Pulmonary disease from occupational exposure to an artificial aluminium silicate used for cat litter

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ABSTRACT All available workers engaged in bagging an artificial crystalline aluminium silicate—the kiln-dried residue from the calcining and water extraction of alunite (a hydrated sulphate of aluminium and potassium) that is currently classified as a nuisance dust—were studied after a complaint of respiratory and systemic symptoms, including arthritis, by an employee of the factory, who showed physiological and radiographic evidence of diffuse pulmonary fibrosis and in whom lung biopsy showed diffuse fibrosis with granulomas. Inhalation challenge produced a transient decrease in transfer factor and transfer factor standardised for alveolar volume. Twenty-five subjects were known to have been exposed at some time to the dust of alunite-residue. Of the 17 who could be contacted, all agreed to attend for respiratory questionnaire and occupational history, pulmonary function testing (spirometry, lung volumes, gas transfer), and posteroanterior chest radiograph. Six subjects considered that occupational exposure to the dust was responsible for respiratory symptoms. Three subjects had abnormality of the chest radiograph consistent with pulmonary fibrosis. The mean percentage of predicted transfer factor standardised for effective alveolar volume was 71.1% in subjects with abnormal chest radiographs and 86.6% in subjects with normal radiographs ($p = 0.10$). There was a trend in the correlation between the percentage of predicted transfer factor standardised for effective alveolar volume and total dust exposure (sum of the products of grade of severity of each exposure period and duration of each exposure period in months) ($r = 0.40$ $p = 0.10$). This study suggests that there may be a relation between inhalation of the dust of this form of aluminium silicate and pulmonary fibrosis.

Although pulmonary fibrosis has been described from occupational exposure to dusts of aluminium powder¹ and aluminium oxide,² and asthma has been associated with the smelting of aluminium,³ there is no record of pulmonary disease in man resulting from exposure to other compounds containing aluminium, although sillimanite, an aluminium silicate, may cause diffuse and nodular pulmonary fibrosis in rabbits.⁴ An artificial silicate of aluminium has been reclaimed from a dump in rural Western Australia since 1975. The dump of about 100 000 tons was created during World War II when alunite clay from a salt lake was collected for the extraction

of potash. Alunite, a hydrated sulphate of aluminium and potassium, was calcined and then leached to yield potash (K_2SO_4). The residue was dumped in a pile on the shores of the lake. This material, when dried to a water content of 2-3%, has been found to be highly absorbent, and since 1975 it has been reclaimed, dried, and packaged for retail as cat litter. Analysis of this alunite-residue has shown it to consist predominantly of crystalline aluminium silicate (mullite) with no fibrous content (table 1). It has been classified as a "nuisance dust" in industry with permissible occupational exposures up to 10 mg/m³.⁵⁻⁷

This study was undertaken because an employee of the firm engaged in packing the dried alunite-residue complained of respiratory symptoms related to dust exposure.

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Table 1 *Chemical analysis of alunite-residue**

Constituent	Percentage of dry weight
Water soluble	
K ₂ SO ₄	2.0
Na ₂ SO ₄	2.5
Mg SO ₄	3.0
Water insoluble	
Al ₂ O ₃	48.5
SiO ₂ (as silicate)	35.0
Fe ₂ O ₃	5.0
K ₂ O	4.0
	100.0

*Western Australian Government Chemical Laboratory.

Subjects

All 11 production staff who had ever worked for more than three months with the firm were studied. Of the 14 production staff who had worked for the firm for less than three months, six were traced and all participated. The study group therefore comprised 4 women and 13 men aged 15 to 52 years.

Methods

RESPIRATORY QUESTIONNAIRE

The British Medical Research Council Questionnaire on Smoking and Respiratory Symptoms was used to provide smoking category and scores for dyspnoea, cough, and phlegm.⁹ In addition the subjects were asked: "Do you think that work with 'kitty litter' affected your chest?" and "Have you ever had any joint troubles or arthritis?"

EXPOSURE HISTORY

Dried alunite-residue from the reclaiming site is stored in large bins at the outlet of which are automatic weighing machines and filling chutes. Bags are held under the chutes by an operator and filled with a preset weight of material at a rate of 30-40 bags every minute. A second worker stands opposite the filling operator and removes the bags on to a conveyor belt where they are closed with a sewing machine and packed on to pallets for transport.

Dust exposure has not been quantitatively measured in the plant. When production started in 1975 there was no ventilation on the bagging machine. Complaints of the amount of dust in the work place led to the provision of a domestic fan to blow it away from the operator but subsequently exhaust ventilation was installed and appeared effective.

A complete occupational history was obtained for each subject. Exposure to the dust of alunite-residue during periods of employment was graded light (= 1), moderate (= 2), or heavy (= 3) on the

detailed information obtained from each subject about his job assignment and the knowledge of the bagging process. Subjects working on the semi-automatic bagging machine before the installation of exhaust ventilation were considered heavily exposed. Subjects employed on the bagging machine since the installation of exhaust ventilation were considered moderately exposed, and those employed on stacking and moving the filled and closed bags within the factory were considered lightly exposed. Subjects working in the open reclaiming the clay from the lakeside dump were considered lightly exposed. Total exposure (the sum of the products of grade of severity of each exposure period and duration of each exposure period in months) was calculated for each subject.

CHEST RADIOGRAPHS

Standard posteroanterior chest radiographs were taken with the tube-object distance of 6 ft (1.82 m). The usual procedure required 150 kv, for 6-10 m sec using a falling load tube current with ionisation chamber automatic exposure (Siemen's Iontomat) and a chest Buckey.

PULMONARY FUNCTION

The forced expiratory volume in one second (FEV₁) and forced vital capacity (FVC) were obtained from a digital spirometer (Hewlett-Packard, Burlington, Massachusetts). Transfer factor for carbon monoxide (TL) was measured by the single breath carbon monoxide method as modified by Ogilvie *et al*.¹⁰ using a Resparameter (PK Morgan). Effective alveolar volume (V_A) was estimated from the dilution of helium during the measurement of TL. Each estimate was the mean of two measurements that differed by less than 10%. The subdivisions of total lung capacity (TLC), vital capacity (VC), and residual volume (RV) were measured in a "flow" plethysmograph¹¹ (JG Emerson, Cambridge, Massachusetts) by the method of Dubois *et al*.¹² The lung volume-transpulmonary pressure relationship of the employee presenting with respiratory symptoms was measured by the method of Milic Emili *et al*.¹³ Pulmonary compliance (CL) was taken as the slope of the curve over the litre above functional residual capacity. Maximum transpulmonary pressure (P_L max) was the mean of the two highest recorded measurements at sustained maximum inspiration.

ANTHROPOMETRIC MEASUREMENTS

Height in stockinged feet was measured using a stadiometer.

STATISTICAL ANALYSIS

Because of the small population the pulmonary

Fig 1 Posteroanterior chest radiograph taken August 1976 three months after onset of symptoms showing no definite abnormality.

function results were standardised for age, height, and sex by expressing them as a percentage of predicted normal value. FEV₁ and FVC were predicted from the regressions of Cherniack and Raber.¹⁴

Fig 2 Posteroanterior chest radiograph taken March 1977 at presentation showing abnormal small irregular opacities throughout both lung fields.

TLC, RV, TL, and V_A were predicted from Cotes.¹⁵ PL max and CL were predicted from H J H Colebatch (personal communication).

CASE REPORT

This 42-year-old woman had never smoked cigarettes, had no history of previous hazardous exposure, and was well until the onset of her current illness. She was employed on the semi-automatic packaging machine filling bags with dried alunite-residue. When she first started work in August 1975 there was no effective exhaust ventilation on the machine. A domestic fan was placed by her right shoulder to provide a stream of air to carry the dust away from her, but it tended to disseminate the dust locally. About eight months after starting this job she noticed the onset of dry cough and shortness of breath. Initially these symptoms came on during the morning at work and would subside during the evening at home, but they progressed and within three months they persisted throughout the day, improving only at weekends. She remained in her job for a total of 18 months, during which time her symptoms became more troublesome. After leaving the plant her symptoms improved, and her cough subsided completely after about three months. During the period of exposure she also complained of pain and morning stiffness in her metacarpophalangeal joints, wrists, elbows, and right knee. These symptoms also subsided within three months of cessation of exposure. Additionally, exposure was associated with general malaise, headache, and anorexia. Corticosteroid treatment with prednisone started after an open lung biopsy in March 1977, two months after cessation of exposure, was stopped in October 1979. At her worst she was persistently short of breath and coughing at rest. Currently she notices dyspnoea walking up hills or stairs but can keep up with others of her own age walking on level ground at an ordinary pace.

Physical examination throughout her period of observation showed the presence of coarse crackles in the mid and lower zones of her lungs bilaterally. There has been no finger clubbing or cyanosis. Her chest radiograph was normal in August 1976, three

Table 2 Pulmonary function tests of patient—January 1979

	Predicted	Feb 1978	Feb 1979	Nov 1979
FEV ₁ (l)	2.4	2.0	2.0	1.7
VC (l)	2.9	2.3	2.3	2.1
TLC (l)	4.6	4.3	4.1	3.9
TL (mmol/min/kPa)	8.1	3.9	4.7	5.0
TL/V _A (mmol/min/kPa/l)	1.8	1.5	1.3	1.5
CL (l/kPa)	2.1	—	0.90	—
PL max (kPa)	2.98	—	8.37	—

Fig 3 (a) Response of T_L to challenge with alunitite-residue (continuous line) and control (lactose powder). (b) Response of T_L/VA to challenge with alunitite-residue (continuous line) and control (lactose powder).

months after the onset of symptoms (fig 1) but showed diffuse small irregular opacities throughout both lung fields at the time of her presentation in March 1977 (fig 2). Pulmonary function tests in February 1978 and subsequently have shown a decrease in T_L and T_L/VA and abnormal transpulmonary pressure-lung volume relationships (table 2). There has been no change in T_L or T_L/VA since February 1978.

Fig 4 Histology of presenting case from open lung biopsy. (Haematoxylin and eosin $\times 100$.)

Quantitative serum protein electrophoresis showed a moderately raised gammaglobulin level of 22 g/l (normal 9-16 g/l). Results of tests for rheumatoid factor using sensitised sheep red cells (Rheumaton, Hyland Laboratory) and Latex particles (Latex fixation test, Denver Laboratory) and for antinuclear factor were negative. Tests for cell-mediated immunity showed no response to intradermal injection of purified protein derivative or candida but a strong response to Varidase (streptokinase/streptodornase). Serum complement fractions were normal. Precipitins to antigens of *Aspergillus* sp and birds were negative by agar gel diffusion. Barium swallow was normal. A six-hour provocation test with non-quantitated exposure to the dust of powdered lactose as control material produced no change in FEV_1 , FVC, T_L or T_L/VA . Similar respiratory provocation with the dust of alunitite-residue on the next day produced no effect on FEV_1 or FVC, but a 20% reduction in T_L and T_L/VA (fig 3).

Histology from open lung biopsy in March 1977 showed interstitial infiltration with small round cells, variable fibrosis, and scattered granulomas. The alveoli were distorted and the granulomas were moderately well formed with multinucleate giant cells and epithelioid histiocytes (fig 4). One hilar lymph node was obtained and showed reactive changes only. X-ray microanalysis of the pulmonary tissue showed the presence of aluminium.

In summary there was a clear temporal relation between the onset and remission of her symptoms and exposure to alunitite-residue in the work place. Functional and radiographic evidence of pulmonary fibrosis was confirmed by histology, the interest being in the presence of granulomas within the lung. Since starting corticosteroids in April 1977 there has been no further deterioration in pulmonary function. Steroids were withdrawn in October 1979.

Results of work force study

The average age of the subjects was 29.1 years (range 15.1-52.1). Age was correlated with duration of employment ($r = 0.77$) and severity of exposure ($r = 0.59$) in that the older subjects stayed in employment longer and were assigned to the more dusty job of filling bags with alunitite-residue on the bagging machine. Overall, the group was comparable to predicted levels of FEV_1 , VC, and TLC (tables 3 and 4). T_L and T_L/VA were less than predicted.

The $T_L\%$ predicted of smokers and ex-smokers (86.0%) was similar to that of non-smokers (85.3%) but $T_L/VA\%$ predicted tended to be lower in smokers and ex-smokers (85.3%) than non-smokers (87.8%). Smokers were not disproportionately represented in the group with greater total dust exposure: mean

Table 3 Table of pulmonary function tests for all subjects

Subject	Age (yr)	Height (cm)	TLC litre (pred)	VC litre (pred)	FEV ₁ litre (pred)	FVC litre (pred)	FEV ₁ /FVC% (pred)	TL (mmol/min/kPa)	TL/VA (mmol/min/kPa/l)	Total exposure (Σ Grade × months)
Men										
1*	18	175.9	6.5 (6.8)	4.8 (5.2)	4.0 (4.4)	4.6 (5.2)	86.7 (85.1)	10.35 (12.08)	1.64 (1.97)	3
2	29	182.9	8.3 (7.4)	5.6 (5.3)	4.7 (4.3)	5.4 (5.3)	86.1 (81.0)	11.72 (12.11)	1.54 (1.82)	36
3*	18	181.0	6.9 (7.2)	4.1 (5.4)	4.2 (4.6)	5.0 (5.4)	83.4 (85.1)	10.42 (12.63)	1.61 (1.97)	6
4*	17	170.8	6.2 (6.3)	4.4 (4.9)	4.0 (4.2)	4.3 (4.9)	92.7 (85.5)	9.50 (11.59)	1.54 (1.98)	2
5*	16	162.6	4.8 (5.6)	4.0 (4.5)	3.2 (4.0)	3.8 (4.5)	84.8 (85.8)	8.53 (10.76)	1.67 (1.99)	2
6*	19	183.5	7.7 (7.4)	5.1 (5.5)	5.1 (4.6)	5.8 (5.5)	87.7 (84.7)	9.01 (12.84)	1.17 (1.95)	48
7†	31	181.6	8.7 (7.3)	6.0 (5.2)	5.3 (4.2)	6.5 (5.2)	82.9 (80.2)	14.21 (11.83)	1.74 (1.80)	30
8	15	172.1	4.9 (5.7)	4.0 (4.4)	3.5 (3.8)	3.8 (4.4)	91.8 (85.6)	7.93 (11.86)	1.64 (2.00)	6
9*	18	166.4	5.5 (5.9)	4.0 (4.7)	4.1 (4.1)	4.3 (4.7)	96.0 (85.1)	8.34 (11.04)	1.37 (1.97)	24
10	23	192.4	7.6 (8.2)	5.4 (5.9)	4.6 (4.8)	5.6 (5.9)	82.5 (83.2)	14.36 (13.54)	1.97 (1.90)	24
11*	17	179.7	7.2 (7.1)	5.2 (5.4)	4.8 (4.6)	5.4 (5.4)	89.1 (85.5)	9.46 (12.56)	1.77 (1.98)	10
12*‡	41	161.9	6.1 (5.5)	4.3 (3.9)	3.4 (3.2)	4.2 (3.9)	80.9 (76.5)	7.47 (9.01)	1.20 (1.67)	144
13†	29	167.6	6.7 (6.0)	4.9 (4.5)	4.3 (3.8)	4.9 (4.5)	86.1 (81.0)	13.07 (10.43)	2.11 (1.82)	8
Women										
14‡	42	158.8	4.1 (4.6)	2.3 (2.9)	2.0 (2.4)	2.4 (2.9)	83.3 (81.1)	4.62 (8.12)	1.30 (1.78)	54
15	36	160.7	4.7 (4.9)	3.1 (3.1)	2.5 (2.6)	3.2 (3.1)	79.2 (82.7)	7.31 (8.58)	1.64 (1.82)	6
16	50	158.8	5.5 (4.5)	3.7 (2.7)	2.6 (2.3)	3.4 (2.7)	76.3 (79.0)	7.68 (7.69)	1.61 (1.72)	72
17†‡	52	153.0	4.8 (4.1)	2.3 (2.4)	2.3 (2.1)	2.8 (2.4)	82.2 (78.5)	4.85 (7.16)	1.17 (1.71)	126

* = Smoker.

† = Ex-smoker.

‡ = Abnormal chest radiograph.

Table 4 Mean values of pulmonary function and percentage of predicted for all subjects

	Mean (SD)	% Predicted (SD)
FEV ₁	3.80 (1.01) l	101.0 (12.0)
VC	4.31 (1.06) l	97.4 (14.7)
FEV ₁ /FVC	85.4 (5.0) %	103.3 (4.5)
TLC	6.25 (1.37) l	101.8 (11.7)
TL	9.34 (2.82) mmol/min/kPa	85.8 (18.6)
TL/VA	1.57 (0.26) mmol/min/kPa/l	83.8 (13.9)

total exposure for smokers and ex-smokers was 36.6 exposure-months, and for non-smokers 33.0 exposure-months.

There was no relation between grade of dyspnoea or the presence of cough and sputum, and pulmonary function. Nor was there any difference in pulmonary function between the six subjects who stated that exposure to the dust of alunite-residue had affected their chests and those who considered it had not or between the five subjects who had ever had arthritis and those who had not.

The mean TL% predicted for the whole group was 85.8 and the mean TL/VA% predicted was 83.8. Two subjects together with the index subject showed small irregular opacities on chest radiography. These three subjects had a significantly greater mean total exposure (108 exposure-months) and a tendency to lower mean TL% predicted (69.2) and TL/VA% predicted (71.1) than the 14 subjects with normal chest radiographs (mean total exposure 20 exposure-months ($p < 0.001$), TL% predicted 89.4% ($p = 0.10$), and TL/VA% predicted 86.6% ($p = 0.10$). None of these subjects had previous exposure to hazardous dusts, and no recent chest

radiographs were available for the two with abnormal radiographs who had no symptoms of respiratory disease.

The TL/VA% predicted tended to correlate with the measurement of total dust exposure ($r = -0.40$ $p = 0.10$) (fig 5). TL% predicted showed less tendency to correlate with total dust exposure ($r = -0.23$).

Fig 5 Relation between total exposure to alunite-residue (sum of the products of grade of each exposure period and duration of each exposure period in months) and TL/VA% predicted. $n = 17$ $r = 0.40$ $p = 0.10$.

Discussion

Several problems that were encountered in interpreting this study arise from the small size of the exposed population, the possible confounding effect of smoking, and the association between age and total exposure. We have had to compare our data with external "predicted normal" values rather than carry out multivariate analysis or internal standardisation of the results. Nevertheless, the data from the initial case and from the work force suggest a relation between exposure to the dust of alunite-residue and impairment of the rate of gas transfer of the lung: the mean values of TL and TL/VA of the group were less than predicted, there was a tendency to an inverse relation between TL/VA % predicted and magnitude of exposure to alunite-residue, and subjects with abnormal radiographs were among the four with the highest exposures. The closer relation between TL/VA % predicted and total exposure than between TL % predicted or lung volumes and total exposure suggests that the pulmonary reaction had a greater effect on the rate of gas transfer than on the effective alveolar volume.

The physiological and radiographic findings of the group are consistent with the pathological appearance of the lung biopsy specimen. We are planning to investigate the mechanism by which alunite-residue may produce pulmonary fibrosis. Immunological mechanisms were suggested by the time course of the transfer-factor response to bronchial challenge and the presence of granulomas in the lung, but they appear unlikely because of the inorganic nature of the material. The precedent for such a reaction, however, has been long recognised in beryllium¹⁶ and tungsten carbide,^{17,18} and it is known that, experimentally, zirconium¹⁹ may also produce pulmonary fibrosis with granulomas, possibly by a foreign body reaction or by combining with protein constituents of the lungs to form an antigen. The presence of systemic symptoms of malaise and arthritis is somewhat against the possibility of a purely local foreign body reaction: challenge studies in our patient resulted in a recrudescence of systemic as well as respiratory symptoms, and change in TL and TL/VA. We have no other evidence, however, to suggest multiple organ involvement. We are aware that clays (palygorscite)²⁰ may have a fibrous form, but our material contains no fibres on electron microscopy.

Our study suggests that a silicate of aluminium may be responsible for pulmonary fibrosis, and industrial users of this type of material should be vigilant. It suggests that the classification of such materials as nuisance dusts should be reviewed.

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