a specific inhibitor of reaginis antibody-antigen mechanisms. Nature 1967; 216:1328-29
14 Orr TSC, Cox JSG. Disodium cromoglycate, an inhibitor of mast cell degranulation and histamine release induced by phospholipase A. Nature 1969; 233:197-98
15 Bouhuys A, Ortega J. Improvement of "Irreversible" airway obstruction by thiazinamium (Multergan). Pneumologie 1976; 15:185-95
16 Groggins RC, Milner AD, Stokes GM. The bronchodilator effects of chlorpheniramine in childhood asthma. Br J Dis Chest 1979; 73:297-301
17 Schachter EN, Brown S, Zuskin E, Kolack B, Buck M, Bouhuys A. The relation of cotton bract sensitivity to histamine sensitivity. Am Rev Respir Dis 1979; 119:234
18 Lam S, Wong R, Young M. Nonspecific bronchial reactivity in occupational asthma. J Allergy Clin Immunol 1979; 63:28-34
19 Nathan RA, Segall N, Glover GC, Shocket AL. The effect of H_1 and H_2 antihistamines on histamine inhalation challenges in asthmatic patients. Am Rev Respir Dis 1979; 120:1251-58
20 Schachter EN, Gerstenhaber B, Brown S. Histamine receptors in airways of healthy subjects (abstr). Clin Res 1978; 26:635
21 Schachter EN, Kreisman H, Littner M, Beck GJ, Voncken F. Airway responses to exercise in mild asthmatics. J Allergy Clin Immunol 1978; 61:390-98
22 Bouhuys A, Mitchell CA, Zuskin E. A physiological study of byssinosis in colonial America. Trans NY Acad Sci 1973; 35:537-46

Pulmonary Function Response to Dust from Standard and Closed Boll Harvested Cotton

Brian Boehlecke, M.D.; Joseph Cocke;† Kenneth Bragg;† John Hancock;* Edward Petsonk, M.D.;* Richard Piccirillo, M.D.*; and James Merchant, M.D., Dr.P.H.**

Although the characteristic feature of byssinosis in workers exposed to cotton dust is the symptom of chest tightness occurring on the first day back to work after an absence, changes in objective measurements of pulmonary function also have been demonstrated. Not all byssinotic patients show objective changes, but as a group they tend to have greater reductions in the FEV_1 over the workshift than asymptomatic workers and those not exposed to cotton dust.[1] The prevalence of symptoms and decrements in pulmonary function increase with increasing dust exposure,[2] but even high dust levels may be associated with a low prevalence of byssinosis if the dust is of low "biologic activity."[3] Reduction of the biologic activity of the dust may be important, since extrapolation of dose-response curves suggests that even low levels of dust may be associated with symptoms of byssinosis in some workers.[2]

The US Department of Agriculture recently harvested a small quantity of cotton before the opening of the bolls to minimize the amount of contamination of the fiber with other materials. We exposed healthy volunteers to dust generated when this cotton was carded in a model cardroom and measured pulmonary function before and after exposure to determine if closed boll harvested cotton dust produced less biologic reaction than dust from standard harvested cotton.

*National Institute for Occupational Safety and Health, Appalachian Laboratory for Occupational Safety and Health, Morgantown, WV.
†US Department of Agriculture, Science and Education Administration, Cotton Quality Research Station, Clemson, SC.
Reprint requests: Dr. Merchant, 944 Chestnut Ridge Road, Morgantown, West Virginia 26505

Materials and Methods

Volunteers were screened to exclude those with a history of asthma, use of medications affecting airway response, recent acute respiratory illness, significant heart disease, or any other medical condition precluding safe participation in an exposure study. Baseline spirometry was performed on an Ohio 840* waterless spirometer with flow volume curves recorded on FM analog tape. At least three acceptable maneuvers were obtained with the difference between the two largest values for FEV_1 less than 5 percent. Those with a baseline FEV_1 less than 80 percent of predicted[4] were excluded from participation.

Those subjects not excluded by the screening procedure were next exposed to a concentration of approximately 1 mg/m^3 of respirable dust from standard cotton for six hours in the model cardroom at the US Department of Agriculture Cotton Quality Research Station in Clemson, SC. Spirometry was performed before and after the exposure. These subjects also performed spirometry before and after six hours of sitting in the model cardroom without exposure to cotton dust (designated "background" exposure). Subjects who demonstrated at least a 5 percent decrement in FEV_1 after six hours of exposure to standard cotton relative to the change in FEV_1 with background exposure were selected for participation. Those selected also completed a modified Medical Research Council Questionnaire for occupational and smoking history and respiratory symptoms.

On exposure days, each subject performed spirometric tests and then immediately entered the model cardroom. Subjects sat in chairs placed around the carding machine and were moved each 30 minutes, so that they had made a complete circuit during the exposure period. Subjects were allowed to leave the cardroom only for restroom breaks and were not allowed to smoke at any time during the study. After six hours of exposure, spirometric testing was repeated using the same spirometer and technician as in the pre-exposure testing. The participants also answered the questions "Do you feel different from when the exposure began?" and "If yes, how?"

Respirable dust sampling was performed continuously with four vertical elutriators (flow rate, 7.4 L/min) around the card. Dust concentrations were maintained at the desired level by varying the card exhaust ventilation.

Four types of closed boll harvested cotton were used for

*Mention of brand names or commercial concerns does not constitute endorsement by the US Public Health Service.

Table 1—*Selected Characteristics of the 26 Participants**

	11 Nonsmokers	12 Smokers	3 Exsmokers
Age, yr	28 (18-74)	40 (20-61)	23, 24, 70
Pack-years of cigarette smoking	...	19 (2-48)	4, 6, ?
Baseline spirometry as % pred			
FVC	114 (95-125)	108 (82-144)	106 (91-117)
FEV_1	107 (88-126)	101 (81-119)	91 (75-105)
No. with:			
Chronic bronchitis	1	3	0
Byssinosis	0	1 (Grade 1/2)	0
Previous cotton dust exposure	2 (25 years spinning) (1 yr weaving)	2 (40 years carding) (1 yr weaving)	2 (40 years weaving) (4 yr weaving)

*Numbers are the mean value and range in parentheses for age, pack-years, and spirometry.

exposure studies. Cotton grown in the Stoneville, Miss, area and hand-harvested before the opening of the bolls will be referred to as Stoneville closed boll cotton. The unopened bolls were washed in a 0.5 percent sodium hypochlorite solution and then placed in wire trays to open. After opening, the lint was mechanically separated from the burr. This cotton is the Stoneville closed boll bract intact cotton (SCBI). Stoneville closed boll bract removed cotton (SCBR) was handled in exactly the same manner, except that the bract material was manually removed from the boll before opening and the lint removed from the burr by hand. Cotton from the same field was later harvested by a mechanical picker after the bolls had opened naturally and was then processed in the usual manner. This cotton is referred to as Stoneville standard cotton.

Cotton grown in the Lubbock, Tex, area was harvested by a machine stripper early in the season and unopened bolls were selected by hand, washed in a 0.5 percent sodium hypochlorite solution, and placed in sealed drying bins through which filtered air was passed. Bract was manually removed before placement in the drying bins for cotton referred to as Lubbock closed boll bract removed (LCBR), and the bract material was left intact on cotton referred to as Lubbock closed boll bract intact (LCBI). Bulk samples of each of the types of cotton were analyzed for endotoxin content using standard methods.[5]

Twenty-six subjects participated in the series of exposures (14 females and 12 males), four of whom were blacks. Table 1 gives other demographic and pulmonary function characteristics of the group. Although six subjects had had one or more years of cotton dust exposure in the textile industry, only one subject had a history of grade 1/2 byssinosis using the modified Schilling classification.[6,7]

Table 2 shows the sequence of exposures. Fourteen of the subjects ultimately selected to participate were exposed to standard cotton dust on August 7 as part of the screening studies. These subjects were reexposed on August 9 along with new volunteers from which the final group of 26 was chosen. The group was next exposed to dust from carding of rayon followed by a day in which they

Table 2—*Exposure Sequence*

Date, 1979	No. Exposed	Carding Rate, lb/hr	Exposure Type*	Mean Dust Concentration, mg/m³	Mean Preexposure, FEV_1, L
8/7	14	10	Stoneville standard cotton	0.98	3.19
8/9	25	10	Stoneville standard cotton	0.96	3.43
8/11	24	60	Rayon	0.49	3.41
8/13	26	–	Background	0.03	3.34
8/14	25	50	SCBR	0.73	3.30
8/15	26	–	No exposure		3.38
8/16	25	50	SCBI	1.02	3.37
8/17	26	–	No exposure		3.39
8/18	26	10	Stoneville standard cotton	0.75	3.34
8/20	24	40	LCBR	0.90	3.31
8/22	25	30	LCBI	0.88	3.35
8/23	25	–	No exposure		3.35
8/24	24	10	Stoneville standard cotton	1.04	3.35

*SCBR = Stoneville closed boll bract removed cotton; SCBI-Stoneville closed boll bract intact cotton; LCBR = Lubbock closed boll bract removed cotton; and LCBI = Lubbock closed boll bract intact cotton.

Table 3—*Stoneville Standard Cotton Exposures*

Date	Mean Dust Level, mg/m³	No. Exposed	Mean ΔFEV₁*
8/7	0.98	14	−271 (−8.5)
8/9	0.96	25	−228 (−6.7)
8/18	0.75	26	−83† (−2.4)
8/24	1.04	24	−148 (−4.5)
Combined	0.93	89	−171 (−5.1)

*Mean ΔFEV_1 = Postexposure FEV_1 minus preexposure FEV_1 in ml; change as a percent of preexposure level in parentheses. Means (ml) adjusted for missing participants.
†$P<.01$ compared with average of three other days.

sat in the cardroom, but no material was processed through the card, labeled "background" on the table. The final group of 26 selected for participation was then exposed to the various types of closed boll harvested cotton and Stoneville standard cotton in the order shown. Closed boll harvested cotton generated much less dust when carded at the same production rate as Stoneville standard cotton, so the carding rate was increased in an attempt to produce respirable dust levels comparable to that during the Stoneville standard exposure days.

Days without exposure were always interposed between any two exposures to cotton dust. On days in which no exposure was performed, the subjects' baseline pulmonary function was measured at the same time of day as that on exposure days to determine if recovery had occurred and to see if any trend of baseline pulmonary function was occurring.

Results

As shown in Table 2, mean preexposure FEV_1 values did not change significantly during the study. Table 3 shows the pulmonary function results on the days in which the subjects were exposed to dust from Stoneville standard cotton. Although the decrement in FEV_1 showed some variability, only the decrement on August 18 (on which the dust level was 0.75 mg/m^3) was significantly smaller than the others. To simplify comparisons in the tables, the decrements in FEV_1 for the four days on which the subjects were exposed to Stoneville standard cotton dust were combined to give an average combined decrement of 5.1 percent, or 171 ml. However, the actual decrements and variability of decrements for all days on which a given subject was exposed to standard cotton were used in the statistical comparisons to responses from the other types of exposures.

Table 4 shows that the average change in FEV_1 on the day in which the subjects sat in the cardroom, but no material was processed through the card (background exposure), was a rise of 60 ml, or +1.8 percent. This was not likely a learning effect, since the background exposure day was actually the third or fourth study day for a given subject, and thus the subjects had performed spirometry at least four times previously. Exposure to dust from rayon produced a small but significant decrement in FEV_1 compared with the background exposure day. The SCBR, SCBI, and LCBR cotton dust exposures produced decrements of FEV_1 not significantly different from that of rayon but significantly smaller than that produced by Stoneville standard cotton dust exposures. The LCBR cotton dust exposure produced a significantly greater decrement in FEV_1 than Stoneville standard cotton dust.

Table 5 shows the results for participants separated into smokers and nonsmokers. The smokers had greater decrements in FEV_1 for each exposure type, but the biologic activity relative to Stoneville standard cotton was different between smokers and nonsmokers only for LCBR cotton.

On most exposure days, only one or two subjects complained of respiratory tract symptoms, usually coughing, when questioned after exposure. Only one subject complained of the classic cotton exposure complaint, chest tightness, during the experiment. On the LCBI exposure day, however, 13 of the 25 subjects complained of coughing. This is consistent with the biologic activity of this dust as measured by the average decrement in FEV_1, which also was most pronounced for the group on this exposure. However, as shown in Table 6, symptomatic subjects had only a slightly greater decrement in FEV_1 than asymptomatic subjects.

Endotoxin content of the different cottons has been completed only on bulk samples (Table 7). LCBI cotton, which had the highest endotoxin content, also produced the greatest decrement in FEV_1, but the overall correlation between endotoxin content and decrement in FEV_1 was not significant.

Discussion

The nature, source, and mechanisms of action of the substances in cotton dust that cause the physiologic response during exposure are still not known. Cotton fibers which have been thoroughly washed and bleached for medical use have low biologic activity.[8] Extracts of bract have been shown to release histamine

Table 4—*Exposure Results*

Exposure Type	Mean Dust Concentration, mg/m³	No. Exposed	Mean ΔFEV₁,* ml
Background	0.03	26	+ 60 (+1.8)
Rayon	0.49	24	− 45† (−1.5)
SCBR	0.73	25	− 70† (−2.1)
SCBI	1.02	25	− 74† (−2.1)
LCBR	0.90	24	− 85† (−2.7)
Stoneville Standard (4 exposures combined)	0.93	89	−171 (−5.1)
LCBI	0.88	25	−352† (−10.4)

*Mean ΔFEV_1 = Postexposure FEV_1 minus preexposure FEV_1, with change as a percent in parentheses. Means (ml) adjusted for missing participants.
†$P<.01$ compared with background or Stoneville standard exposure.

Table 5—*Exposure Results by Smoking Category*

Exposure Type	Mean Dust Concentration, mg/m³	Nonsmokers		Smokers	
		No. Exposed	Mean ΔFEV₁*	No. Exposed	Mean ΔFEV₁*
Background	0.03	11	+2.4	12	+ 1.2
Rayon	0.49	10	−1.5	11	− 1.8
SCBR	0.73	11	−1.5	11	− 3.1
SCBI	1.02	11	−0.6	11	− 3.0
LCBR	0.90	11	−0.3	10	− 6.7
Stoneville standard	0.93	39	−4.0	40	− 6.0
(4 exposures combined)					
LCBI	0.88	11	−7.2	11	−14.2

*Change in FEV_1 after exposure as percent of preexposure value.

from lung tissue and when aerosolized and inhaled, to produce signs and symptoms of byssinosis in volunteers.[8] Although bronchoconstriction may be a direct effect of a chemical substance present in cotton plants, others have suggested that endotoxin from associated bacteria play a role.[9,10] Water washing of cotton appears to decrease the bronchoconstricting properties of the dust,[11] but difficulties in processing washed cotton into yarn have so far prevented this method of control from use in the textile industry.

Harvesting of cotton before the natural opening of the boll allows better control over contamination of the fibers with material from outside the boll. Carding of closed boll harvested cotton produced much less dust than standard cotton, and even with reductions in ventilation, a carding rate of three to five times that for standard cotton had to be used to attain roughly equivalent respirable dust concentrations. Thus, it appears that significant reductions in dust concentration could be achieved in textile mills and other phases of cotton processing without any change in air-cleaning equipment if closed boll harvested cotton could be successfully adapted for commercial use.

Decrements in FEV_1 after six hours of exposure were significantly less for Stoneville closed boll harvested cotton than for Stoneville standard cotton. This was true in both smokers and nonsmokers and seemed unrelated to development of tolerance or decreased ability to respond. No fall in average preexposure FEV_1 for the group occurred during the study, and the largest decrement in FEV_1 was seen on the next to last exposure day. Return to the baseline preexposure value of FEV_1 had occurred by the following morning after all exposures.

Smokers consistently showed greater decrements in FEV_1 than nonsmokers, but, except for the LCBR cotton, the relative biologic activity of the cottons was the same in smokers and nonsmokers. In studies of chronic exposure to cotton dust, smoking appears to increase the risk for symptoms of byssinosis and decreased preexposure pulmonary function for a given amount of dust exposure.[6,12,13] The difference noted for the LCBR cotton could have been a chance occurrence among the multiple comparisons, but the Lubbock cotton may also have been different from the Stoneville cotton in some fundamental way. Both Lubbock cottons had greater endotoxin content than any of the Stoneville cottons, including the standard type, and the methods for drying the unopened bolls were quite different for Stoneville and Lubbock cottons. Further studies in a second group of subjects to be reported separately have continued to show differences in response to Lubbock and Stoneville closed boll cottons at equivalent dust concentrations. In these latter studies, constant carding speed was maintained for all cottons to preclude qualitative differences in the dust generated, as might have occurred in the present study.

Some of the differences in response detected in this

Table 6—*Exposure Results for Lubbock Closed Boll Bract Intact Cotton by Symptom Category*

	Symptomatic	Asymptomatic
No.	13	12
Nonsmokers	3	8
Smokers	8	3
Exsmokers	2	1
ΔFEV₁,* ml	−368	−334

*ΔFEV_1 = Postexposure FEV_1 minus preexposure FEV_1.

Table 7—*Endotoxin Content of Bulk Cotton Samples*

Cotton Type	Endotoxin Content, μg/g
Stoneville standard	1.93
SCBR	2.48
SCBI	1.65
LCBR	4.85
LCBI	7.35

study may have been due to the differences in dust concentrations for the different cottons. An accurate adjustment for these differences cannot be made because only two closely spaced points on the dose-response curve for standard cotton dust were obtained, and it may not be accurate to assume a similar slope for the dose-response to closed boll cotton dust even if the slope for standard cotton dust were known precisely. However, using a simple extrapolation based on the observed dose-response slope for standard cotton dust, response to SCBI and LCBR cotton dusts remained significantly lower than the response to standard cotton dust. The same adjustment applied to the response to rayon, results in a larger decline in FEV_1 than observed with standard cotton exposure. Whether bract removal is important in reducing the biologic activity of closed boll cotton cannot be determined from this study. Likewise, although the correlation of endotoxin content and pulmonary function response was not significant, the inhaled dose of endotoxin may not be accurately reflected in measurements on random bulk samples. Analysis of airborne endotoxin from this and future studies may allow more definite conclusions to be made.

Finally, whether the acute pulmonary function response to a six-hour exposure in nonbyssinotic subjects is a valid predictor of the potential of a given type of cotton dust to produce byssinosis or permanent pulmonary impairment after long-term exposure can only be determined from carefully controlled prospective studies. However, short-term exposure studies seem to be useful and safe in rapidly estimating the relative effectiveness of various experimental treatments in decreasing the biologic activity of cotton dust.

References

1 Berry G, McKerrow C, Molyneux M, Rossiter C, Tombleson J. A study of the acute and chronic changes in ventilatory capacity of workers in Lancashire cotton mills. Br J Ind Med 1973; 30:25-36

2 Merchant J, Lumsden J, Kilburn K, et al. Dose response studies in cotton textile workers. J Occup Med 1973; 15:222-30

3 Batawi MA, Shash El, El-Din S. An epidemiological study on aetological factors in byssinosis. Int Arch Gewerbepath Gewerbehyg 1962; 19:393-402

4 Knudson R, Slatin R, Lebowitz M, Burrows B. The maximal expiratory flow-volume curve normal standards variability and effects of age. Am Rev Respir Dis 1976; 113:587-600

5 Olenchock S, Mull J, Boehlecke B, Major P. Cotton dust and complement *in vivo*. Chest 1981; 79:53S-55S

6 Roach SA, Schilling RSF. A clinical and environmental study of byssinosis in the Lancashire cotton industry. Br J Ind Med 1960; 17:1-9

7 Schilling RSF, Vigliani EC, Lammers B, Valie F, Gilson JC. A report on a Conference on Byssinosis. In: Proceedings of the XIVth International Congress on Occupational Health, Madrid. Amsterdam; Exerpta Medica, 1963:137-45

8 Douglas J, Zuckerman A, Ridgway P, Bouhuys A. Histamine release and bronchoconstriction due to textile dusts and their components. Second International Conference on Respiratory Disease in Textile Workers. Alicante, Spain; 1968:148-55

9 Cavagna G, Foa V, Vigliani E. Effects in man and rabbits of inhalation of cotton dust or extracts and purified endotoxins. Br J Ind Med 1969; 26:314-21

10 Cinkotai F, Lockwood M, Rylander R. Airborne microorganisms and prevalence of byssinotic symptoms in cotton mills. Am Ind Hyg Assoc J 1977; 38:554-59

11 Merchant JA, Lumsden J, Kilburn K, et al. Pre-processing cotton to prevent byssinosis. Br J Ind Med 1973; 30:237-47

12 Bouhuys A, Schoenberg JB, Beck GJ, Schilling RSF. Epidemiology of chronic lung disease in a cotton mill community. Lung 1977; 154:167-86

13 Merchant JA, et al. Byssinosis and chronic bronchitis among cotton textile workers. Ann Intern Med 1972; 76:423-33

Pulmonary Function and Symptoms in Herbal Tea Workers*

Robert M. Castellan, M.D.; Brian A. Boehlecke, M.D.; Martin R. Petersen, M.S.; Terry D. Thedell, Ph.D.; and James A. Merchant, M.D., Dr. P.H.

Occupational respiratory disease caused by inhalation of dust generated during the manufacture of tea was first reported in terms of "tea factory cough" by Castellani and Chalmers.[1] Occupational asthma in a tea factory worker was later labeled as "tea maker's asthma" by Uragoda.[2] Ebihara[3] described two persons whose illnesses, allergic rhinitis in one and asthma in the other, were related to cultivating and harvesting tea.

Several surveys of groups of tea workers have been reported. One revealed by questionnaire an excessive prevalence of chronic bronchitis and asthma.[4] Another reported shift reductions in FEV_1 related to dust exposure.[5] Yet another demonstrated a chronic effect of tea dust exposure on expiratory flow rates.[6]

We evaluated a potential occupational health hazard at an herbal tea processing and packing plant where black tea (the basis of the above-mentioned reports) is only one of dozens of raw ingredients processed. During a preliminary site visit, a NIOSH physician interviewed workers and reviewed data from the company's pulmonary function surveillance program. Because of frequent respiratory symptoms, including one case history strongly suggestive of occupational asthma, and because of objective documentation of shift decre-

*From the Division of Respiratory Disease Studies, National Institute for Occupational Safety and Health, Morgantown, WV.

Use of commercial names does not imply endorsement by the NIOSH.

Reprint requests: Dr. Castellan, 944 Chestnut Ridge Road, Morgantown, West Virginia 26505