CARBORUNDUM PNEUMOCONIOSIS

R. BÉGIN, M.D. • A. Dufresne, Ph.D. • A. Cantin, M.D. • Massé, M.D. • P. Sébastien, Ph.D. • P. Durand, Ph.D. • G. Perrault, Ph.D.

Université de Sherbrooke, Sherbrooke (QC), Dust Disease Unit, McGill School of Occupational Health, Montréal (QC) and Institut de Recherche en Santé et Sécurité au Travail, Montréal (QC)

INTRODUCTION

Silicon carbide (SiC) also called carborundum is a universally used abrasive produced by the fusion of high-grade silica and finely ground carbon in electric furnace at 2400°C. A recent review of the subject in Parkes textbook[6] led to the conclusion that there was no evidence that exposure to silicon carbide dust gave rise to a pneumoconiosis.

Nonetheless, pneumoconiosis has been reported in long term workers engaged in the manufacturing of SiC and it was suspected that sick workers had been previously exposed to other dust hazards or to quartz dust in the raw materials of the manufactures. One pathological report raised the possibility of a carborundum pneumoconiosis.[4]

Recent investigations in the Quebec carborundum industry have documented an excess of radiographic abnormalities compatible with pneumoconiosis, particularly in older workers of the industry.[7] In view of these findings, collaboration with the industry was established and a thorough multidisciplinary investigation was initiated.

Pathological studies of available lung tissue from long term workers of the SiC industry were analyzed in detail.[5] Recent chest radiographs of 1984 and 1979 of some 128 workers were reviewed.[3] Evaluation of occupational exposures in the industry was conducted and reported in detail.[1,2] A review of the occupational hygiene led to the preparation and characterization of reference samples of respirable particles collected in the SiC production industry for use in this experimental research.

The objectives of this study were to evaluate the in vivo lung biologic activity of the mineral dusts found in the carborundum manufacturing industry, to identify the offending dust in order to establish appropriate control of dust level in the workplace.

MATERIALS AND METHODS

Experimental Design

Seventy-two sheep were used in this study. The flock was divided into 9 groups of 8 sheep. Following pre-exposure (control) studies, the sheep tracheal lobe was exposed to:

- 100 ml saline = Sa group (control);
- 100 mg latex beads in 100 ml saline = latex group;
- 100 mg graphite in 100 ml saline = graphite group;
- 100 mg SiC raw particles in 100 ml saline = SiCp group;
- 100 mg SiC ashed particles in 100 ml saline = SiCpa group;
- 100 mg Minusil-5 in 100 ml saline = Si group;
- 100 mg crocidolite fibers in 100 ml saline = Cro group;
- 100 mg SiC raw fibers in 100 ml saline = SiCf group;
- 100 mg SiC ashed fibers in 100 ml saline = SiCfa group.

Exposure to the tracheal lobe was carried out via bronchoscopic infusion of the suspension in the lobe. The animals were studied prior to exposure and post-exposure at month 2, 4, 6, and 8 by BAL and by histopathological methods at month 8.

The Minerals

The materials for exposure were obtained from the following sources: Latex beads from Sigma Chemical Co., St-Louis, MO; these particles are uniform in size with a mean diameter of 1 μ. Minusil-5 from Pennsylvania Glass Co., Pittsburgh, PA; the silica particles are well characterized with 99.9% of diameter $< 5\,\mu$, and 95% $< 1\,\mu$. Crocidolite fibers from the Union Internationale Contre le Cancer (UICC); these fibers have a known diameter of $0.17 \pm .01\,\mu$ with an average length of $3.9 \pm 0.2\,\mu$ 95% of fibers with a length $< 10\,\mu$, 82% $< 5\,\mu$.

All other samples were obtained from the Quebec SiC industry, prepared and characterized. Briefly, these materials were collected from the production sites in the Acheson furnaces of two Quebec SiC plants. The non-fibrous SiC was collected from the center of large lumps of produced materials. The SiC fibers were collected mainly from the outside part of the main cylindrical lump produced by the process. The graphite was extracted from the core of a fired Acheson furnace. The raw particulate and fibrous SiC were, as expected, contaminated with graphite flakes on surface, which at least in theory, could alter biological activity. To eliminate these contaminants, reference samples of fibrous and particulate SiC were ashed. Graphite particles were 98.8% $< 5\,\mu$, particulate SiC raw or ashed were 99.5% $< 5\,\mu$. For the SiC fibers, seventy percent of fibers were less than 5 μ, with some longer than 20 μ. The fibrous SiC raw or ashed were of an average of $0.27\,\mu \pm 0.27$ diameter with an average length of $6.8 \pm 11.2\,\mu$. These morphometric data were considered in the

selection of the asbestos fiber crocidolite, for comparison in these experiments.

Assessment of Lung Reaction

To evaluate the disease process induced by exposure to these respirable minerals, we looked at lung lavage cellularity and biochemistry as biologic indicators of alveolitis. The severity of lung tissue damage was evaluated at autopsy, 8 months after exposure, by histopathology. To assess interstitial lung matrix changes we looked at the glycosaminoglycan accumulation in BAL fluid. We also measured the production of fibronectin by BAL cells in culture.

Lung lavage fluid was analyzed for the presence of molecules capable of enhancing fibroblast proliferation.

Histopathology

At month 8 of the study, all sheep were sacrificed and the lungs removed from the chest cavity. The tracheal lobe was identified and 9 samples of the lobe of each sheep were obtained each time for microscopic examination.

RESULTS

The Particulates

In comparison to Sa group, all the particulate exposed groups had a slight and transient early increase in cellularity except for the Si group, which had an early 500% increase in cellularity which decreased to 250% at month 4, but remained elevated to the end of experiment. This was largely due to increase in the macrophage population, but increases in lymphocytes and neutrophils were also significant and sustained in the Si group. Similarly, in the biochemical and cell culture analyses, only the Si group had significant increases in BAL lactate dehydrogenase, glycosaminoglycan, and increased production of fibronectin and fibroblast growth activity. The lung morphology of the sheep was normal in groups Sa and latex. The lung tissue of sheep in the graphite group, SiCp and SiCpa groups contained accumulation of particles in alveoli and interstitium without cellular reaction. In the graphite exposed sheep, the morphologic changes are reminescent of the early simple pneumoconiosis of coal workers.[6] In the Si exposed sheep, the lung changes are characterized by a diffuse alveolitis with early nodular silicotic lesions as reported in our earlier studies. The pathological scores were 0 ± 0 for Sa group, latex group, graphite group, SiCp group and 2.9 ± 1.0 for the Si group ($p < 0.01$ for Si group vs others).

The Fibers

Briefly, cellularity of BAL was increased in all the fiber groups following exposure with a larger attenuation for the SiCf group. This effect was pancellular and was also seen in the pattern of response of LDH overtime. Fibronectin production was significantly increased, again with some attenuation for the SiCf group. Fibroblast growth activity was increased significantly in all fiber groups.

Pathologic analysis of lung tissue in the crocidolite exposed sheep revealed a peribronchiolar fibrosing alveolitis as previously reported in other asbestos exposure. In the fibrous carborundum exposed sheep, we found nodular lesions in the parenchyma which were not located around the bronchioles. These nodules were composed of multinucleated macrophages, monocytes and a few neutrophils and contained several carborundum fibers and "bodies." The intensity and profusion of lesions in the fiber groups were: 1.9 ± 0.25 for Cro group, 1.2 ± 0.21 for the SiCf and 1.6 ± 0.2 for the SiCfa group ($p > 0.05$ between the 3). The slightly lower score ($p > 0.05$) in the SiCf compared to SiCfa could suggest a partial inhibitory effect of the graphite on surface of the SiCf fibers.

DISCUSSION

In recent years, several epidemiological and clinical investigations have suggested that carborundum workers may have a specific occupational lung disease. This experimental study of the airborne dust particles and fibers in the carborundum industry provides significant new information on the pathogenesis of interstitial lung disease in workers of that industry. It documents that of all the non-fibrous particulate minerals encountered on site, only silica appears to be potentially responsible for some of the lung injury. In addition, this study documents clearly that fibrous SiC has significant biologic activity and can initiate a fibrosing lung disease. In SiC manufactures, SiC fiber inhalation can contribute to the genesis of an interstitial lung disease. Therefore, it is appropriate to recommend that surveillance of the work environment in that industry should include an assessment of airborne fiber levels.

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IMAGING THE PNEUMOCONIOSES IN 1988: A MULTIDISCIPLINARY APPROACH

R. BÉGIN, M.D. • S. Massé, M.D. • A. Cantin, M.D. • G. Bisson, M.D. • D. Bergeron, M.D.

Centre Hospitalier Universitaire, Sherbrooke, Québec, Canada J1H 5N4

INTRODUCTION

In recent years, it has become increasingly clear, on the basis of human and experimental data, that lung fibrosis associated with mineral dust inhalation was the end-stage phenomenon of a long chronic inflammatory process initiated by the retention of biologically active mineral particles in the lung tissue.

The early stages of lung tissue reaction to mineral dust deposition is characterized by an excessive accumulation and activation of macrophages in the peripheral bronchoalveolar tissue. This is well documented both in animal studies[9] and in humans.[4,5,16] Asbestos dust inhalation produces the fundamental early lesion of asbestosis the peribronchiolar fibrosing alveolitis; quartz dust inhalation produces the more nodular, often perivascular accumulation of macrophages and lymphocytes in the alveolar spaces of lung tissue.

As these mineral dust diseases progress, they are associated with extension of the process to the adjacent alveolar and interstitial lung tissues which leads to diffuse interstitial lung fibrosis. However, we know now that this process can be limited to its early peribronchiolar reaction and leave the lung tissue nearly intact. This is particularly the case for asbestos-induced lung disease. In silica-induced lung disease,[11] after the initial nodular lesion, the process becomes less inflammatory, fibroblasts accumulate in the nodules with excessive deposition of reticulin and collagen in and between the cells in the nodule, and eventually the fibrotic collagenous process aggregates the individual nodules to form masses of fibrotic tissue.

Knowing these fundamental pathological processes, strategies to detect these diseases at an early inflammatory stage have been developed.

MODES OF DETECTION

Rales

The observation of bilateral basilar end-inspiratory in asbestos workers with or without asbestosis suggest that auscultatory rales are found in most workers with asbestosis; their profusion correlates fairly radiographic and functional parameters of severity of asbestosis.[3] However, rales are the initial finding of disease in asbestos workers in less than 5% of cases and when present, they likely reflect a fibrotic process already in place. In quartz exposed workers, rales are usually absent and of limited interest in detection of silicosis.

Chest Radiograph

The standard PA high kilovoltage chest radiograph is the definite indicator of the mineral dust pneumoconiosis and its value has been well established for the detection of both asbestosis and silicosis. However, it has been documented that the chest radiograph can be normal in up to 10% of symptomatic patients with proven interstitial lung disease. In asbestosis, we have documented similar findings,[3-5] and in silicosis substantial pathological changes in the lung tissues have been observed in stone cutters with normal chest radiograph.[11] Thus, whereas chest radiograph is a useful mode of detection of disease, cannot be considered as a sensitive indicator of early disease.

Computed Tomograph of the Thorax

In asbestos related pleuropulmonary diseases, earlier clinical studies[13,14] on relatively small populations of patients have found that the CT scan was significantly more sensitive than conventional chest X-rays in the detection of disease. We obtained a CT scan of the thorax in 127 long term asbestos workers who were also evaluated by conventional posteroanterior (PA), lateral and obliques (4-view) X-rays, and clinical and functional evaluations.[2] Our analysis of the total scores of the pleuropulmonary changes and profusion of parenchymal opacities shows that the three methods can detect about the same total amount of abnormalities in each subset of workers, which is at variance with previous clinical reports.[13,14] Pleural plaques were scored slightly higher on the four-view films than on the PA film, in agreement with a previous report comparing these methods,[13,14] but pleural plaques were scored significantly lower on the CT scan, mostly because of the lower yields at the costophrenic angles and diaphragms. The largest discrepancies between the three methods were observed in the evaluation of pleural calcifications. On PA films, calcified pleural plaques were often suspected, but could be confirmed by one of the other methods in only two of nine cases. Of the 27 definite pleural calcifications detected in our 127 asbestos workers, however, 14 were detected only by CT scan and all those detected by the PA and four-view films were also observed on the CT scan. Our data on asbestos workers without sufficient criteria for asbestosis but with rigid P-V curve and increased Ga-67 lung uptake show that the CT scan does not detect significantly more pleuropulmonary abnormalities than PA films. With both methods, workers with early asbestos alveolitis could not be separated from those without asbestos alveolitis or asbestosis.

In 58 silica-exposed workers, we have also used computed tomography of the thorax.[7] On the basis of chest radiograph, 6 were without silicosis, 30 had simple silicosis without coalescence or large opacity, 13 had silicosis with coalescence and 9 had silicosis with large opacity. In the presence of simple silicosis without coalescence or large opacity on plain chest film, CT scanning of the thorax revealed conglomerations in 10/30 cases, 70% of which could not be seen with the addition of lateral and oblique chest films. This additional information on the presence of conglomeration is particularly important as it identifies the presence of a complicated disease which could be either early coalescence of silicotic nodules, tuberculosis or other lung processes such as lung tumor. Further investigations documented that of the 10 conglomerations detected by CT scan only, 2 were tuberculous lesions, 1 was a carcinoma and 7 were of silicotic origin. It has been reported in the last year that the use of ultra-thin CT scan cuts (1-2 mm) may improve the imaging of interstitial reticular or nodular lung lesions. However, these clinical observations by others and ourself have not been scientifically validated.

Gallium-67 Scan

Ga-67 scanning has been used in clinical medicine for over 15 years in the detection of tumors and sites of occult infection, two disease processes associated with chronic inflammation. The mechanisms of localization of the radionuclide in the inflammatory site, however, has been only partially clarified recently. After intravenous injection of the radionuclide, Ga-67 is rapidly bound to serum proteins, transferrin, haptoglobin and albumin, and less than 1% is transferred to the leucocytes. Gallium-67 lung uptake is primarily associated with activated macrophages producing excessive amount of fibronectin[4] and to correlate with histopathological scores of inflammation in lung tissue and with BAL levels of Ga-67 radioactivity retrieval.[4]

In asbestos workers of the mines and mills of Quebec, we have obtained routinely Ga-67 scans in over 300 workers who can be divided into 4 categories:

A = workers without asbestosis and normal scan,
B = workers without asbestosis and abnormal scan,
C = workers with asbestosis and abnormal scan,
D = workers with asbestosis and normal scan.

The workers in groups A and B have chest radiograph in the ILO categories 0/1 or 0/0 and they do not have bilateral rales on auscultation. Their lung volumes are within normal prediction but some 66% of the workers in group B have increased rigidity of the lung pressure-volume curve and exercise induced hypoxemia.[3,11] On lung biopsy, they have a peribronchiolar macrophagic alveolitis. The workers in groups C and D have radiographic changes of category $\geqq$ 1/0, the majority of them have bilateral rales and a restrictive pattern of lung function. What differentiates groups C and D is that workers with asbestosis in group C have increased Ga-67 lung uptake whereas those in group D have a normal scan. These differences between groups A and B or C and D are not related to pleural disease,[15] but relate best to the rate of fall of vital capacity; the workers with enhanced Ga-67 lung uptake have increased rates of decline of vital capacity per year.

We have obtained computer-based quantitative analysis of Ga-67 uptake in a group of 46 long term workers exposed to silica dust at work in the granite industry or in foundry and in a group of 13, age, sex and smoking habit matched controls. In the controls, Ga-67 scan index averaged 1.77 ± 0.46; in the 11 workers exposed to silica dust without silicosis, the index was 3.05 ± 0.69. In 12 workers with simple silicosis 3.75 ± 0.70; in 8 workers with silicosis and coalescence it was 7.25 ± 2.23 and in 15 workers with large opacities it was 7.97 ± 1.03. These data therefore confirm the work of Siemsen in documenting that Ga-67 lung uptake is enhanced in silicosis and document that in long term silica-exposed workers with or without simple silicosis, Ga-67 lung uptake is increased at 200% control value and when the disease becomes complicated by coalescence and/or large opacity, the Ga-67 uptake is further enhanced to 400% control value.

Bronchoalveolar Lavage

In the interstitial lung disease which could be related to asbestos exposure, BAL analyses are of interest: 1) to eliminate other etiologies of lung injury, 2) to document asbestos exposure, 3) to support other clinical information, 4) to study the biological mechanisms. Following our initial report of a substantial number of long term workers with abnormal Ga-67 scan in the absence of other criteria for asbestosis,[1] we have investigated several asbestos workers and similar studies were conducted by Dr. Rom at NIH. In these studies, it was documented that macrophages of the bronchoalveolar space of asbestos exposed workers demonstrated marked structural changes, were producing excessive amount of fibronectin, fibroblast growth factor and increase γ-interferon which could participate in the pathogenesis of asbestosis. In our experimental studies in the sheep model, we have fully reported similar evidences of activated macrophages producing excessive amount of fibronectin, fibroblast growth factor and neutrophil chemotactic factors. Thus, these data document that in support of a diagnosis of early asbestosis (asbestos alveolitis), BAL analyses can provide additional information which pertains to several mechanistic features of disease activity.

Among our silica workers presented in the Ga-67 scan section of this paper, we obtained BAL in 17. In the workers without silicosis (group 2), our results demonstrated increases in total cellularity (× 2), macrophage (× 2), lymphocyte (× 1.5), neutrophil (× 4), eosinophil (× 2), albumin (× 2.5) and immunoglobulin IgM (× 5), without increases in fibronectin or procollagen. These data in silica exposed long term workers without overt silicosis are essentially in agreement with the data of Christman et al[10] in documenting the presence of a sub-clinical quartz alveolitis in these workers. In the workers with simple silicosis, cellularity of BAL is further increased, particularly for lymphocytes (× 4 control), neutrophils (× 8 control) but with BAL biochemical results comparable to those of group 2. In the workers with complicated silicosis (coalescence and/or large opacity), cellularity is also increased but, whereas albumin in BAL is now comparable to control, immunoglobulins IgG, IgA, IgM are the

highest, fibronectin and procollagen are highly increased ($P < 0.05$), which would agree with the current concepts of an activated fibrotic process. Of interest, we have also documented that when the disease was radiographically detectable, there was a significant increase in fibroblast growth factor which was observed even in the absence of coalescence and/or conglomeration.[8]

Pulmonary Function Tests

In the evaluation of early disease in asbestos workers, several investigators have suggested that spirometry, diffusion and gas exchange studies could identify workers with asbestosis as well as chest radiograph. Futhermore, it has been documented by Jodoin et al,[12] and confirmed in our own investigations that rigidity of the lung pressure-volume curve could be seen in several workers without radiograph changes.[3,4] We have further documented that this finding was usually associated with enhanced gallium-67 lung uptake and when a lung biopsy was obtained, it showed the fundamental early macrophagic peribronchiolar alveolitis associated with early asbestosis. Also we found that early peribronchiolar disease did not significantly reduce the spirometric flow rates but caused a slight increase in upstream resistance only at low lung volumes.[6]

In silica-exposed workers, we have also obtained the usual lung function tests as well as pulmonary mechanics. This is the subject of distinct report.

DISCUSSION

Recent researches in the biology of the mineral dust pneumoconioses have substantially increased our understanding of the sequence of events leading to fibrosis of the lung. Fibrosis in the mineral dust pneumoconioses is an end-stage result of a chronic inflammatory process which is continuously activated by the chronic retention of the mineral particles in the lung tissue. In parallel, in-depth clinical investigations of mineral dust exposed workers with or without pneumoconiosis have identified workers without the classical findings of the pneumoconiosis but with significant abnormalities of CT-scan, lung lavage, Ga-67 lung scan and lung pressure-volume curves similar to those of early disease in the animal studies. These abnormalities can detect the early inflammatory lesion of mineral dust pneumoconioses before its fibrotic stage. Newer approaches to prevent fibrosis of the lung tissue are currently under animal investigation in several laboratories.

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EXPERIENCE WITH THE ILO CLASSIFICATION (1980) IN RELATION TO EXPOSURE TIME IN $ COAL MINES IN THE FRG

W.T. ULMER • U. Bengtsson • H.L. Reischig • B. Speckmann • H.-J. Vautrin • I. Zimmermann

Pneumoconiosis Research Institute, Bochum (FRG)

ABSTRACT

2347 coal miners were examined in 4 coal mines. The relation between exposure time and X-ray changes following the ILO-classification 1980 is relatively linear. Therefore, for a single coal miner as for the mean value of a mine, an "ILO-classification-step-time" can be determined. Assessed according to ILO-classification categories, on the X-rays the increase shows the same augmentation after termination after 15 years of exposure time as the group of workers still active. In the ILO-classification-step-time, there are tremendous differences (1:10) between different coal workers as well as between mean values of different mines (1:7). From the ILO-classification-step-time, the useful time interval of X-ray reexaminations of coal workers can be detected, too.

No Paper provided.

LUNG FUNCTION MEASUREMENTS ON COAL MINERS

W.T. ULMER • U. Bengtsson • H.L. Reischig • B. Speckmann • H.-J. Vautrin

Pneumoconisis Research Institute, Bochum (FRG)

ABSTRACT

We performed measurements of airway resistance, thoracic gas volume and arterial blood gases at the same time as X-ray examination with 2496 coal miners. The reagibility of airways was controlled by metacholine-challenge tests, too.

There are age-dependents in 2 to 6,5% miners with signs of an obstructive airway disease. 9,5% showed a hyperreagibility of airways. The hyperreagibility was not age-dependent. There was no correlation between these lung function disturbances and X-ray changes. For the health situation of miners it is important to find out persons with obstructive airway disease in order to avoid a further deterioration of this affection.

No Paper provided.

VISCERAL PLEURAL THICKENING IN ASBESTOS EXPOSURE: THE OCCURRENCE AND IMPLICATIONS OF THICKENED INTERLOBAR FISSURES

S. DAVID ROCKOFF,* M.D., F.A.C.R. • Arnold Schwartz,* M.D. • William Hix,*M.D. • Prashant Rohatgi,* M.D. • Elliot Kagan,† M.B., BCh, MRCPath • David Kriebel,‡ Sc.D.

*The George Washington University Medical Center (GWUMC), Washington, DC, USA
†Georgetown University Medical School, USA
‡School of Public Health, Harvard Medical School, USA

INTRODUCTION

The interlobar fissures are lined by visceral pleura. We have noticed, radiographically, the frequent occurrence of thickened interlobar fissures in asbestos exposed individuals, even when the lungs have been normal otherwise. Visceral pleural thickening in asbestos exposure has not received much attention in the diagnosis of asbestos-related thoracic disease, having been considered mainly to be an extension of a more diffuse pleural reaction to asbestos dust.[1] However, in the 1980 revision of the I.L.O. classification, provision was made to indicate fissural thickening as being present or absent. We studied the significance of such thickening[2] and describe the potential practical application of fissural thickening on radiographs as an early sign of asbestos exposure. The peripheral deposition of inhaled asbestos fibers in the lung[3-5] and the fact that visceral pleural thickening is the usual finding histologically in asbestosis,[6] provides a reasonable expectation for a relationship between asbestos exposure and visceral pleural thickening radiographically.

METHODS

A *control group* of 100 adult male patients with no known asbestos exposure, with good quality posterior-anterior (PA) and lateral chest radiographs read as "no active disease" and admitted for non-thoracic problems were selected from 257 consecutive admissions, after 157 were excluded for inadequate radiographs and/or radiographic evidence of obvious cardiopulmonary disease. The radiographs were classified as to the presence and degree of fissural thickening. All had otherwise normal appearing lungs.

The *study group* was comprised of 220 asbestos-exposed workers drawn from 241 consecutively encountered individuals participating in an occupational screening program, with 21 being eliminated for absence of adequate radiographs or the presence of cardiopulmonary disease which could interfere with the interpretation. The number of years since first occupational contact was recorded as a measure of asbestos exposure. The radiographs of the study group subjects were analyzed for the following factors:

1. *Parietal pleural plaque formation* was noted to be present, absent or questionable.
2. *Interstitial pulmonary fibrosis* was noted as the presence or absence of accentuation of the nonvascular, fine linear lung markings of the type generally referred to as "small irregular opacities," without an attempt to grade the degree of profusion.
3. *Fissural thickening* was graded as 0 = Normal fissures, being <0.5 mm throughout; +/- = Questionable thickening, with areas of apparent thickening (>0.5 mm), which could represent either localized fissural thickening or superimposed fissures; 1 + = Minimal fissural thickening with definite, localized thickening of >0.5 and <1.0 mm; 2 + = Moderate fissural thickening with definite, diffuse fissural thickening >0.5 and <1.0 mm, involving the equivalent of a large portion of the length of a major or minor fissure, with or without localized plaques; 3 + = Marked fissural thickening was extensive, diffuse involvement of the fissure(s) as evidenced by thickening of virtually all of the major and/or minor fissures and/or thickening predominantly >1.0 mm.

In addition to the control and study groups, a series of individuals with *clinically and/or histologically diagnosed asbestosis* were studied to see whether asbestos-induced fissural thickening occurs in the absence of pulmonary fibrosis and, regardless of the presence of radiographically-evident pulmonary fibrosis, to analyze the plain film and computed tomographic appearances of visceral pleural thickening in interlobar fissures.

STATISTICAL METHODS

Group means were examined with Student's "t" test and the relationship between years since first exposure to asbestos and the occurrence of pleural abnormalities was investigated by fitting logistic models, as described in our earlier paper.[2] These models corrected for the effect of the person's age on the data.

RESULTS

A. *Control Group:* Combining fissural thickening of 0 and

+/- degrees as "normal" and 1+ to 3+ as abnormal, 84% had "normal" fissures while 16% had fissural thickening. Of those with fissural thickening, none was marked (i.e., 3+) with an equal distribution between "slight" and "moderate" thickening.

B. *Study Group:* Definite fissural thickening was observed in 54.5% while 45.5% had radiographically "normal" fissures. The relationship between fissural thickening and years from first exposure is shown in Figure 1 where it is seen that the 50% probability of having fissural thickening occurs at 21 years after first exposure. With regard to parietal pleural plaques, 38.2% had definite plaque formation while 61.8% had none. As shown in Figure 2, the 50% probability of having pleural plaques occurs 31 years after first exposure. Both the pleural plaques and the fissural thickening were associated with the length of time since first exposure. These data show not only that fissural thickening occurs some 10 years earlier than pleural plaque formation, but also that it is a more common lesion (i.e., 54.5% vs. 38.2%). However, the two types of pleural changes generally occurred together with 85% of those with parietal pleural plaques also having fissural thickening. Further, it was relatively uncommon to see radiographic evidence of pulmonary fibrosis in the absence of fissural thickening.

C. *Fissural Thickening in Clinical Asbestosis:* In studying our series of asbestosis patients, the radiographic finding of fissural thickening was uniformly found even in the *absence* of diffuse chest wall pleural thickening. Pulmonary asbestosis was found histologically in the absence of radiographic changes in the lungs. (Figure 3) The uncalcified fissural thickening as seen on plain chest radiographs and on computed tomograms is demonstrated in Figure 4. In one of our cases, the fissure was calcified on CT only.[7]

DISCUSSION AND CONCLUSIONS

The data presented suggest some interesting possibilities with regard to the earlier radiographic diagnosis of pulmonary asbestosis. While the relationship between radiographically visualized fissural thickening and underlying asbestos-induced pulmonary fibrosis has yet to be clarified definitively, the visceral pleura is part of the lung (unlike parietal pleural plaques) and thickening of it has been shown to be related to the concentration of asbestos fibers and bodies.[8]

A few comments are in order about radiographic techniques. The I.L.O. method[9] uses only the frontal view, on which only the minor fissure of the right lung is routinely visualized. To achieve the results presented in our work, the lateral as well as the frontal view is required in order to visualize the major as well as the minor fissures.

Based upon the observations we have made using frontal (PA) and lateral chest radiographs, we conclude the following:

1. Fissural thickening is common in asbestos exposed individuals (54.5%) although it is not specific, being also seen in 16.0% of an unexposed control group.
2. Fissural thickening was found to be more common than pleural plaque formation in the asbestos-exposed population (i.e., 54.5% vs. 38.2%).
3. An age adjusted analysis using logistic models showed that fissural thickening occurs, on an average, 10 years earlier after asbestos exposure than does pleural plaque formation (i.e., 21 years vs. 31 years). This means that fissural thickening can serve as an earlier, if not more specific, sign of asbestos-related disease of the thorax.
4. The severity of the fissural thickening, when adjusted for age, increases with length of time since first exposed to asbestos, suggesting its direct relationship to the asbestos exposure.
5. The plain film and computed tomographic appearances of the fissural thickening ranges from isolated visceral pleural plaques to thickening involving entire fissures. Our cases rarely showed any relationship to diffuse, generalized pleural thickening.

There are two potential practical clinical applications of the finding of fissural thickening on radiographs. First, if a person is known to have been exposed to asbestos, it could be a marker of early involvement of the lungs as the result of the exposed and lead to appropriate inquiries. In individuals without known occupational exposure, the finding of unexplained fissural thickening could lead to inquiries which might indicate unusual spousal or environmental contact with asbestos dust, bearing in mind that isolated fissural thickening is a non-specific finding.

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Note: Consult with author for figures.

PREVALENCE OF CLINICAL AND RADIOGRAPHIC ABNORMALITIES IN 150 WORKERS EXPOSED TO NON-CALCINED DIATOMACEOUS EARTH IN CENTRAL CALIFORNIA

JOHN HOWARD,* M.D. • B. Dwight Culver,* M.D. • E. Nicholas Sargent,† M.D.

*Southern Occupational Health Center, University of California, Irvine, CA, USA
†Department of Radiology, University of Southern California, Los Angeles, CA, USA

INTRODUCTION

Diatomaceous earth, or diatomite, is a siliceous sedimentary rock composed essentially of the skeletal remains of microscopic single-celled aquatic plants called diatoms. Diatomite is a valuable material with a range of industrial uses. World production is approximately 1.6 million short tons, 45% of which is from the United States. California accounts for more than half of United States production.[1]

Diatomite consists primarily of an amorphous silica containing a small percentage of crystalline silica detectable by conventional X-ray diffraction analysis. In the past, diatomite processing included calcination which involves heating the natural diatomite to high temperatures, with or without an alkaline flux, thereby converting the amorphous silica into a fibrogenic crystalline form called cristobalite. The cristobalite content of natural (uncalcined) diatomite in typically less than 1%; that of straight-calcined 10-20%; and that of flux-calcined products 40-60%.

Pneumoconiosis in the diatomite industry has been associated with exposure to calcined products containing cristobalite. In 1953, a United States Public Health Service survey in California demonstrated a 25% prevalence rate of pneumoconiosis among diatomite workers who had been employed for five years or more.[2]

Since that time, dust control measures have been instituted throughout the diatomite industry and calcination of the natural diatomite has largely been eliminated. Subsequent surveys of the diatomite industry have demonstrated the effectiveness of dust control measures.[3]

In 1983, a medical surveillance program was begun at Excel Mineral Company, which processes sedimentary rock (characterized as diatomaceous earth) into cat litter absorbent. This report summarizes data on the respiratory symptoms, pulmonary function studies and chest roentgenograms of 150 employees with at least five years of continuous employment at Excel Mineral Company.

SUBJECTS AND METHODS

Study Population

Excel Mineral Company is located in the southern San Joaquin Valley of California and operates two plants at Taft and McKittrick. All current employees at both plants participated in two medical surveillance surveys done by the Southern Occupational Health Center of the University of California at Irvine. Only employees with at least five years of continuous employment at Excel were included in this report.

Exposure Index

Since only scant personal monitoring data existed on the level of past dust exposure, an exposure index (E.I.) was constructed. First, employee tasks were subdivided into eight categories: (1) mining; (2) milling; (3) packaging; (4) loading dock; (5) delivery; (6) administration; (7) maintenance (inside plant); (8) maintenance (outside plant). Next, these eight job categories were divided into "dusty" 1, 2, 3, 7 and "non-dusty" 4, 5, 6, 8 jobs based on the results of a 1977 personal hygiene study. A dusty job was one in which dust concentrations exceeded 10 mg/cc[3]. A year spent at a dusty job prior to 1971 (when dust controls were nonexistent) was counted as the equivalent of two dust-years of exposure after 1971. A year spent in a non-dusty job either before or after 1971 did not contribute to the exposure index. Therefore, the E.I. represents the sum of twice a pre-1971 dust-year plus a post-1971 dust-year.

Study Protocol

All current employees participated in medical surveillance surveys done in 1983 and 1988 which included a self-administered health history questionnaire, pulmonary function studies and chest roentgenograms.

The questionnaire elicited information about general medical conditions, specific respiratory system complaints and a complete occupational history. The presence of any one of the following respiratory complaints of cough, wheezing, chest tightness and dyspnea was included in calculation of a total respiratory symptom score. The symptom score ranged from zero (no symptoms present) to four (all four symptoms present).

Spirometric pulmonary function studies were done on site and consisted of a forced vital capacity (FVC) and forced expiratory volume in one second (FEV_1). Spirometry was performed by a NIOSH-trained technologist on an 8-L Collins portable recording spirometer (Warren E. Collins, Braintree, MA) which met NIOSH apparatus criteria. Predicted values were based on Knudson's regression equations.[4]

A single posteroanterior chest roentgenogram was obtained at a nearby physician's office and was interpreted blindly by one of the authors (ENS) according to the ILO Classification of the Pneumoconioses (1980).[5]

Mineral Analysis

Ore from the opencast mine was sent to Clayton Environmental Consultants, Inc. (Southfield, Michigan) for complete mineral content analysis. In addition, dust from several areas in both plants was sent for microscopic particle sizing and mineral analysis including a determination of the proportional content of amorphous and crystalline silica (alpha-quartz, cristobalite and tridymite).

Statistical Analysis

Comparisons between exposure groups were done with Student's two-tailed, chi-square test with and without Yates' continuity correction, and Fisher's exact test.

RESULTS

One hundred fifty (121 males and 29 females) employees present for the 1983 survey who were continuously employed at Excel and present for the 1988 survey were included in this analysis. All subjects were subdivided into three approximately equal categories based on exposure index. Group I (n=82) had an E.I. of zero to eight years, Group II (n=47) had an E.I. of nine to sixteen years, and Group III (n=21) had an E.I. of seventeen or more years. All three groups were comparable ($P > .13$) in sex, age, race, and tobacco smoking history.

Respiratory Symptoms

Respiratory symptom scores increased with exposure index. Group I had a symptom score of 0.8, Group II 1.0 and Group III 1.4. ($P = .048$) In all three Groups, a large proportion of employees complained of wheezing (Group I 26%, Group II 23% and Group III 43%).

Pulmonary Function Tests

Spirometry revealed no obstructive or restrictive defects. Group I had an FVC of 90.6%, and FEV_1 of 78.9% of predicted. Group II had an FVC of 88.0%, and FEV_1 of 79.8% of predicted. Group III had an FVC of 87.9%, and FEV_1 of 79.1% of predicted. There was no significant difference in pulmonary function among the three groups.

Roentgenographic Findings

Eleven employees (7%) had chest roentgenograms which demonstrated parenchymal abnormalities of doubtful significance for pneumoconiosis (profusion score of 0/1 or 1/0). Three employees (2%) had parenchymal abnormalities on chest roentgenograms consistent with pneumoconiosis (profusion score of 1/1 or greater).

Of the three employees with films consistent with pneumoconiosis, one employee's film in Group II had a profusion score of 2/1 and two employees' films in Group III had scores of 2/1 and 2/2. Of note, the three employees whose films demonstrated pneumoconiosis were employed for a total of 9, 20, 21 years, respectively. There were no parenchymal abnormalites suggestive of irregular or large opacities. In addition, no pleural findings were seen.

Mineral Analysis

Microscopic sizing of dust samples taken from the mill area at both plants revealed a respirable dust content (two microns or less) of 91% of particles. Mineral analysis by X-ray diffraction of both ore and dust samples revealed a mean proportional silica content of 75%, chiefly in the form of amorphous silica (mean 69%) and crystalline silica (mean 6%). Crystalline silica was present in two forms: alpha-quartz (mean 2%) and cristobalite (mean 4%). The mineral content of ore and area dust samples did not differ appreciably.

DISCUSSION

In the past, the prevalence rate of pneumoconiosis in the diatomite industry in California was 25%. Recent surveys of employees in the California diatomite industry have demonstrated a steadily decreasing pneumoconiosis prevalence rate. In fact, a survey in 1984 revealed that only 6 employees out of 473 (2.3%) had films which were classified 1/2 or higher and these employees had been employed in diatomite processing for more than 25 years.[3]

In our survey, we expected to find an even lower pneumoconiosis prevalence rate than previously published surveys for several reasons. First, calcining at Excel antedated the employment of nearly all members of the current workforce. Second, control measures at Excel have reflected the industry standard for a number of years. Third, we expected that mineral analysis of the natural, uncalcined diatomite would yield a crystalline silica content lower than the 6% mean figure obtained.

In our survey, we found a pneumoconiosis prevalence rate (2%), which was slightly less than previous surveys. Of concern, however, is the fact that employees with positive films had worked in the diatomite industry for much shorter periods of time than those employees with positive films described in other studies.

Mineral analysis of the ore and dust may provide some explanation for the pneumoconiosis prevalence rate found. Since the content of fibrogenic crystalline silica seen in the Excel ore and dust exceeds what is generally found in uncalcined diatomite, employees at Excel may be at greater risk than other employees in the diatomite industry. Further study of this population is planned.

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PROGRAM TO PREVENT ASBESTOS-INDUCED HEALTH HAZARDS IN FINLAND—ASBESTOS PROGRAM IN FINLAND

M.S. Huuskonen • H. Koskinen • H. Vainio • A. Tossavainen • J. Rantanen

Institute of Occupational Health, SF-00250 Helsinki, Finland

The Institute of Occupational Health (IOH) started a program to prevent asbestos-induced hazards in 1987. Special emphasis is placed on primary and secondary prevention of asbestos-related cancers. The program involves the dissemination of information, training, services, and research. The IOH is carrying out the program together with the authorities, industry, unions, the health care system, and insurance companies. The program aims to prevent asbestos-related health hazards (by minimizing exposure to asbestos and by educating workers already exposed), to assess the risks caused by exposure to asbestos, and to improve the diagnosis of asbestos-related diseases in Finland.

EXPOSURE TO ASBESTOS IN FINLAND

The use of asbestos in new production was highest between 1965-1975 (about 12,000 tons annually). Some asbestos products are still produced, but the authorities have stipulated that the manufacture of all asbestos products should cease by 1995. This stipulation, however, does not mean that exposure to asbestos will cease, because asbestos is present in nearly all buildings, ships, etc. built before1975-1980. More and more old buildings are being renovated. Potential asbestos sources have been assessed only in a few cases. Because of this insufficiently controlled, and on-going, situation, both direct and indirect exposure to asbestos has been more common than is generally realized. Besides occupational environments there are many non-occupational sources of asbestos exposure: refitting schools, hospitals, garrisons, and other public buildings. The goal is to stop using asbestos in new production and to assess the potential asbestos exposure before planning work to renovate old buildings. When asbestos is present, work should always be done so that neither workers nor the environment is exposed.

According to a rough estimate, there are more tnan 200,000 currently active or retired workers in Finland who have been exposed to over 2 fb/ml for a period of at least two months. Altogether some 50,000 workers (mainly from the construction industry) over 40 years of age have been working in the construction branch for more than 10 years. Thus, on the basis of what is known about the exposure situation in Finland, incidence of asbestos-related diseases will reach its peak during the first decade of the next century.

ASBESTOSIS

A total of about 550 asbestosis cases were diagnosed between 1938-1987. In the last few years, 30-40 cases of asbestosis have been diagnosed annually. Preliminary data from the screening of about 1,000 construction workers suggest that there are many more undiagnosed asbestosis cases. The mean age of the surveyed groups was 59 years, and the workers had been employed in the construction branch in 1967. One in four screened construction workers had positive parenchymal and/or pleural findings; almost all of them were ignorant of their clinical status. When interviewed, they reported an average of 3.7 years of asbestos exposure. Half of them were retired. The routine health care system had been unable to trace the subjects for further clinical evaluation. It can be inferred that the number of undiagnosed cases of asbestosis is thus equal to or even higher than the number of diagnosed cases.

ASBESTOS AND CANCER

A large proportion of those who develop asbestosis will eventually die of cancer. Of the previously diagnosed Finnish asbestosis patients, about 40% have died of lung cancer, 5-10% of mesothelioma, and 10% of other cancers. At the IOH 130 asbestosis patients have been followed from 1980 to 1985. Eighteen of these 130 patients have contracted lung cancer within this observation period. The rough annual lung cancer incidence is thus 2.3/100.

About 2,000 incident lung cancers are found annually in Finland. Smoking is the most important etiological factor. The etiologic fraction of occupational exposures in the rise of lung cancer varies between 13% and 35%. Asbestos is the most important single occupational cause of lung cancer.[5,6] In one study it was estimated that 23% of lung cancers could have been prevented by eliminating asbestos exposure.[6]

About 50 pleural mesothelioma cases are diagnosed in Finland each year. The number has tripled in the last 10-15 years. More than 80% of the diagnosed mesothelioma cases have been exposed to asbestos.[12] Only a few peritoneal mesotheliomas have been diagnosed in Finland.

TIME FACTORS IN ASBESTOS-INDUCED CANCER

The studies on asbestos insulation workers suggest that the risk of lung cancer may decline as the length of the observation period increases. In a cohort of 17,800 asbestos insulation workers, Selikoff et al[11] found that the relative risk of lung cancer begins to increase ten years from the first such employment, rises to a maximum at 30 to 40 years from the first employment, and then falls. A symmetrical bell-shaped curve with a peak at 35 years from the first employment is a good representation of this relationship.[8] Asbestos and smoking increases the risk of lung cancer multiplicatively; asbestos increases the relative risk of lung cancer similarly among both smokers and nonsmokers.[2,3,4]

Peto et al[9] have shown that, among asbestos-exposed working, the mesothelioma death rates are proportional to the third and fourth power of time from the first exposure. This relationship occurs in a wide range of conditions of exposure and is independent of the worker's age when initially exposed. These findings suggest that asbestos induces mesothelioma by acting in the early stages of carcinogenesis, while asbestos induces lung cancer by acting in the late stages of carcinogenesis. This means that slight exposure at early age could have an important effect in inducing mesothelioma but a negligible effect in inducing lung cancer. In contrast, a high exposure level when middle-aged has an important effect in inducing lung cancer after a relatively short period which is approximately linearly proportional to the dose.

Time considerations may have an important bearing on calculations to determine the amount of asbestos-related malignant disease that can be expected to occur in the future. It may also be important with respect to chemoprevention, especially chemoprevention of lung cancer caused by asbestos.

CANCER CHEMOPREVENTION AMONG ASBESTOS-EXPOSED WORKERS

Vitamin A and beta-carotene (provitamin A) have attracted attention as possible cancer prevention agents.[1,13] In retrospective epidemiological studies, subjects with low serum concentrations or low estimated dietary intakes of carotenoids, beta-carotene, or retinol have had an increased incidence of developing cancers as compared with matched cohorts having high to normal serum concentrations of these micronutrients.

Vitamin E is able to act as a radical trap in lipid membranes. Some experimental studies have suggested that vitamin E has an inhibitory effect on the development of tumors in experimental animals induced by chemical carcinogens. Relevant epidemiological studies are limited. In two cohort studies, no relationship was found between vitamin E levels and risk of cancer at all sites combined[13] or for various sites.[10] However, in two other cohorts, significantly lower vitamin E levels were observed among women[14] and men[7] who subsequently developed cancer than among their controls.

A prospective intervention trial involving administration of beta-carotene and vitamin E to asbestosis patients and subjects heavily exposed to asbestos is presently being planned. The aim is to determine whether daily treatment with beta-carotene (20 mg) and/or vitamin E (50 mg) could result in a lower incidence of (lung) cancer in groups receiving the active treatment as compared to the incidence in the group receiving a placebo.

DIAGNOSTICS AND COMPENSATION

Asbestos-related diseases, including malignancies, have been known for decades. According to the Finnish occupational health legislation, all those with asbestos-induced diseases are eligible for compensation. The information on occupational exposures should therefore be gathered for every mesothelioma and lung cancer patient. In every case the causal importance of asbestos should be evaluated from the medical point of view.

SUMMARY

There is no known safe level of exposure to asbestos at work. Primary prevention is the main goal of the asbestos program of the IOH. Primary prevention carried out today can reduce the disease incidence in future decades. The present disease panorama is the consequence of past exposures (mainly before the 1970s). The peak in asbestos-induced diseases will be reached 15–20 years from now. The annual number of asbestos-related premature deaths is estimated at present to be about 150, which exceeds the annual number of fatal occupational accidents. The number of pleural mesotheliomas has tripled in the last 10–15 years, and is now about 50/year. Only in a few cases of mesothelioma has there been no relevant asbestos exposure. However, clinicians have paid very little attention to exposure to asbestos. Therefore most cases are not registered as occupational diseases, and no claims are filed with insurance companies. Informing and training hospital medical staff is essential to improve the situation. The termination of exposure, antismoking campaigns, improved diagnostics, and careful attention to compensation issues, as well as clarifying the potential for chemoprevention, are the central points of the asbestos program of the IOH.

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STUDY ON HAEMOLYTIC ACTIVITIES OF 10 TYPES OF COAL MINE DUSTS AND THEIR EFFECT FACTORS

XING GUO-CHANG • Lui Tie-Min • Lui Zung-Qi • Zhou Chen
Institute for Occupational Medicine of Ministry of Coal Industry, Beijing, China

INTRODUCTION

Prevalence rate of C.W.P. differs not only in different countries, but also in different coal mines in one country.[1,2,3] It is so in China. Of course, the difference is due to many factors. Walton, et al[4] and Reisner, et al[5] suggested that an unknown factor or factors must play a major role in determining the pneumoconiotic potential of individual dusts.

The haemolytic test is a simple and reliable method for estimating cytotoxicity of silica mineral dusts, which was one of the first systems used for exploring mineral dust cytotoxicity[6] and later on for cytotoxicity of colliery dust.[7] Reisner, et al[5] found that cytotoxicity or coal dust was correlated with the pneumoconiosis risk obtained by epidemiological survey.

In the present study, a vitro haemolytic technique was used to estimate preliminary cytotoxicity of most colliery dusts in China, providing scientific basis for fibrogenic potential of different colliery dusts.

MATERIALS AND METHODS

Preparation of Erythrocyte Suspensions

Healthy male New Zealand rabbits weighing 3 Kg were used for this study (provided by Animals Centre of Academy of Medical Sciences of China). Blood was drawn from the heart, centrifuged at 2000 rpm for 20 min., diluted with sterile physiological saline to make a 2% erythrocyte suspension.

Preparation of Dust Suspensions

10 types of coals used in this study were Fat Coal, Anthracite, Cindery Coal, Meagre Coal, Candle Coal, Weak Caking-Coal, Gas Coal, Lignite, Non-Caking Coal and Lean Coal, provided by Academy of Coal Science of China. The elemental compositions were listed in Table I and Table II. These coal samples were crushed in agate mortar to the particle size distribution less than 5 μm in dia. accounting for over 95%. Standard quartz dust less than 5 μm in dia. accounts for over 99%, provided by Academy of Preventive Medical Science of China.

A series of dust samples were dried, sterilized by ultraviolet ray for 30 min., suspended in sterile physiological saline to make the certain concentration and shaken in a high-speed water bath shaker for complete suspension.

Experiment Groups

Coal groups:

10 types of coals were divided into 10 groups. 3 ml erythrocyte suspensions were added into 2 ml of 20 mg/ml to 10 types of coal dust suspensions respectively and then incubated in IDI Water Bath Oscillator (at 37 ± 0.5 temperature, 120 times per min, cyclo-oscillation) for 60 min. The suspensions were centrifuged at 2000 rpm for 60 min and the optical density of the suspensions was measured at 540 nm in a 721 Spectrophotometer.

Quartz control groups:

- Quartz control I: 0.16 mg/ml.
- Quartz control II: 1.25 mg/ml.

Different Concentrations of Coal Groups

A series of Anthracite, Candle Coal and Non-Caking Coal were used as different doses of coal-groups (5, 10, 20 and 40 mg/ml).

Completely Lysed Control and Erythrocyte Fragility Control

3 ml of 2% erythrocyte suspension was centrifuged at 2000 rpm for 20 min and added with 5 ml distilled water to make a complete lysis control. 2 ml of 2% erythrocyte suspension was mixed with 2 ml physiological saline to make an erythrocyte fragility control.

$$\%\ \text{of haemolysis} = \frac{OD_{540}\ \text{Test Sample} - OD_{540}\ \text{Fragility Control}}{OD_{540}\ \text{Fully Lysed Control}} \times 100$$

RESULTS

Comparison of Haemolytic Activities among 10 Types of Coal Dusts

Results of tests done repeatedly 17–20 times are shown in Figure 1 and Table III. It is clearly seen that haemolytic activities of 10 types of coal dusts were different. Degree of haemolysis by Lean Coal and Fat Coal was respectively lowest and highest (range 10–35%). Statistics showed that haemolytic activities of quartz control I and II were significantly higher than those of coal dust-groups and that haemolytic activities of different doses of coal dust-groups were significantly

Table I
Composition of 10 Types of Coals

Types of Coal	Ash (g %)	Volatility	% of Carbon	% of Hydrogen	% of Nitrogen
Anthracite	22.962	3.471	79.944	1.086	0.715
Lean Coal	16.390	16.067	73.293	3.776	1.111
Cindery Coal	24.796	18.623	64.671	3.746	1.012
Gas Coal	11.244	29.332	76.436	4.640	1.323
Candle Coal	11.369	35.763	70.424	4.593	0.723
Lignite	10.042	41.623	63.925	4.020	0.960
Weak Caking Coal	10.340	26.150	71.680	4.380	
Non-Caking Coal	5.940	28.550	63.430	3.430	
Fat Coal	35.780	22.290	57.380	3.700	1.040
Meagre Coal	25.640	14.800	67.200	4.300	1.560

Table II
Composition of Ashes of 10 Types of Coals

Types of Coals	% of SiO_2	% of Fe_2O_3	% of Al_2O_3	% of CaO	% of MgO	% of SO_3	% of TiO_2	% of K_2O	% of Na_2O	% of P_2O_5
Anthracite	52.67	5.31	30.89	4.13	0.99	1.08	1.13	1.48	0.80	0.47
Lean Coal	46.59	13.83	30.08	3.40	0.67	1.96	1.57	0.76	0.45	0.11
Cindery Coal	46.47	11.33	25.05	7.07	1.59	4.59	1.12	0.89	0.75	0.09
Gas Coal	59.42	5.42	26.75	2.367	0.67	1.61	1.16	1.26	0.33	0.08
Candle Coal	49.08	7.94	32.81	3.49	1.26	1.23	1.44	1.13	0.42	0.34
Lignite	50.42	12.25	22.18	6.68	1.16	3.58	1.06	1.52	0.552	0.18
Weak Caking Coal	52.16	21.47	17.15	2.38	1.09	2.54	1.92	1.06	0.12	
Fat Coal	48.67	4.90	35.04	3.78	1.92	2.90	1.48			
Meagre Coal	49.77	3.34	35.71	3.95	1.54	0.54	1.31			

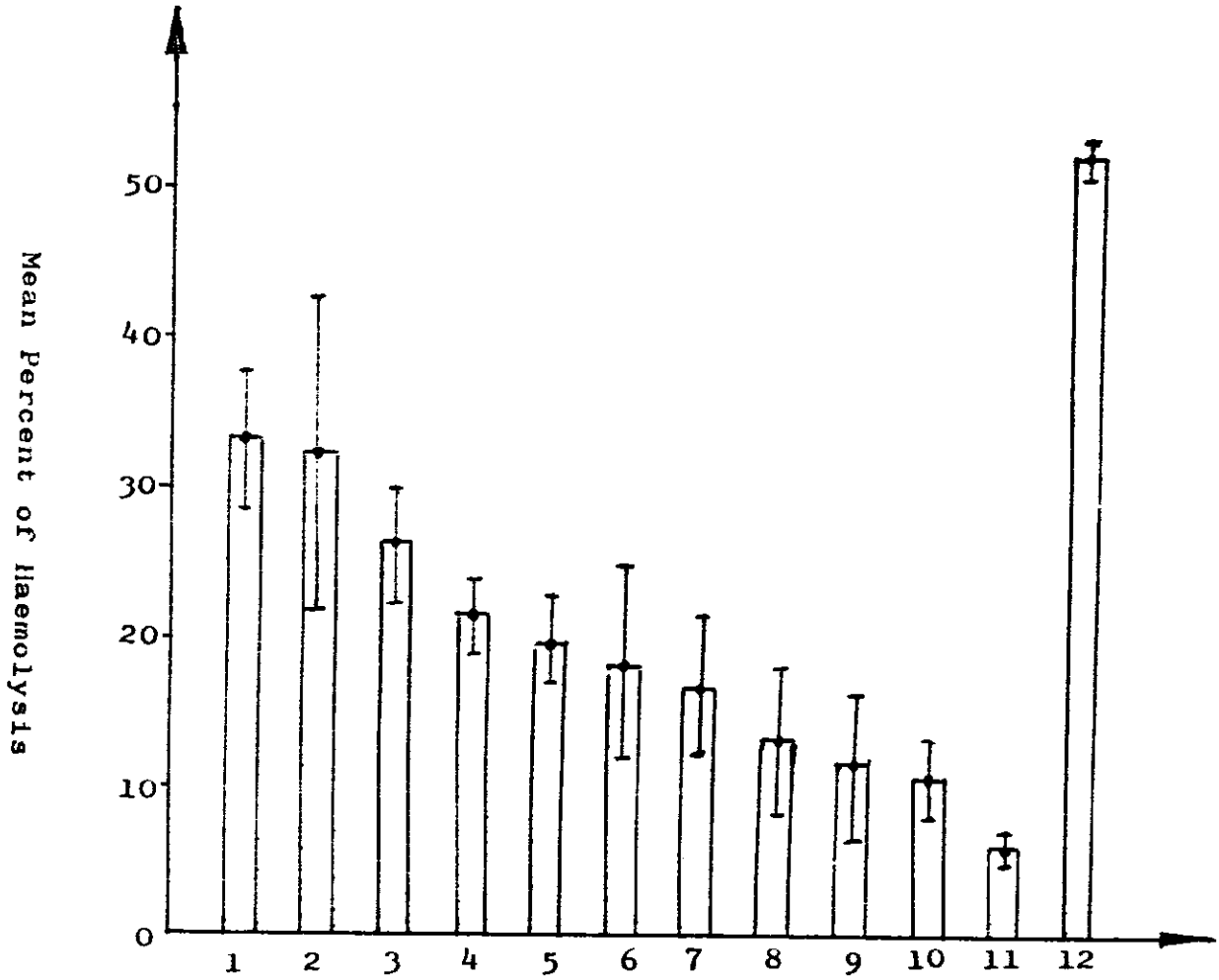

Figure 1. Mean percent of haemolysis of 10 types of coals—(1) Fat Coal, (2) Anthracite, (3) Cindery Coal, (4) Meagre Coal, (5) Candle Coal, (6) Weak Caking Coal, (7) Gas Coal, (8) Lignite, (9) Non-Caking Coal, (10) Lean Coal, (11) Quartz I, (12) Quartz II.

Table III
Endangerment Levels of Coal Dusts

Types of Coals	% Haemolysis	Levels
Fat Coal Anthracite Cindery Coal	33-26	Highest
Meagre Coal Candle Coal Weak Caking-Coal Gas Coal	21-16	High
Lignite Non-Caking Coal Lean Coal	13-10	Low

different ($P < 0.01$, analysis of Variance). Further F-Test showed that except for Anthracite and Candle Coal, Lignite and Lean Coal, haemolytic activities of remaining coal dusts showed statistical significance. Therefore, 10 types of coal dusts were divided into three levels by haemolytic activities, listed in Table III.

Comparison of Haemolytic Activities by the Different Doses of Coal Dusts

Anthracite, Candle Coal and Non-Caking Coal were selected as representatives of three levels of coals as defined above for dose-response test. The results are shown in Figure 2. Haemolytic activities of Anthracite, Candle Coal and Non-Caking Coals were respectively highest, high and low. But at the dust dose less than 10 mg/ml, their haemolytic activities were not significantly different. Starting from the dose of 10 mg/ml, their haemolytic activities increased with increasing dust doses.

Analysis of Effect Factors on Cytotoxicities of Coal Dust

Experimental data were analysed by multiple regression technique using computer to investigate the relationship among % Carbon content (X_1), % Ash content (X_2), % SiO_2 content (X_3) and % AlO_3 content (X_4) in dusts and haemolytic activities of dusts (Y). The analysis results were as follows.

Relationship between Y and X_1, r = 0.89
Relationship between Y and X_2, r = 0.98
Relationship between Y and X_3, r = 0.92
Relationship between Y and X_4, r = 0.94

Where r is Correlation coefficient.

Maximum amount comtributing variance were put into the equation. The result was:

$$Y = -2.382418 + 1.651106X_2 + 2373641X_3$$

Statistics showed that % of Ash content and SiO_2 in dusts made the largest contribution to variance.

DISCUSSION

Many scholars suggested a lot of hypothesis to explain the difference of C.W.P incidence rate in different coal mines with same dust concentration and similar workers' exposure time to dust. Some[5] thought that it was related to geological age and coal rank. Some[2] have identified rank and volatility of coal as factors associated with pneumoconiosis. Others[10] thought that it was related to non-coal mineral component and

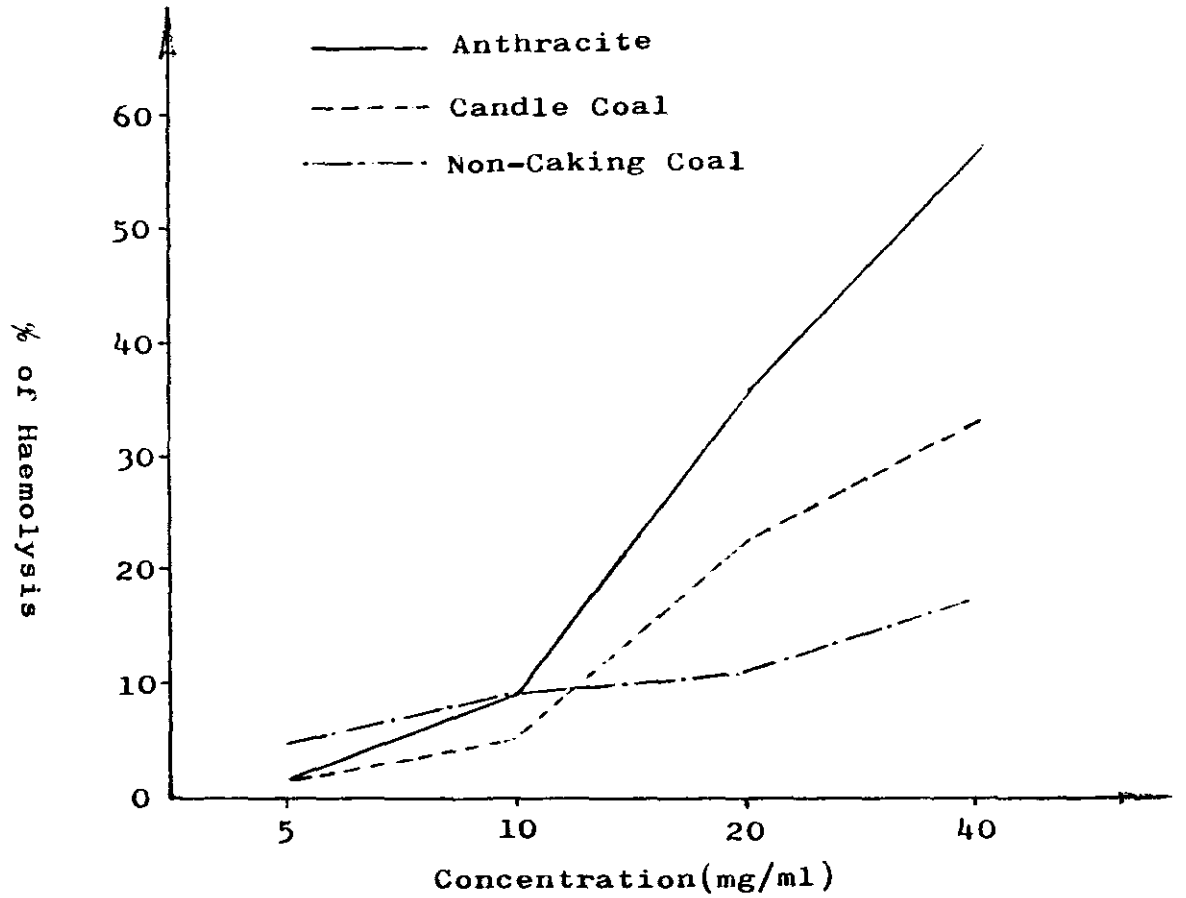

Figure 2. Relation between concentration and percent of haemolysis.

Table IV
Statistical Analysis of Mean Percent of 10 Types of Coals

Types of Coals	Number of Replicates	% of Haemolysis		Variance
		Mean	Standard Error	
Fat Coal	20	33.04	3.95	15.60
Anthracite	17	32.30	12.41	154.01
Cindery Coal	18	26.17	3.23	10.43
Meagre Coal	19	21.10	2.22	4.93
Candle Coal	18	19.43	2.43	5.91
Weak Caking Coal	20	18.48	6.92	47.89
Gas Coal	17	16.39	3.04	9.24
Lignite	19	13.14	4.21	17.72
Non-Caking Coal	19	11.60	4.46	19.89
Lean Coal	18	10.63	2.74	2.51

ash content. Others[7] thought rank and chemical composition of coal were important. It must be pointed out that unanimity of opinion has not been reached on the role played by SiO_2 in the development of pneumoconiosis. Some scholars[11,12] think that quartz, even if a small amount of it exists in dust, plays a role in developing pneumoconiosis, but others[13] don't agree with this opinion. Our experiment showed that from large to small sequence of haemolytic activities of coal dusts were Fat Coal, Anthracite, Cindery Coal, Meagre Coal, Candle Coal, Weak Caking Coal, Gas Coal, Lignite, Non-Caking Coal, and Lean Coal.

The mean haemolytic activities of 10 types of coals were listed in Table IV. It was clearly seen that haemolytic activity of coal was associated with coal type which is related to the geological age. Although times and conditions of coal formation and country rock component have an effect on coal quality, i.e. ash content and component, coal rank and carbon and ash content in 10 types of coals are in above order of haemolytic activity but volatility increased. Therefore, we think that SiO_2 in coal dusts plays an important role in cytotoxicity, which effect of coals themselves is related to period of coal formation. But other factors such as coal rank, volatility carbon content, ash content and SiO_2 content etc. are related to period or coal formation and are affected by condition of coal formation and country rock component.

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HIGH-SPEED, HIGH-RESOLUTION X-RAY COMPUTED TOMOGRAPHS IN THE DIAGNOSIS OF PNEUMOCONIOSIS

HISAO SHIDA,* M.D. • Keizo Chiyotani,† M.D. • Yutaka Hosoda,‡ M.D.

*Div. of Radiology, Rosai Hospital for Silicosis, Japan
†Div. of Internal Medicine, Rosai Hospital for Silicosis
‡Radiation Effect Foundation

INTRODUCTION

Improvement in CT scanner technology now allows imaging of the lung with excellent anatomic detail demonstrating both normal and abnormal interstitium, patterns of pulmonary abnormalities caused by dust inhalation and morphologic characteristics of localized or generalized parenchymal processes, by circumventing the summation of lung structures in complex anatomic regions such as apices, paratracheal, perihilar, pericardiac, lateral margin of chest walls and diagphragmatic regions. The Fourth generation CT (TOSHIBA TCT 900S) can confirm the presence of pneumoconiotic nodular or interstitial fibrosis associated with areas of lung destruction and disorganization of lung architectures results in a cystic appearance to the lung, bulla, bleb, pulmonary emphysema, broncho-bronchiolectasis, pneumothorax, pleural thickening or plaque and effusion, even if conventional plain chest radiographs cannot visualize these abnormalities.

METHOD

A comparative study between CT and P-A view of computed radiography or conventional chest radiography was made of 108 cases of pneumoconiosis including silicosis, asbestosis, welder's lung, foundry worker's lung and activated carbon pneumoconiosis, the profusion of which ranged from 0/1 to 3/3 according to the ILO 1980 International Classification of Pneumoconiosis.

Special filter function of FC3 and FC4 were provided to visualize detailed images of pulmonary parenchymal or interstitial abnormalities.

RESULTS

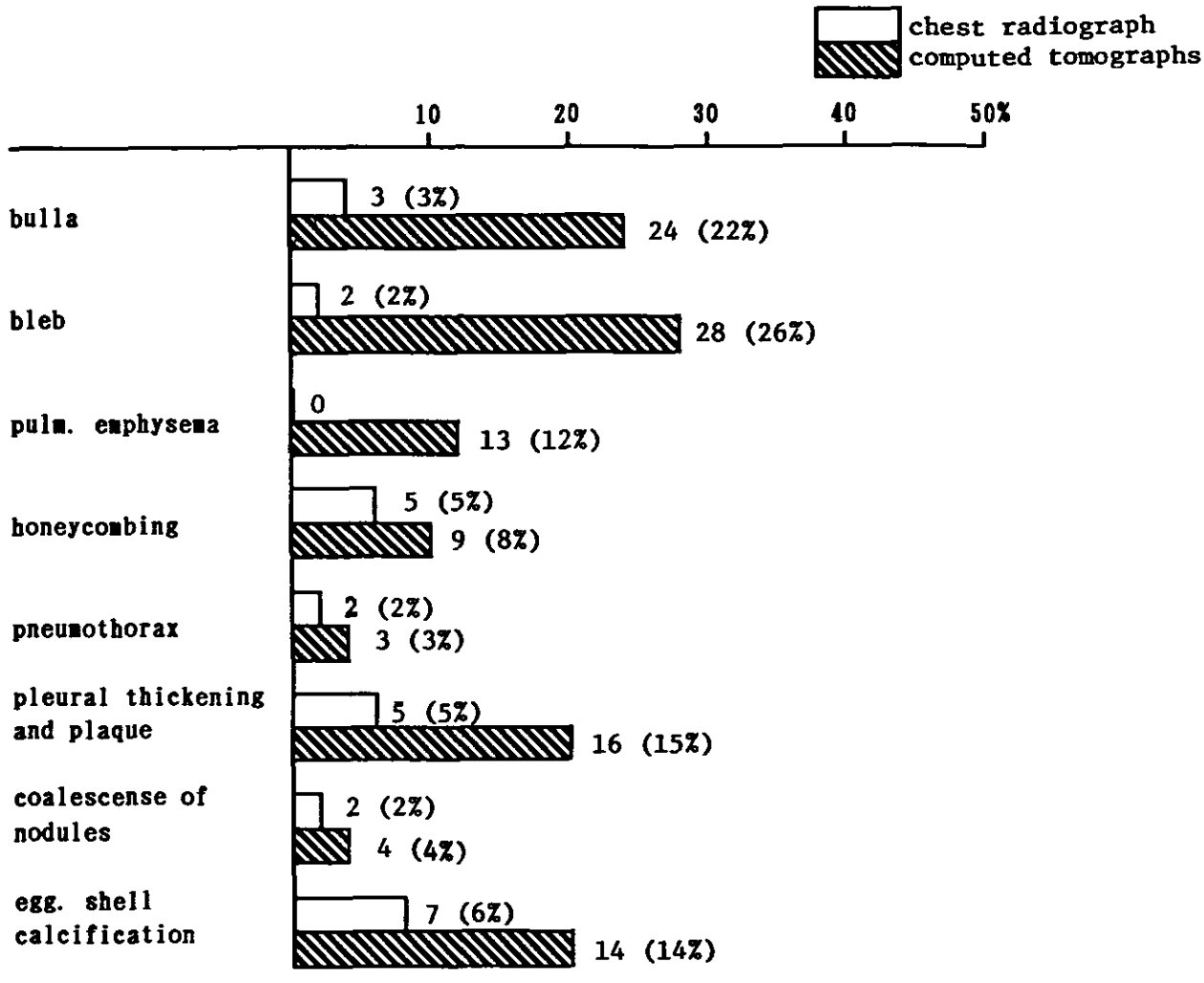
The high-speed, high-resolution CT has a high detectability for the abnormalities of pulmonary parenchyma or interstitium and pleura. The presence of emphysematous changes including bulla, bleb, honeycombing, pleural thickening or plaque, septal thickening, subpleural strand, broncho-bronchiolectasis and very small rounded or very fine irregular opacities, can be confirmed, as shown in Table I.

It is considered that the CT will greatly increase the sensitivity of imaging techniques in detecting pneumoconioses and it is a useful procedure in the diagnosis of pulmonary disease at present.

DISCUSSION

In some cases of pneumoconiosis, very small rounded opacities can be difficult to distinguish from vessels seen in the thin cross-section. As general use it is recommended to take image with 5.0 to 10.0 mm in slice thickness.

Table I
Detectability of CR and CT in 108 Cases of Pneumoconiosis



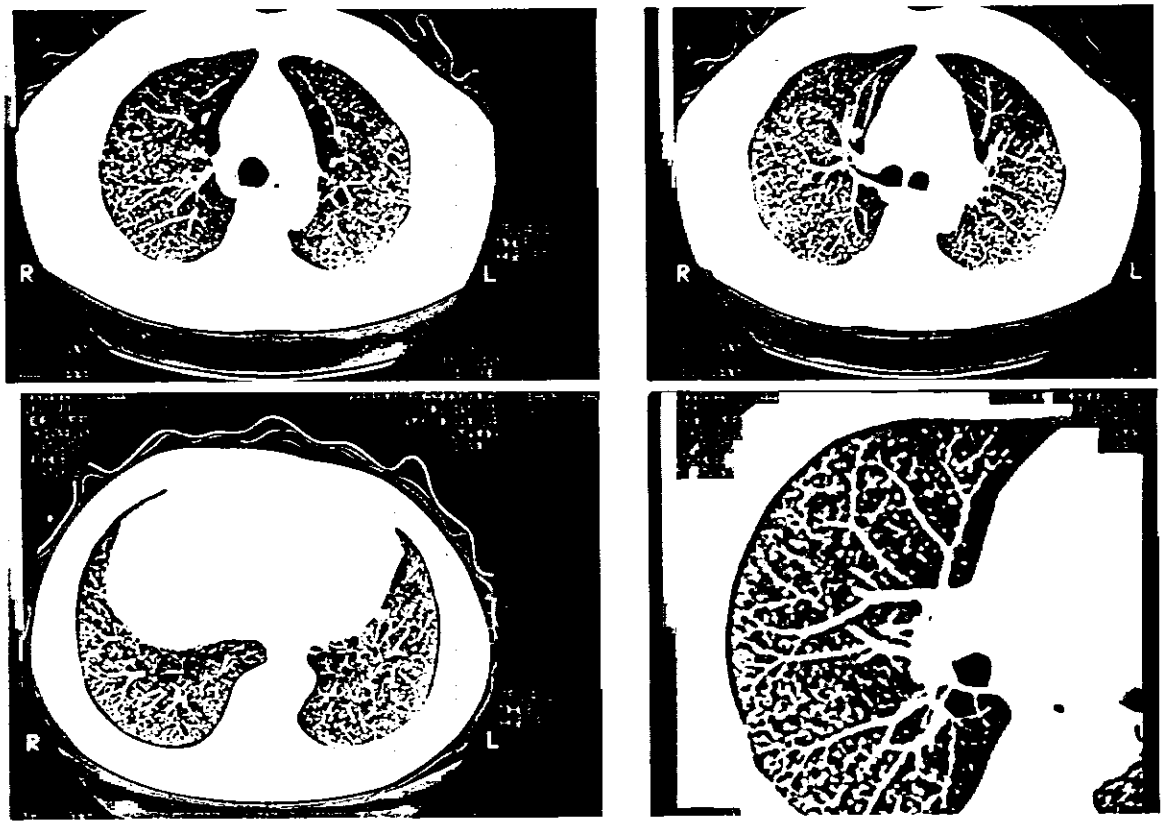


Figure 1. Case 1. 55 year-old, male, silicosis 1/1, P.
CT images demonstrate dense dissemination of fine silicotic nodular high densities throughout lungs. It is noteworthy that these nodules are more clearly and densely distributed than the conventional chest radiograph.

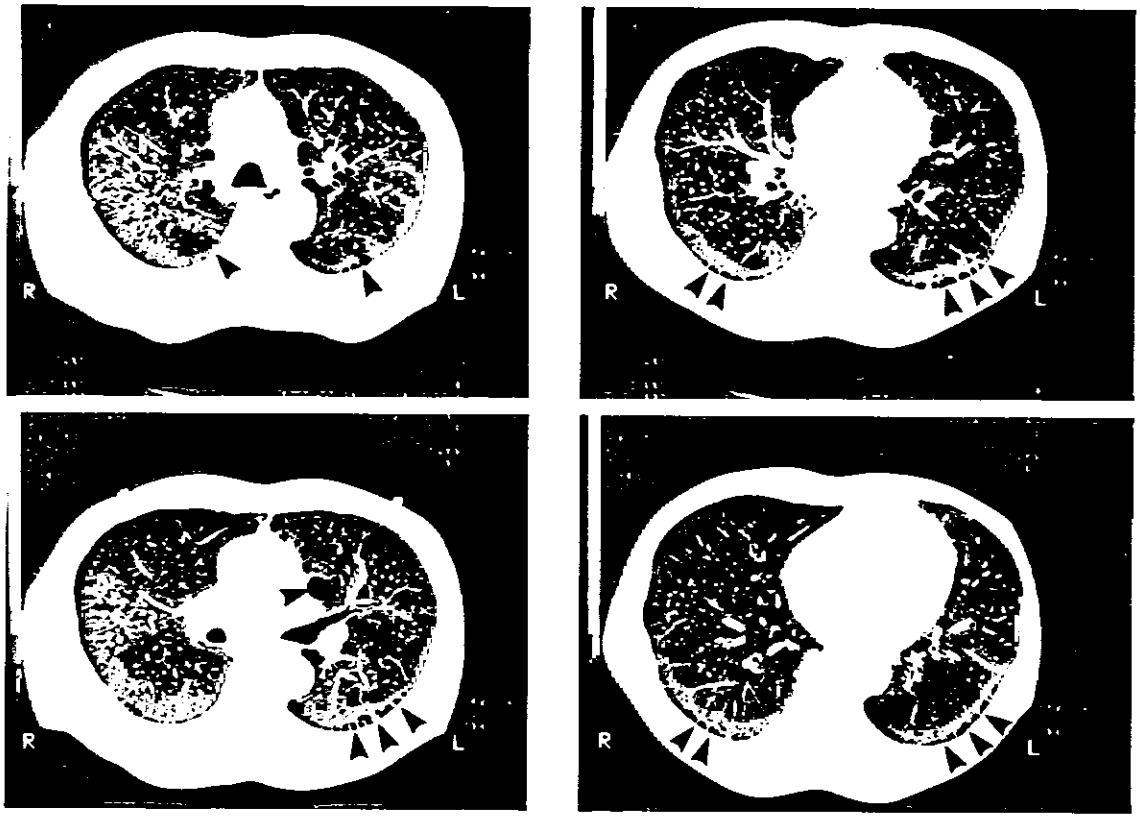


Figure 2. Case 2. 60 year-old, male, silicosis 2/2, q.
CT images reveal dense dissemination of silicotic nodular high densities throughout lungs of which diameter is larger than that of the case 1. Subpleural blebs and bullae are characterized on the CT images. (arrow)

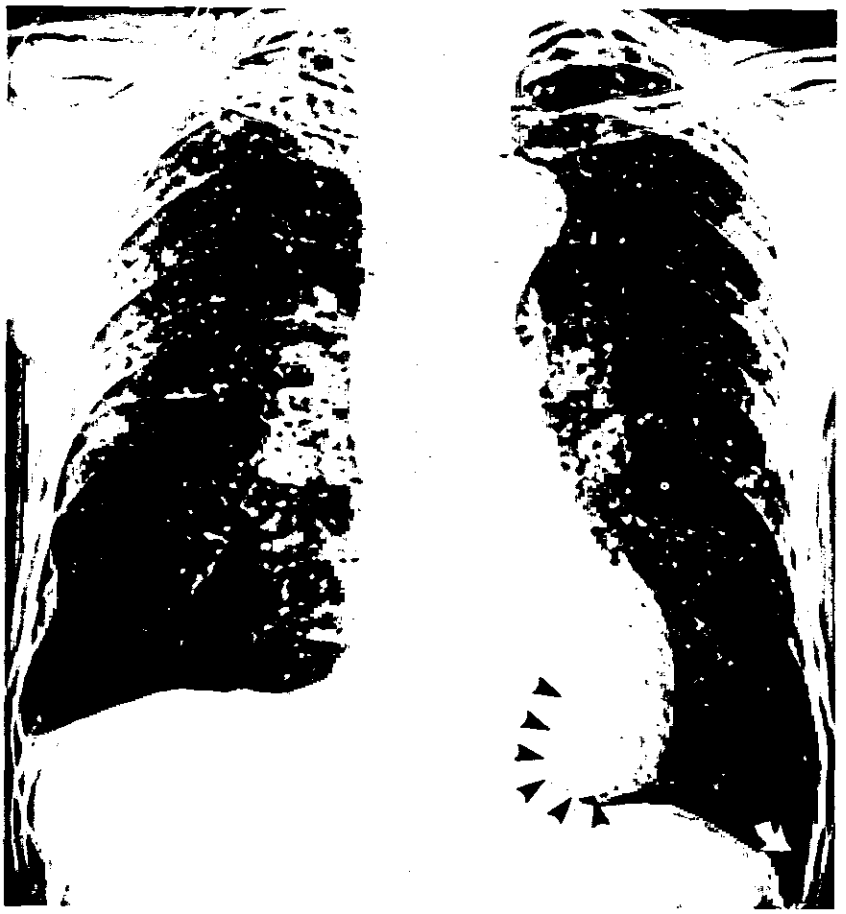


Figure 3. Case 3. 67 year-old, male, silicosis 2/2, q, es, px.
A chest computed radiograph shows dissemination of silicotic nodular high densities throughout lungs and minimal pneumothorax of the left lower lateral margin (white arrow) associated with collapsed lobe. (black arrow)

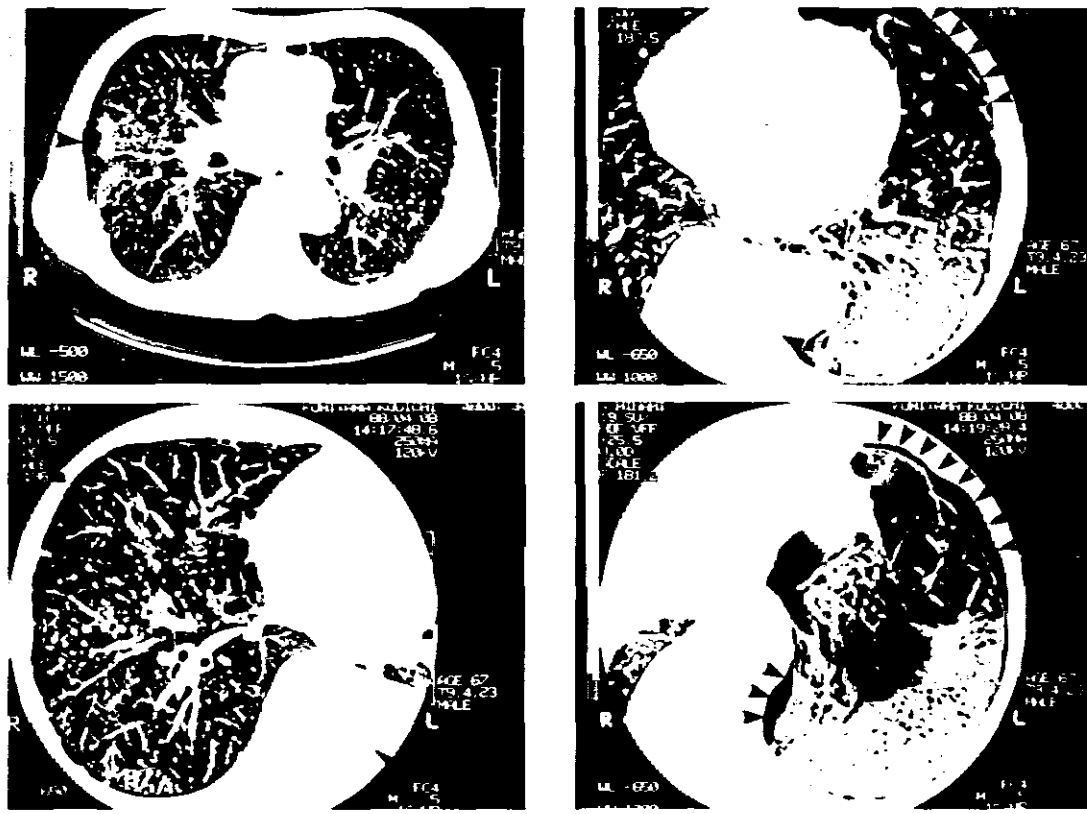


Figure 4. CT images of demonstrate more evident pneumothorax, the collapsed lower lung and bullae. (arrow) These bullae and blebs are not visualized on the conventional chest radiograph. Dissemination of silicotic nodular high densities are also clearly visualized which are located in the middle and posterior lung regions.

Figure 5. Case 4. 59 year-old, welder's lung, 2/2, s.
A chest computed radiograph shows densely distributed fine irregular opacities throughout lungs and the left lung is more hyperlucent than the right.

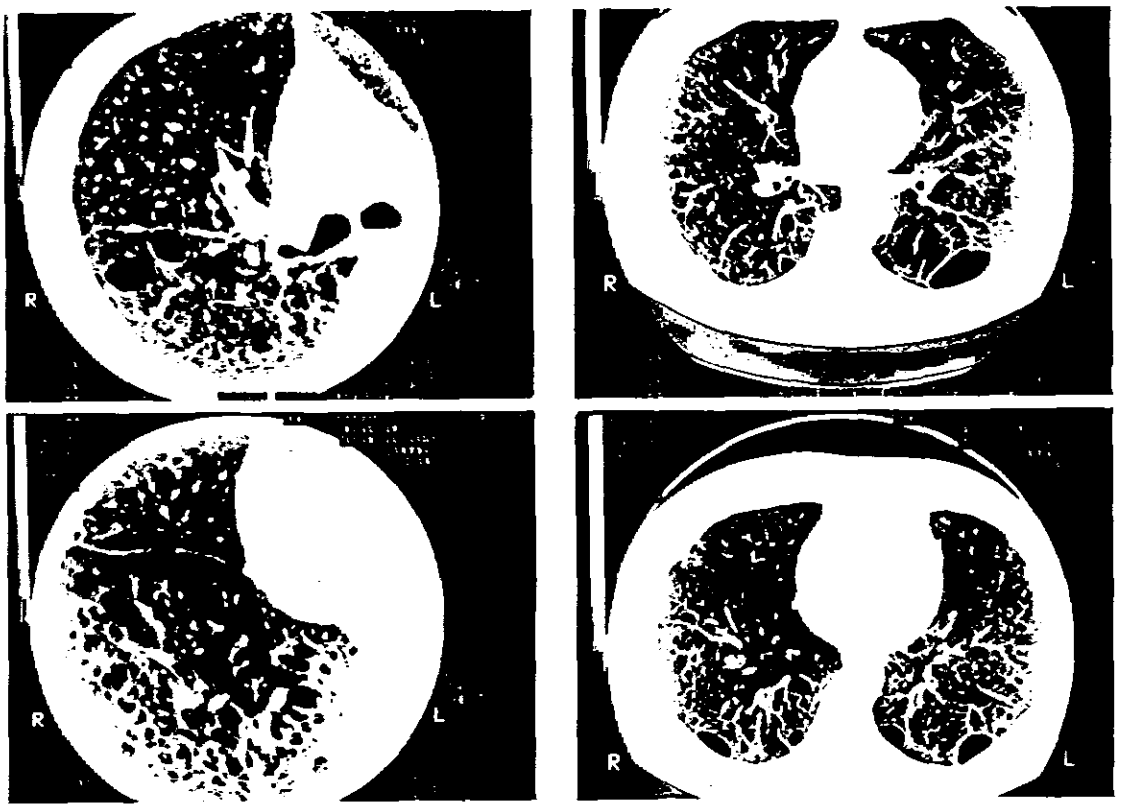


Figure 6. CT images evidently demonstrate strand or streak like interstitial fibrosis, pulmonary emphysema and bullae. On the left super resolution mode images taken by 1.0 mm slice thickness clearly demonstrate impaired lung parenchyma and pulmonary vessels caused by emphysema. The presence of large bullae of the left lung posterior region shows hyperlucency on the chest radiograph.

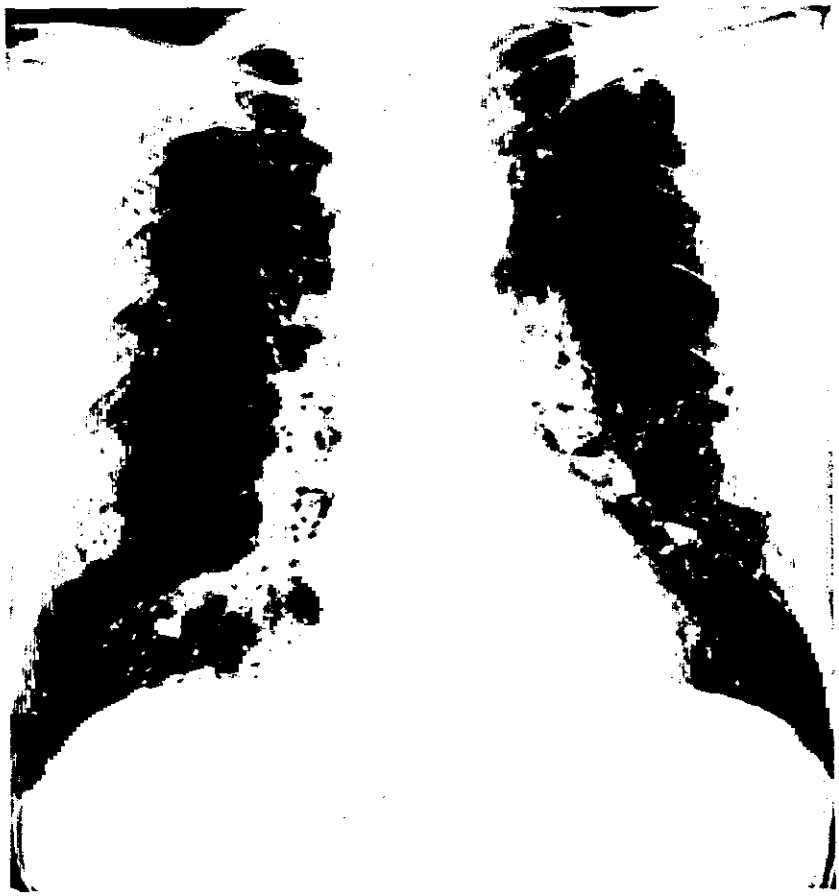


Figure 7. Case 5. 42 year-old, male, foundry worker's lung 2/2, s.
A chest computed radiograph reveals densely distributed fine irregular opacities throughout lungs and on the left upper lung hyperlucency is noted.

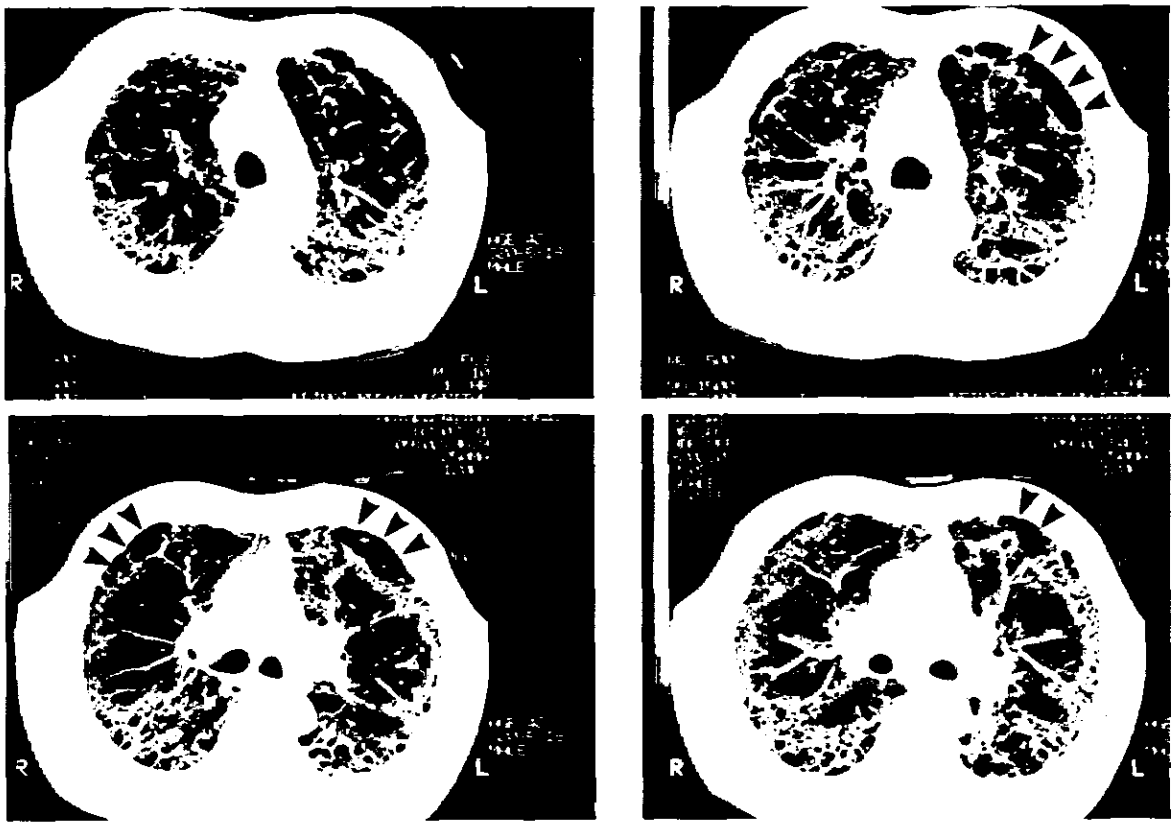


Figure 8. CT images demonstrate strand or streak like interstitial fibrosis associated with pulmonary emphysema, bullae (arrow) and honeycombing.

A CASE CONTROL STUDY OF PNEUMOCONIOTIC COAL MINERS IN BRAZIL*

EDUARDO ALGRANTI, MSc
FUNDACENTRO, São Paulo, SP, Brazil

INTRODUCTION

Coalworkers' pneumoconiosis (CWP) has been known for approximately 150 years. It is one of the respiratory diseases which coal miners are at risk. It is generally accepted that the development of pneumoconiosis depends on a number of variables such as the amount of inhaled dust, the dust composition, the number of years of exposure, the residence time of dust in the lungs and the individual susceptibilities. Except this latter, the other factors are quantifiable, and to date there are reliable studies on the probability of acquiring CWP.[6]

In Brazil, it is known that dust exposure conditions in underground coal mines are critical. Moreover, the dust composition differs from that of the countries where classical studies on CWP were carried out. Brazilian coal has plenty of ashes. Only approximately 60-70% of the mined material is coal. Quartz concentrations are high, often above 10%,[8] making us assume that CWP in Brazil is distinct from classic CWP. The high quartz content makes dose-response relations (dose = quantity of dust retained in the lungs; response = pneumoconiosis) to be not so strong since the pathogeny of classic CWP and silicosis is different.

With the purpose of identifying discriminant variables between pneumoconiotic and non-pneumoconiotic miners a case control study was carried out with the coal miners—studied in the Projeto Mineração, 1984 (Mining Project—Brazil).

METHODS

A random sample of about 50% of the underground miners in six mines (manual, semimechanized and mechanized) was selected. The chosen miners were engaged in different underground jobs. Out of the 956 miners investigated, 816 had their radiographs read independently by three experienced readers in the ILO Radiological Classification of pneumoconiosis.[5]

One hundred and eight (108) radiographs were considered to be inadequate for reading. From the 708 analysed radiographs, 40 cases of pneumoconiosis (Profusion 1/0 or above) were found, and 80 cases of suspicious radiographs were detected (Profusion 0/1). For analysis the cases were divided in two groups:

Group 1: Single job underground miners (pure exposure)
- 1A) Profusion 1/0 or above (cases: 12; controls: 33).
- 1B) Profusion 0/1 or above (cases: 37; controls: 102).

Group 2: Multiple-job underground miners
- 2A) Profusion 1/0 or above (cases: 32; controls: 91).
- 2B) Profusion 0/1 or above (cases: 80; controls: 227).

*Supported by grant from the Brazilian Ministry of Labour (SSMT/MTb No. 014/83).

These cases were matched in the ratio of 1:3 or 1:2 based in the following parameters:

1. Years worked underground ± 1
2. Age ± 2
3. Control subjects with profusion 0/0
4. Non-repetitive control subjects
5. Control subjects working in the same mine.

Additionally, for groups 1A and 1B, we selected control subjects performing the same job groups, i.e. supervision, face and maintenance.

These matching criteria excluded 20% to 30% of the cases, due to the lack of controls or only one control.

The analysed variables were cough, phlegm, breathlessness, recent acute respiratory episodes (RARE), FEV_1, FVC and FEV_1/FVC. Cough and/or phlegm were considered positive, when present for more than 3 months. Breathlessness was considered positive, if related to great efforts.

The respiratory functional parameters were calculated by using a dry spirometer (Vitalograph, Vitalograph Limited, Buckingham, UK) and transformed into BTPS. Other data were obtained through a questionnaire on respiratory symptoms, adapted from the questionnaire on Chronic Bronchitis (MRC, UK, 1976).

For calculating the differences concerning cough, phlegm, breathlessness and RARE, we used chi-squared tests from contingency tables 2 × 2. For FEV_1, FVC, FEV_1/FVC and pack years, we analysed the difference between the means through the Student "t" value. With both tests we rejected the null hypothesis at the 5% level.

RESULTS

The results are shown in Tables I and II. The mean of pack years of the four subgroups of cases and controls did not differ significantly. In subgroup 1A, only FEV_1 was significantly lower in the cases. In subgroup 2A the FVC was significantly lower in the cases and the occurrence of RARE was more frequent in the cases.

The inclusion of miners having radiographs 0/1 or above as cases (subgroups 1B and 2B) made all the differences among the variables of cases and controls non-significant.

Table I

X^2 Values of Contingency Table of Cases and Controls with Cough, Phlegm, Breathlessness and Recent Acute Respiratory Episodes (RARE)

SUBGROUP	COUGH	PHLEGM	BREATHLESSNESS	RARE
1A	0.02	1.02	1.70	0.50
1B	0.15	0.15	0.01	1.02
2A	0.09	0.69	3.74	4.68*
2B	1.07	1.07	0.47	3.30

* $p \leq 0.05$

Table II

Means and Standard Deviations of Lung Function Parameters+

SUBGROUP		FEV_1	FVC	FEV/FVC
1A	Ca	3.33 ± 0.28 *	4.21 ± 0.66	0.80 ± 0.12
	Co	3.62 ± 0.57	4.63 ± 0.79	0.79 ± 0.11
1B	Ca	3.69 ± 0.73	4.70 ± 0.78	0.79 ± 0.12
	Co	3.71 ± 0.67	4.67 ± 0.78	0.79 ± 0.11
2A	Ca	3.44 ± 0.59	4.19 ± 0.71 *	0.82 ± 0.11
	Co	3.72 ± 0.62	4.62 ± 0.67	0.80 ± 0.11
2B	Ca	3.66 ± 0.71	4.59 ± 0.73	0.80 ± 0.11
	Co	3.74 ± 0.66	4.69 ± 0.75	0.81 ± 0.09

* $p \leq 0.05$

+ The number of cases and controls are about 20% less than Table I because of rejected spyrometries.

Ca = Cases

Co = Controls

DISCUSSION

The studied variables were somewhat discriminating as to differentiate pneumoconiotic from non-pneumoconiotic miners. The findings in the group of pure miners (FEV_1) did not repeat in the multiple job undergroup miners, who in their turn presented FVC and the occurrence of RARE different from that of the control. As approximately 20% of the lung function tests in the original group of 956 miners have been rejected,[1] this may have contributed to the inconsistency of the differences found in the FEV_1 and FVC of subgroups 1A and 2A, as miners with rejected tests (188/956), showed a significantly higher mean of years of exposure than those with accepted tests ($p < 0.01$). The presence of breathlessness was nearly significant in subgroup 2A. Breathlessness, together with the number of years of exposure, FEV_1/FVC, and FEV_1, were the variables most closely associated with pneumoconiosis, when subgroup 2A was analysed through a probit regression analysis.[1]

When the suspected subjects (profusion 0/1) were included as cases there was no difference between cases and controls in both groups. This is an indirect indication that they were probably classified correctly as category 0.

Respiratory symptoms are related to both dust exposure and cigarette smoking.[7] The average pack years of the analyzed groups did not differ between cases and control subjects, and the effect of dust exposure was also controlled. The low capacity of discrimination presented by the variables cough and phlegm reinforces that pneumoconiosis is independent of the effects of dust on the bronchial tree.[4]

Autopsy studies on coal miners showed that pneumoconiosis did not correlate with hypertrophy of the bronchial glands, which was related to both cigarette smoking and dust exposure.[2]

Although case control studies are often inappropriate for conclusive analyses of the cause-effect relationships,[3] especially when we are studying high prevalence diseases, these findings concerning pneumoconiosis and respiratory symptoms are in accordance with classic studies on respiratory disease in coal miners.

This group of miners will be followed up in 1989.

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