the radiographic category and dyspnea score.

Studies on pulmonary function were VC 95.7 ± 17.9 percent (mean SD) of predicted value,$FEV_{1.0}$/FVC 64.2 ± 15.6 percent, flow at 75% FVC(V25) divided by height (meter) 0.38 ± 0.24 L/sec/m, RV/TLC 37.4 ± 10.3, $\%DL_{co}$ 106.2 ± 27.5%, $PaO_2$ ± 78.7, 6.8 torr, A -$aDO_2$ 24.0 ± 7.4 torr (Table I).

No clear correlation was found between conventional radiographic findings nor HR-CT findings and pulmonary function parameters except emphysema score by CT and $FEV_{1.0\%}$ which showed mild inverse relationship.

Nodular opacities, interstitial fibrosis, bullae and emphysema were more clearly and specifically demonstrated on HR-CT scans than on conventional chest radiographs in most patients.

Radiologic-pathologic correlation was performed on the specimens of transbronchial lung biopsy in 4 patients. One case was illustrated in Figure 2. This 54-year-old retired silica brick factory worker showed combined restrictive and obstructive ventilatory disturbance with VC of 57%, $FEV_{1.0\%}$ of 42%, flow at 75% FVC of 0.13L/sec/m. Plain X-P (Figure 2a) was categorized as PRlp. HRCT also revealed dense nodular opacities in upper and middle level of slice (Figure 2b). Subpleural thickening of interlobular septum was also observed. Specimen of transbronchial biopsy revealed well defined pneumoconiotic nodules and mild thickening of alveolar septum (Figure 2c). Small opacities in HRCT may well reflect these small pneumoconiotic nodules seen in TBLB.

Figure 3a shows plain X-P of 88-year-old retired coal miner with an occupational history of 37 years. His autopsied lungs were fixed, dried and, scanned by HRCT and compared with radiograph by soft X-ray or macroscopic findings (Figure 3). Excellent spatial resolution of HRCT was clearly demonstrated from their comparison.

## DISCUSSION

HRCT examination of the lung using an extended scale and three-to-four fold magnification imaging format presented the most recent improvement in CT. It has excellent spatial resolution in high-contrast regions which have been expected

Table I

Age, Smoking Index, Duration of Occupational Exposure, RRCT, and Pulmonary Function Parameters According to Radiographic Categories (mean ±SD)

| X-P category | No | Age | Smoking Index | Duration of Expo. (year) | Dyspnea | CT | | | %VC (%) | RV/TLC (%) | $FEV_{1.0}$ %Z (%) | $V_{max}$/Ht L/sec/m | %DLco (%) | DLco/VA | PaO2 (torr) | A-aDO2 (torr) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | Nodular Profusion | Subpl. Emphy. | Central Emphy. | | | | | | | | |
| I | 10 | 58.5 ± 9.3 | 805.0 ± 350.7 | 27.2 ± 8.6 | 2.4 ± 1.2 | 0.3 ± 0.5 | 12.5 ± 24.3 | 37.5 ± 33.8 | 93.4 ± 17.5 | 42.5 ± 13.2 | 59.1 ± 19.8 | 0.33 ± 0.29 | 106.8 ± 19.5 | 4.74 ± 1.15 | 80.1 ± 6.2 | 21.2 ± 6.2 |
| 2 | 13 | 62.0 ± 8.0 | 654.2 ± 541.3 | 22.2 ± 8.3 | 2.0 ± 0.9 | 1.3 ± 1.3 | 20.5 ± 27.0 | 32.7 ± 27.7 | 97.6 ± 13.2 | 35.0 ± 6.5 | 65.3 ± 9.9 | 0.30 ± 0.12 | 106.3 ± 25.7 | 4.91 ± 1.29 | 79.0 ± 5.6 | 24.4 ± 7.9 |
| 3 | 6 | 58.8 ± 9.7 | 615.0 ± 145.8 | 21.0 ± 12.9 | 2.8 ± 0.8 | 1.2 ± 1.2 | 45.0 ± 27.4 | 55.0 ± 32.6 | 96.7 ± 28.0 | 33.9 ± 9.9 | 76.7 ± 6.7 | 0.57 ± 0.21 | 91.3 ± 41.2 | 4.21 ± 0.79 | 74.5 ± 7.2 | 28.2 ± 10.3 |
| 4 | 8 | 64.0 ± 12.8 | 417.5 ± 238.0 | 24.8 ± 7.6 | 3.4 ± 0.9 | 1.7 ± 1.3 | 12.5 ± 20.9 | 20.8 ± 10.2 | 92.4 ± 19.6 | 35.8 ± 11.3 | 60.8 ± 17.9 | 0.40 ± 0.33 | 112.4 ± 30.1 | 5.05 ± 0.96 | 79.5 ± 9.1 | 23.5 ± 7.1 |
| Total | 37 | 60.9 ± 9.6 | 655.8 ± 398.0 | 23.5 ± 8.9 | 2.5 ± 1.0 | 1.1 ± 1.2 | 22.4 ± 27.0 | 35.3 ± 28.9 | 95.7 ± 17.9 | 37.4 ± 10.4 | 64.2 ± 15.6 | 0.38 ± 0.24 | 106.3 ± 27.5 | 4.80 ± 1.00 | 78.7 ± 6.8 | 24.0 ± 7.4 |

to give the advantages in evaluating interstitial diseases such as pneumoconiosis. Several investigators have already reported the value of HRCT in evaluating pneumoconiosis.

We compared HRCT with conventional chest radiograph and pulmonary function studies.

Contrary to our expectation there are substantial discrepancies between radiological and CT evaluation. Concerning nodular opacities, HRCT showed good spatial resolution but lower profusion score than conventional chest radiographs. This may reflect the effect of summation in postero-anterior profection of plain X-P compared with the horizontal thin slice in CT. Attenuation of nodular opacities by emphysema also may contribute to this emphysematous cases because it is speculated that progress of emphysema may attenuate the nodular opacities.

Interstitial fibrosis, bullae, and emphysema were more clearly and specifically demonstrated on CT scan than conventional chest radiographs in most patients. The subpleural distributions of bullae were particularly well demonstrated in CT which may not be reflected in pulmonary function studies.

HRCT is useful for performing detailed morphological analyses of abnormalities of the peripheral portions of the lung, but no clear correlation was found between HRCT findings and pulmonary function parameters.

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Figure 2a. 54-year-old man with a history of silica-brick factory worker for 35 years. Chest radiograph showing small round opacities.

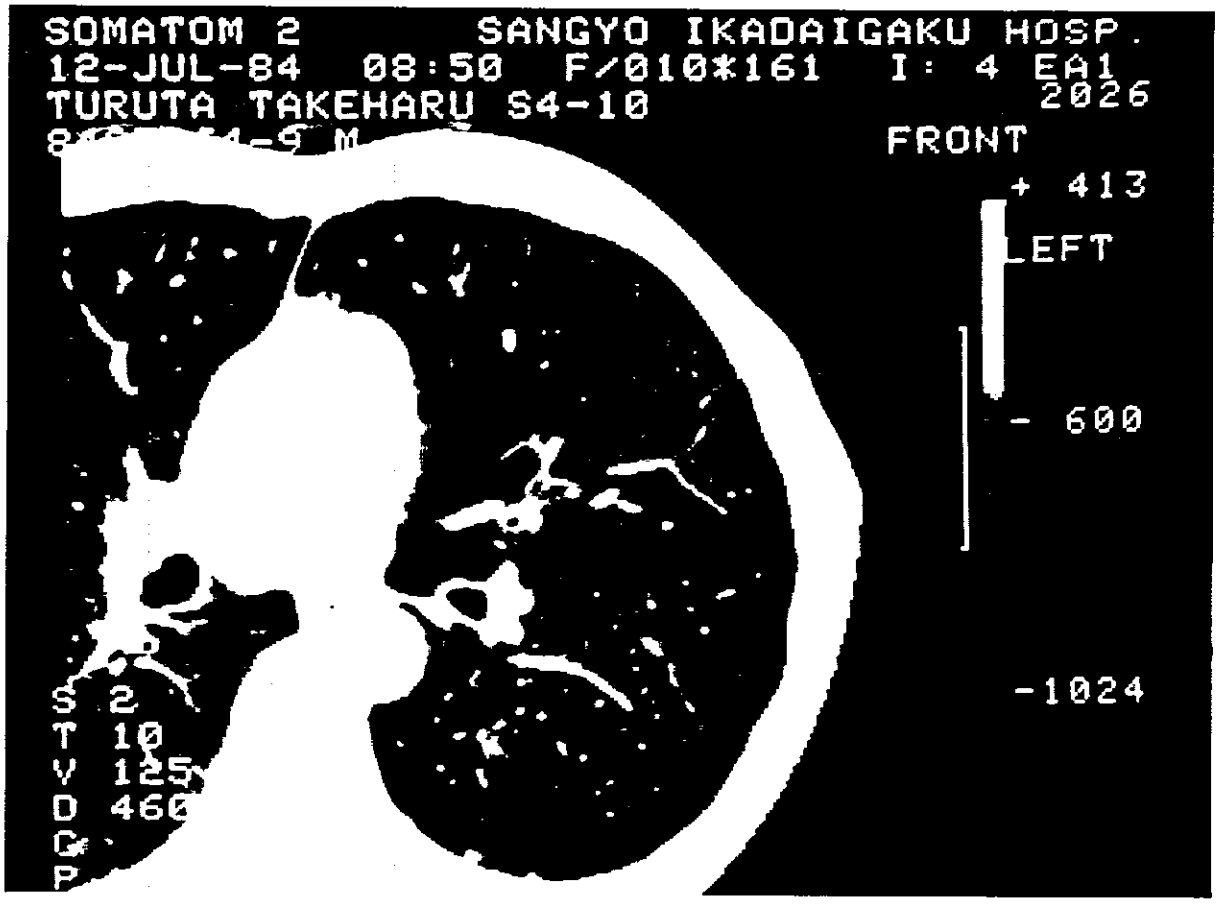


Figure 2b. HRCT. Diffuse well-defined small opacities in the middle lung fields.

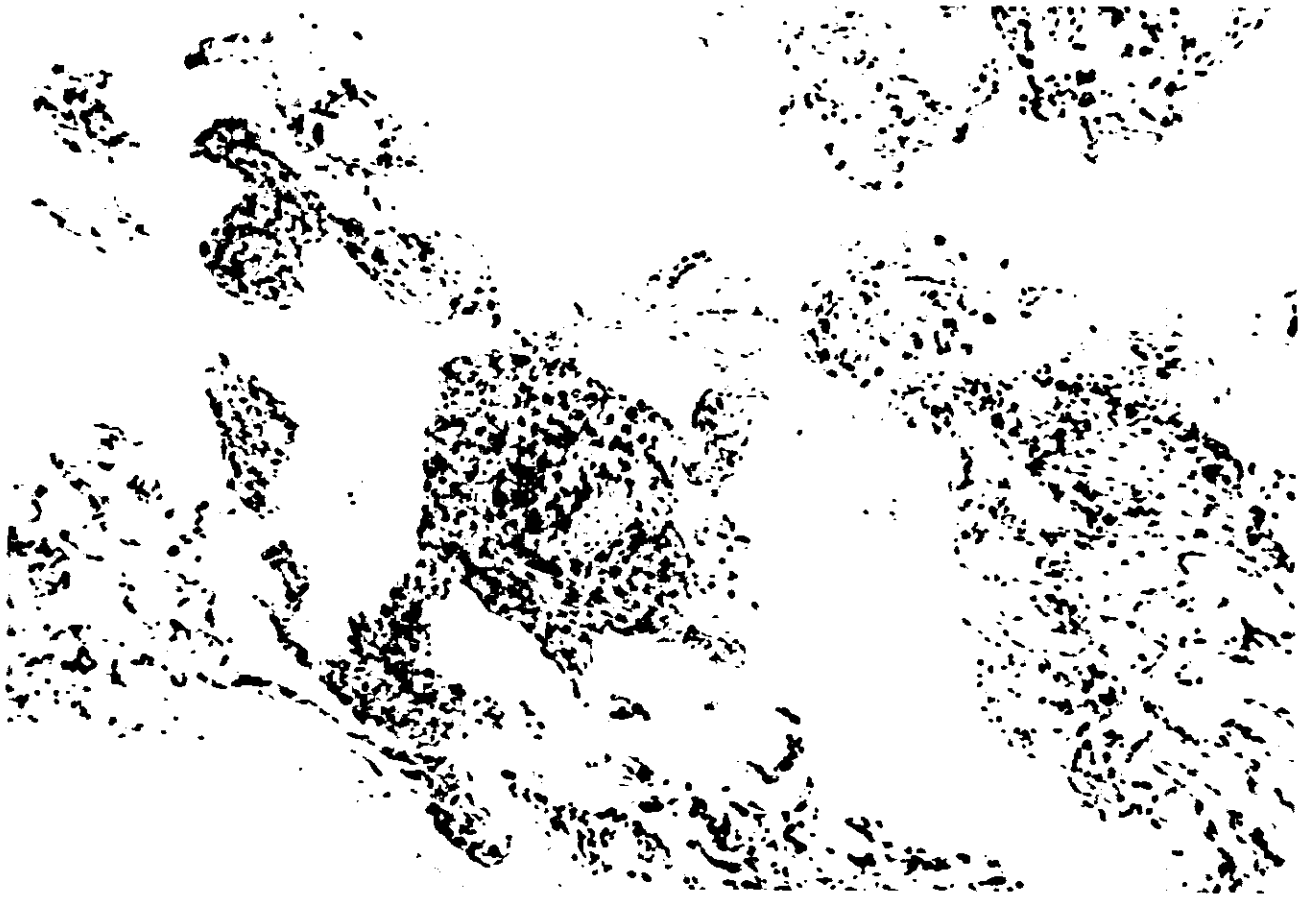

Figure 2c. Photomicrograph of transbronchial lung biopsy showing well-defined pneumoconiotic nodule. Hematoxylin and eosin stain, x40.

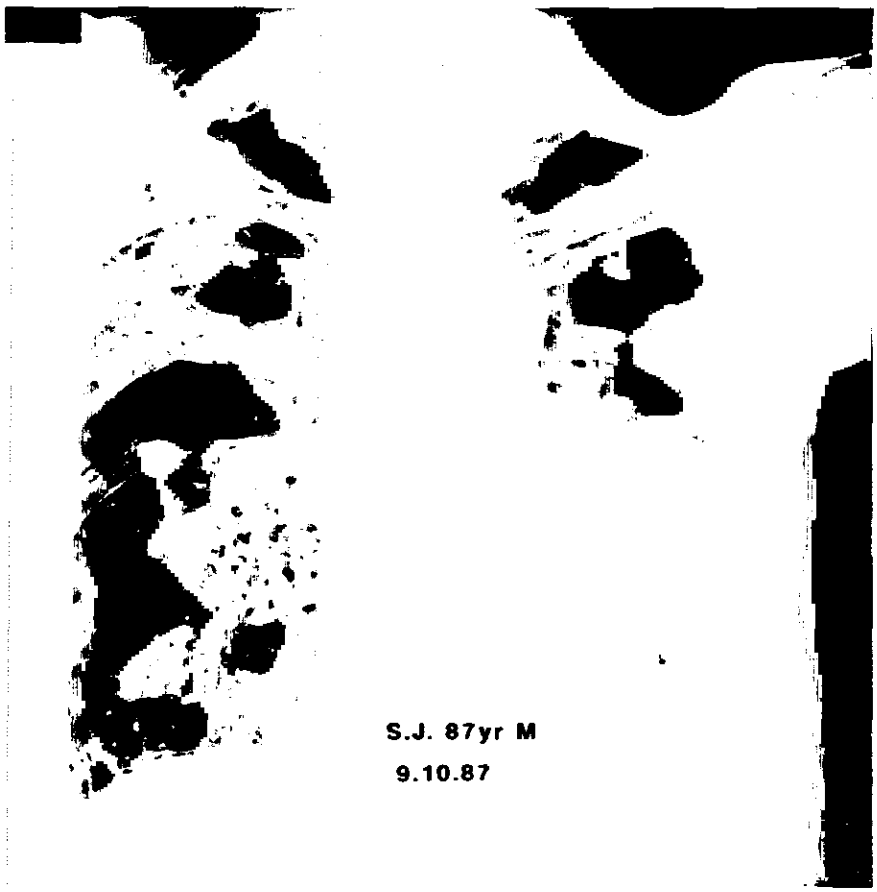


Figure 3a. 88-year-old man with a history of coal miner for 37 years.
Chest radiograph eight month prior to his death shows large opacities and fibrocalcified tuberculous change with few nodular opacities.

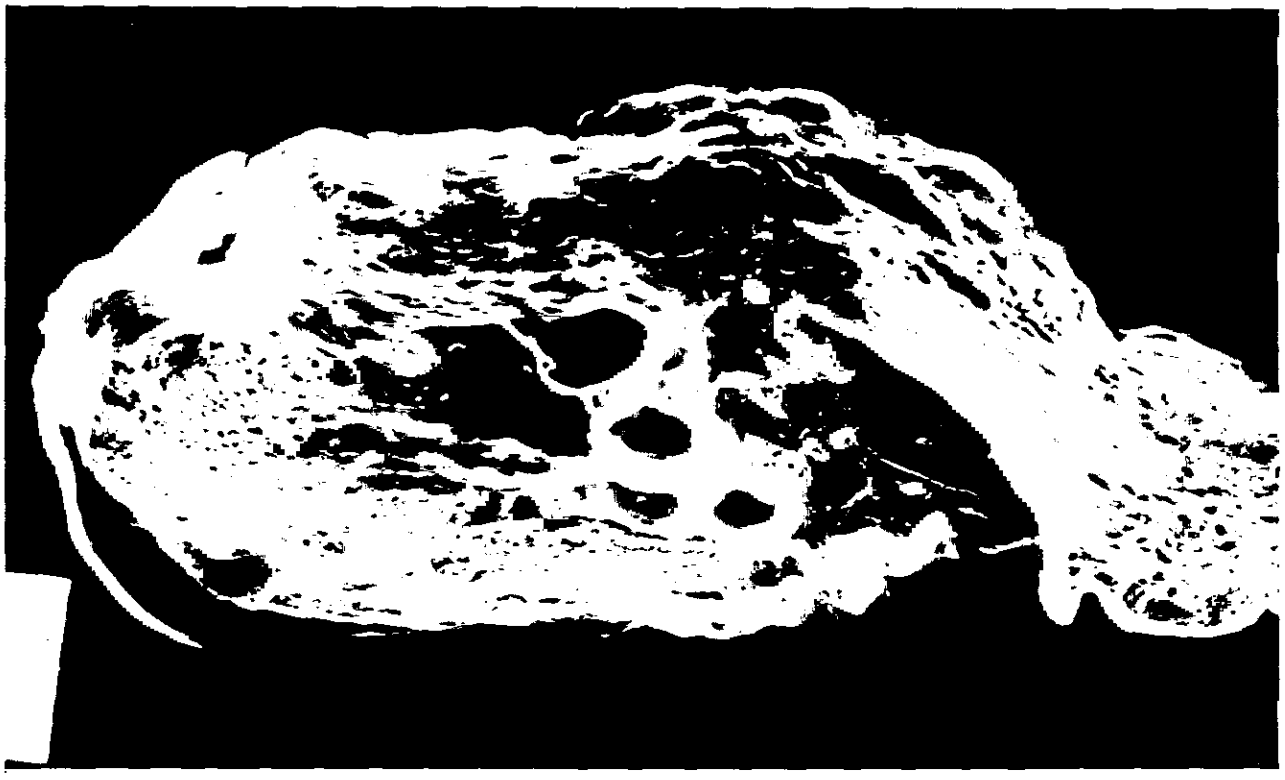

Figure 3b. HRCT of autopsied lung after fixation at the level of middle lung field.

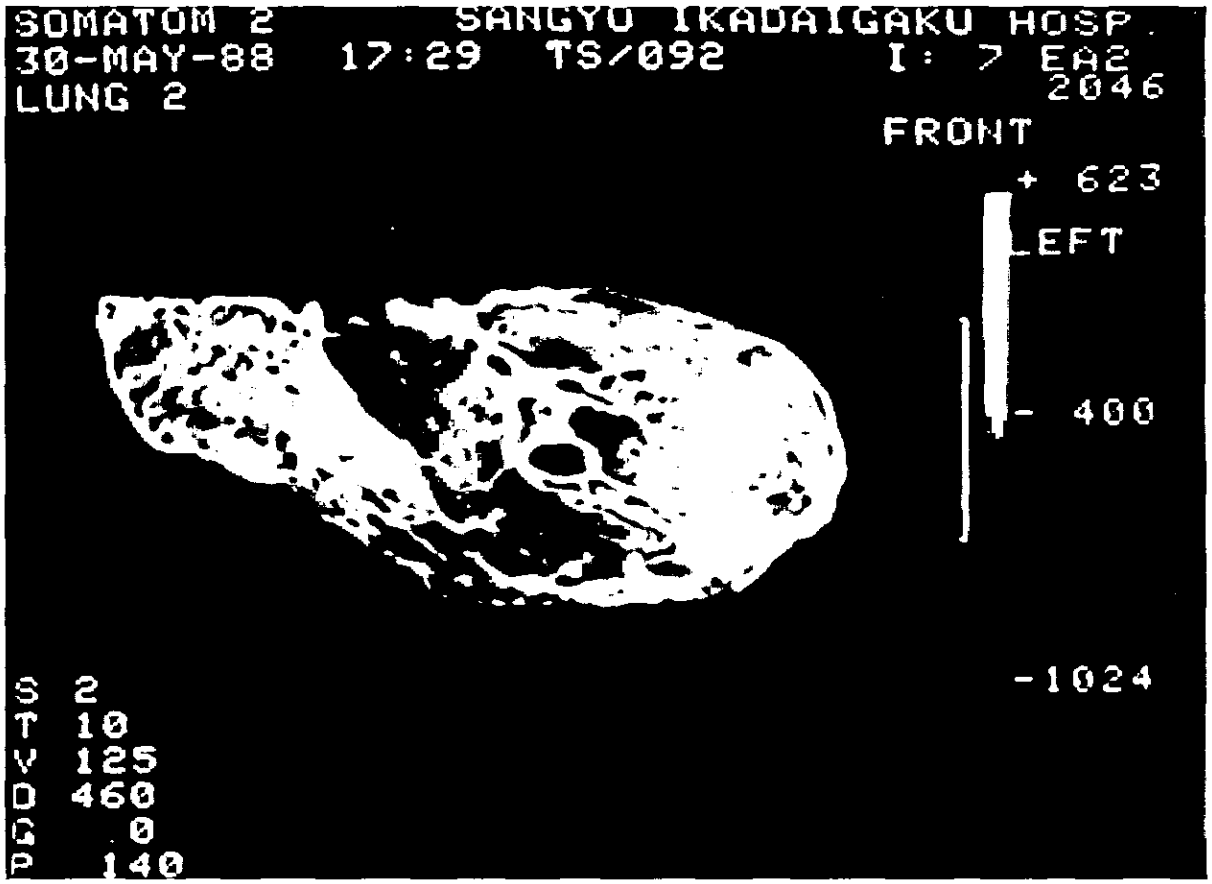


Figure 3c. Post-fixation radiograph of lung in the horizontal slice at the same level as HRCT.

Figure 3d. Macroscopic view of lung at the same level.

# ASBESTOS-ASSOCIATED ROUNDED ATELECTASIS IN A COHORT OF INSULATION WORKERS

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## ABSTRACT

Insulation workers with more than 30 years elapsed time since entering the trade were invited to participate in a nationwide screening. Twenty-nine hundred and seven men were examined between 1981 and 1983 in 20 U.S. cities. Twelve cases of lung cancer and two cases of pleural mesothelioma, previously undiagnosed, were discovered during the survey. By 1988, twelve were dead and two alive. Thirteen cases of asbestos-associated rounded atelectasis were also found. All were alive and free of cancer after a minimum of four years follow-up. Comparison of clinical parameters (duration from onset of exposure, ILO radiographic categories, pulmonary function test results, respiratory symptoms, smoking histories, findings on clinical examination) showed no major differences between the two groups. Asbestos-associated rounded atelectasis is not rare among workers with substantial asbestos exposure and latency.

## INTRODUCTION

Because of the well known increased risk of malignant disease among asbestos exposed workers, discovery of a lesion suspicious for neoplasm on the chest radiograph of an asbestos exposed individual is a cause for considerable concern.[1,2] Rounded atelectasis (RA) is a nonmalignant consequence of exposure to asbestos which, on chest radiographs, can mimic neoplasia. Since the first report in 1966,[3] asbestos associated rounded atelectasis (AARA) has been described in a number of case reports or case series.[4,5,6,7,8,9] One report has enumerated cases of AARA within a defined community, thus permitting an estimate of incidence of this condition,[9] though the methods and characteristics of the population differ substantially from those used in the present investigation.

We describe the prevalence of AARA within a well-defined cohort of asbestos insulation workers. Clinical parameters of cases of AARA are compared to those of cases of lung cancer and mesothelioma discovered during the same survey of workers. The cross-sectional prevalences of newly-discovered cancer and AARA were similar. No clinical features, aside from possible radiographic appearance, were capable of distinguishing AARA from cases of lung cancer or mesothelioma in this survey.

## METHODS

A cohort of asbestos insulation workers in the United States and Canada was established on 1 January 1967.[10] It included all 17,800 members on the roles of the insulation workers union (The International Association of Heat and Frost Insulators and Asbestos Workers (IAHFIAW), AFL-CIO, CIC) in the United States and Canada on that day.

A total of 5377 members of the cohort who were alive in 1981 and had reached 30 years from onset of work exposure were invited to appear for a comprehensive medical examination. Twenty-nine hundred and seven insulators were examined in 1981–1983, of which 2815 had greater than 30 years elapsed time since onset of exposure to asbestos. Reasons for non-participation (employment requirements, unrelated illness, family responsibilities, travel constraints, lack of interest) were ascertained and did not suggest significant selection bias. All survey participants are included in this analysis. Examinations were undertaken in Chicago, Columbus, Baltimore, Boston, Atlanta, Tampa, Seattle, Anchorage, San Francisco, Los Angeles, Denver, Omaha, St. Louis, Albuquerque, Dallas, Houston, New Orleans, New York, New Jersey, and Syracuse. The examinations included occupational, medical, and smoking history, review of symptoms, respiratory symptom questionnaires, physical examination, chest radiographs, pulmonary function tests, and laboratory tests.

Following completion of the survey in 1983, all chest radiographs were interpreted according to the 1980 International Labour Office guidelines for classification of chest radiographs for pneumoconioses.[11] In 1987, the radiographic interpretations of all 2907 insulation workers were reviewed. All cases in which the radiographic interpretation included comments such as "cancer," "mesothelioma," "pseudotumor," "rounded atelectasis," "nodule," "granuloma," "effusion," or suggested the presence of a nodule, effusion, or mass lesion were re-examined. In addition, all cases in which the recorded interpretation included ILO symbols suggestive of cancer ("ca"), effusion ("ef"), enlarged hilum ("hi"), or other lesions

("od") were also studied. One hundred thiry-nine cases were reviewed.

The initial review consisted of re-evaluation of the 139 chest radiographs obtained during the survey, without knowledge of patients' examination results or follow-up status. On the basis of the radiographs, patients were classified as "possible" cancer/AARA, or not cancer/AARA; the latter cases were excluded from further consideration. Previously published radiographic features of AARA were used as guidelines in the identification of AARA.[6] Each of the remaining cases was then reviewed using all available materials, including all data obtained at the time of the survey, subsequent correspondence with patients and/or their physicians, hospital records, previous and subsequent radiographs and radiology reports, death certificates, necropsy reports, independent analysis of pathologic material,* and direct contact with patients.

It was determined that twelve cases of lung cancer and two cases of pleural mesothelioma were discovered during the surey. (There were thirteen additional cases of lung cancer identified among participants of the survey, but these cases had been known or suspected prior to the survey and are not included in the analysis.) Thirteen study participants were classified as having AARA following a thorough review of available data and determination of clinical status after at least four years follow-up. Vital status of each of the 27 cases of interest was determined in one of two ways: death certificate; direct telephone contact with the patient or the patient's spouse.

## RESULTS

Two thousand nine hundred and seven men participated in the nationwide suvrey of insulation workers. As outlined above, 139 cases were reviewed in detail for this report. Using all available information and determination of vital status after a minimum of four years of follow-up, 13 cases of AARA and 14 cases of newly discovered cancer were identified. Twelve of the latter were lung cancer, and two were pleural mesothelioma. The prevalence of AARA among men who participated in the survey was 13/2907 = .45%, which is comparable to the prevalence of newly discovered chest cancers (14/2907 = .48%).

Twelve deaths occurred among newly discovered lung cancer and mesothelioma patients and were confirmed via death certificate. In addition to the underlying cause listed on the death certificate, ascertainment of the cause of death was supplemented by physician notes, hospital records, autopsy reports, and independent analysis of pathologic material. All deaths occurred less than four years after each individual's survey date, and all deaths were attributed to neoplasms discovered during the survey.

The remaining 15 patients were determined to be alive at least four years after their survey examinations on the basis of direct telephone contact with the patient (12 cases), or patients' wives (3 cases). At the time of telephone contact, all patients with AARA (or their wives) denied any history of chest cancer or chest surgery on direct questioning. Two patients with lung cancer were alive at the time of follow-up, at least four years after they participated in the survey. The diagnosis of cancer in these two patients was confirmed by pathologic analysis of surgical specimens.

Features of patients with cancer and AARA at the time of their survey examination are listed and compared in Table I. The mean age of the two groups did not differ greatly, although the cancer patients were 5 years older on average. Both groups had long latency periods, which is partly a reflection of the criteria used to invite workers to participate in the survey. The total number of current and former smokers was similar between the two groups, as were the mean number of pack-years among smokers. It is interesting to note that those with AARA more frequently reported having stopped smoking at the time of the survey than those discovered to have cancer. Results of spirometry, respiratory symptoms, physical examination findings, the frequency of pleural fibrosis, and the distribution of ILO parenchymal profusion scores were comparable. Although some differences between those with AARA and cancer were present (such as the incidence of cough, clubbing, or former versus current smoking), there is great overlap between the groups. The number of cases involved is small and does not merit statistical inference. More importantly, none of the clinical parameters examined (Table I) would permit differentiation of cancer from AARA in individual patients.

## DISCUSSION

Identification of AARA in this cohort of men with extensive exposure to asbestos and prolonged duration from onset essentially was a radiologic diagnosis, confirmed by follow-up of all cases after at least four years. Excluding radiographic appearance, cases of AARA could not be distinguished from what were determined to be newly discovered cases of lung cancer and mesothelioma. The cross-sectional prevalence of AARA was almost the same as that of newly diagnosed lung cancer.

In a radiographic survey of adults, Hillerdal identified 891 individuals with pleural changes presumed to be related to asbestos during a population survey of approximately 250,000 persons.[9] During a ten year period of follow-up, six cases of AARA were known to have developed among the 891 patients with pleural disease. All cases of AARA were confirmed at surgery. No details regarding exposure to asbestos, latency, or other clinical parameters were provided, and no mention is made of incidence of cancer within the cohort during the same period of follow-up. The ten year cumulative incidence of AARA, 6/891 = .67%, is similar to the prevalence of AARA discovered among the participants of our survey (.45%). However, these numbers should not be compared directly; one represents a 10 year cumulative incidence, and the other is a cross-sectional prevalence.

Asbestos insulation workers are known to have a high lifetime risk of developing lung cancer or mesothelioma.[1,2] AARA is a nonmalignant radiographic finding related to asbestos exposure. We have shown that the number of new cases of lung cancer and mesothelioma discovered during a survey of insulation workers is comparable to the prevalence of AARA. Among patients with a history of exposure to asbestos, clinical evaluation of suspicious lesions must be pursued aggressively. It must also be remembered that the

same population can develop AARA. Short of surgery and/or long term follow-up, the nonradiographic clinical features can be similar.

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Table I

Clinical Features of Patients with Newly-Discovered Cancer and Asbestos-Associated Rounded Atelectasis Among Insulation Workers

| | Cancer | AARA |
|---|---|---|
| Total Number of Cases | 14 | 13 |
| Mean Age at Examination (range) | 64.5 (53-73) | 59.4 (51-71) |
| Mean Years from Onset of Exp. (range) | 40.3 (31-52) | 36.2 (27-49)@ |
| Smoking History, number (%) | | |
| Current | 6 (42.9) | 1 (7.7) |
| Former | 6 (42.9) | 10 (76.9) |
| Never | 2 (14.3) | 2 (15.4) |
| Mean Pack-Years (smokers only) | 45.1* | 45.3* |
| Spirometry, mean percent predicted (range) | | |
| Forced Vital Capacity | 66.4 (36-105) | 69.5 (37-113) |
| Forced Exp. Volume 1 sec. | 59.4 (37-89) | 62.8 (20-106) |
| Forced Exp. Flow 25-75 | 60.1 (19-112) | 62.4 (9-105) |
| Symptoms, number (%) | | |
| Dyspnea | 10* (76.9) | 10 (76.9) |
| Hemoptysis | 1 (7.1) | 1 (7.7) |
| Cough | 8 (57.1) | 5 (38.5) |
| Physical Examination Findings, number (%) | | |
| Rales | 11 (78.6) | 12 (92.3) |
| Rhonchi | 3 (21.4) | 2 (15.4) |
| Clubbing | 6 (42.7) | 3 (23.1) |
| 1980 ILO Radiographic Scores | | |
| Parenchymal Fibrosis, number | | |
| Zero (-/0, 0/0, 0/1) | 1 | 3 |
| One (1/0, 1/1, 1/2) | 5 | 7 |
| Two (2/1, 2/2, 2/3) | 5 | 3 |
| Three (3/2, 3/3, 3/+) | 3 | 0 |
| Pleural Fibrosis, number (%) | 14 (100) | 12 (92.3) |

@ = one patient had less than 30 years
* = missing results from one case

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