

ENVIRONMENTAL PULMONARY MINERAL BURDEN CORRELATED WITH SMOKING, PULMONARY EMPHYSEMA AND LUNG CANCER

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INTRODUCTION

In order to be able to identify a significant lung particle burden exceeding the background, it is necessary to know the basic pulmonary level of inhaled particles in a population. The amount of asbestos fibers in lung tissue which could originate from environmental sources would be an especially important piece of information. Numbers of asbestos fibers reported in the lung tissue of occupationally non-exposed people in the literature have varied from less than half a million to several millions per gramme of dry lung tissue.¹⁻³ Some of the differences may be due to inter-laboratory variation in fiber determinations, which has been reported to be vast.⁴

Environmental exposure to minerals varies at least due to local climatic conditions, the earth's crust and environmental pollution. The worst personal source of pollution is smoking. Smoking in itself, and diseases related to it, including chronic obstructive lung disease, pre-cancerous bronchial epithelial changes and cancer, may alter the deposition and retention of inhaled particles. Pulmonary emphysema is a morphological counterpart of chronic obstructive lung disease, and its severity also serves as an objective indicator for the duration of smoking in the course of the subjects life. The present paper describes pulmonary mineral content in a series of occupationally non-exposed subjects from Northern Finland and compares it with smoking history, the grade of pulmonary emphysema and the presence of lung cancer.

MATERIAL

20 cases were selected from an initial series of 42 male subjects who had died of non-malignant diseases and been autopsied and 53 male patients operated on for lung cancer. Smoking habits, measured in smoking time, pack years and time since stopping smoking, and also occupational history, were determined from the patient or from the next of kin by means of a questionnaire and/or personal interview. The effects of smoking, pulmonary emphysema and lung cancer on the pulmonary mineral content were studied in 13 pairs matched in terms of given background characteristics (Tables I-III).

METHODS

The lungs and lung lobes obtained from the autopsies and surgical operations were radiographed during continuous air inflation⁵ and the severity of emphysema was graded into normal, mild, moderate and severe from these radiographs

on the grounds of peripheral vascular changes, tissue defect translucencies and changes in the shape of the lung or lobe.⁶ The lungs were fixed transbronchially with hyperosmolar formalin. The grade of emphysema was also estimated from gross specimens and histological sections and these data were used if grading from the radiographs did not produce an unambiguous result. The histological type of cancer was determined according to the WHO classification of tumours.

A 0.5-1 g peripheral sample of fresh lung tissue containing no pleural surface or cancer tissue was taken from the (apico) posterior segment of the upper lobe and the apical segment or basal segments of the lower lobe after radiographing. The samples were ashed in aluminium cups in a low temperature asher with an oxygen plasma, after which the ash was dissolved in 1 M nitric acid to remove excess salt and then in absolute ethanol and distilled water. The residue was sonicated and various dilutions filtered onto a Nuclepore filter of pore size 0.1 μm . The filter, coated with carbon, was transferred onto a gold grid and dissolved slowly in chloroform vapour. The grid was coated again with carbon to minimize charging.

Electron microscopy was performed using a JEOL 100CX scanning transmission electron microscope (STEM) and PGT SYSTEM III energy dispersive spectrometry (EDS). At least a hundred particles ($> 0.1 \mu\text{m}$) per specimen were identified using EDS analysis and electron diffraction. Two dimensions on each particle were measured on the STEM image, the thickness being assumed to be equal to the width for all minerals other than phyllosilicates ($0.2 \times$ width). Approximate volumes were calculated for the minerals, after which their masses could be determined from their known densities. To determine the number of fibers, 100 fibrous particles having the length to diameter ratio $\geq 3:1$ were searched and identified. Statistical comparisons were performed using paired t-tests, in which p values less than 0.05 were considered significant.

RESULTS

The pulmonary particle burden, measured as total mass, volume and surface area, showed very narrow variation depending on smoking, pulmonary emphysema or lung cancer, whereas the number of particles and the mean particle size showed some dependence on these factors. The mean total number, volume, surface area and mass of mineral particles in the material (\pm SD) were $155 \pm 194 \times 10^6$, $0.15 \pm 0.16 \text{ mm}^3$, $655 \pm 670 \text{ mm}^2$ and $0.41 \pm 0.43 \text{ mg}$ per

Table I
 Characteristics of the Case-Control Pairs Chosen for
 Studying the Effect of Smoking on the Pulmonary Mineral Burden

	Age	Smoking	Smoking time	Grade of emphysema	Occupation	Lung cancer	Site of sample*
1.	75	Non-smoker	0	No	Farmer	No	BLL
	71	Smoker	25	Mild	Unknown	No	AUL
2.	79	Non-smoker	0	Mild	Unknown	No	BLL
	75	Smoker	44	No	Roadman	No	BLL
3.	73	Non-smoker	0	Mild	Car driver	No	AUL
	61	Smoker	46	Mild	Road scraper driver	No	AUL
4.	77	Non-smoker	0	No	Unknown	No	BLL
	72	Smoker	25	No	Salesman	No	BLL

* AUL= apical upper lobe, ALL= apical lower lobe, BLL= basal lower lobe

Table II
 Characteristics of the Case-Control Pairs Chosen for Studying
 the Effect of Pulmonary Emphysema on the Pulmonary Mineral Burden

	Age	Smoking	Smoking time	Grade of emphysema	Occupation	Lung cancer	Site of sample*
1.	72	Smoker	25	No	Salesman	No	BLL
	71	?	?	Severe	Unknown	No	BLL
2.	71	Smoker	25	Mild	Unknown	No	AUL
	60	Ex-smoker	25	Moderate	Clerk	No	BLL
3.	75	Non-smoker	0	No	Farmer	No	BLL
	68	Ex-smoker	25	Moderate	Farmer	No	AUL
4.	77	Non-smoker	0	No	Unknown	No	BLL
	73	?	?	Severe	Roadman	No	AUL
5.	75	Smoker	44	No	Roadman	No	BLL
	69	Smoker	50	Moderate	Caretaker	No	AUL

* AUL= apical upper lobe, ALL= Apical lower lobe, BLL= Basal lower lobe

Table III
 Characteristics of the Case-Control Pairs Chosen for Studying
 the Effect of Lung Cancer on the Pulmonary Mineral Burden

	Age	Smoking	Smoking time	Grade of emphysema	Occupation	Lung cancer	Site of sample*
1.	68	Ex-smoker	25	Moderate	Farmer	No	AUL
	65	Ex-smoker	35	Moderate	Farmer	Yes	BLL
2.	71	Smoker	57	Moderate	Mason	No	ALL
	60	Smoker	40	Moderate	Sawyer	Yes	AUL
3.	71	Smoker	25	Mild	Unknown	No	AUL
	63	Ex-smoker	40	Mild	Surveyor technician	Yes	ALL
4.	74	Smoker	50	Moderate	Caretaker	No	AUL
	73	Ex-smoker	25	Moderate	Roadwork foreman	Yes	ALL

* AUL= apical upper lobe, ALL= apical lower lobe, BLL= basal lower lobe

gramme of dry lung tissue respectively. In individual cases the number of particles varied from 10×10^6 to 670×10^6 , and the number of fibers from less than a hundred thousand to 10×10^6 per gramme of dry weight. The asbestos fibers were mostly anthophyllite and crocidolite, but not many amosite and chrysotile were found.

Smoking

The number of particles, including every particle type except fibers, aluminium, plagioclase and talc, was greater in the lung tissue of the smokers than in their matched non-smoking counterparts. Kaolinite particles were especially numerous in the lungs of the smokers as compared with the non-smokers. The differences in the number and type of particles between the non-smokers and smokers were not statistically significant, however. The mean particle size (mean volume of single particles) was larger in the non-smokers than in the smokers ($p=0.065$) (Table IV).

Pulmonary Emphysema

The total number of particles in patients with moderate or severe pulmonary emphysema was lower than in their matched pairs with mild or no emphysema. Plagioclase was the only particle type which was more numerous in the emphysematous lungs. The mean size of single particles was significantly larger in the patients with moderate or severe emphysema as compared with controls who had mild or no emphysema ($p<0.05$) (Table V).

Lung Cancer

All the cancers included in the material were histologically of the squamous cell type. The total number of particles did

not differ significantly between the patients with lung cancer and their matched controls, but the numbers of fibers, plagioclase, and particles containing aluminium, iron or titanium only, were higher in the lung cancer patients, the difference in the number of fibers being statistically significant ($p<0.05$) (Table VI).

DISCUSSION

The pulmonary mineral particle burden was measured here in terms of total number, mass, volume and surface area. The number of particles varied from case to case and due to smoking and pulmonary emphysema more than the other parameters did. The total number of particles found in the lung tissue of the patients without known occupational exposure to minerals is in a fairly good agreement with the findings of Churg and Wiggs.⁷ In the present study smokers' lung tissue contained more particles than that of the non-smokers, although the difference was not statistically significant. The total volume of particles did not differ between the smokers and matched non-smokers, but the average volume of the individual particles was smaller in smokers, the difference approaching statistical significance. Churg and Wiggs⁷ found more particles in the lungs of heavy smokers than in those of light smokers. It is not known whether the numerous small particles such as kaolinite in smokers' lung tissue originate from the tobacco smoke or whether their additional presence is due to a deterioration in mucociliary clearance in smokers.

The effect of pulmonary emphysema on the total number of particles and the mean volume of single particles seemed to be the opposite of that of smoking. The small number of particles in the emphysematous lungs may be attributable firstly to tissue destruction, and secondly by a reduction in the inhalation of particles from tobacco smoke, since many people

with marked emphysema stop or cut down their smoking because of dyspnoea.

The lung cancer patients did not differ significantly from their matched controls in terms of pulmonary particle burden. Churg and Wiggs² found a greater number of particles in lung cancer patients than in controls without cancer, but this could not be found here. On the other hand, the number of fibers was significantly higher in the lungs of the present lung cancer patients than in those of the controls, even though none of them had any known occupational exposure to asbestos.

The same observation is recorded by Churg and Wiggs,² but the number of fibers they found in both the lung cancer and control patients was about ten times higher than we could detect. Similarly, ten to fifteen times higher pulmonary concentrations of fibers are reported in lung cancer patients in another study from Great Britain⁸ than we found in our patients. The difference may be due to the slightly different methods used, but it is also possible that the finding is real and reflects the degree of local environmental outdoor pollution or an unrecognized presence of asbestos materials in buildings.

Table IV
Mean Number and Type of Particles in Lung Tissue from Non-Smokers and Smokers

	Non-smoker (4 pairs)	-	Smoker	t	p
Total number ($\times 10^6$ /g dry w.)	106	-	214	- 0.6	NS
Total volume (mm^3 /g dry w.)	0.2	-	0.2	- 0.2	NS
Total surface (mm^2 /g dry w.)	736	-	798	- 0.1	NS
Total mass (mg/g dry w.)	0.4	-	0.5	- 0.2	NS
Mean particle volume (um^3)	1.5	-	0.8	2.5	<0.07
Numbers of particles ($\times 10^6$ /g dry w.):					
Fibers	3.2	-	1.2	0.6	NS
Al	0.9	-	0.5	0.5	NS
Fe	8.1	-	14.8	- 0.4	NS
Kaolinite	7.6	-	29.9	- 0.8	NS
K-feldspar	18.2	-	27.8	- 0.5	NS
Mica	23.4	-	60.5	- 0.7	NS
Plagioclase	15.4	-	9.6	1.0	NS
Quartz	14.8	-	27.8	- 0.5	NS
Talc	2.1	-	2.0	0.1	NS
Ti	5.5	-	10.0	- 0.4	NS
Others	10.5	-	29.0	- 0.8	NS

Table V
 Mean Number and Type of Particles in Lung Tissue from
 Patients with and without Pulmonary Emphysema

	No emphysema - Emphysema (5 pairs)		t	p
Total number ($\times 10^6$ /g dry w.)	194	- 50	1.1	NS
Total volume (mm^3 /g dry w.)	0.2	- 0.2	0.1	NS
Total surface (mm^2 /g dry w.)	718	- 453	0.5	NS
Total mass (mg/g dry w.)	0.5	- 0.4	0.1	NS
Mean particle volume (μm^3)	1.0	- 2.8	- 2.8	<0.05
Numbers of particles ($\times 10^6$ /g dry w.):				
Fibers	0.9	- 0.3	0.9	NS
Al	0.9	- 1.0	- 0.1	NS
Fe	15.4	- 0.1	1.5	NS
Kaolinite	26.2	- 3.6	1.1	NS
K-feldspar	25.7	- 10.5	1.0	NS
Mica	50.4	- 6.0	1.1	NS
Plagioclase	11.1	- 13.4	- 0.6	NS
Quartz	27.3	- 5.4	1.3	NS
Talc	2.2	- 0.6	1.5	NS
Ti	11.5	- 2.0	1.2	NS
Others	22.8	- 7.5	0.8	NS

Table VI
Mean Number and Type of Particles in Lung Tissue from
Patients with and without Lung Cancer

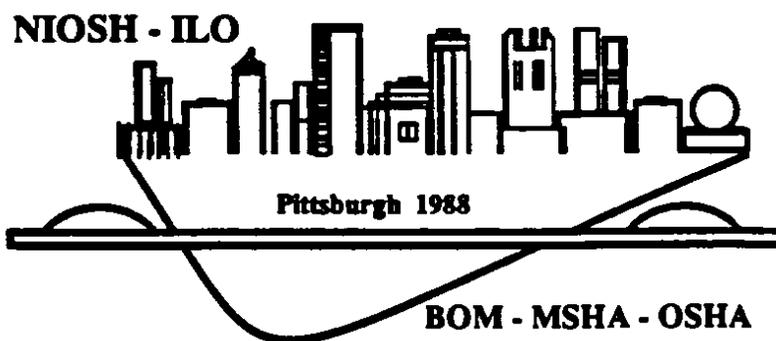
	No cancer - Lung cancer (4 pairs)			t	p
Total number ($\times 10^6$ /g dry w.)	218	-	164	0.3	NS
Total volume (mm^3 /g dry w.)	0.3	-	0.1	1.5	NS
Total surface (mm^2 /g dry w.)	1098	-	541	0.8	NS
Total mass (mg/g dry w.)	0.9	-	0.3	1.4	NS
Mean particle volume (μm^3)	2.7	-	0.9	2.0	NS
Numbers of particles ($\times 10^6$ /g dry w.):					
Fibers	0.2	-	1.2	- 2.9	<0.05
Al	0.6	-	5.3	- 0.8	NS
Fe	13.2	-	16.2	- 0.1	NS
Kaolinite	29.5	-	9.5	0.7	NS
K-feldspar	29.3	-	23.6	0.3	NS
Mica	58.9	-	13.7	0.9	NS
Plagioclase	12.7	-	26.4	- 1.4	NS
Quartz	30.0	-	16.6	0.5	NS
Talc	0.2	-	0.0	1.0	NS
Ti	11.4	-	41.2	- 0.8	NS
Others	32.1	-	11.9	0.9	NS

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