CANCER MORTALITY AMONG SILICOTIC CASES

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INTRODUCTION

This study takes into consideration the mortality related to all site cancer, to lung and laryngeal cancer, to silicosis and silico-tuberculosis, and to chronic non-malignant respiratory diseases among workers professionally exposed to silica.

The aim of the investigation is to ascertain whether a cancer mortality excess, particularly from lung cancer, exists, and to identify from which factors is affected.

The role of different working exposures and smoking habits in inducing lung cancer has been investigated.

METHODS

The Archives of Turin office of the National Institute of Insurance (I.N.A.I.L.) were examined and the clinical documentation was collected for each male worker who received compensation for silicosis and died between 1970 and 1983; 746 subjects were included in the study.

The following data were obtained: date of birth, type of occupation in industry, year of starting and ceasing exposure, compensation year and percentage, year and cause of death through death certificate; smoking habits were also investigated.

Mortality analysis has been carried out using the Standardized Proportional Mortality Ratio (SPMR).[1,2]

RESULTS

In Table I overall mortality data, and observed and expected deaths related to specific causes as well as Standardized Proportional Mortality Ratios (SPMR) are shown.

A lung cancer mortality excess (81 observed cases versus 59.50 expected—PMR 136; 95% C.L. 111—162) was found, together with a high mortality rate (27.8%) related to silica dust exposure.

In Tables II, III, and IV, observed and expected deaths related to specific causes are arranged according to exposure in the different working activities.

The 746 cases were divided in three groups: the first one covering mine, quarry and tunnel workers, the second one

Table I
Mortality: Overall and by Causes

	OBSERVED (%)	EXPECTED	PMR
ALL CAUSES	746 (100)	-	-
ALL CANCERS	158 (21.2)	198	80
LUNG CANCER	81 (10.8)	59.5	136 *
LARYNX CANCER	6 (0.8)	7.86	76
CHRONIC NMRD	45 (6)	46.97	95
SILICOSIS	176** (23.6)	-	-
SILICO-TB	31** (4.2)	-	-

* $p < 0.05$
** 27.8 % as mentioned in the text

Table II
Mortality: Overall and by Causes According to Job
Underground Workers and Stonecutters

	OBSERVED (%)	EXPECTED	PMR
ALL CAUSES	239 (100)	-	-
ALL CANCERS	37 (15.5)	65.41	57.6
LUNG CANCER	21 (8.8)	19.88	106
LARYNX CANCER	2 (0.8)	2.66	75
CHRONIC NMRD	4 (1.7)	14.55	27
SILICOSIS	96 (40.2)	-	-
SILICO-TB	31 (7.1)	-	-

Table III
Mortality: Overall and by Causes According to Job
Foundry Workers

	OBSERVED (%)	EXPECTED	PMR
ALL CAUSES	457 (100)	-	-
ALL CANCERS	111 (24.3)	119.65	93
LUNG CANCER	56 (12.3)	35.22	159 *
LARYNX CANCER	4 (0.9)	4.79	84
CHRONIC NMRD	36 (7.9)	29.60	122
SILICOSIS	67 (14.7)	-	-
SILICO-TB	8 (1.7)	-	-

* $p < 0.05$

covering foundry workers and the third one assembling all other remaining works in which a silicogenic risk is attributable: pottery, tile, glass, refractory material industries, etc.

According to this analysis a mortality excess from lung cancer is present only in the category of foundry workers (56 observed cases versus 35.2 expected—PMR 159; 95% C.L. 126—192); in the first group (miners, quarrymen, stonecutters) an increased mortality from silicosis and silicotuberculosis is observed close to a markedly reduced mortality from chronic non-malignant respiratory diseases (NMRD) (4 observed cases versus 14.55 expected).

This result led to focus a few parameters, among those better documented, which could affect the lung cancer excess confined to foundry workers. We meant particularly to stress out the possible role in inducing pulmonary neoplasm of the type of industry, and related different intensity of silica exposure, and of the smoking habits.

Information concerning smoking habits has been collected for more than 2/3 of the group under examination. Table V shows a significant mortality increase from lung cancer in smoking foundry workers: 38 observed cases versus 21.82 expected—PMR 174; 95% C.L. 132.13–215.94.

The group of non-smoking silicotic foundry workers is numerically too small to provide statistical significance to apparent mortality increase from lung cancer observed also in this group (10 observed cases versus 6.31 expected—PMR 158). Nevertheless by means of a procedure formerly used by

Saracci[3] to assess expected values in cohorts of smokers and non-smokers, is possible to assume that mortality rates from lung cancer in the general population (which in Italy includes1/2-1/3 of smokers) are at least four times greater than those of the non-smokers. Therefore lung cancer mortality risk in non-smoking foundrymen seems to be underestimated. Table VI shows the results adjusted for smoking habit, that is 10 observed cases versus 1.57 expected; this data achieves the conventional limits of statistical significance.

In Table VII lung cancer mortality has been related to exposure length. This sorting criteria shows a lung cancer mortality excess, both in the group whose exposure duration is covered between 11 and 20 years (21 observed cases versus 12.15 expected—PMR 173; 95% C.L. 116.5-229.1), and in that whose exposure duration is more than 20 years (29 observed cases versus 18.26 expected—PMR 159; 95% C.L. 113.05-204.8).

In Table VIII foundry workers have been divided in two

Table IV

Mortality: Overall and by Causes According to Job Other Activities

	OBSERVED (%)	EXPECTED	PMR
ALL CAUSES	50 (100)	-	-
ALL CANCERS	10 (20)	13.96	71
LUNG CANCER	4 (8)	4.23	94
LARYNX CANCER	0	-	-
CHRONIC NMRD	5 (10)	3.06	160
SILICOSIS	13 (26)	-	-
SILICO-TB	6 (12)	-	-

Table V

Lung Cancer—Observed and Expected Deaths and PMR According to Smoking Habit—Foundry Workers

	OBSERVED	EXPECTED	PMR
NON SMOKERS	10	6.31	158
SMOKERS	38	21.82	174 *

* p < 0.05

Table VI

Lung Cancer—O/E Deaths and PMR According to Smoking Habit —Expected Values Adjusted for Smoking

	OBSERVED	EXPECTED	PMR
NON SMOKERS	10	1.57	636 *
SMOKERS	38	27.27	139 *

* p < 0.05

groups in accordance with the average exposure characteristic of job title:[4] (1) lower risk of silica exposure (melting, furnace worker, pouring, coremaking, cut-off saw, molding, crane driving, gathering motormen, mechanical and electrical maintenance staff). (2) higher risk of silica exposure (earths and sands system, muller, grinder, chipper, sandblaster, shot blaster, tumbler, relining and repair).

In the first group the excess risk for lung cancer is statistically significant (36 observed cases versus 21.93 expected—PMR 164; 95% C.L. 122.3–206), whereas in the second group such an excess is still present but doesn't attain the conventional limits for statistical significance. Thus no relationship between lung cancer prevalence and silicotic exposure estimate seems to be present in foundry workers group.

DISCUSSION

The assumption that silica has a causal role in inducing pulmonary neoplasm is still under debate.

In a recent literature review Goldsmith[5] agreed with this hypothesis and acknowledged that silica exposure allows an enhanced risk of developing lung cancer. In historical cohort studies[6,7] and in a recent Italian case-referent study[8] an overall excess risk for lung cancer was found in workers compensated for silicosis in different industrial activities.

On the other hand the same assumption has been strictly criticized by Heppleston[9] who considered these inferences not sufficiently demonstrated, chiefly as regards the confounding effect of smoking habits. Further on, Swaen[10] argues that it is unlikely that the confounding effect of smoking can explain the high relative risk for lung cancer in workers with silicosis.

This study considers silica exposure as predominant in three categories of workers, namely miners, foundry workers and employees in other industrial fields like glass manufacturing, potting and brick works, etc. For this third group it is impossible to draw valid appraisals.

Table VII

Lung Cancer—Observed and Expected Deaths and PMR According to Exposure Duration—Foundry Workers

	1 - 10 years			11 -20 years			> 20 years		
	OBS.	EXP.	PMR	OBS.	EXP.	PMR	OBS.	EXP.	PMR
ALL CAUSES	50			146			253		
LUNG CANCER	6	4.95	121	21	12.2	173 *	29	18.3	159 *

* p < 0.05

Table VIII

Lung Cancer—Observed and Expected Deaths and PMR According to Exposure Level—Foundry Workers

	high risk of silica exposure			low risk of silica exposure		
	OBSERV.	EXPECT.	PMR	OBSERV.	EXPECT.	PMR
ALL CAUSES	175			282		
LUNG CANCER	20	13.39	149	36	21.93	164 *

* p < 0.05

In the first group, which is mainly formed of underground workers and stonecutters, almost exclusively exposed to silica, the collected data don't point out a mortality excess from lung cancer. This result, as far as concerns talc miners, confirms our data on miners of Piedmont (Italy Region).[11,12] Previous researches by Goldman,[13] Ashley,[14] Enterline,[15] Liddel[16] and Howard,[17] did not underline an increased mortality for lung cancer in coal miners. So that it may be assumed that no relationship exists between lung cancer and mine and quarry working activities, when specific carcinogenic agents (ionizing radiations, asbestos, etc.) are absent. This conclusion has been debated by Finkelstein[18] who reported an increased mortality for lung cancer in an Ontario miners population compensated for silicosis; no final estimate was drawn about the possible causal role of silica dust in inducing neoplasm. No definite statements are any more expressed in the report by Thomas[19] in which the role of silica itself as a cofactor in inducing lung cancer in pottery workers exposed to silica and non-fibrous talc cannot be ruled out.

On the contrary, through the analysis of data concerning silicosis cases in foundry workers, an increased mortality risk for lung cancer emerges.

This special risk does not seem solely related to smoking habit, since also in the group of non-smoking workers a significant mortality excess from lung cancer is present.

A similar result has been reported by Blot[20] in an investigation on a group of steel plant workers in which the mortality excess from lung cancer still persists after cigarette smoking adjustment.

Other reports confirm as well the presence of an increased lung cancer mortality in foundry workers.[21,22,23,24,25]

In our study the enhanced mortality risk for pulmonary neoplasm does not seem related to silicotic risk: an increased risk is not present in the group of underground workers (exposed to high silica level) and a significant excess of lung cancer is present in the group of foundry workers rated at low silica exposure. This remark agrees with a Tola's[26] observation in which the relationship between lung cancer mortality and specific occupation is evaluated.

In conclusion we can hypothesize that in foundry workplaces other risk factors (Polycyclic Aromatic Hydrocarbons?) than silica are present and they can play a role at least concomitant in inducing pulmonary cancer.

REFERENCES

1. Kupper, L.L., McMichael, A.H., Symons, M.J., Most, B.M.: On the utility of proportional mortality analysis. *J. Chron. Dis.* 31:15-22 (1978).
2. Zeighami, E.A., Morris, M.D.: The measurement and interpretation of proportionate mortality. *Am. J. Epidemiol.* 117:90-97 (1983).
3. Saracci, R.: Asbestos and lung cancer: an analysis of the epidemiological evidence on the asbestos-smoking interaction. *Int. J. Epidemiol.* 20: 323 (1977).
4. Rubino, G.F., Pettinati, L.: *Elementi di Medicina del Lavoro*, 3rd Ed., p. 86. Minerva Medica Edizioni, Torino (1985).
5. Goldsmith, D.F., Guidotti, T.L., Johnston, D.R.: Does occupational exposure to silica cause lung cancer? *Am. J. Ind. Med.* 3:423-440 (1982).
6. Westerholm, P.: Silicosis, observations on a case register. *Scand. J. Work Environ. Health* 6 (Suppl. 2): 5-86 (1980).
7. Zambon, P., Simonato, L., Mastrangelo, G., Winkelmann, R., Saia, B., Crepet, M.: Mortality of workers compensated for silicosis during the period 1959-1963 in the Veneto region of Italy. *Scand. J. Work Environ. Health* 13:118-123 (1987).
8. Forastiere, F., Lagorio, S., Michelozzi, P., Covariani, F., Arca, U., Borgia, P., Perucci, C., Axelson, O.: Silica, silicosis and lung cancer among ceramic workers: A case-referent study. *Am. J. Ind. Med.* 10:363-370 (1986).
9. Heppleston, A.G.: Silica, pneumoconiosis and carcinoma of the lung. *Am. J. Ind. Med.* 7:285-294 (1985).
10. Swaen, G.M.H., Meijers, J.M.M.: Lung cancer risk among workers with silicosis: potential confounding by smoking habits. *Am. J. Ind. Med.* 12:223-225 (1987).
11. Rubino, G.F., Scansetti, G., Piolatto, G., Gay, G.: Mortality and morbidity among talc miners and millers in Italy. *Dusts and Disease*, Pathotos. Pub., 357-363 (1979).
12. Rubino, G.F., Scansetti, G., Piolatto, G., Romano, C.: Mortality study of talc miners and millers. *J. Occup. Med.* 18:186-193 (1976).
13. Goldman, K.P.: Mortality of coal miners from carcinoma of the lung. *Brit. J. Ind. Med.* 22: 72-77 (1975).
14. Ashley, D.G.B.: The distribution of lung cancer and bronchitis in England and Wales. Brit. J. Cancer 21: 243 (1967).
15. Enterline P.E.: Mortality among coal miners in the U.S.A. *Am. N.Y. Acad. Sci.* New York (1971).
16. Liddel, F.D.K.: Mortality in British coal miners in 1961. *Brit. J. Ind. Med.* 30:15-24 (1973).
17. Howard, D., Rockette: Cause specific mortality of coal miners. *J. Occup. Med.* 19:795-801 (1971).
18. Finkelstein, M., Kusiak, R., Suranyi, G.: Mortality among miners receiving workmen's compensation for silicosis in Ontario 1940-1975. *J. Occup. Med.* 24:663-667 (1982).
19. Thomas, T.L., Stewart, P.A.: Mortality from lung cancer and respiratory disease among pottery workers exposed to silica and talc. *Am. J. Epidemiol.* 125:35-43 (1987).
20. Blot, W.J., Brown, L.M., Pottern, L.M., Stone, B.J., Fraumeni, J.F.: Lung cancer among long-term steel workers. *Am. J. Epidemiol.* 117: 706-716 (1983).
21. Gibson, E.S., Martin, R.H., Lockington, S.N.: Lung cancer mortality in a steel foundry. *J. Occup. Med.* 19:807-812 (1977).
22. Egan, Baum E., Miller, B.A., Waxweiler, R.J.: Lung cancer and other mortality patterns among foundry men. *Scand. J. Work Environ. Health* 7 (suppl.4): 147-155 (1981).
23. Palmer, W.G., Scott, W.D.: Lung cancer in ferrous foundry workers: a review. *Am. Ind. Hyd. Ass. J.* 42: 329-340 (1981).
24. Fletcher, T: The mortality of a cohort of british foundry workers. Proceedings International Symposium *Silice, Silicosi e Cancro.* 27-43. Padova, Italy (10/5/1985).
25. Silverstein, M., Maizlish, N., Park, R., Silverstein, B., Brodsky, L., Mirer, F.: Mortality among ferrous foundry workers. *Am. J. Ind. Med.* 10:27-43 (1986).
26. Tola, S., Koskela, R.S., Hernberg, S., Jarvinen, E.: Lung cancer mortality among iron foundry workers. *J. Occup. Med.* 21: 753-760 (1979).

ALVEOLITIS IN OCCUPATIONAL LUNG DISEASES (OLD)

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INTRODUCTION

The prevalence of inhalatory pulmonary diseases, caused by many occupational and environmental exposures to organic and inorganic substances, remains a problem that may be underestimated because, in many instances, the disease has an insidious character and the host lung response protect and smoulder the clinical picture.

Although many primary industries, such as granite sheds and asbestos mines, improved control measures, the exposure remains in secondary and tertiary manufacturing trades, which use those products.

The correct diagnosis can be missed and to avoid it the physician must use all his sense of purpose and curiosity in the study of the suspect OLD patient. It is also expected that a better knowledge of the OLD mechanisms constitute the foundation for the understanding and diagnosis of these diseases.

The bronchoalveolar lavage (BAL) seems to fulfil this goal as it is now well known that the study of BAL fluid closely mimics the events happening in the interstitial space.[4,8,9,12]

Confirming this in Extrinsic Allergic Alveolitis, it is generally accepted that the study of BALF discloses an alveolitis although it is not completely established if and how there is a correlation between the gravity of disease and the intensity of the alveolitis found. However it is considered that the increased number of effector cells found in BALF of these patients, is the local expression of the basic immunologic mechanisms of the disease, evolving to the formation of granulomas and, lately, contributing to fibrosis.[4,11,16]

Regarding the interstitial lung diseases caused by inorganic dusts, only recently has the occurrence of an alveolitis been accepted,[2,3,4,13,14] and Begin et al., even found that the alveolitis in subsets of silica exposed workers, with distinct clinical stages of disease, was found to have distinct biological characteristics.[2]

In this study we tried to evaluate the existence or not, and the type of alveolitis found in a group of 48 patients with occupational lung disease confirmed by the usual criteria. We also compared the patients with occupational history of exposition to organic dust (Group I) with the patients exposed in work environment to mineral dust (Group II). Finally we tried to correlate the findings with clinical manifestations and evolution.

MATERIAL AND METHODS

Patients

We studied 48 patients, being 28 males and 20 females. The average age was 42 ± 13 years old, ranging from 73 to 28 years old.

Twenty-four patients had smoking habits. None of the patients had history of other concomitant pulmonary disease.

All patients were referred to the Outpatient Clinic of Occupational Diseases because of respiratory complaints and 10 (21%) had also systemic complaints—fever, weight loss and asthenia.

Thirty of the patients were exposed to mineral dusts (63%): silica (8 patients), iron (7 patients), cement (1 patient), asbestos (1 patient) and the other 13 patients to various other mineral dusts.

Eighteen patients were exposed to organic dusts (37%), mainly pigeon dregs (10 pt), wood (4 pt), cork (2 pt), wool (1 pt) and flour (1 pt).

All patients were submitted to a standard posteroanterior and lateral X-ray, read by 3 observers, according to ILO classification (10) and to a functional respiratory study by body plethysmography.

In all patients bronchofibreoscopy was performed followed by bronchoalveolar lavage, being the effluent fluid recovered.

Fourteen patients, during diagnosis procedures, were submitted to a transbronchial lung biopsy.

After the diagnostic assessment in all patients with an alveolitis disclosed by BAL a treatment with corticosteroids was prescribed (Prednisone—1 mg/Kg of body weight).

Methods

Bronchoalveolar Lavage:

Briefly the BAL was performed with 200 ml saline serum, warmed up to 37°C, instillated by syringe in 4 alliquots of 50 cc, through a wedge bronchofibreoscopy in a subsegment of the medium lobe followed a few seconds after by recovery of the lavage effluent proceeded by gentle syringe suction.

After remotion of mucus, cells were counted in a hemocytometer and cytocentriphuge smears were prepared and stained by May—Grunwald-Giemsa method for identification of the cellular populations.

The cellular pellet was obtained by centrifugation—500 G at 4°C during 20 minutes—washed three times with PBS balanced solution and resuspended in PBS solution at the final concentration of 5×10^6 cells/ml.

T-Lymphocytes

The T-lymphocytes and its subpopulations were characterized by indirect immunofluorescence after banding to specific monoclonal antibodies (Ortho—OKT_3, OKT_4 and OKT_8) following procedures previously described.[7,14]

Statistical Analysis

The results are expressed as the mean ± SD. The data were tested by the Student's test for differences between groups—and by Chi-Square test when appropriate.[1]

RESULTS

The cellular analysis of BALF stated increased number of cells with a significative difference in Group I, as compared to controls (Table I), 67% of Group I and 40% of Group II patients fulfilled the criteria for an alveolus defined by a number of cells per ml of BALF superior to that of controls average + SD.

The alveolitis in both groups is mainly due to a significative increase of lymphocytes: 35.7 ± 21.6% (Group I) and 28.0 ± 15.0 (Group II). There was also a slight but not significative increase in the PMN cells. The percentage decrease on macrophages is not accompanied by a diminishing of the absolute number of these cells; on the contrary a slight increase was found.

The observation of cytocentrifuge smears frequently proved foamy macrophage, the existence of Spontaneous Rosetts Macrophage-Lymphocyte and a number of giant cells above 3% on average.

Regarding the T-lymphocytary populations we found an increase in the number of T cells in both groups being significative in Group I. The analysis of the T-lymphocyte subsets proved a predominance of the T supressor cells in the groups of patients leading to an inversion of T helper/T supressor ratio. So in 16 pt (88%) of the Group I and in 26 patients (86%) of the Group II the T_h/T_s ratio was below 1 (Table II).

The incidence of a lymphocytary alveolitis was significantly higher in patients of Group I than in those of Group II: 67% and 40% respectively—$p<0.02$—(Table III).

In the patients with systemic symptoms the BAL disclose an alveolitis in 60% of them and a normal pattern in others 40%—$p<0.02$—(Table IV).

Among the 14 patients in which lung biopsy was performed alveolitis was found in the BAL of 9 patients. From these 9 patients 8 (88%/) showed granulomas or lymphoplasmocytary infiltration of the alveolar septa (Table V). From the 5 patients without alveolitis in BAL only one presented granulomas in the lung biopsy (20%). The difference between the two groups is significative for a $p<0.02$.

Besides aggressive dust evication of all patients we submitted the 24 patients with alveolitis to corticotherapy (Prednisone 1mg/Kg of body weight). Only 53% of this group of patients improved clinically and functionally, compared

Table I

Differential Cell Count—Bronchoalveolar Lavage

	GROUP I	GROUP II	CONTROLS
nº cells/ml	$46.6 \pm 39.5 \times 10^4$ *	$36.3 \pm 36.0 \times 10^4$	$17.4 \pm 4.3 \times 10^4$
Macrophages	*** 56.1±21.8 %	*** 67.0±18.4 %	90.8±2.2
Lymphocytes	** 35.7±21.6 %	*** 28.0±15.0 %	8.0±1.6
P M N	5.4±6.4	3.2±5.9	1.1±0.9

* S $p < 0.05$ ** S $p < 0.01$ *** S $p < 0.001$

Table II
Lymphocytary Subpopulations—Bronchoalveolar Lavage

	GROUP I	GROUP II	CONTROLS
T_3	83.9±6.5 % ***	75.2±11.3 N.S.	70.1±3.3
T_4	32.7±12.4 *	28.2±6.3 ***	42.0±2.1
T_8	50.8±13.7 ***	43.4±10.8 ***	26.5±1.9
T_4/T_8	0.7±0.3	0.8±0.7	1.4±0.3

S * $p < 0.05$ S *** $p < 0.001$

Table III
Patients with Lymphocitary Alveolitis

	GROUP I	GROUP II
Lymphocitary Alveolitis	12 pts (67%)	12 pt (40%)
	→ p < 0,01 ←	
T_4 / T_8 Inversion	26 pts (86%)	16 pt (88%)
	N.S.	

Table IV
Clinic and Alveolitis

	SYSTEMIC SYMPTOMS	
Alveolitis	60%	↓
		p < 0,02
Without Alveolitis	40%	↑

Table V

Lung Biopsy and Alveolitis

	Granuloma or Lymphoplasmocitary Infiltration	Other Pathological Findings	TOTAL
Alveolitis	8 pt (88%)	1 pt (11%)	9
Normal BALF	1 pt (20%)	4 pt (80%)	5

$\chi^2 = 6.57$ S ** $p < 0.02$

Table VI

Treatment and Alveolitis

	ALVEOLITIS	NORMAL BALF	TOTAL
Clinical Improvement	13 pt (53%)	20 pt (83%)	33
No response or worsening	11 pt (46%)	4 pt (17%)	15
TOTAL	24	24	48

$\chi^2 = 4,76$ S ** $p < 0.05$

to 83% of the patients without alveolitis in BAL—$p<0.02$—(Table VI).

DISCUSSION

Being an heterogeneous population it is difficult, in a certain way, to take conclusions from the results. Anyway it becomes evident that an important number of OLD patients presents an alveolitis which has the same characteristics: it is an lymphocytary alveolitis. This suggests that at least some of the pathogenic pathways are similar in spite of the nature of the inhaled noxious dust. Besides, a great number of patients show an inversion of the T helper/T supressor ratio, that could indirectly demonstrate an activation of the immunologic local mechanisms of defense in almost all the studied patients.

It is easy to accept the immunologic via to the patients exposed to organic dust, but more difficult for those exposed to inorganic materials. Taking into consideration the findings that the number of macrophages is also increased besides the above referred morphologic modifications (foamy cells, rosetts lymphocytes—macrophage and numerous giant cells), we could think that the alveolar macrophages are activated. This activation can be provoked either by immunologic and no immunologic stimulation and leads to the realization of mediators like IL_1 able to activate the T-lymphocyte.[5,6]

Once again we found a good correlation between the histological data and the study of BALF proving the interest of this technique in the study of the interstitial lung diseases.[9,12,15]

The fact that only 53% of the patients that presented an alveolitis in BALF improved, in despite of being under corticotherapy, is in striking contrast with the improving of 83% of the patients without alveolitis in which the only therapeutic measure was the withdrawal of the causing dust. So the BALF study has some predictive value and the existence of an alveolitis signifies, in our opinion, not only an involvement of the lung interstitium but also expresses the existence of amplification and perpetuation mechanisms centered in the activated alveolar macrophage and T-Lymphocyte.[5,6]

In this study we found a marked increase in the T supressor cells. This is also reported by others and is common to almost all occupational lung diseases with some exceptions such as the case of berylliosis and asbestosis.[3,4,11,14] This fact can contribute to the differential diagnosis and real meaning of this immunologic abnormality is not well established; perhaps

it signifies one attempt to brake the local immunologic processes.

In conclusion, we think that BAL is a good method to the study and comprehension of the occupational lung diseases. It contributes to the stagging and understanding of the pathogenic mechanisms.

The study of the cellularity is, although insufficient, being crucial, the study of the lymphocytary populations and the quantification of various chemical mediators released by the different cells involved in the pathogenesis of these diseases.

REFERENCES

1. Bahn, A.K.: Basic Medical Statistics. Grune and Straton Inc. (1972).
2. Bégin, R.O., Cantin, A.M., Boileau, R.D., Bisson, C.Y.: Spectrum of Alveolitis in Quartz—Exposed Human Subjects. *Chest*, 92:1061-1067 (1987).
3. Costabel, U., Bross, K.J., Huck, E., Cuzman, J., Mathys, A: Lung and Blood Lymphocyte Subsets in Asbestosis and in Mixed Dust Pneumoconiosis. *Chest*, 91:110–112 (1987).
4. Crystal, R.C., Reynolds, H.Y., Kalika, A.R.: Bronchoalveolar Lavage: the Report of an International Conference. *Chest*, 89:122-131 (1986).
5. Davis, C.S.: Pathogenesis of Silicosis: Current Concepts and Hypothesis. *Lung*, 164:139-154 (1985).
6. Davis, G.S., Calhoum W.J.: Occupational and Environmental Causes of Interstitial Lung Disease. Interstitial Lung Disease. *Scharzw King, Ed., B.C. Decker Inc.*, pp. 63-109 (1988).
7. Ginns, L.C., Goldenheim, P.D., Miller, L.C. et al.: T-Lymphocyte Subsets in Smoking and Lung Cancer: Analysis by Monoclonal Antibodies and Flow Cytometry. *Am. Rev. Resp. Dis.*, 126:265–269 (1982).
8. Hunninghake, C.W., Cadek, J.E., Kawanami, O. et al.: Inflammatory and Immune Processes in the Human Lung in Health and Disease: Evaluation by Bronchoalveolar Lavage. *Am. J. Pathol.*, 97:149-206 (1979).
9. Hunninghake, G.W., Kawanami, O., Ferrans, V.Y. et al.: Characterization of Inflammatory and Immune Effects Cells in the Lung Parenchyma of Patients with Interstitial Lung Disease. *Am. Rev. Resp. Dis.*, 123:407-412 (1981).
10. ILO/UC International classification of radiographs of pneumoconiosis, 1980 No. 22 revised. Occupational Safety and Health Series. *Geneve International Labour Office* (1980).
11. Keller, R.H., Swartz, S., Schlueter, D.P., Bar-Sela, S., Fink, J.N.: Immunoregulation in Hypersensitivity Pneumonitis: Phenotypic and Functional Studies of Bronchoalveolar Lavage Lymphocytes. *Am. Rep. Resp. Dis.*, 130:766-771 (1984).
12. Reynolds, H.Y., Chretien, J.: Respiratory Tract Fluids: Analysis of Content and Contemporary Use in Understanding Lung Diseases. *Year Book Medical Publisher; Disease-a-Month*, February (1984).
13. Robinson, B.W.S., Rose, A.H., James, A., Whitaker, D., Musk, A.W.: Alveolitis of Pulmonary Asbestosis. *Chest*, 90:396-402 (1986).
14. Teles de Araujo, A., Alfarroba, E., Freitas e Costa, M.: The Role of Monoclonal Antibodies in the Study of Chronic Inflammatory Diseases Caused by Dust Inhalation. *Eur. J. Resp. Dis.*, Supl. 146:203-210 (1986).
15. Teles de Araujo, A., Raymundo, E., Rosal, Goncalves J., Correia, I., Moniz, D., Freitas e Costa, M.: Bronchoalveolar Lavage and Lung Biopsy in Interstitial Lung Diseases. 4th Congress of the European Society of Pneumology, A 166 (1985).
16. Voisin, C., Tonnel, A.B., Layette, C. et al.: Bird Fancier's Lung: Studies of Bronchoalveolar Lavage and Correlations with Inhalation Provocation Tests. *Lung*, 159:11-12 (1981).

NEW DUSTGRAVIMETER FOR UP-TO-DATE EXAMINATION OF DUST CONDITIONS AT MINING WORKING PLACES

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ABSTRACT

Mineral dusts originating at deep mining are polydisperse of a broad spectrum. The size of the largest particles is about 50 to 200 μm. At inspiration the particles undergo a selection according to their size: the particles exceeding 200 μm are not inhalable /H-fraction/, particles exceeding a size of 15 to 20 μm remain in the tracheobronchial tract /NPL-fraction/, granules smaller than 5 to 8 μm will be deposed in the alveolar region /A-fraction/. Selection of dust has been characterized by international conventions, i.e., the A-fraction by BMRC-characteristic.

In the case of inert and fibrogenous mineral dust environment—from the five dust fractions—the A-fraction as the risk factor for pneumoconiosis and the TB-fraction as the risk factor for "dustbronchitis" may have an importance. Therefore concentration of these two fractions has to be systematically measured. The paper presents a dustgravimeter—new in its structural composition—suitable for measuring concentration of the two fractions simultaneously and separately.

The preselector of the static dustgravimeter is a vertical /laminar/ flow-classifier, the medical collector for the selection of TB-fraction is an axial ciklon, and the postcollector for the A-fraction is a filter from microglassfiber. The installation of the gravimeter of 3 kg mass and 20 dm^3/min capacitance is under process.

No Paper provided.

MEASURES FOR THE IMPROVEMENT OF THE MEANS AND METHODS OF DUST CONTROL AND THE PREVENTION OF PNEUMOCONIOSIS IN THE COAL INDUSTRY

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ABSTRACT

The main cause of dust formation in mines is the constantly increasing mechanization and intensification of mineral products output, the increasing volumes of mining works using mechanical and explosion methods of mountain-mass disintegration.

The main factors determining the intensity of dust formation, are: physical-chemical properties of rocks, methods and intensity of rock disintegration, the possibility of reaching the places of dust formation by ventilation flows.

In order to create safe conditions of work according to the dust factor, ensuring the prevention of pneumoconiosis, a number of research projects is at present carried out in the USSR; new methods of mineral excavation with lower levels of dust formation are being developed, the theoretical basis of hydraulic processes of dust suppression are developed, the theoretical basis of the parameter optimization of dry methods of entrapment are developed, the methods and instruments for dust control are improved and developed.

The engineering-technical problems of the prevention of pneumoconiosis are of great importance, as they are directed at the control of its initial cause—the dust. The solution of these problems is based on the information and research of mining aerosols and physical chemistry in general, on physics and mechanics of rock and other fundamental branches of science.

No Paper provided.

UNEXPECTED SARCOIDOSIS FOLLOWING PNEUMOCONIOSIS —CLINICAL OBSERVATIONS

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ABSTRACT

The authors report two observations of workers, a cement charger and a metal sand-blaster, with clinical, X-ray and BAL findings of interstitial pneumoconiosis.

Unexpected occurrence of sarcoidosic granuloma appeared in both cases, four and two years later, respectively. The diagnosis was ascertained by means of a lung biopsy performed because of a sudden worsening of the clinical and radiological findings.

The possible relationship between pneumoconiosis and sarcoidosis will be discussed to clarify whether silica and other industrial dusts, i.e., diatomaceous earth, asbestos, talc, cement, copper, could be in some cases responsible for sarcoid-like reaction or sarcoidosis.

No Paper provided.

ASBESTOS EXPOSURE AMONG FINNISH MESOTHELIOMA PATIENTS

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INTRODUCTION

During the past 70 years, a total of about 175,000 tons of chrysotile, 120,000 tons of anthophyllite and 5,000 tons of amosite or crocidolite has been used in Finland. Most exposures to asbestos have occurred in construction and shipbuilding industries when asbestos-containing materials have been manufactured, installed, handled or demolished.[1] About 50,000 current or retired workers have been employed for more than ten years in such occupations.

In Finland the annual incidence rate of pleural mesothelioma is about 10 per million which shows a five-fold increase since the 1960's.[2] Most cases are associated with occupational exposure to asbestos, and therefore, a detailed interview and fibre analyses from lung tissues are of great importance for the diagnosis and etiology of the disease.

MATERIALS AND METHODS

Subjects

In 1986–87, forty pleural mesotheliomas (33 males, 7 females) were diagnosed at three central hospitals. The cases and 31 sarcoidosis patients as referents were interviewed and their past occupational, domestic or environmental exposures to asbestos were recorded. Unaware of the case-referent status, a team of two occupational hygienists and a medical doctor classified the data into the following categories.

Group I Definite exposure (*e.g.*, lagging or insulation work. asbestos spraying and manufacture of asbestos products)

Group II Probable exposure (*e.g.*, construction, shipyard and maintenance work)

Group III Possible exposure (*e.g.*, transport, garage and power plant work)

Group IV Unlikely or unknown exposure (*e.g.*, agriculture, forestry and office work)

Exposures with a duration of less than one month were excluded.

For 19 mesothelioma patients (mean age at diagnosis 57 years, range 42–73 years) and 10 autopsied persons (mean age at death 56 years, range 37–70 years) with no known exposure to asbestos, lung tissue samples were analyzed for the mineral fibre content with scanning electron microscopy.

Lung Tissue Analysis

At autopsy, a tissue sample of 1–5 cm^3 in size was taken from the upper left lobe and stored in 4% formalin solution. A 1 cm^3 piece was cut below the pleural surface, dried at 80°C for 24 hours, weighed, and ashed in a low-temperature asher (Nanotech Plasmaprep 100). The ash residue was dispersed in 0.1-N hydrochloric acid, ultrasonicated and filtered on Nucleopore filters with a pore size of 0.2 micrometer. The samples were gold-coated in a Jeol JFC 1100 sputtering device and analyzed in a Jeol Temscan 100 CX electron microscope equipped with an energy dispersive X-ray spectrometer (Tracor Northern TN-5500). The fibre content was measured in SEM mode at a magnification of 5000X. The intensity ratios of Si, Mg, Fe and Na were utilized to identify the type of asbestos. All inorganic fibres with roughly parallel sides and with an aspect ratio greater than 3:1 were counted. At least 400 fields of view were included in the measurement which corresponds to an analytical sensitivity of 0.1 million fibres/g dry tissue. All liquids used in the sample preparation were filtered before use and a blank sample was added to each series of analyses.

RESULTS

In the series of 40 mesothelioma cases, 22 persons (55%) had been employed in occupations such as shipbuilding, construction and maintenance in which their past exposure to asbestos was classified as possible, probable or definite. In similar standardized interviews, 8 of 31 referents (26%) adjusted for age, sex and residential area reported some exposure to asbestos (Table I).

Amosite, crocidolite and anthophyllite were the predominant fibrous minerals in parenchymal tissue while chrysotile and inorganic fibres other than asbestos were found in some samples. The fibres were 1 to 35 μm (median 3.7 μm) in length and 0.1 to 3 μm (median 0.2 μm) in diameter and the concentration ranged from 0.4 to 370 million fibres/g dry tissue. About 35% of the particles were longer than 5 μm and the number of asbestos bodies averaged 4% of the total, coated and uncoated fibres. The highest levels (over 100 million fibres/g dry tissue) were found in an insulation worker and in two shipyard electricians. In 80% of the mesothelioma patients, the content exceeded 1 million fibres/g dry tissue. The fibre concentration was <0.1 to 0.9 million fibres/g dry tissue in 10 autopsied persons with no known exposure to asbestos who had died from unrelated causes such as myocardial infarction or suicide.

DISCUSSION

According to the criteria used in this study, 55% of the mesothelioma patients reported past occupations or tasks which may have entailed to some exposure to asbestos. In 80% of the cases, the fibre concentration in the lungs ex-

Table I
Asbestos Exposure Among 40 Mesothelioma Cases and 31 Referents

Exposure category	Mesothelioma patients		Sarcoidosis patients	
	Males	Females	Males	Females
Definite	4	0	0	0
Probable	12	0	1	0
Possible	6	0	7	0
Unlikely or unknown	11	7	17	6
	33	7	25	6

ceeded a level which may presumably arise from environmental or domestic exposure. Neither the interview nor electron microscopic analyses indicated any occupational exposure to asbestos for about 10% of the cases. The results are consistent enough and similar to those from other studies[3] that the two methods, alone or in combination, can establish a valid evidence from the cumulative exposure of an individual.

REFERENCES

1. Huuskonen, M., Ahlman, K., Mattson, T., Tossavainen, A.: Asbestos Disease in Finland. *J. Occup. Med.* 22:751-754 (1980).
2. Nurminen, M.: The Epidemiologic Relationship between Pleural Mesothelioma and Asbestos Exposure. *Scand. J. Work Environ. & Health 1:128-137 (1975).*
3. Mowe, G., Gylseth, B., Hartveit, F., Skaug, V.: Fiber Concentration in Lung Tissue of Patients with Malignant Mesothelioma. *Cancer* 56:1089-1093 (1985).

FACTORS THAT MAY INFLUENCE INTERACTIONS BETWEEN MINERAL DUSTS AND LUNG CELLS

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ABSTRACT

Sup. .natant media of dust-exposed pulmonary alveolar macrophages (PAMs) were inactive in assays for both Interleukin-1 and fibroblast growth factors (FGF). We have begun to evaluate several factors that may interfere with dust-PAM interactions.

To determine the effect of sterilization on the activity of dusts, PAMs were exposed to autoclaved dust, heat-sterilized dust or to dust that had not been heated. Supernatants from the first two groups were inactive in the FGF assay, but supernatant from PAMs exposed to unheated dusts stimulated growth of lung fibroblasts.

Recent data have revealed that freshly crushed mineral dusts possess labile free radicals that are absent in dust that has been stored for more than a few days. Suspensions were prepared of a "stale" sample of anthracite dust 867 and of a freshly ground sample of the same dust. These suspensions were instilled intratracheally into guinea pigs under general anesthesia. Two, five or eight days later, PAMs were collected from the lungs by bronchoalveolar lavage, and the cells were counted. At two and five days after instillation, all lavage suspensions contained 70 to 85% PAMs, of which 5 to 18% contained phagocytized dust particles. On day eight there were again 80–84% PAMs in all suspensions, but in the presence of "fresh" dust, 48% of PAMs had phagocytized particles in comparison to 16% in the presence of "stale" dust. A similar experiment was performed in short-term cell culture. During 24-hours, >95% of PAMs phagocytized dust particles, whether or not the dust was "stale" or "fresh." Our studies are being extended to determine the effect of (1) removing surface oil contaminants by organic extraction and (2) suspending dusts without surfactant.

No Paper provided.

ELECTRON MICROSCOPIC FINDINGS OF HYPERSENSITIVITY PNEUMONITIS

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ABSTRACT

Ultrastructure in open lung biopsies of 13 patients with hypersensitivity pneumonitis were studied. Eleven of the patients had farmer's lung and two had been exposed to other mouldy dust. Numerous lymphocytes, macrophages and giant cells were found in the alveolar and bronchiolar lumina. Loss of microvilli on the ciliated cells, granulomas, detachment of basal cells from each other, as well as disintegration of the basement membrane could be detected in bronchioles. In the alveoles hyperplasia and hypertrophy of type II (granular) pneumocytes often loosely connected with the basement membrane, were frequently demonstrated. Disintegration of the basement membrane accompanied by detachment of the pneumocytes was found occasionally. In the interstitium lymphocytes, mast cells and plasma cells predominated. Some lymphocytes with pseudopods were detected both in alveolar lumen and in the interstitium. Mast cells were found in close connection with plasma cells occasionally. Granulomas consisting of these cells and giant cells were usually present. Foreign material resembling hyphal fragments was found in the giant cells of two patients. The present series emphasizes the role of lymphocytes, macrophages, giant cells and mast cells, in the pathogenesis of hypersensitivity pneumonitis. The presence of numerous plasma cells in the lung parenchyma suggest the possibility of local antibody response caused by exposure to inhaled antigens.

No Paper provided.

MUSCULARIZATION OF PULMONARY ARTERIES IN COAL WORKERS PNEUMOCONIOSIS

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INTRODUCTION

Smooth muscle hypertrophy occurs in the walls of small pulmonary arteries in coal workers pneumoconiosis (CWP), and has been suggested as a pathogenetic cause for cor pulmonale.[1] There are two types of muscular hypertrophy in the terminal pulmonary arterial tree in CWP, namely longitudinally oriented and circularly oriented smooth muscle hypertrophy. The purpose of this study is to examine the differences between their etiology and pathophysiology and to correlate the changes with right ventricular hypertrophy (RVH) in CWP. For this study, 72 autopsies without heart valvular or severe coronary lesions and without hypertensive left ventricular hypertrophy were drawn from a series of 120 unselected consecutive autopsies carried out in a southern West Virginia hospital serving mainly a coal mining community.

LONGITUDINALLY ORIENTED SMOOTH MUSCLE HYPERTROPHY

Etiology

In CWP, a longitudinally oriented smooth muscle layer or bundle may be seen in the walls of the terminal pulmonary arteries. This muscle layer is more prominent in the intimal wall, and sometimes in the adventitia, of terminal pulmonary arteries (diameter $>120\mu$) than in those of small pulmonary arterioles (diameter $< 100\mu$) The development of such muscle fibers may be due to repeated elongation or stretch forces of the vessels as they pass around an abnormal air sac, as in emphysema, or around a fibrotic mass.[2,3] Pulmonary hypertension and alveolar hypoxia may help to stimulate its formation. The combination of high intravascular pressure and repeated stretch forces potentially exaggerates the development of longitudinal muscle hypertrophy in the pulmonary arteries.[4] Other factors such as smoking and chronic bronchitis may also induce some longitudinal muscle fibers in the intimal wall[5] but they are not as abundant as in emphysema or in CWP. It is believed that the longitudinal muscle fibers could make the vessel wall more stable and help to prevent its over distension when it is subjected to repeated stretching forces.[6]

Pathologic Features

At first, a small fasciculi of longitudinally oriented muscle fibers may develop in the intima of the vessels. Such small fascicular fibers may develop into a thicker continuous band of muscle (Figure 1) and then became separated from one another by collagen ana elastic fibrils. With the passage of time, fibrous tissue progressively replaces the muscle fibers leaving the appearances of a "nonspecific intimal fibrosis." These developments in the intima are the result of activity of myofibroblasts, which have the capacity to form smooth muscle cells and secrete collagen and elastin.[7] The ultimate outcome of the process is narrowing or occlusion of the lumen with fibroelastosis (Figure 2).

Correlation with Right Ventricular Hypertrophy

In emphysema, the development of longitudinal muscle in the pulmonary artery wall is not related to RVH and hence to pulmonary hypertension.[8] Measurements on the noncircularly oriented muscle in coal workers' vascular lesions in an earlier study of the Appalachian region also failed to demonstrate such a correlation.[9,10] In our recent study of 10 CWP cases with significant longitudinal muscle hypertrophy in the intimal walls of small pulmonary arteries, the thickness of such a muscle layer, expressed in percentage of longitudinal muscle area (PLA)*, did not show any correlation with RVH ($r = -0.205$) (Figure 3). This implies that the simple loss of vascular bed due to longitudinal muscle hypertrophy or intimal fibromuscular proliferation is not the main cause of cor pulmonale in CWP. The lungs may develop compensation mechanisms such as recanalization, collateral circulation or bronchopulmonary anastomosis which may ameliorate the pulmonary circulation.[3,11] The response of longitudinal muscle to stimuli is, therefore, unlikely to constrict the vessels and hence augment the pulmonary vascular resistance as circular muscle does.

CIRCULARLY ORIENTED SMOOTH MUSCLE HYPERTROPHY

Etiology

A newly formed or hypertrophied circularly oriented smooth muscle layer may exist in the medial wall of terminal pulmonary arteries in CWP, but is usually more prominent in the segment of pulmonary arterioles (diameter $<100\mu$) sandwiched between an outer original and inner newly formed elastic lamina (Figure 4). In the normal, the medial circular muscle layer exists only in the pulmonary arteries (diameter 100–500μ), gradually turns to spiral fibers in the wall of arterioles (diameter 90–100μ), and vanishes in small arterioles (diameter $<60\mu$) after birth.[12] Hypertrophy of medial circular muscle in these vessels appears to imply

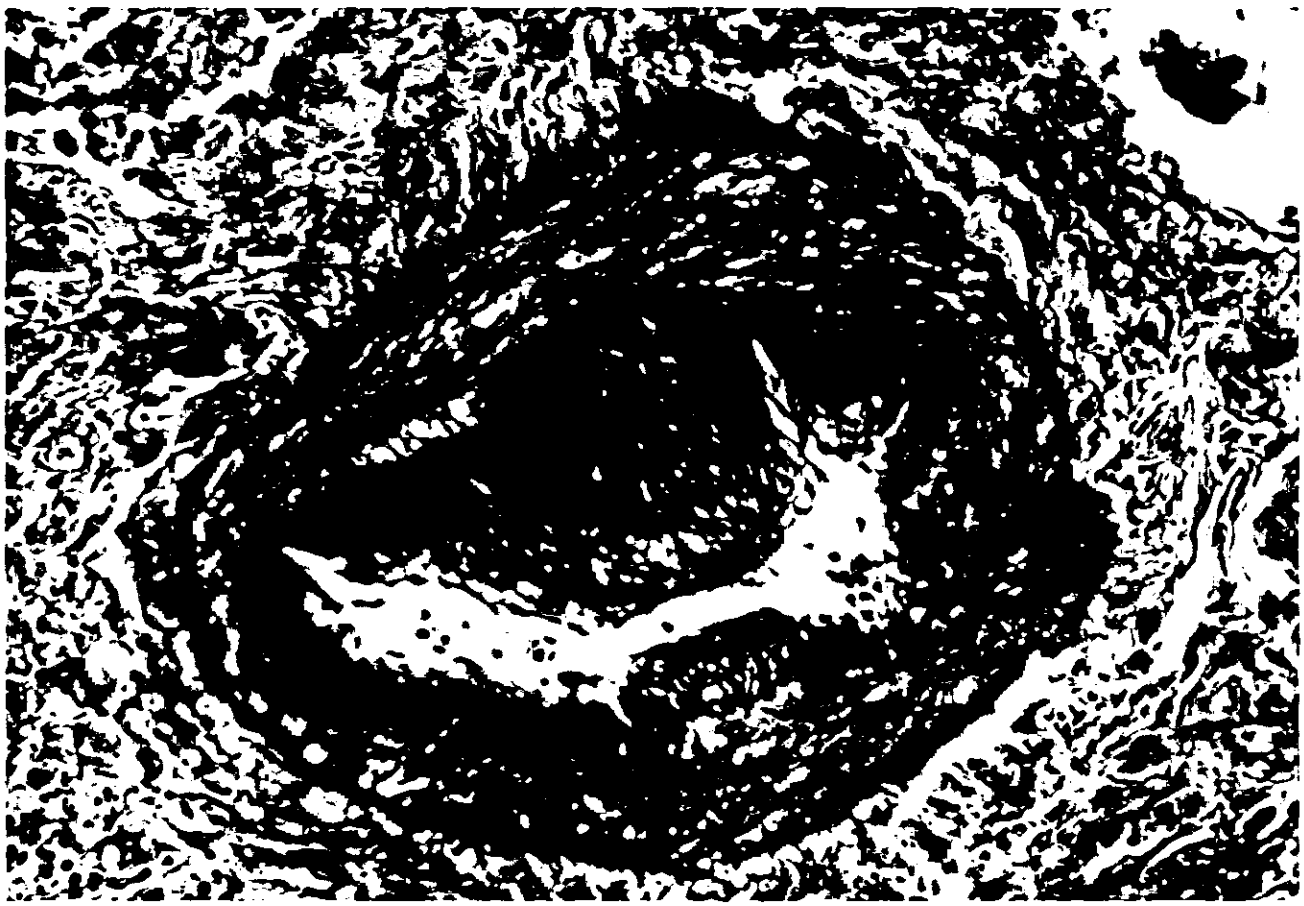

Figure 1. A 67-year-old coal worker with 25 years of underground mining exposure. He had PMF, CALD and severe emphysema with complications of cor pulmonale and right ventricular failure. Note the band of longitudinal smooth muscle in the intimal wall of a small pulmonary artery located in fibrotic tissue. (Van-Gieson elastin stain) (380X).

active vasoconstriction and increased muscular work intermittently or continuously for a prolonged time.[13] The most potent stimulant is chronic alveolar hypoxia which causes the terminal pulmonary arteries to constrict and gives rise to an increased quantity of smooth muscle in the medial layer.[5,9,14] Another stimulant is pulmonary hypertension, that is, the small arteries will also constrict in response to a sudden increase in pressure.[15] There are genetic differences in the responsiveness of the pulmonary circulation to hypoxia, pulmonary hypertension and other various physiological and pathological stimuli.[16,17] The pulmonary vascular resistance of individual CWP may be modified by many factors.

Pathophysiology

In CWP, especially in progressive massive fibrosis (PMF) or complicated with other chronic airway lung diseases (CALD), such as chronic bronchitis, brochiolitis, bronchiectasis and pulmonary tuberculosis, disorders of ventilation and perfusion and decreases of diffusing capacity may be severe enough to cause chronic alveolar hypoxia and hypoxemia.[18,19] Chronic hypoxemia and pulmonary hypertension may exert their functional effects throughout the entire pulmonary arterial tree, but the most reactive part is at the arterioles both in affected and normal areas (Figure 5).[20] Although the presence of a hypertrophied medial muscle layer does not cause constriction, once it is stimulated, a thicker circular muscle layer has a stronger contraction. Thus, a vicious cycle between constriction, medial hypertrophy and pulmonary hypertension will be formed leading to RVH.[4]

Correlation with Right Ventricular Hypertrophy

There are close correlations between the development of arteriolar muscularization and RVH in emphysema as well as in CWP.[7,21,22] This suggests the possibility that such muscularization represents the organic basis for the increased pulmonary resistance in these diseases. The percentage of medial wall thickness (PMT) in pulmonary arterioles (diameter $< 100\mu$) of 57 coal miners and 15 controls in

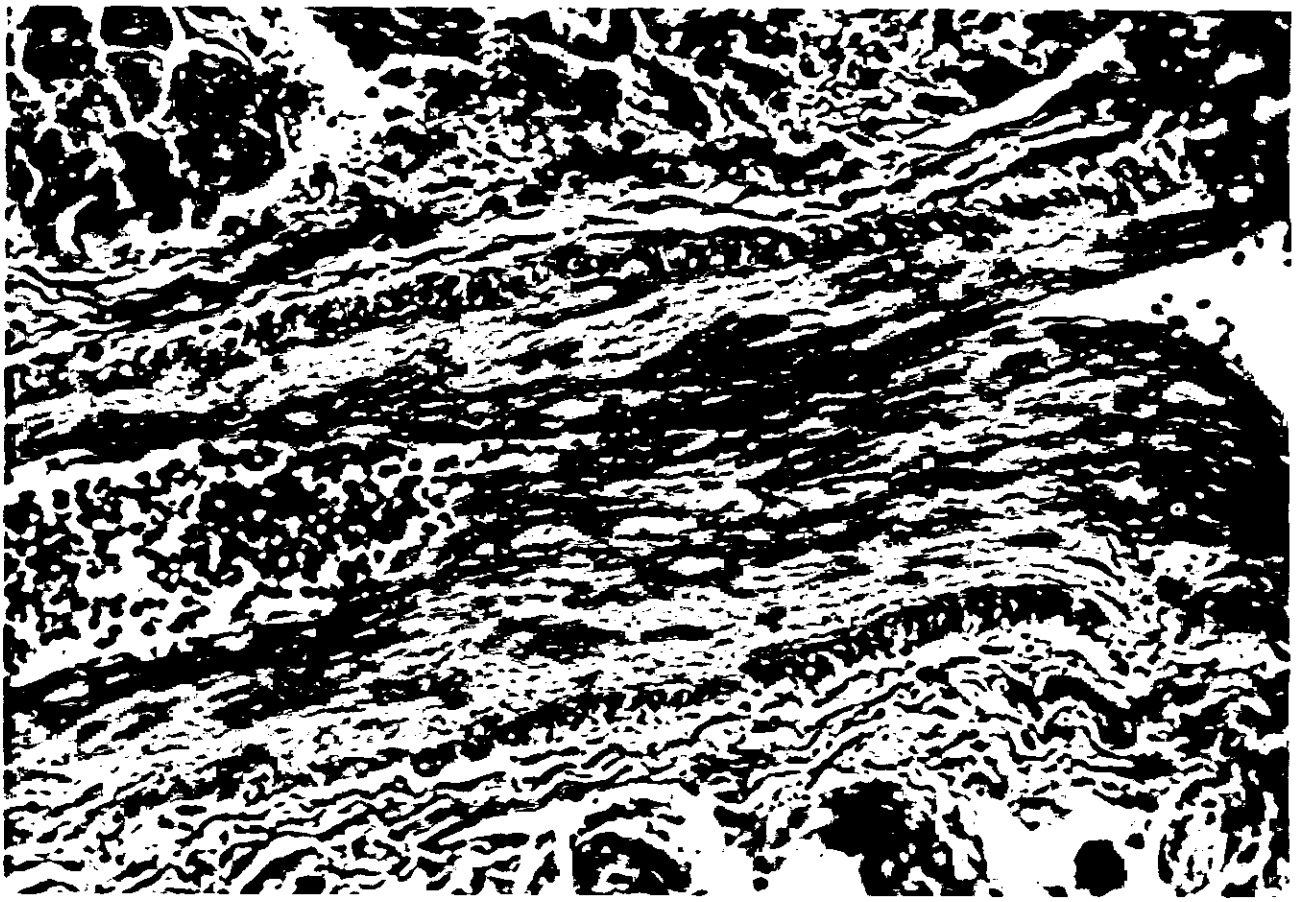

Figure 2. A 65-year-old coal miner with 35-years of underground exposure shows nodular lesions of CWP and silicosis. The severe intimal longitudinal smooth muscle hypertrophy appears to occlude the lumen of a small pulmonary artery. (Masson stain) (380X).

the Appalachian region were recently evaluated with a standard stereology program and showed a high correlation with the RV weight in percentage of LV weight (RV/LV).[22] When the cases were grouped according to the literature of RVH index into normal (RV/LV<74%), mild (RV/LV = 75–79%), moderate (RV/LV = 80–89%) and severe (RV/LV >90%)[1,23] with comparable average ages and underground exposure years, the mean PMT increased from 23 to 33, 36 and 40%, respectively ($p < 0.001$) (Table I).

On the other hand, medial thickness of small pulmonary arteries with external diameter larger than 100μ (grouped into 101–300μ and 301–500μ) in 25 CWP cases showed less or no correlation with the incidence of RVH ($r = 0.4690$ and 0.0726 respectively), while those of pulmonary arterioles (diameter <100μ) showed a significant correlation with RVH ($r = 0.8146$) (Figure 6).

Right Ventricular Hypertrophy in Different CWP and Controls

In the same study,[22] progressive massive fibrosis (PMF) caused a higher incidence of moderate and severe RVH than simple CWP did, 60% vs 16%. When they were complicated with chronic airway and lung diseases, both incidences of RVH increased, 87% vs 54% (Table II).

CONCLUSION

Circular smooth muscle hypertrophy in the medial wall of pulmonary arterioles (diameter <100μ) showed a high correlation with the incidence of RVH in 57 CWP and 15 controls from the Appalachian region. Intimal longitudinal muscle hypertrophy, or medial circular muscle hypertrophy in small pulmonary arteries (diameter >100μ), did not show such correlation with RVH.

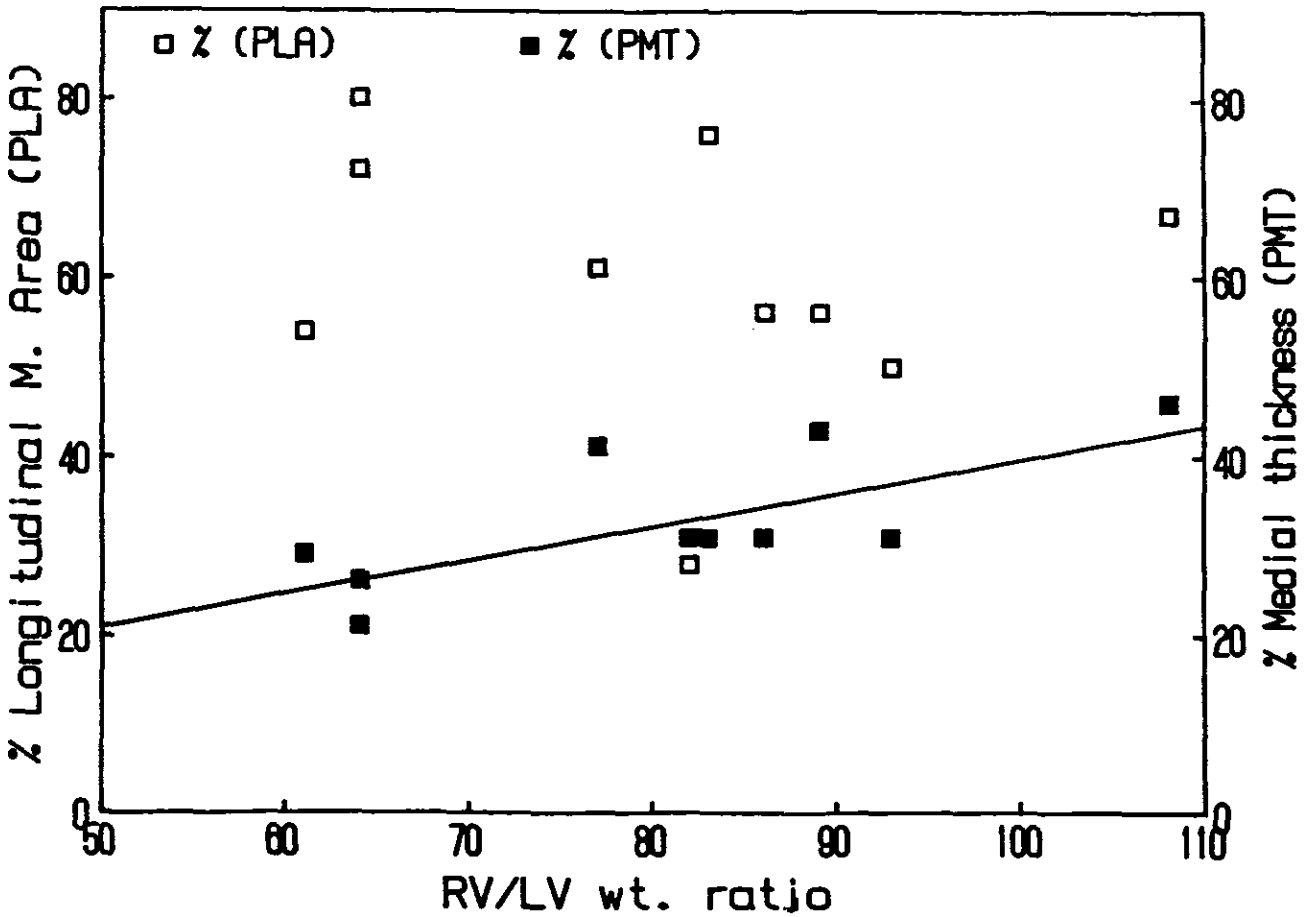

Figure 3. Correlation between RV/LV wt. ratio and percentage longitudinal muscle area (PLA) and percentage medial thickness (PMT) in 10 CWP.

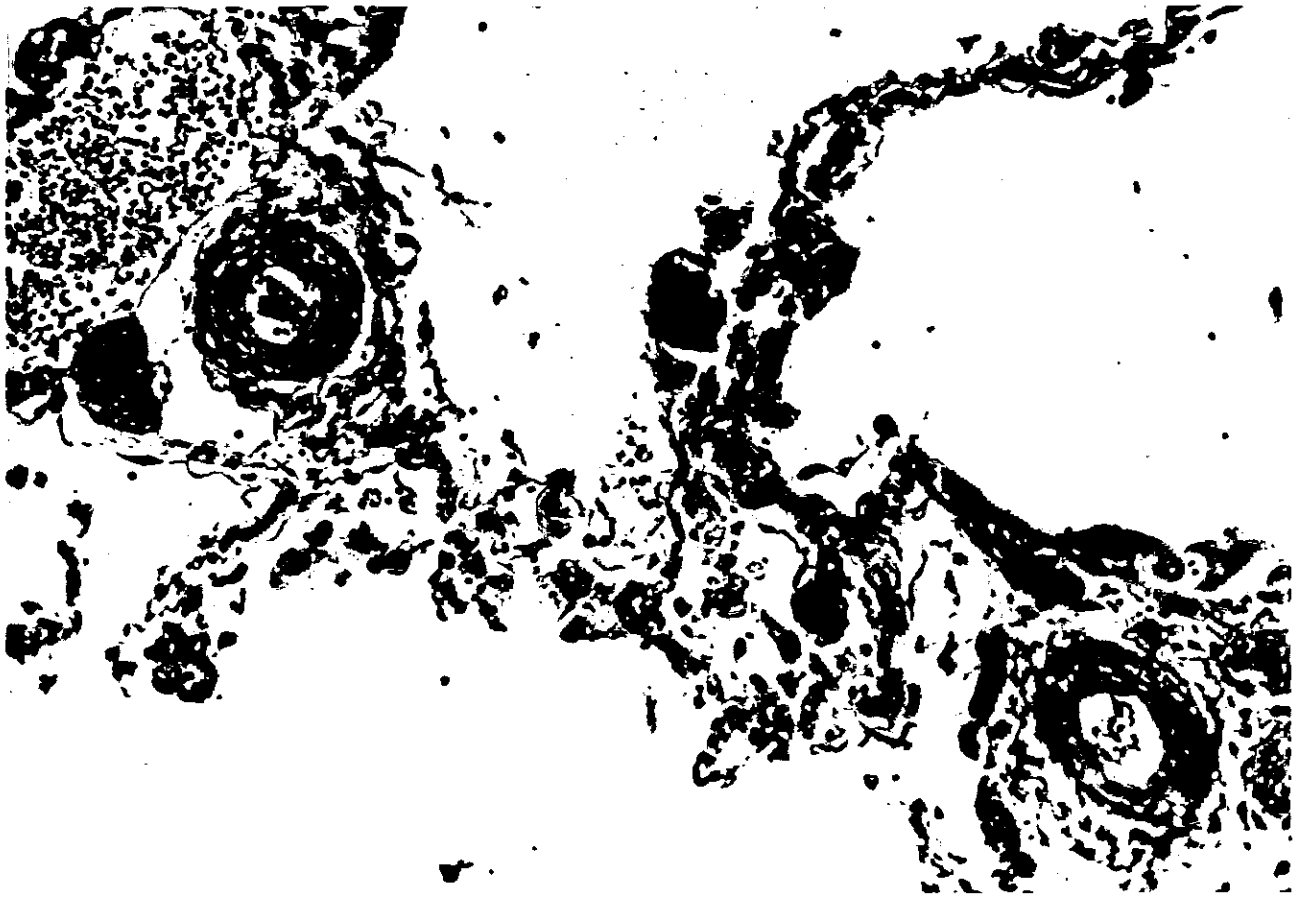

Figure 4. A 78-year-old coal miner with 25-years of underground exposure who had severe PMF and cor pulmonale. Note the medial hypertrophy of his pulmonary arterioles. (Van-Gieson elastin stain) (240X)

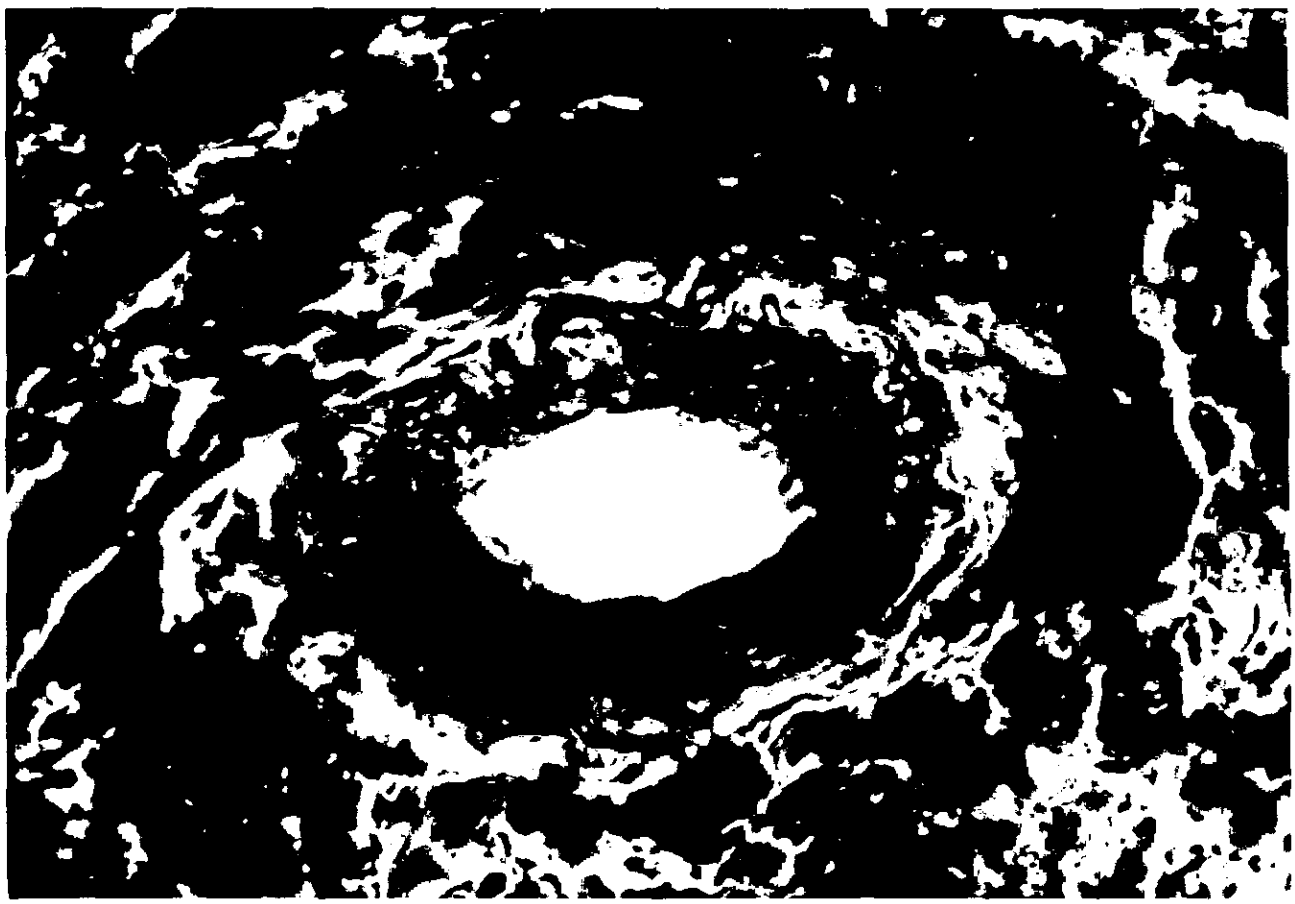

Figure 5. A 69-year-old coal miner with 45-years of underground exposure and CWP, CALD and mild cor pulmonale. Notice the arteriolar muscularization within a macular lesion. (V.G. stain) (960X)

Table I

The Severity of RVH of 57 CWP Cases (in 4 groups) Correlated with Other Parameters

	GROUP I	GROUP II	GROUP III	GROUP IV
COR PULMONALE (RVH)	NORMAL	MILD	MODERATE	SEVERE
RV/LV WEIGHT RATIO:	<74%	75-79%	80-89%	>90%
CASES	17	10	13	17
AGE	67±9♦	68±11	68±6	66±7
UNDERGROUND EXPOSURE (YRS)	32±8	39±10	37±9	33±7
RV/LV (%)	60±10	77±1	85±3	104±16
RV FAILURE (CASES)	0	1	8	15
PMT (%)	23±8	33Δ±5	36†±5	40§±6

♦ mean ± standard deviation

Δ statistically significant ($P < 0.05$) from Group I

† statistically significant ($P < 0.05$) from Group I and II

§ statistically significant ($P < 0.05$) from Group I, II, and III

Table II

Incidences of RVH and Mean PMT in Different CWP and Controls

Diff. Lung Dis.	RVH (RV/LV > 80%) (%)	(cases)	Mean RV/LV (%)	Mean PMT (%) ± (SD)
PMF-CALD	87	14/16	94	38.6 ± 6.6
PMF	60	3/5	83	31.8 ± 9.5
CALD-Simple CWP	54	13/24	79.5	31.9 ± 7.3
CALD	30	3/10	73.5	27.0 ± 9.5
Simple CWP	16	2/12	69.8	27.2 ± 9.5
Normal	0	0/5	< 60	10.9 ± 2.5

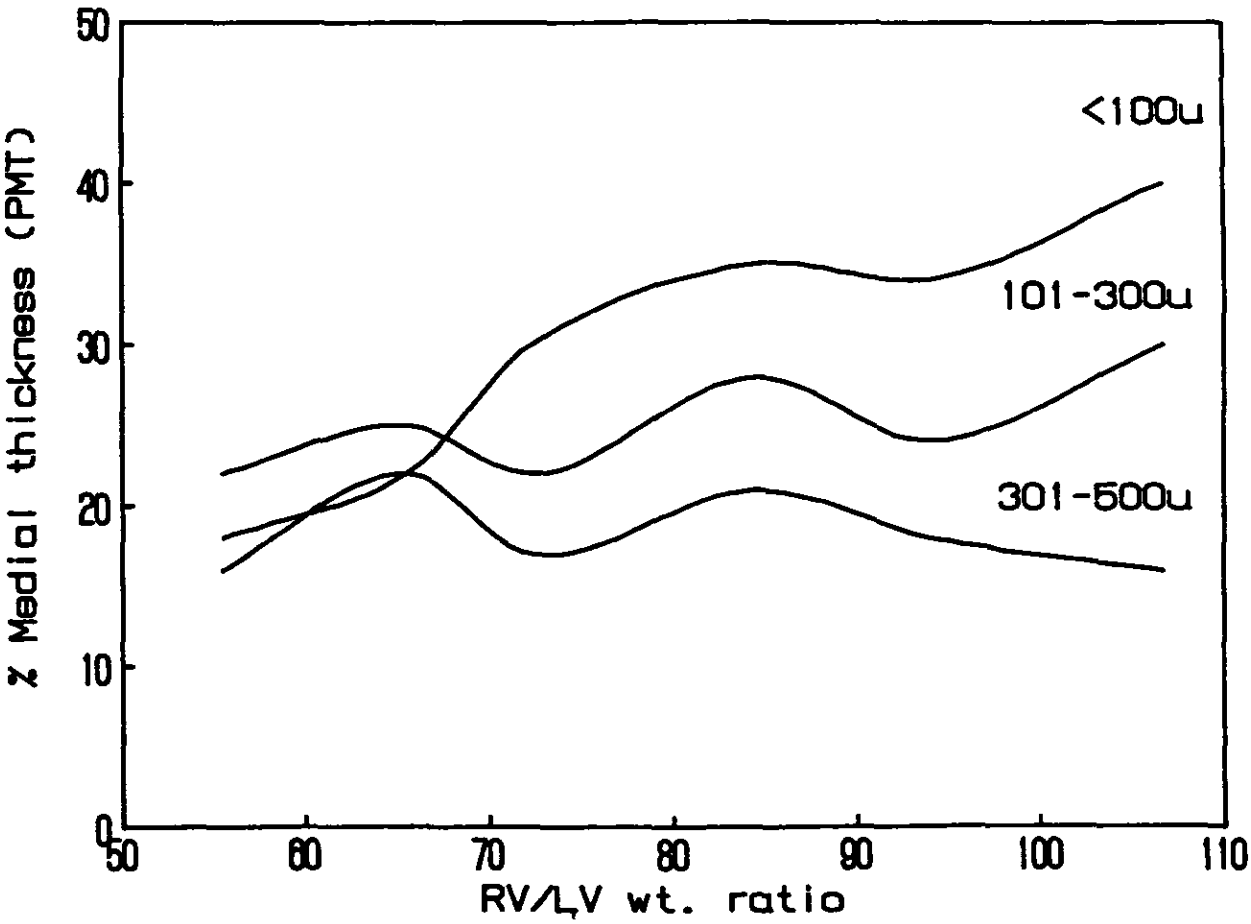

Figure 6. Correlation between RV/LV wt. ratio and percentage medial thickness (PMT) of terminal pulmonary arteries in diameters < 100. 101–300μ and 301–500μ in 25 CWP cases.

REFERENCES

1. Thomas, A.J., James, W.R.L.: The Right Ventricule and the Small Pulmonary Arteries in Coal Workers. *B. Heart. J.* 20:403-410 (1958).
2. Dunnill, M.S.: An Assessment of the Anatomical Factor in Cor Pulmonale in Emphysema. *J. Clin. Pathol.* 14:246-258 (1961).
3. Heath, D., Smith, P.: Pulmonary Vascular Disease Secondary to Lung Disease, in Moser K.M. (ed): *Pulmonary Vascular Diseases,* pp. 407-415. Marcel Dekker Inc., New York (1979).
4. Harris, P., Heath, D.: The Relation Between Structure and Function in the Blood Vessels of the Lung in Pulmonary Hypertension, in: *The Human Pulmonary Circulation, Its form and function in health and diseases,* 3rd ed., pp. 284-297. Churchill Livingston, Edinburgh (1986).
5. Naeye, R.L., Delliger, W.S.: Pulmonary Arterial Changes With Age and Smoking. *Arch. Pathol.* 92:284-288 (1971).
6. Burton, A.C.: Relation of Structure to Function of the Tissues of the Wall of Blood Vessels. *Physiol. Rev.* 34:619 (1954).
7. Harris, P., Heath, D.: The Pulmonary Vasculature in Emphysema, in: *The Human Pulmonary Circulation,* 3rd ed., pp. 507-521. Churchill Livingston, Edinburgh (1986).
8. Hicken, P., Health, D., Brewer, D.B., Whitaker, W.: The Small Pulmonary Arteries in Emphysema. *J. Pathol. Bacteriol.* 90:107 (1965).
9. Naeye, R.L., Laqueur, W.A.: Chronic Cor Pulmonale: Its Pathogenesis in Appalachian Bituminous Coal Workers. *Arch. Pathol.* 90:487-493 (1970).
10. Kleinerman, J. et al. (eds): Pathology Standards for Coal Workers Pneumoconiosis: Reports of the Pneumoconiosis Committee of the College of American Pathologists to the National Institute for Occupational Safety and Health. *Arch. Pathol. Lab. Mea.* (special issue) 103:375-429 (1979).
11. Turner-Warwick, M.: Precapillary System Pulmonary Anastomosis. *Thorax.* 18:225-237 (1963).
12. Wagenvoort, C.A., Wagenvoort, N.: Pulmonary Vascular Bed: Normal Anatomy and Response to Disease, in Moser K.M. (ed): *Pulmonary Vascular Diseases,* pp. 14-26. Marcel Dekker Inc., New York (1979).
13. Harris, P.: Patent Ductus Arteriosus With Pulmonary Hypertension. *B. Heart. J. 17:85 (1955).*
14. Naeye, R.L., Greenberg, S.D., Valdivia, E.: Small Pulmonary Vessels in Advance Pulmonary Emphysema. *Arch. Pathol.* 97:216-220 (1974).
15. Johansson, B.: Vascular Smooth Muscle Reactivity. *Ann. Rev. Physiol. 43:359 (1981).*
16. Grover, R.F., Vogel, J.H.K., Averill, K.H., Blount, S.G.: Pulmonary Hypertension, Individual and Species Variability Relative to Vascular Reactivity. *Am. Heart. J.* 66:1 (1963).
17. Heath, D., Smith, P., Rios Dalenz, J., William, D., Harris, P.: Small Pulmonary Arteries in Some Natives of La Pazi Bolivia. *Thorax.* 36:599 (1981).
18. McNeill, R.S., Rankin, J., Forster, R.E.: The Diffusing Capacity of the Pulmonary Membrane and the Pulmonary Capillary Blood Volume in Cardiopulmonary Disease. *Clin. Sci.* 17:465-482 (1958).
19. Bates, D.V., Varis, C.J., Donevan, R.E., Christie, R.V.: Variations in the Pulmonary Capillary Blood Volume and Membrane Diffusion Component in Health and Disease. *J. Clin. Invest.* 39:1401-1412 (1960).
20. Wagenvoort, C.A., Wagenvoort, N.: Pulmonary Vascular Bed: Normal Anatomy and Response to Disease. In Moser K.M. (ed): *Pulmonary Vascular Diseases.* p. 48. Marcel Dekker Inc., New York (1979).
21. Hicken, P., Heath, D., Brewer, D.B., Whitaker, W.: The Small Pulmonary Arteries in Emphysema. *J. Pathol. Bacteriol.* 90:107 (1965).
22. Hu, S.N., Vallyathan, V., Green, F.H.Y., Weber, K.C., Laqueur, W.:

Pulmonary Arteriolar Muscularization in Coal Workers Pneumoconiosis (CWP) and Its Correlation With Right Ventricular Hypertrophy. (unpublished)

23. Wells, H.A., Laqueur, W.A.: Right Ventricular Hypertrophy in West Virginia Coal Miners. *U.S. Dept Health Education and Welfare* (1966).

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APPENDIX

$$PLA^{*} = \left(1 - \frac{\text{Peri. Lumen}^{2}}{\text{Peri. Int.}^{2}} \right) \times 100\%$$

where, PLA is the longitudinal muscle area in the percentage of original intact lumen area bounded by internal elastic lamina; Peri. Lumen and Peri. Int. are perimeters of the remaining lumen and internal elastic lamina respectively.

Since:

$$PLA = \frac{\text{Longitud. Muscle Area}}{\text{Original Lumen Area}} \times 100\%$$

and,

$$\text{Longitud. Muscle Area} = \text{Original Lumen Area} - \text{Remaining Lumen Area}$$

$$\text{Original Lumen Area} = \left(\text{Peri. Int.} / 2\pi \right)^2 \pi$$

$$\text{Remaining Lumen Area} = \left(\text{Peri. Lumen} / 2\pi \right)^2 \pi$$

therefore,

$$PLA = \frac{\text{Original Lu. Area} - \text{Remain. Lu. Area}}{\text{Original Lu. Area}} = 1 - \frac{\text{Remain. Lu. Area}}{\text{Orig. Lu. Area}}$$

$$= 1 - \frac{(\text{Peri. Lu.} / 2\pi)^2 \pi}{(\text{Peri. Int.} / 2\pi)^2 \pi} = \left(1 - \frac{\text{Peri. Lumen}^{2}}{\text{Peri. Int.}^{2}}\right) \times 100\%$$

STUDY OF SILICOSIS IN THE INDUSTRIAL DISEASE HOSPITAL (ESI HOSPITAL) MADRAS

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ABSTRACTS

14 cases of silicosis who were working in Madras Stone Industry is reported. Only four cases were suffering from silicosis and 10 from solice tuberculosis. They were all working in the industry for a period of 10 to 20 years. 85.7% were in the 40–49 age group. X-ray mottling in 85.7% of cases. Sputum AFB positive in 71% of cases.

With the positive history of occupation in the stone industry with quartz cystals, feldspar and dried dust of finely powdered material, the cases were investigated. Chest X-ray, sputum analysis and lung biopsy were done to confirm the diagnosis. Literature of silicosis is reviewed.

MATERIALS AND METHODS

Patients who are referred for symptoms of chest disease are examined after getting detailed history of their stone-dust exposure. Blood examination, sputum examination and radiological examination were done in all the cases. Radiological, findings with a positive occupational exposure history were taken as confirmatary of the diagnosis. Lung biopsy, though done in one case, is not indicated in all the cases.

CASE REPORT

Case I

Mr. M, 38 years old working in a factory at Porur, Madras, came to the hospital first on 29/10/85 with the complaints of cough with expectoration and chest pain of one month duration. O.E. Afebrile, few scattered rales heard at the apices. Sputum-AFB negative; TC-8600/cells. P 65 to 20 E15 ESR-12/30 for half and one hour. X-ray chest PA view-mottling over both lung fields, more dense at the apices. Diagnosis of miliary tuberculosis was made and treatment started with INH/SM and Eifa with Prednisolone. He was on treatment regularly; On 29/9/86 he came with cough and chest pain of one month duration. O.E. Afebile, R.S. few rales heared TC-8800/cm DC-P62 L30 E8 ESR/32/72 for one and one-half hour sputum AFB-negative: X-ray chest PA view increased mottling with fibrosis of both lung fields with dense hilum; occupational history—worked as rolling shift worker for more than twenty years. Operator for mixing of sand and stones into fine powder; white stones (quartz), red stones (feldspar) and sands are mixed and made into powder form. Lung biopsy was done by Menghini's aspiration needle. Occupational history with clinical features, the diagnosis of Silico-tuberculosis was made.

Case II

Mr. S, 36 years—working in the above company as Grinder Operator. C/O cough with minimal sputum of one month duration R.S. Rales over high infraclavicular area present. TC-9400/10mm DC-P50 L 34-E-16 ESR 3/7mm for half and one hour sputum for AFB negative. Culture negative, X-ray chest PA view shows right special hazziness with rounded densities all over lung fields suggestive of Silico-tuberculosis.

Case III

Mr. P, 30 years—working in the above company; sand stones are pressed into moulds, trimming is also done under pressure in the heat room. Mantoux-negative, sputum AFB-negative TC 8400 DC: P60 L30 E10 ESR 7/14, half an hour C.S. No growth in culture, X-ray chest PA view patch of opacity right base.

Tables I, II, and III indicate that 85.7% were in the 40–49 years of age group and X-ray evidence also 85.7%. Sputum possibility of AFB is 71%.

Table I
Age Incidence

Age	No. of Cases	%
20–29	0	—
30–39	2	14.2%
40–49	12	85.7%

Table II

Chest X-ray	No.
Mottling—both lungs	12.85%
Patchy Opacity—Pneumonia	2–14%

Table III
Investigations

Sputum—AFB	10	71.4%
ESR	7	50.0%

Case IV

Mr. K, 36 years—working in the above industry for twelve years. Had treatment for tuberculosis with history of cough and expectoration for one year. Now on examination he is afebrile R.S. Rales over infraclavicular area present. Mantoux negative, sputum AFB negative. Culture—No organism grown; X-ray chest PA view shows fine reticular pattern over both lung fields. With a positive history of occupation in the above industry with exposure for more than twelve years diagnosed as silico-tuberculosis and treatment started.

DISCUSSION

Silica may exist in the combined forms called SILICATES which are themselves fibrogenic. It is respirable free silica incrystalline forms that causes SILICOSIS. Quartz, crystals (white stones), Feldspar (red stones) and dried dusts of finely powdered materials may become airborne before wetting or after drying.

PATHOGENESIS

When silica particles are installed and deposited in the lung periphery, they are ingested by macrophages. They enter these cells surrounded by an envelope of all membrane, the phagozome. Enzymes are secreted into this envelope; Silica particle destablizes the membrane, which ruptures and release these enzymes into the cytoplasm, killing the cell. Cell rupture releases the silica particles into the environment where they are encountered by successive waves of macrophages that meet the same fate. The process continues until macrophages can no longer reach silica particles. This can result, if silica is localized and resulting tissue reaction forms an effective barrier. What properties of silica accounts for cyto-toxicity? Angularity and sharpness of the crystals and silicic acid may cause rupture of macrophages—Fibrosis may be due to fibrogenic factor released from dusted macrophages. Silica by altering the immune system provide supply of macrophages to an area containing silica. Silicotic lessions contain plasma cells and immune globulin.

PATHOLOGY

In the chronic form of silicosis, the characteristic lession is the silicotic nodule. These are more numerous in the upper lobes. Lesions consists of concentric whorls of hyalinised, relatively acellular material.

Outside this zone of cellular connective tissue infiltrated with lymphocytes. Central hyalinised zone may contain some silica and most of the particles are found in the periphery.

IN SIMPLE SILICOSIS

The disease does not progress beyond the state of isolated silicotic nodules. Silicotic nodules become conglomerate forming masses of organizing fibrous tissue. This process called progressive Massive Fibrosis (PMF) attended by Massive obliteration of underlying lung tissue.

SILICO-TUBERCULOSIS

Mycobacterial infections may complicate silicosis because of the central role of macrophages in defense of the lungs against those infecting organisms.

Accelerated silicosis: seen in circumstances of more intense exposure—Progression is faster.

Acute Silicosis is due to heavy exposure to respirable free silica.

Silicotic lymphonodes may contain silicotic nodules.

CLINICAL FEATURES

1. Breathlessness on exertion.
2. Cough
3. Little sputum.

X-ray (1) rounded small opacity –1.5 mm; (2) Enlargement of hilar lymphnodes-nodes have peripheral calcification egg-shell pattern; (3) PMF—Coalescence of rounded small opacities to form larger aggregates bilateral and upper zones. They lead to large pneumoconiotic opacities; (4) These masses begin to contract, leaving clear spaces between their lateral margins and pleural surface (Angel Wings) appearance produced by sub-pleural emphysema and contracting large opacities; (5) Later leads to shrunken lungs and kinking of trachea; (6) Calcification rarely in silicotic nodules enhancing their radiographic visibility; (7) Acute silicosis produces lung consolidations in middle and lower zones.

PHYSIOLOGY

Obstruction, mixed obstruction and restriction, and restriction or pure restriction lead to abnormal spirometric tests.

COMPLICATIONS

1. Infections include tuberculosis and nocardia commonly.
2. High risk of developing collagen disease.
3. FMF leads to pneumothorax bronchopleural fistula, chronic cor pulmonale and respiratory failure.

PROGNOSIS

Is guarded because of progression of fibers is despite cessation of silica exposure. A patient with silicosis and positive tuberculin reaction has high risk of developing active P.T. and PMF.

TREATMENT

There is no satisfactory treatment for established fibrosis due to silica. Ssurveillance and treatment for complicating infections are indicated. Further exposure in fibrogenic dust is to be stopped. Jobs and habits (e.g.) sucking, that increase the risk of developing obstructive lung disease should be avoided.

REFERENCES

1. Dauber, J.H.: Silicosis in Update-Pulmonary diseases and disorders, A.P. Fishman (ed) New York, McGraw-Hill, 1982, pp. 149–166.
2. Guideline for the use of International Labour Office—classification of radiographs of pneumoconiosis occupation safely and health sciences, 22 (Revised 1980).
3. Rom, William N.: Environments and Occupational Medicine, 197–205, First edition 1983.

ON THE BLASTOMOGENIC CAPABILITY OF SUBMICROSCOPIC ASBESTOS DUST: IS ITS FIBROUS STRUCTURE THE ONLY PHYSICAL PROPERTY DETERMINING ITS BLAST POTENTIAL?

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ABSTRACT

Ground to complete isometry and submicroscopicity of fibres after the author's own method (soft aqueous medium grinding) crocidolite (UICC), Bulgarian and Soviet antophyllites were injected intraperitoneally and intrapleurally in Wistar domestic line white rats. The percentage of induced mesotheliomas of the intraperitoneal method was 22, while that of the intrapleural one was 12. The investigations on the experimental dusts carried out at the Berghau-Forschungsinstitut in Essen, West Germany, under the personal supervision of Prof. Dr.rer.nat. K. Robock, indicated that when subjected to observation under screen electron microscope all specimens showed no fibrous structure, while electron sonde investigations indicated that the isometric material had the same chemical composition as the initial one. These results give grounds to assume that in spite of the importance of the length and diameter of fibres in asbestos blastomogenesis, experimentally proved by Stenton and other authors, they are not the only and most substantial determining factor. Purposeful investigations on this problem are necessary.

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