Factors Influencing the Interpretation of FEV₁ Declines Across the Working Shift*

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Guidelines for the evaluation and management of workers exposed to cotton dust have been defined by the Department of Labor in the recently adopted cotton dust standard. The success of this standard is dependent on the precision with which an acute or chronic change in lung function can be detected at the workplace. Although strict requirements have been adopted for test instruments and procedures, the inherent variability of measurements of lung function still pose a significant problem in distinguishing reactors from nonreactors. According to the standard, possible acute reactors are defined as those exhibiting a fall in Monday FEV₁ in excess of 5 percent or 200 ml, whichever is less. Since for some persons the within-subject SD for FEV₁ is in excess of 200 ml, individual variability can cause the cutoff for reactors to be exceeded, yielding both false-positive and false-negative results. To quantify this effect, the individual and group variability of data collected at four cottonseed crushing mills was examined relative to symptoms, smoking status, and work shift.

MATERIALS AND METHODS

Four cottonseed crushing mills in the southern United States were visited in 1975, 1977, and 1978. Lung function measurements were performed before work and after the subjects had been away from the mill for at least 36 hours and after at least five hours at the workplace. Spirometric tests were conducted on a dry, rolling-seal spirometer with the output displayed on a Hewlett-Packard XYY recorder.

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This work was supported by U.S. Public Health Service grant HL-15092 of the National Heart, Lung, and Blood Institute.
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as volume-time or flow-volume plots of the maximal forced expiratory vital capacity maneuver. The measurements included the 7-sec forced vital capacity (FVC), the forced expiratory volume in .5 and 1 second (FEV₀.5 and FEV₁), and the forced expired flow between 25 and 75 percent of the forced vital capacity (FEF25-75%). The beginning of time for calculating the FEV₅ and FEV₁ was obtained by the method of backward extrapolation, and all measurements were corrected to the body temperature and pressure saturated with water vapor (BTPS). Subjects were tested in the standing position, nose clips were used, and at least four maximal expiratory maneuvers were performed at each testing session.

A trained interviewer administered a British MRC questionnaire modified for detection of byssinosis. Responses to the questionnaire were analyzed for the prevalence of byssinosis by the Schilling definition and for chronic bronchitis, atopy, dyspnea, and groups of upper and lower respiratory tract symptoms.

An analysis of variability within subjects for FEV₁ was performed using the four largest preshift and postshift volumes obtained on 192 subjects tested at the four mills in 1977. For each individual, within-subject SD was computed as the square root of the average preshift and postshift FEV₁ variances. This within-subject SD was analyzed in relation to symptoms, smoke status, and work shift. The SD of the preshift-postshift FEV₁ difference for each individual was computed by multiplying the within-subject SD by the square root of (1/N₁ + 1/N₂), where N₁ and N₂ represent the number of preshift and postshift measurements.

Acute changes in lung function in relation to shift were analyzed for all mills and for all visits. Only subjects with acceptable over-the-shift spirometry values were included in analyses. Acceptable spirometry required visually acceptable curves, with the added stipulation that the two largest FVC values differed by less than 3 percent. Acceptable over-the-shift spirometry was obtained at least once for 185 linter area workers at three visits.

RESULTS

The individual within-subject SD for the 192 subjects studied in 1977 ranged from .020 to .428 L, with 74 percent less than .100 L. The average within-subject variability was .102 L SD across the shift ranged from .014 to .302 L, with .072 L as a representative value.

Figure 1 displays the average FEV₁ within-subject variability between groups answering "yes" or "no" to

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lower or upper respiratory tract symptom complexes, chronic bronchitis, dyspnea, and byssinosis. The variability of groups answering “yes” to bronchitis and byssinosis (.141 L and .192 L, respectively) was significantly different (P = .001) from the nonbronchitic subjects and the subjects without symptoms of byssinosis (.099 L and .102 L, respectively). No statistical difference in variability was exhibited between groups answering “yes” or “no” to lower or upper respiratory tract symptom complexes or dyspnea.

Figure 2 displays the average within-subject variability in FEV$_1$ as a function of smoking status and shift. For smoking, there was no significant difference in variability between current, exsmokers, and never-smokers. In addition, the morning, evening, and night shifts yielded statistically similar repeatability.

Changes over the working shift were related to time of day for all three visits and for all four mills, even though preshift measurements were not significantly related to shift. For FVC, FEV$_1$, and FEF25-75%, there was no significant difference between morning and night shifts. However, there was always a significant difference for all of these parameters between evening shift and the morning and night shifts. Table 1 shows the mean change for all visits collapsed for all mills. The significant difference in FEV$_1$, FVC and FEF25-75% between shifts persisted even though there was no significant difference between shifts in smoking status, symptoms, exposure (all were linter area workers), race, age, years employed in mill, and work area.

**DISCUSSION**

The ability with which one can detect a meaningful change in FEV$_1$ is related to shift and is an inverse

| Table 1—Mean Change in Spirometric Values for All Visits to All Mills |
|---------------|-----------------|-----------------|-----------------|
| **Shift**     | **Mean Time of Preshift Spirometry** | **Mean Change Over All Visits (Linter Area Workers)** |
|               | **N** | **FVC** | **FEV$_1$** | **FEF25-75%** |
| Morning       | 72    | .042    | .051         | .148           |
| Evening       | 64    | .083    | .135         | .465           |
| Night         | 49    | .031    | .030         | .098           |
function of within-subject variability. This variability is related to symptoms of byssinosis and chronic bronchitis. The current practice of comparing individual decline in FEV₁ across the shift to a fixed value, eg, > 200 ml, in order to classify reactors, is misleading, since the across-shift SD of some subjects is in excess of 250 ml. Conversely, very repeatable subjects (SD < 50 ml) should be classified as reactors if their across-shift decline is in excess of 100 ml. In addition, the excessive variability of subjects with symptoms of byssinosis is a possible explanation of the lack of correlation between acute decline and symptoms. The shift effect implies that an adverse change in FEV₁ observed across the day shift or night shift would be significantly lower than an equally meaningful change observed in the evening. Therefore, a more accurate classification of reactors should take into account symptoms, shift, and an assessment of individual variability.

**Summary**

An analysis of variability within individuals was conducted for FEV₁, obtained from subjects employed in the cottonseed industry. Individual SDs ranged from .020 to .428 L. The within-subject SD of the preshift-postshift difference ranged from .014 to .302 L. When within-subject variability of FEV₁ was analyzed in relation to symptoms, smoking history, and shift, the only statistical difference occurred in the 14 bronchitic subjects (.141 L) relative to the 179 without bronchitis (.099 L), and the three subjects with byssinosis (.192 L) relative to those without symptoms (.102 L). Changes over the working shift were significantly different for evening relative to morning and night shifts, even though there was no significant difference in smoking status, symptoms, exposure, race, age, years employed in the mill, and work area. In addition, baseline measurements were not significantly related to shift. Therefore, the effect of individual variability, symptoms, and shift should be considered if an accurate classification of reactors based on change in FEV₁ across the shift is to be obtained.

**Acknowledgment:** The authors would like to acknowledge the programming and technical assistance of Daniel Seale, B.S., in the preparation of this manuscript.

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The Effect of Mediator Modifying Drugs in Cotton Bract-Induced Bronchospasm*

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**Byssinosis** is a chronic occupational lung disease associated with the inhalation of cotton and other textile dusts.\(^1\) In its early phases acute reversible symptoms, such as wheezing, chest tightness, and shortness of breath, accompany reversible changes in pulmonary function.\(^2\) The therapy for this disease remains incompletely defined. However, considerable evidence from both in vitro and in vivo studies indicates that the mechanism underlying acute airway obstruction in this disease is related to the nonantigenic release of histamine and possibly of other mediators by the action of an airway constricting agent in cotton bracts.\(^3\)\(^4\) To test the therapeutic implications of these findings, we studied the effect of mediator modifying drugs on cotton bract-induced bronchospasm in healthy subjects. Two classes of agents were studied, a cromone, disodium cromoglycate, and two antihistamines, an H₁-blocking agent, chlorpheniramine, and cimetidine, an H₂-blocking agent.

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CHEST, 79: 4, APRIL, 1981 SUPPLEMENT

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