Notes

Pneumoconiosis and Lung Function in a Group of Kaolin Workers[1-3]

SUMMARY In June 1981, 65 current and former workers at a kaolin mine and mill were examined by chest radiography, spirometry, and a questionnaire. Five (13%) of 39 current workers and 3 (19%) of 16 former workers with 5 yr or more of exposure had radiographic evidence of pneumoconiosis. Among the 8 workers with pneumoconiosis, conglomerate upper lobe lesions were present in one half. No pneumoconiosis was observed among 8 current workers with less than 5 yr of exposure. Lung function testing showed significant reductions ($p < 0.05$) in FVC, FEV_1, and peak flow rate in kaolin workers compared with that in a control group. Environmental sampling during the testing period showed airborne dust to be composed of kaolinite (96%) and titanium dioxide (4%). Additional controlled epidemiologic studies among kaolin workers are needed to generate reliable prevalence data for pneumoconiosis and to assess the impact of dust exposure on pulmonary function.
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The term kaolin (china clay) derives from the Chinese "Kau-Ling" or high ridge, the name given a hill near Jauchau Fu, China, where the clay was first mined. It is one of several clay varieties exploited for its content of the aluminum silicate kaolinite. In the United States, deposits are primarily concentrated in a belt extending from central Georgia to west central South Carolina. Mining is by conventional open-pit methods, and processing involves either dry milling or wet particle separation and drying. Industrial uses for kaolin include the manufacture of paper products, refractory materials, ceramics, and as a filler in plastics, rubber, and paints.

The potential for dust-induced lung disease in the kaolin processing industry was noted by Middleton in 1936 (1). Pathologic findings in kaolin workers with pneumoconiosis were subsequently described by Lynch and McIver (2) and Hale and coworkers (3). Nodular and large coalescent lesions and alveolar wall fibrosis were reported. Few respiratory surveys have been conducted among kaolin workers (4–7). The characteristic radiographic finding in these has been diffuse, bilateral discrete nodulation, sometimes accompanied by massive conglomerate upper lobe lesions. These studies, however, have rarely included complete occupational histories, pulmonary function testing, or environmental dust data.

This report presents the results of a recent medical and environmental survey at a kaolin plant in Georgia. Study findings are discussed in relation to previously published epidemiologic studies and future research needs.

In 1981, a health study was conducted by representatives of the National Institute for Occupational Safety and Health (NIOSH) at a kaolin mine and mill in northcentral Georgia. All current workers were invited to participate. Former workers with a minimum of 5 yr kaolin tenure since January 1970 were also recruited for the study. The minimal exposure criteria for ex-workers was selected to identify those at risk for pneumoconiosis, given the observation that disease has rarely been reported in workers with less than 10 yr of exposure (4–7). The study population was identified from personnel records and was composed entirely of males.

A comparison group of 189 males working in respiratory hazard-free environments in the southeastern United States was chosen for the analysis of pulmonary function. One third of this group was from Georgia and the remainder was from Alabama, Mississippi, North Carolina, and South Carolina. The population was tested in the same general time period as the study group and included workers from soft drink bottling companies, candy factories, a power tool company, the fabric department of a tire manufacturer, and shipping clerks in a poultry packing plant.

Breathing zone samples of respirable dust and area samples of total dust were collected at the kaolin operation on the days of health testing using portable battery-powered pumps. Respirable dust was measured in all job categories with pumps employing dust cyclone preselectors and area total dust measurements were made in designated work stations. Particle size distribution of airborne dust by aerodynamic dimension was determined with Andersen particle fractionating samplers in several mill areas and near the baghouse. Data were collected over full shifts, and tared filters were analyzed gravimetrically. Free silica content of respirable dust samples was determined according to NIOSH Physical and Chemical Analytical Method 259 (8). Air samples were also collected for fiber and trace metal content, and filters were analyzed by electron microscopy using the Zumwalde-Dement procedure (9).

Dust monitoring in comparison group workplaces was performed using vertical elutriators and, as in the study group, results are presented as 8-h time-weighted averages. Vertical elutriators will yield higher estimates of respirable dust concentrations than will cyclone pumps because of their larger aerodynamic particle cutoff (15 versus 3.5 μ).

Health screening included spirometry, a chest roentgenogram, and administration of a modified British Medical Research Council questionnaire by experienced interviewers. The questionnaire detailed occupational and smoking histories as well as pulmonary symptomatology. Lung function testing consisted of forced expiratory maneuvers into an Ohio 840 waterless, rolling-seal spirometer. Standing height was obtained with shoes worn, and heels were measured and subtracted. Each worker performed at least 5 maneuvers, which were recorded electronically as flow-volume curves. From a minimum of 3 maneuvers meeting the American Thoracic Society criteria for spirometry (10), the largest forced vital ca-

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pacity (FVC), forced expiratory volume in one second (FEV_1), and peak flow rate were chosen for analysis regardless of the curve(s) on which they occurred. Values were corrected to BTPS given ambient temperature and barometric pressure. Test results of each participant were compared with predicted values from Knudson and coworkers (11). For blacks, the predicted values for FEV_1 and FVC were multiplied by a factor of 0.9. Obstructive lung disease was defined as an FEV_1/FVC percent less than 70% and restrictive impairment as a percent predicted FVC less than 80% (12).

Standard 14- by 17-inch posteroanterior roentgenograms of the chest were submitted by NIOSH for three independent readings by certified pneumoconiosis ("B") readers using the 1971 ILO/UC International Classification of Radiographs of the Pneumoconioses (13). Recent films of current kaolin workers were obtained from the company, and former workers were examined at the time of the study. Roentgenograms were interpreted without knowledge of worker occupation or exposures. Pneumoconiosis was considered present if at least two of three readers categorized small opacity profusion as 1/0 or greater. For purposes of description, simple pneumoconiosis was defined as the presence of small opacities alone, and complicated pneumoconiosis as the presence of both small and large opacities. Chest radiography was not performed on the comparison population.

Analysis of covariance was employed to assess the effect of kaolin dust on lung function (14). A linear model fit of age, height, race, smoking status, and pack/years was used. Exposure to kaolin dust, expressed dichotomously as exposed or nonexposed, was the remaining independent variable in the model. Least squares means were derived for FVC, FEV_1, and peak flow rate for kaolin and comparison groups overall and by smoking class. Two-tailed t tests were computed to compare differences in pulmonary function between exposed and comparison groups.

Environmental. Air samples were collected in the kaolin milling operation and examined for fibrous constituents and elemental composition by transmission electron microscopy with backscattered electron imaging. Analysis of the airborne dust demonstrated no asbestiform fibers. Particle morphologic features and aluminum-to-silicon ratio indicated the dust to be 96% kaolinite and 4% titanium dioxide. Andersen aerodynamic particle size data for five mill work stations showed respirable dust fractions (below 10 μ) of over 50% adjacent to pulverizers and to the baghouse (dust collection site). Other locations sampled exhibited respirable dust fractions of 10 to 20%.

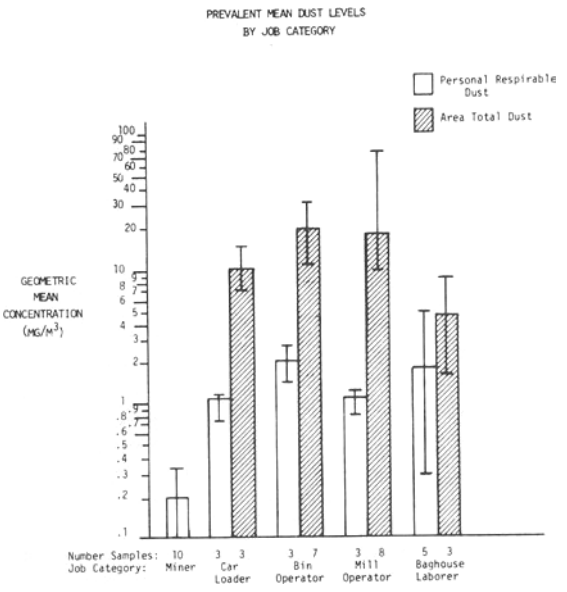

Fig. 1. A histogram of the range and geometric mean of respirable and total dust measurements obtained during the days of health testing.

Breathing zone samples of respirable dust were obtained, and results for selected occupations are shown in figure 1. In all job categories, mean values were below the nuisance particulate threshold limit value for respirable dust (5 mg/m³) recommended by the American Conference of Governmental Industrial Hygienists (15). Each personal respirable dust sample (n = 44) was analyzed for free silica content by X-ray diffraction and none was detected. Total dust levels by area in the kaolin facility revealed means for three of five work stations in excess of 10 mg/m³ (figure 1).

Worksites of the comparison workers were visited prior to the study and no recognized occupational respiratory hazards were noted. On the day of health testing a mean of 4 dust samples were taken at each facility. Mean concentrations of dust, 15 μ or less by aerodynamic dimension, were below 0.33 mg/m³ at all 8 plants. Five had mean dust concentrations below 0.16 mg/m³ and 3 had levels between 0.16 and 0.32 mg/m³.

Medical. Demographic data for kaolin and comparison populations are shown in table 1. All current kaolin workers (n = 49) participated in the study. Sixteen (76%) of 21 former workers with at least 5 yr of exposure were also examined. Ex-workers were principally retirees and this is reflected in a greater mean age and mean exposure years compared with that in current workers. The racial composition of study and comparison populations was similar, black workers constituting 51 and 61% of the respective groups. The comparison population is seen to differ in mean age and pack/years of smoking. Differences in these characteristics are accounted for in the statistical analyses.

The prevalence of pneumoconiosis among kaolin workers is reported in table 2. No current worker with fewer than 5 yr of exposure had pneumoconiosis. A prevalence rate of 13% was ob-

TABLE 1

DEMOGRAPHIC CHARACTERISTICS OF PARTICIPANTS

	Number	Mean Age (yr)	Mean Kaolin Exposure (yr)	Smokers (%)	Ex-Smokers (%)	Never Smokers (%)	Mean Pack/ year
Comparison population	189	37	0	97 (51%)	62 (33%)	30 (16%)	15
Current kaolin workers	49	44	16	27 (55%)	12 (25%)	10 (20%)	25
Ex-kaolin workers, 5 yr or more exposure	16	61	28	7 (44%)	7 (44%)	2 (13%)	34

TABLE 2

PREVALENCE OF PNEUMOCONIOSIS BY CHEST RADIOGRAPH*

	Number	Simple Pneumoconiosis	Complicated Pneumoconiosis	Total
Current workers				
Less than 5 yr kaolin exposure	8	0	0	0 (0%)
5 yr or more kaolin exposure†	39	4	1	5 (13%)
Ex-workers				
5 yr or more kaolin exposure	16	0	3	3 (19%)
Ex-workers + current workers				
5 yr or more kaolin exposure	55	4	4	8 (15%)

* Category 1/0 or greater; ILO/UC 1971 Classification (13).
† Two workers refused radiographs.

TABLE 3

LUNG FUNCTION* AND RELATED DATA AMONG WORKERS WITH PNEUMOCONIOSIS

Worker No.	Age (yr)	Smoking Status	Pack/ Years	Exposure (yr)	Mill Jobs† (yr)	FEV_1 (% pred)	FVC (% pred)	FEV_1/FVC (%)
1‡	69	SM	28	34	34	R	R	R
2‡	62	SM	22	26	26	32	56	45
3‡	60	ES	21	35	18	89	91	77
4	60	ES	31	39	0	75	79	73
5	38	SM	22	15	15	98	93	86
6	44	ES	23	22	16	101	98	83
7‡	56	ES	20	35	16	82	100	64
8	43	ES	2	20	7	101	94	86

Definition of abbreviations: SM = current smoker; ES = ex-smoker; R = refused spirometry.
* Knudson (11); blacks 0.9 predicted values.
† Total years in bin, bagging, car loading, and screen work.
‡ Complicated pneumoconiosis.

TABLE 4

ADJUSTED LUNG FUNCTION BY SMOKING GROUP*

	Never Smokers (n = 74)	Ex-Smokers (n = 49)	Smokers (n = 130)	Total (n = 253)
Mean adjusted FVC, L				
Comparison group	4.57 (62)	4.69 (30)	4.57 (97)	4.59 (189)
Kaolin workers	4.42 (12)	4.24 (19)	4.37 (33)	4.32 (64)
p value†	0.49	0.07	0.17	< 0.05
Mean adjusted FEV_1, L				
Comparison group	3.54 (62)	3.71 (30)	3.51 (97)	3.58 (189)
Kaolin workers	3.44 (12)	3.31 (19)	3.31 (33)	3.34 (64)
p value†	0.57	< 0.05	0.08	< 0.05
Mean adjusted peak flow, L/s				
Comparison group	9.53 (62)	9.84 (30)	9.21 (97)	9.53 (189)
Kaolin workers	8.48 (12)	8.97 (19)	8.27 (33)	8.57 (64)
p value†	0.13	0.24	< 0.05	< 0.05

* Least squares mean adjusted for age, height, race, and pack/years.
† p value of two-tailed *t* test.

served among current workers with 5 yr or more of exposure. Small opacities were of the rounded variety in each instance. Past exposure to other noxious respiratory hazards was noted in only one current worker with pneumoconiosis, i.e., asbestos. Small rounded opacities on his chest roentgenogram were not characteristic of asbestosis and pleural abnormalities were absent.

Participating ex-workers with 5 yr or more of exposure demonstrated a 19% prevalence rate of pneumoconiosis. Rounded opacities were present in 2 workers and combined rounded and irregular opacities were observed in the other. All had conglomerate upper lobe lesions. None had known previous exposure to other occupational or environmental respiratory hazards.

Total years of kaolin exposure exceeded 19 yr in all but 1 worker with pneumoconiosis (table 3). Seven of 8 workers with pneumoconiosis had dust exposure limited to mill work, and mill tenure was largely in the dustier occupations. Pneumoconiosis was present in only 1 employee whose primary work area had been the open-pit mine (Worker 4). Pulmonary function was obtained in 7 of the 8 workers with pneumoconiosis. Abnormal lung function profiles (12) were present in 3 of these, all with prominent smoking histories (mean pack/years, 24).

Mean adjusted lung function is reported for kaolin and comparison workers in table 4. Comparison of both groups as a whole showed significantly lower values ($p < 0.05$) for FVC, FEV_1, and peak flow rate among the kaolin workers. Results by exposure group and smoking status revealed significant differences ($p < 0.05$) in mean spirometric values for FEV_1 in ex-smokers and for peak flow in current smokers. In this comparison, our ability to detect significant differences was limited by the small size of each kaolin-smoking group.

* * *

Prevalence rates for pneumoconiosis among active kaolin workers vary in published reports from 0.7 to 9% (4–7). The present study found a prevalence rate of 13% among current workers and 19% among participating former workers, all with a minimal exposure to kaolin of 5 yr. The radiographic spectrum of disease observed was consistent with previous observations (1–7) and included simple and complicated forms of pneumoconiosis. Total years of kaolin exposure in the 8 workers with pneumoconiosis (15 to 39 yr) supports the general notion that this disease tends to occur only after many years of exposure (4–7).

Workers with pneumoconiosis had also been employed at the facility at a time when the work environment was reported to have been considerably dustier. Historical air sampling data was insufficient, however, to provide reliable estimates of past exposure. The long tenure of workers with pneumoconiosis did not permit an assessment of the relative contribution to observed disease of past versus more recent exposure levels. In contrast, detailed work histories and our environmental sampling identified the handling of milled kaolin as higher exposure tasks. Similar observations have previously been made in kaolin workers with pneumoconiosis (3, 6).

Pneumoconiosis was found exclusively in workers who were current or former cigarette smokers (table 3). Of 8 workers with pneumoconiosis, 7 had considerable smoking histories, but 1 had only a 2 pack/year history. The distribution of affected workers by smoking habit was examined and found not to be significant (Fisher's exact test, $p = 0.17$). The relation, if any, between pneumoconiosis and smoking cannot be adequately addressed in a small population with only 12 never smokers.

Meaningful correlations of lung function and symptoms by radiographic severity of pneumoconiosis were not possible in this study because of the small size of the population examined. Rawlings and coworkers (7) examined chest roentgenograms, symptoms, and pulmonary function correlatives in a population of Georgia kaolin workers. Pneumoconiosis by chest roentgenogram bore no relation to the occurrence of sputum production, cough, wheezing, or breathlessness. Although percent predicted FVC was found to decline with increasing severity of radiographic change, methodologic problems with the pneumotachygraph employed (16) make this observation difficult to interpret. In the current study, no association was observed between pneumoconiosis radiographically and abnormalities of lung function. This has also been reported in underground coal miners with uncomplicated pneumoconiosis (17) and workers with less advanced forms of simple silicosis (18).

Analysis of adjusted lung function showed FVC, FEV_1, and peak flow rate to be reduced in each kaolin-comparison group contrast (table 4). The differences were significant ($p < 0.05$) when the groups as a whole were compared. Group totals presented the most powerful test of observed differences because the largest number of observations were retained in this comparison. Adjusted lung function for kaolin workers showed a FVC of 94%, a FEV_1 of 93%, and a peak flow rate of 90% of comparison group values (table 4, group totals). The equivalent decrements in adjusted FVC and FEV_1 for the study group resulted in an FEV_1/FVC ratio of 77% compared to 78% for the reference population. This suggests that the ventilatory defect in the kaolin workers is predominantly restrictive. Although it is possible that an unknown systematic difference between groups compared accounts for these findings, it is important to consider the possibility of a dust-induced decrement in ventilatory capacity. Dust related reductions in FEV_1, which were independent of age and smoking habit, have, for example, been reported in underground coal miners (17). Lung function in kaolin workers requires further controlled studies that are more representative of the industry and are better able to assess observed differences.

Free silica exposure appears to be a variable, yet important, consideration in assessing the occurrence of pneumoconiosis among some kaolin-exposed workers. Lesser and associates (19) described 9 cases of pneumoconiosis among kaolin firebrick workers, and pathologic study of tissue in 2 was thought to be consistent with silicosis. Analysis of airborne dust collected at several firebrick factories showed a free silica content of as much as 4.5%. In our study, free silica was not detected in numerous respirable breathing zone air samples. It is unlikely, moreover, that the crystalline silica content has differed historically because the plant under study has always exploited and processed the same local kaolin seam.

The pathogenic potential of kaolin dust for the lungs in the absence of crystalline silica contamination is not universally accepted (15). Epidemiologic studies have shown the occurrence of pneumoconiosis in kaolin mill workers (4–7), but these have lacked clear definition of the nature and extent of the exposure, previous exposures to noxious respiratory hazards, and population selection factors operative in each. Animal models of pneumoconiosis have been developed for asbestos- and silica-induced lung diseases, but none has proved satisfactory for kaolin (20). Animals exposed to kaolinite dust have shown pulmonary responses limited pathologically to reticulin formation and macrophage reactivity, whereas simultaneous inoculation of dust and avirulent microorganisms has resulted in marked fibrosis (20). *In vitro* models of dust biologic activity have demonstrated cytotoxic responses to kaolinite in erythrocyte and macrophage systems (21), but the significance of these findings to human disease has yet to be elucidated.

In the interim, kaolin continues to be regarded as a nuisance particulate, a designation implying little fibrogenic potential to the lungs assuming compliance with recommended exposure limits (15). Available evidence neither supports nor refutes such a determination. Studies designed to characterize exposure and generate reliable prevalence data for adverse pulmonary effects are needed. Controlled epidemiologic investigations including both environmental and medical assessments are indicated. Prospective surveillance of workers entering the industry after implementation of the nuisance particulate standard can provide data on the incidence of lung function and radiographic abnormalities at this exposure level. Such epidemiologic research, together with continued laboratory investigation, should provide a more informed basis for decisions regarding the protection of the health of these workers.

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Morphologic Evidence that Large Inflations of the Lung Stimulate Secretion of Surfactant[1]

SUMMARY **We ventilated rats at normal tidal volume without periodic deep breaths, or with a 4-times tidal volume inflation every 5 min for 1 h. The volume density of lamellar bodies in alveolar type 2 cells was about one-third lower after 60 min of ventilation in sighed than in unsighed rats, and this effect of sighs was not blocked by bilateral cervical vagotomy. These morphologic data support previously reported biochemical studies indicating that large inflations are potent stimuli of surfactant secretion.**

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Reports from several laboratories have provided biochemical evidence supporting the notion that large inflations stimulate the secretion of pulmonary surfactant (1-5). These investigators used the amount of radioactive phospholipid, or increases of nonradioactive phospholipid, in lung lavage returns as indexes of surfactant secretion. Although there is unanimity among these reports, potential pitfalls in this approach (vide infra) have led us to seek morphologic support for the biochemical findings. A morphologic approach seemed appropriate because, in virtually all systems, stimulated secretion results in a fall in the volume density of secretory granules in secretory cells. Therefore, we undertook the present study in which we used electron microscopy and morphometry to evaluate the effect of intermittent large breaths (sighs) on the volume fraction of lamellar bodies, which are the intracellular storage granules for pulmonary surfactant in alveolar type 2 cells (6).

We used male Long-Evans-descended hooded rats (Charles River Farm, Wilmington, MA), which were allowed food (Rodent Laboratory Chow 5001; Ralston-Purina Co., St. Louis, MO) and water ad libitum, and were kept on a 12-h light-dark schedule. After they were intraperitoneally anesthetized (sodium pentobarbital, 50 mg/kg) we gave them 15 mg of tubocurarine chloride in 0.1 ml of 0.15 M NaCl intraperitoneally and inserted a plastic tube into the trachea and ventilated the rats with humidified room air. The nomogram of Kleinman and Radford (7) was used to determine the tidal volume appropriate for the animals' body weight and a respiratory rate of 40 breaths/min. Bilateral vagotomy was performed by identifying both cervical vagi, placing a ligature beneath each, and then cutting each nerve. Sham-operated rats were treated in the same manner, but the nerves were not cut.

After 1 h of ventilation a bilateral pneumothorax was produced by puncturing the diaphragm from its abdominal surface. We then infused cold 2.5% glutaraldehyde in 0.1 M sodium cacodylate buffer (pH, 7.4) into the trachea at a transpulmonary pressure of 20 cm H_2O. The trachea was then ligated, and fixation was continued (8, 9). The methods of preparing lung tissue for electron microscopy examination, the tissue sampling procedures, and the criteria for identification of alveolar type 2 cells were identical to those previously described in detail (10-12). Morphometric analysis was performed with a double lattice test system (9) using the method of Weibel (13).

The volume density of lamellar bodies relative to the cell was determined by dividing the number of points of the test system that fell on the lamellar bodies by the number of points that fell over the entire cell (including the lamellar bodies) and multiplying this quotient by 100. Because changes in the volume density could reflect either an absolute change in the volume of lamellar bodies or in cell volume, we also calculated the volume density of the type 2 cell relative to the fixed number of points on the test system. We measured the surface-to-volume ratio of the lamellar bodies, as previously described (8).

All measured or calculated values for individual animals were averaged per experimental group, and the standard error of the group mean was calculated. Multiple group comparisons were made by use of an analysis of variance and Duncan's multiple range test (14); Kramer's extension of Duncan's test (15) was used to identify intergroup significant differences.

The lamellar body volume density of rats sighed once every 5 min was about one-third less than the lamellar body volume density of rats ventilated at a constant tidal volume without sighs (table 1). Vagotomy did not alter the response to intermittent large inflations. These differences in volume density were not due to changes in volume of the type 2 cells, because the number of test system probe points that fell on type 2 cells divided by the fixed number of test system probe points was not different between groups (table 1). The fall in volume density in the three sighed groups took place without changes in the surface-to-volume ratio of the lamellar bodies (table 1).

The amount of phospholipid in lung lavage returns may be affected by processes other than the secretion of surfactant; these include the number of airway macrophages (16), the rate of physical clearance of airway surfactant (17, 18), and the rate at which surfactant is biochemically altered. Furthermore, even ignoring these potential

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