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by [Tielemans E](#), [Heederik D](#), [van Pelt W](#)

Affiliation: Department of Epidemiology and Public Health, University Wageningen, The Netherlands.

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Changes in ventilatory function in grain processing and animal feed workers in relation to exposure to organic dust

by Erik Tielemans, MSc,¹ Dick Heederik, PhD,¹ Wilfrid van Pelt, PhD²

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OBJECTIVES — The effects of organic dust exposure on the configuration of the maximum expiratory flow volume (MEFV) curve was examined multivariately.

METHODS — Data from 390 male workers in the animal feed industry in The Netherlands were analyzed. A multivariate technique called nonlinear canonical correlation analyses was used to study the relationship between a set of organic dust exposure variables and a set of ventilatory function variables.

RESULTS — The results indicate an almost independent effect of the overall mean organic dust exposure and the number of years of organic dust exposure on ventilatory function. Increasing mean organic dust exposure was associated with a decrease in both forced expiratory volume in 1 s (FEV_{1.0}) and forced vital capacity (FVC) and decreased flows at high lung volumes only. Increasing number of years of dust exposure was associated with a decrease in FEV_{1.0} and a decrease in flow at all lung volumes, while the FVC seemed relatively constant. These two distinct patterns of reduction in ventilatory function may represent two different pathological processes. Whereas workers with prolonged exposure showed reduced values for all of the MEFV curve variables, except the FVC, those with only a few years of exposure especially showed a decrease in FVC and peak expiratory flow. The effect of current organic dust exposure was more evident for nonsmokers than for ex-smokers and current smokers.

CONCLUSION — The major finding of this study was an independent effect of overall mean organic dust exposure and the number of years of organic dust exposure on the MEFV curve.

KEY TERMS — grain dust, lung function, multivariate analysis, organic dust, pathology.

Studies of grain elevator workers (1–4) and workers in the cotton industry (5) have shown that occupational exposure to organic dust is associated with the development of respiratory symptoms and airway obstruction. This finding has recently been confirmed by several cross-sectional studies in the grain processing and animal feed industry (6, 7). The etiology of lung disease in relation to exposure to organic dust is hardly understood. There is some experimental evidence that endotoxins may play an important role in the etiology of the acute lung function changes related to organic dust exposure (8). A relation between endotoxin exposure and chronic lung disease was found in two epidemiologic studies (5, 6). However, whether these originate from disease processes in central and peripheral airways or in the lung parenchyma is not clear. Furthermore, little is known about short-term (acute) and long-term

(chronic) effects of organic dust exposure on ventilatory function.

This paper reports results from a cross-sectional study of 390 workers in the Dutch animal feed industry. We studied the relationships between exposure to organic dust and ventilatory function using maximum expiratory flow volume (MEFV) curves. In most epidemiologic studies it is common to examine ventilatory function variables separately. A few studies (9–10) have described the use of the principal component analysis to investigate the main directions of variability (principal components) of a whole set of ventilatory function variables. However, this multivariate technique is hampered by the fact that the principal components are not necessarily focused on the sources of variability in the MEFV curve. In the present study a multivariate technique called nonlinear canonical correlation analyses was used to study the relationship between a set of organic dust exposure variables and a set of ventilatory function variables. This technique extracts information from the MEFV curve in relation to organic dust exposure and summarizes it in (two) newly created independent variables. This procedure allows a parsimonious description of patterns of abnormality in ventilatory function in relation to organic dust exposure (i.e., the configuration of the MEFV curve).

¹ Department of Epidemiology and Public Health, University Wageningen, Wageningen, The Netherlands.

² National Institute of Public Health and Environmental protection, Bilthoven, The Netherlands.

The multivariate analysis facilitated a more comprehensive description of relationships between several indices of organic dust exposure and ventilatory function as a whole, and a comparison of these effects among nonsmokers, ex-smokers, and current smokers.

Subjects and methods

Subjects

We studied a population of Caucasian male workers in the Dutch animal feed industry. Three hundred and fifteen workers came from a cross-sectional study carried out between 1986 and 1988 in two animal feed elevators where grain is processed. Details of this study have been reported previously (6, 11). Additional data on 78 workers were obtained from a follow-up study carried out four years later in the same animal feed elevators, the result being a study population of 393 animal feed workers. Of the 393 animal feed workers, 390 were used in the analyses because three had missing values for the exposure variables. The characteristics of the study population are given in table 1.

Table 1. Characteristics of the 390 male animal feed workers. (EXPYEAR = years of organic dust exposure, MEANDUST = overall mean organic dust exposure, CUMDUST = cumulative organic dust exposure)

	Mean	SD	%
Age (years)	39.6	10.0	·
Height (cm)	178.1	6.5	·
Years smoked (years)	15.3	12.7	·
Current smokers	·	·	51
Ex-smokers	·	·	24
Nonsmokers	·	·	25
EXPYEAR (years)	10.5	9.6	·
MEANDUST ($\text{mg} \cdot \text{m}^{-3}$)	9.6	10.8	·
CUMDUST ($\text{years} \cdot \text{mg} \cdot \text{m}^{-3}$)	108.5	127.3	·

Lung function and exposure

The ventilatory function was characterized by maximum expiratory flow volume (MEFV) curves that were obtained from all 393 subjects by normal spirometry with a Vicatest 5 spirometer (Mijnhardt, Bunnik). Measurements and procedures including BTPS adjustments for body temperature and pressure (saturated with water vapor) and procedures of data selection, were in accordance with the standards of the European Community for Coal and Steel (12); they have been described in detail elsewhere (6). The variables derived from the MEFV curve were forced vital capacity (FVC), forced expiratory volume in 1 s ($\text{FEV}_{1.0}$); maximum mid-expiratory flow (MMEF); peak expiratory flow (PEF); and maximum expiratory flow rates at 75, 50 and 25% of the FVC (MEF_{75} , MEF_{50} , and MEF_{25} , respectively). For each animal feed worker, age- and height-specific reference values (predicted values) of the MEFV curve variables were calculated from reference equations of the European Community for Coal and Steel for adult males (12) (table 2). The residuals were computed as follows: MEFV curve variables "measured" - MEFV curve variables "predicted." They were then used in the multivariate analysis. In eight randomly selected facilities, 8-h personal inspirable dust samples were taken among the production workers. Detailed information on the exposure assessment strategy of organic dust has been described in earlier papers (6, 13). For all group members a complete occupational history was available. These histories allowed calculations of the following exposure variables: cumulative organic dust exposure (CUMDUST), years of organic dust exposure (EXPYEARS), and overall long-term mean organic dust exposure (MEANDUST), which is CUMDUST/EXPYEAR (table 2).

For comparing the groups of workers in the multivariate analysis of variance (see table 4 in the Re-

Table 2. Characteristics of the transformations and range of the variables used in the canonical correlation analyses. (FVC = forced vital capacity; $\text{FEV}_{1.0}$ = forced expiratory volume in 1 s; PEF = peak expiratory flow, MEF_{75} , MEF_{50} and MEF_{25} = flow rate at 75, 50 and 25%, respectively, of the FVC; MMEF = maximum midexpiratory flow; MEANDUST = overall mean organic dust exposure; CUMDUST = cumulative organic dust exposure; EXPYEAR = years of organic dust exposure)

Variables	Transformation	Range
MEFV curve set (residuals)		
FVC (l)	Linear	-1.74—+2.39
$\text{FEV}_{1.0}$ (l)	Linear	-2.16—+1.90
PEF ($\text{l} \cdot \text{s}^{-1}$)	Linear	-5.65—+6.88
MEF_{75} ($\text{l} \cdot \text{s}^{-1}$)	Linear	-6.56—+5.00
MEF_{50} ($\text{l} \cdot \text{s}^{-1}$)	Linear	-4.10—+4.07
MEF_{25} ($\text{l} \cdot \text{s}^{-1}$)	Linear	-2.01—+1.94
MMEF ($\text{l} \cdot \text{s}^{-1}$)	Linear	-3.42—+3.38
Organic dust exposure set		
MEANDUST ($\text{mg} \cdot \text{m}^{-3}$)	Second degree monotone Spline Knots: 0.001 2.9 6.7 12.1	0—46.6
CUMDUST ($\text{years} \cdot \text{mg} \cdot \text{m}^{-3}$)	Second degree monotone Spline Knots: 0.01 20.8 62.5 158.3	0—803.3
EXPYEAR (years)	Second degree monotone Spline Knots: 0.1 5 10 20	0—40

sults section) and in the graphic presentations in figures 2 and 4 (see the Results section for figures 2 and 4), the workers were divided into groups according to their exposure. First they were divided into two groups, one with present organic dust exposure levels $<5 \text{ mg} \cdot \text{m}^{-3}$ ($N = 230$) and one with levels of $>5 \text{ mg/m}^3$ ($N = 160$). The workers were also divided into the following five groups according to their years of organic dust exposure (EXPYEAR): unexposed workers ($N = 76$), 0.5–5 years exposed ($N = 65$), 5.5–10 years exposed ($N = 88$), 10.5–20 years exposed ($N = 93$), >20 years exposed ($N = 68$). A worker was categorized as a current smoker if he currently smoked or had stopped within one year prior to the study.

Statistical analysis

The nonlinear canonical correlation analysis was used to determine relationships between the set of age- and height-adjusted MEFV curve variables and the set of exposure variables. This technique extracts information on the adjusted MEFV curve variables in relation to organic dust exposure and summarizes this information in one or more newly created independent variables. Such variables are called canonical variables, and they are linear combinations of the original adjusted MEFV curve variables. In our analyses only two canonical variables were computed. The nonlinear canonical correlation analysis can, to a certain extent, cope with nonlinear relationships so that more information about the relationships between the two sets can be summarized with fewer canonical variables (14). Only the exposure variables were allowed to be nonlinearly transformed. (See figure 3 in the Results section.) The scaling method chosen allows for monotone, piecewise second-order spline transformations. The nonlinear transformations were chosen to be smooth except for a possible jump at the first knot, which separated the unexposed and exposed workers. The knot placement is given in table 2. The determination of both optimal transformations and the construction of canonical variables was done with SAS software (procedures TRANSREG and CANCORR) (15).

To present results of the nonlinear canonical correlation analysis graphically, vector diagrams were made in which the components of both sets of variables are depicted with respect to the canonical variables of the MEFV curve set. The canonical variables form a referential frame of perpendicular axes in which the variables are indicated by vectors. The length of a vector is a measure of the correlation between the variable and the canonical variables. The fraction of variance of a variable "explained" by its correlation with the two canonical variables is equal to the sum of the squares of these two correlations (ie, equal to the squared length of the corresponding vectors) (figure 1 and table 3).

The numerical value of a worker on the first or second canonical variable is called a (canonical)

score. These two scores represent a worker's ventilatory function as measured with the MEFV curve. Scores can be averaged according to subgroups leading to what are called centroids. Similar to the scores of different workers, the relative positions of the centroids of the subgroups can be studied with respect to the vector diagram. (See figures 2 and 4 in the Results section.)

An interaction between exposure to organic dust and smoking habits was formally tested with a multivariate analysis of variance (MANOVA) with all age- and height-adjusted MEFV curve variables as dependent variables and smoking habits, present organic dust exposure, and years of organic dust exposure (EXPYEAR) as independent variables. (See table 4 in the Results section.) The independent variables were categorized as described earlier. The interaction terms between the current organic dust exposure and smoking habits, current organic dust exposure and EXPYEAR, and EXPYEAR and smoking habits were added to the model.

Results

Figure 1 shows the vector diagram depicting the relationship of the organic dust exposure variables with the variables defining the MEFV curve. The first and second canonical correlations are 0.41 and 0.31, respectively. This result indicates that organic dust exposure relates to a fraction of the total variability in lung function. Note that the normal variability of the MEFV-curve variables has been adjusted by age and height with the use of reference equations.

The vector diagram in figure 1 shows that the vectors for the MEFV curve variables and EXPYEAR point in opposite directions. This finding indicates that all of the MEFV curve variables are negatively correlated (ie, decrease with increasing years of organic dust exposure). Both flows at high lung volumes (PEF , MEF_{75}) and flows at low lung volumes (MEF_{50} , MEF_{25} , MMEF) decrease with increasing years of exposure. The FVC was hardly affected, as the vectors for the FVC and EXPYEAR are almost perpendicular and the length of the FVC vector is very small. The latter occurrence is important because the squared length of a vector is equal to its "explained" variance, which is the variance accounted for by the two canonical variables of the MEFV-curve set. As $\text{FEV}_{1.0}$ was negatively correlated with EXPYEAR and FVC was not, the $\text{FEV}_{1.0}:\text{FVC}$ ratio decreased with increasing years of organic dust exposure. In general one can say that when workers are exposed for a longer time to organic dust, a decrease of flows takes place at both the beginning and end of the MEFV curve, while the FVC is not influenced to a great extent. It can be seen from the vector diagram that the flows at the beginning of the MEFV curve (PEF , MEF_{75}) are negatively correlated with MEANDUST, while flows more towards the end of

Figure 1. Vector diagram with the variables for the curve set of the maximum expiratory flow volume (MEFV) curve set and the variables for the nonlinear transformed exposure as projected onto the canonical variables of the MEFV curve set (number of subjects = 390). (CAN1 and CAN2 = the first and second canonical variable, respectively; exposure variables: MEANDUST = overall mean organic dust exposure, CUMDUST = cumulative organic dust exposure; EXPYEAR = years of organic dust exposure; variables of the MEFV curve set: FVC = forced vital capacity; FEV₁ = forced expiratory volume in 1 s; MMEF = maximum midexpiratory flow; MEF₇₅, MEF₅₀ and MEF₂₅ = flow rate at 75, 50, and 25%, respectively, of the FVC; PEF = peak expiratory flow)

Table 3. Variance of maximum expiratory flow volume (MEFV) curve variables, and the nonlinear transformed exposure variables, as explained by the first and second canonical variable (CAN1 and CAN2) of the MEFV curve set (sum of the squared correlations with CAN1 and CAN2) in reference to the nonlinear canonical correlation analysis underlying the results presented in figure 1. (FVC = forced vital capacity; FEV_{1.0} = forced expiratory volume in 1 s; PEF = peak expiratory flow; MEF₇₅, MEF₅₀ and MEF₂₅ = flow rate at 75, 50 and 25%, respectively, of the flow rate; MMEF = maximum midexpiratory flow; MEANDUST = overall mean organic dust exposure; CUMDUST = cumulative organic dust exposure; EXPYEAR = years of organic dust exposure)

Variables	Fraction "explained" variance
MEFV curve set	
FVC	0.20
FEV _{1.0}	0.62
PEF	0.81
MEF ₇₅	0.85
MEF ₅₀	0.62
MEF ₂₅	0.70
MMEF	0.75
Exposure set	
MEANDUST	0.08
CUMDUST	0.15
EXPYEAR	0.17

the MEFV curve are less correlated (MEF₅₀, MMEF) or not correlated (MEF₂₅). A decrease in the FVC and the FEV_{1.0} with increasing mean organic dust exposure was found as well. CUMDUST, the product of

MEANDUST and EXPYEAR, occupied an intermediate position in the vector configuration between MEANDUST on one hand and EXPYEAR on the other.

Figure 2 depicts the vectors of the MEFV curve variables and MEANDUST and EXPYEARS, as well as centroids of five EXPYEAR categories. The centroids suggest two different lung function effects with increasing years of exposure. This result can be evaluated further if the centroids are projected upon the vectors of the MEFV curve variables. When a line is drawn from the first category of EXPYEAR (0 years of exposure) to the second category (0.5–5 years of exposure), the line is more or less parallel to the vectors of FVC and PEF. This result suggests that exposure during the first years of employment in this industry is associated particularly with a decrease in FVC and PEF. Workers who are exposed for a longer time, however, show a reduction for all MEFV curve variables, except FVC, since the line drawn from the second and following categories of EXPYEAR is almost perpendicular to the vector of the FVC and, to a less degree, to the vector of the PEF. The line points more clearly in the same direction as that of the other MEFV curve variables.

We have also investigated EXPYEAR with respect to the MEFV curve variables by further dividing the

five EXPYEAR groups into those for nonsmokers, current smokers, and ex-smokers (not shown). For these groups similar results were found, as depicted in figure 2. This vector diagram suggests an almost independent effect of MEANDUST and EXPYEAR on the ventilatory function with respect to the MEFV-curve configuration. This finding is in accordance with the vector configuration in figure 1.

The transformations of the exposure variables MEANDUST and EXPYEAR are given in figure 3. The original values of the variables are plotted against their transformed values. The transformations of the two exposure variables must be interpreted with respect to the variables of the MEFV curve set with which they are associated. Therefore, rough indications about exposure-response relationships can be derived from figure 3. The transformation of EXPYEAR shows a leveling off at high values. In fact, very little change is found between values higher than 30 years. This finding indicates that the differences in the MEFV curve are less pronounced for those people who performed their job for a long or a very long time. The transformation of MEANDUST does not show such a leveling off at high values.

The vector diagram in figure 4 is the same as shown in figure 2. In addition, centroids of the two categories of current low and high exposure to organic dust are projected for the nonsmokers, ex-smokers, and current smokers onto the canonical variables of the MEFV curve set. In all of the groups of smokers, flows at high lung volumes (PEF, MEF₇₅) and the FVC decreased with increasing current exposure to organic dust, while flows at low lung volumes (MEF₅₀, MMEF, MEF₂₅) and, to a less extent, the FEV_{1.0} were not affected. The centroids show that current organic dust exposure is more strongly related to decreases in lung function among nonsmokers since the line which is drawn between the centroids of current low and high exposure is longer for the nonsmokers than for current or ex-smokers. Such a possible interaction effect of current organic dust exposure and smoking habits with respect to the ventilatory function was tested in a multivariate analysis of variance (MANOVA) (table 4). Because EXPYEAR was not equally distributed among the three smoking categories, an interaction term between current organic dust exposure and EXPYEAR was added to the model. Only the interaction term between current organic dust expo-

Figure 2. Vector diagram with the variables for the maximum expiratory flow volume (MEFV) curve, the variables for the nonlinear transformed exposure, and five centroids corresponding to the years of exposure (EXPYEAR) categories, which have been projected onto the canonical variables of the MEFV curve set (ie, CAN1 and CAN2, the first and second canonical variable, respectively) (number of subjects = 390). (centroids: 0 = unexposed workers, 5 = 0.5–5 years exposed, 10 = 5.5–10 years exposed, 20 = 10.5–20 years exposed, >20 = more than 20 years exposed; exposure variables: MEANDUST = overall mean organic dust exposure; EXPYEAR = years of organic dust exposure; variables of the MEFV curve set: FVC = forced vital capacity; FEV₁ = forced expiratory volume in 1 s; MMEF = maximum midexpiratory flow; MEF₇₅, MEF₅₀ and MEF₂₅ = flow rate at 75, 50 and 25%, respectively, of the FVC; PEF = peak expiratory flow)

Figure 3. Monotone spline transformations of years of exposure (EXPYEAR) and overall mean organic dust exposure (MEANDUST), in reference to the nonlinear canonical correlation analyses of MEANDUST and EXPYEAR with the MEFV curve variables. (Compare with figures 2 and 4.) (MEFV = maximum expiratory flow volume)

sure and smoking habits reached statistical significance, the results of the nonlinear canonical correlation analysis presented in figure 4 being confirmed. It can be deduced from figure 4 that smoking has an adverse effect on lung function that more or less coincides with the effect caused by EXPYEAR. This smoking effect was not confounded by the distribution of EXPYEAR in the smoking categories, as the mean value for EXPYEAR was highest in the intermediate ex-smokers' category. This finding was supported by the MANOVA results in table 4, which shows significant effects of both smoking and

EXPYEAR, while the interaction term between smoking habits and EXPYEAR was not significant.

Discussion

The main objective of this study was to examine the MEFV curve representing ventilatory function with respect to a set of different exposure variables for organic dust. General knowledge about changes in the configuration of the MEFV curve in association with organic dust exposure can add some insight into corresponding pathological processes. An examina-

Figure 4. Vector diagram with the maximum expiratory flow volume (MEFV) curve variables, nonlinear transformed exposure variables, and six centroids corresponding to categories for present organic dust exposure and the smoking categories, which have been projected onto the canonical variables of the MEFV curve set (ie, CAN1 and CAN2, the first and second canonical variable, respectively) (number of subjects = 390). (centroids: 0 = present dust exposure $< 5 \text{ mg} \cdot \text{m}^{-3}$, 1 present dust exposure $> 5 \text{ mg} \cdot \text{m}^{-3}$; exposure variables: MEANDUST = overall mean organic dust exposure, EXPYEAR = years of organic dust exposure variables of the MEFV curve set: FVC = forced vital capacity; FEV₁ = forced expiratory volume in 1 s; MMEF = maximum midexpiratory flow; MEF₇₅, MEF₅₀ and MEF₂₅ = flow rate at 75, 50 and 25% of the FVC; PEF = peak expiratory flow)

tion of the MEFV curve was accomplished with the nonlinear canonical correlation analysis. This multivariate technique extracts those aspects of the MEFV curve which correlate maximally with organic dust exposure and summarizes the MEFV curve essentials in two new independent variables. In other words, available information of the whole MEFV curve (seven flow and volume variables) was extracted and reduced to two new variables that are more strongly related to lung pathology induced by exposure to organic dust.

All of the exposure variables analyzed were negatively correlated with age- and height-adjusted MEFV curve variables. This finding confirms previously published evidence that organic dust exposure in the grain processing and animal feed industries can induce airway obstruction. Changes in the MEFV curve in association with the mean organic dust exposure (MEANDUST) probably reflects, to a large extent, short-term lung effects, as these changes coincide almost completely with those associated with current organic dust exposure (figure 4). On the other hand, changes in the MEFV curve in relation to years of organic dust exposure

Table 4. Results of the multivariate analysis of variance (number of workers = 390). (EXPYEAR = years of organic dust exposure)

Exposure variables	P-value
Smoking	0.02
EXPYEAR	0.0003
Present organic dust exposure	0.02
Smoking $\times$ present organic dust exposure	0.01
EXPYEAR $\times$ present organic dust exposure	0.44
Smoking $\times$ EXPYEAR	0.61

(EXPYEAR), independent of normal aging, are indicative of chronic effects. An important finding is that MEANDUST and EXPYEAR are related more or less independently to the MEFV curve (figures 1, 2, and 4). Evidence for two independent pathological mechanisms leading to acute and chronic lung disease was also found by Kennedy et al (5).

Flows at the beginning of the MEFV curve were negatively correlated (decrease) with MEANDUST, while flows more towards the end of the curve were not. Consequently FEV_{1.0} was only slightly negatively correlated with MEANDUST, and MMEF did

not correlate with it at all. This finding suggests that short-term effects related to MEANDUST probably involves a narrowing of central airways more than a narrowing of peripheral airways, while loss of elastic recoil of the parenchyma is not likely, as the shape at the end of the MEFV curve does not change.

The flows at all of the lung volumes, as well as the FEV_{1.0} and MMEF, decreased with increasing EXPYEAR, while the FVC seemed hardly affected. These effects on the whole shape of the MEFV curve suggest obstruction involving both central and peripheral airways. Recent studies have shown that organic dust exposure affects mainly the airways and probably not the lung parenchyma. Chronic lung diseases such as chronic bronchitis and chronic obstructive airway diseases related to organic dust exposure have been described (16). The chronic effects are (partially) irreversible (17) in contrast with the more reversible acute effects (18–20). In two studies (5, 6) endotoxins have been shown to be associated with chronic obstructive airway disease. Although airway disease is the common effect in workers with prolonged exposure to organic dust, parenchymal lesions have been described a few times. Several animal studies describe emphysema in species exposed to organic dust (16). Hence an additional explanation for the decrease in flows at low lung volumes with increasing EXPYEAR may be, besides a narrowing of peripheral airways because of a thickening of airway walls through inflammation and plugging, a diminished tethering of the peripheral airways through loss of elastic recoil of the parenchyma. Loss of lung elastic recoil is also a possible explanation for the low negative correlation between FVC and EXPYEAR. According to two studies (21, 22) of smokers, total lung capacity can increase due to a loss of parenchymal elasticity. On the other hand, an increased residual volume due to premature airway closure should be expected. A concurrent increase in total lung capacity and residual volume may result in an almost unaffected FVC. This possibility is in agreement with our finding that the MEFV curve changes that occurred in relation to EXPYEAR and smoking habits were very much alike (figure 4). Indeed, Cotton et al (4) showed that the effects of smoking and organic dust exposure are about equal in terms of lung function changes. They could not however separate the acute and chronic effects of organic dust exposure. Thurlbeck (23) and Nagai et al (24) showed that cigarette smoking can cause chronic bronchitis, emphysema, peripheral airway diseases, or any combination of these. As an analogue to studies about cigarette smoking (23, 24), one can hypothesize that airway disease in workers with prolonged organic dust exposure is also multifactorial, involving both peripheral and central airways and possibly also lung parenchyma.

A striking finding is that the FVC and PEF seem to decrease, especially in the first years of exposure,

while workers with prolonged organic dust exposure show reduced values for all MEFV curve variables, except for the FVC (figure 2). Changes in the MEFV curve in the first exposure years may again be the short-term lung effects described for MEANDUST; these short-term effects develop a more chronic nature at a later stage. However, also health selection in the first years might have influenced the observed pattern in figure 2. Such selection in the first years was suggested by a longitudinal study of 164 workers in grain elevators (25).

Our results suggest an interaction effect between smoking and current organic dust exposure (figure 4). This interaction has formally been confirmed by a multivariate analysis of variance (table 4). Nonsmokers seem to be affected more by current organic dust exposure than ex- and current smokers. Such an effect has, to our knowledge, not been described previously. Only additive (26, 27) and synergistic (3, 4) effects of smoking and organic dust exposure have been found with respect to ventilatory function. An explanation for our results might be a selection effect, meaning that ex- and current smokers would represent a survivor population that is less susceptible to present organic dust exposure than a population of nonsmokers. Another hypothesis is that the lungs of ex- and current smokers are already irritated, and therefore the additional acute effect of present organic dust exposure is small.

In conclusion, mean organic dust exposure (MEANDUST) and years of exposure (EXPYEAR) relate to almost independent aspects of ventilatory function. MEANDUST is mainly related to airway obstruction that originates from disease processes affecting central airways and, to a less extent, peripheral airways, and these processes seem to have a short-term nature. EXPYEAR relates to airway obstruction extending to both central and peripheral airways and perhaps also to the parenchyma, and this type of obstruction may have a more chronic nature. EXPYEAR relates to both short-term and long-term effects of organic dust exposure (ie, a decrease of the FVC and PEF in the first exposure years and, in following years, a reduction in all of the MEFV curve variables, except FVC). The long-term effects of organic dust exposure and smoking on ventilatory function are very much alike. In contrast to other studies the effect of current organic dust exposure is greater for nonsmokers than for ex-smokers and current smokers and has no synergistic or additive effect for smokers.

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