Arterial Blood Gas Tensions and Lung Function During Acute Responses to Hemp Dust[1-3]

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SUMMARY

Exposure to hemp fiber dust for one quarter hour to 3 hours of volunteer ex-hemp workers ranging from 42 to 73 years resulted in symptoms of byssinosis, decreases in forced expiratory volume in one second, and decreases of arterial oxygen tension. The decrease in arterial oxygen tension occurred in men with normal control forced expiratory volume in one second as well as in those whose control forced expiratory volume in one second before dust exposure was less than 70 per cent of the predicted value. The decreases of forced expiratory volume in one second and of arterial oxygen tension correlated significantly. Changes of arterial carbon dioxide tension were small in most subjects. Thus, exposure to hemp dust caused changes in gas exchange as well as in lung mechanics. Increased nonuniformity of gas distribution and its effect on ventilation-perfusion relations adequately accounted for the altered gas exchange. This study showed for the first time that acute exposure to textile dust not only can cause changes in lung mechanics and dyspnea, but can also lead to arterial hypoxemia, and reinforced the need for stringent control of dust exposure in textile workers at risk of byssinosis.

Introduction

Inhalation of dust produced during processing of hemp fibers (*Cannabis sativa*) produces acute symptoms similar to those of asthma (1). Barbero and Flores (2, 3) proposed that these acute symptoms form part of a syndrome that includes acute as well as chronic responses to dust. This syndrome was called "hemp disease" (2) or "cannabosis" (4). In due course, the repeated acute episodes that occurred during dust exposure were followed by disabling chronic respiratory disease and premature death (5). More recent studies have provided extensive epidemiologic and physiologic data on both the acute and the chronic components of the respiratory disease in hemp workers (6–9); however, these investigations dealt mainly with changes of ventilatory lung function, both during acute exposures to dust and during long-term employment. The results demonstrated that these responses are

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indistinguishable from those in byssinosis of other textile workers exposed to cotton or flax dust. None of the previous studies included measurements of arterial blood gases in textile workers in relation to acute dust exposure. Such measurements are reported in the present paper.

Materials and Methods

The study was performed in Callosa de Segura, Province of Alicante, Spain, during July 1970. The working conditions in the industry have been described previously (2, 3, 6, 7). A group of 28 volunteer subjects, all men, ranging in age from 42 to 73 years, who had previously worked in the hemp industry participated in the study. They had retired from the trade 3 or more years before the study, either because of closure of the factory or because of retirement.

The severity of respiratory symptoms was graded according to Schilling and associates (10).[4] In addition to this classification, grade 3 was used to denote workers who had continuous dyspnea during slight exercise, even in the absence of dust exposure. Most workers with grade 3 symptoms were totally disabled.

Dust exposure took place in a hackling room. Six subjects processed hemp fiber throughout the exposure period. Six others worked part of the time and rested in the dusty room during the rest of the exposure period. The other subjects did not work during the exposure. The total time each subject spent in the dusty room varied because many subjects discontinued the exposure when they felt tightness in the chest or shortness of breath.

Spirographic recordings of slow as well as maximally forced expiratory maneuvers after a maximal inspiration were made in all subjects before and after dust exposure, using a Godart spirograph.[5] Slow as well as forced expirations were repeated 3 to 5 times, and the maximal values for slow vital capacity (VC) and forced expiratory volume in one second (FEV_1) were read from the appropriate curve. Arterial blood samples were obtained in seated subjects after local anesthesia and puncture of the brachial artery. The samples were immediately analyzed with an IL blood gas analyzer[6] in the field laboratory at an ambient temperature of 28° C. Two or three determinations of arterial oxygen tension (Pa_{O_2}) and arterial carbon dioxide tension (Pa_{CO_2}) were made with each sample. Standard calibration procedures, including tonometry, were carried out regularly throughout the study. Because incomplete data were obtained in Subjects 7 and 27, they were not included in the analysis.

Predicted values for FEV_1 were derived from the prediction equations of the VA–Army Cooperative studies (11). Previous experience had shown that the FEV_1 in a small group of Spanish men not exposed to inhalation of noxious dusts corresponded closely to the values predicted from the VA–Army equations (8). For slow VC, prediction data from the European Coal and Steel Community Study were used (12).

Results

Control data: There were large differences in the VC and FEV_1 among subjects (table 1). These differences were not related to acute dust exposures because none of these men had recently worked in hemp dust. The subjects who had no history of consistent dyspnea on Monday during their employment in the hemp industry (grades 0 to 0.5) had an average VC of 76 per cent of the predicted value, and their FEV_1 was 85 per cent of predicted. Arterial blood oxygen tensions varied within the normal range in this group; carbon dioxide tensions varied from 32 to 38 mm Hg.

In the workers with a history of regular Monday dyspnea (grades 1 and 2), control VC and FEV_1 were lower than in the first group (table 1). Average Pa_{O_2} was slightly but not significantly lower than in the first group; Pa_{CO_2} values were the same. Finally, the disabled workers (grade 3) had severe limitation of ventilatory function, but none of these men had respiratory insufficiency at rest, as judged from their Pa_{CO_2} (table 1).

Acute responses to hemp dust: All subjects, even those who indicated that they never had shortness of breath on Mondays, had a decrease of forced expiratory volumes during

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[4] Grade 0.5, occasional chest tightness on Mondays; grade 1, chest tightness or difficulty in breathing or both every Monday at work; grade 2, chest tightness or difficulty in breathing or both during work on Mondays and other days.

[5] Model EP 6200L, Godart-Statham, Bilthoven, The Netherlands.

[6] Instrumentation Laboratories, Lexington, Massachusetts.

TABLE 1

GRADE OF BYSSINOSIS AND CONTROL PULMONARY FUNCTION DATA IN 26 VOLUNTEER SUBJECTS PREVIOUSLY EMPLOYED IN A HEMP FACTORY

Patient No.	Grade	Age (years)	VC (liter)	VC (% pred.)	FEV_1 (liter)	FEV_1 (% pred.)	Before Work Pa_{O_2} (mm Hg)	Before Work Pa_{CO_2} (mm Hg)
2	0	66	3.00	62	1.70	62	99	32
3	0	73	3.20	91	2:10	102	97	37
15	0	69	2.65	69	1.40	62	125	38
16	0	51	4.00	86	2.70	91	98	36
18	0	53	4.20	70	3.40	100	103	36
19	0	52	3.75	84	3.00	105	126	34
22	1/2	71	2.90	69	1.90	72	108	37
Average of grade 0–0.5		*62*		*76*		*85*	*108*	*36*
1	1	42	3.90	91	2.85	95	111	42
12	1	59	3.10	82	2.25	107	126	36
14	1	61	2.35	56	1.25	51	82	40
21	1	59	2.70	73	1.60	67	90	34
23	1	53	3.25	68	2.25	75	86	31
24	1	61	3.32	75	1.80	66	99	38
25	1	60	3.00	93	1.95	69	85	39
4	2	58	2.95	56	1.80	59	105	38
11	2	62	3.00	100	1.90	95	75	39
17	2	65	2.40	57	1.00	41	96	34
20	2	70	1.58	33	0.90	34	105	36
Average of grade 1–2		*59*		*71*		*69*	*96*	*37*
5	3	65	1.70	47	0.90	40	85	41
6	3	62	2.55	70	1.05	45	121	39
8	3	58	2.50	60	1.30	50	76	32
9	3	61	2.80	61	1.05	41	94	35
10	3	68	2.00	49	0.85	35	120	41
13	3	57	2.40	34	1.40	50	96	42
26	3	68	2.15	65	0.95	46	79	36
28	3	66	2.25	65	1.15	52	85	37
Average of grade 3		*63*		*56*		*45*	*94*	*38*

dust exposure. Vital capacity also decreased after dust exposure; these decreases as a percentage of the control value were either of the same order of magnitude or smaller than the changes of FEV_1. The data on dust exposure are subdivided according to each subject's control FEV_1, as shown in table 2. The absolute decrease of FEV_1 was similar in the group with a control FEV_1 greater than 70 per cent of predicted and in the group with a control FEV_1 less than 70 per cent of predicted. As a percentage of the absolute values, the decrease was larger in the group with decreased control FEV_1, but that reflected the low control value rather than the acute effect of the dust.

The most striking finding in the blood gas data was the decrease in Pa_{O_2} in many subjects. This decrease occurred in subjects with normal (greater than 70 per cent of predicted) FEV_1 as well as in those with lower (less than 70 per cent of predicted) FEV_1 (table 2). In Subject 5, a severely disabled man with an FEV_1 of 0.9 liter, Pa_{O_2} decreased from 85 to 30 mm Hg during the course of 2.5 hours of dust exposure. The decrease of Pa_{O_2} during dust exposure was greater in most subjects whose FEV_1 showed a large decline with exposure to dust. There was a significant correlation between the change (Δ) in FEV_1 and ΔPa_{O_2} (table 3). It is interesting that this correlation was particularly pronounced in subjects whose control FEV_1 was normal (greater than 70 per cent of predicted). In the workers with subnormal FEV_1 values under control conditions, ΔFEV_1 still correlated positively

TABLE 2

CHANGES IN FORCED EXPIRATORY VOLUME AND ARTERIAL BLOOD GAS TENSIONS DURING HEMP DUST EXPOSURE IN 26 VOLUNTEER SUBJECTS PREVIOUSLY EMPLOYED IN HEMP FACTORY

Patient No.	Grade	Exposure *(hours)*	ΔFEV_1 *(liter)*	ΔPa_{O_2} *(mm Hg)*	ΔPa_{CO_2} *(mm Hg)*
9 subjects with control $FEV_1 >$ 70% of predicted					
16	0	1.0	−0.17	− 1	+5
3	0	1.0	−0.20	− 2	+2
23	1	1.0	−0.25	−10	+2
18	0	1.25	−0.25	−39	+2
12	1	2.0	−0.35	−61	−4
19	0	2.25	−0.35	−56	+4
11	2	0.75	−0.50	−21	+3
22	1/2	2.75	−0.65	−42	0
1	1	2.5	−0.75	−39	−5
Average		*1.61*	*−0.38*	*−30*	*+1*
17 subjects with control $FEV_1 <$ 70% of predicted					
5	3	2.5	−0.12	−55	− 5
17	2	1.5	−0.28	−18	+ 6
14	1	2.25	−0.30	−22	− 1
20	2	3.0	−0.30	−38	+ 1
8	3	1.0	−0.35	−16	+ 4
10	3	0.25	−0.35	0	− 2
26	3	1.0	−0.35	−11	+ 6
28	3	1.0	−0.35	−11	0
6	3	2.0	−0.40	−55	− 5
9	3	1.0	−0.40	+ 1	+23
13	3	1.0	−0.40	+29	+18
15	0	2.0	−0.40	−65	− 3
21	1	1.5	−0.41	−12	+ 2
4	2	2.5	−0.52	−39	− 1
2	0	2.0	−0.76	−41	+ 1
25	1	1.25	−0.80	−10	+ 3
24	1	2.5	−1.00	− 5	+23
Average		*1.66*	*−0.44*	*−22*	*+ 4*

with ΔPa_{O_2}, but the correlation coefficient ($r = + 0.559$) was significant only at the 5 per cent level.

The changes in Pa_{CO_2} during dust exposure were small and were not of clinical significance in most subjects. In 3 subjects, Pa_{CO_2} reached values greater than 50 mm Hg after dust exposure, with increases of 18 to 23 mm Hg above the control values. Each of these 3 subjects also had a large decrease of FEV_1 during the exposure, and they had low control values of FEV_1 (41, 50, and 66 per cent of predicted). Other subjects with equally poor control lung function and similar FEV_1 decrements during exposure, however, showed only minor changes in their Pa_{CO_2}. In the group as a whole, the change of Pa_{CO_2} correlated ($r = - 0.447$; $P < 0.05$, table 3) with the change of ventilatory capacity, but this probably reflected merely the presence of the 3 subjects in whom both parameters changed markedly.

Several other relationships were examined statistically. There was no significant correlation between age and grades of byssinosis. The decrease of FEV_1 while in dust correlated positively with the time spent in the dusty atmosphere. This time is, however, not an independent variable because the subjects were told to leave the dusty room when their dyspnea became intolerable to them. The decrease of FEV_1 during the total exposure period, therefore, varied with the duration of exposure as well as with the grade of byssinosis. Because the subgroups in the different categories were too small, a meaningful analysis of these relations was not possible.

TABLE 3

CORRELATIONS BETWEEN BLOOD GAS CHANGES AND VENTILATION CHANGES DURING ACUTE HEMP DUST EXPOSURE IN WORKERS WITH CONTROL ONE-SECOND FORCED EXPIRATORY VOLUMES GREATER THAN AND LESS THAN 70 PER CENT OF PREDICTED

	Control FEV_1		Total Group
	>70% Predicted	<70% Predicted	
r for ΔFEV_1 *vs* ΔPa_{O_2}	+ 0.845*	+ 0.559†	+ 0.654*
r for ΔFEV_1 *vs* ΔPa_{CO_2}	0**	− 0.549†	− 0.447†

*$P < 0.01$.
†$P < 0.05$.
**$\Sigma xy = 0$; see table 2.

Discussion

The subjects of this study were hemp workers who had not worked in the dusty work rooms for at least 3 years. Some of them did not remember any previous symptoms of byssinosis, but they responded to dust exposure in the present study with a large decrease of FEV_1 and with chest tightness and dyspnea. It is well known that the symptoms and changes of lung function in byssinosis are more pronounced after prolonged absence from work (13). The severe function changes in many subjects were most likely due, in part, to the long absence from the dusty environment. The acute effects of hemp dust on the lungs offered a unique opportunity for a study of acute changes in blood gases under relatively well controlled conditions.

Only a few of the subjects (7 of 26) had control FEV_1 values within the normal range (80 to 120 per cent of predicted; table 1). Values for VC were even less, although this might have been due, in part, to the use of the normal values of the European Community for Coal and Steel Study (12). The validity of this standard for Spanish populations has not been tested adequately, and it is likely that the normal values for VC were too high for this group.

Arterial oxygen tensions often decreased markedly during dust exposure, whereas Pa_{CO_2} increased more than 6 mm Hg in only 3 subjects. These gas tension changes correlated significantly with the changes of FEV_1 during the same dust exposure during the same period of time in the same subjects (tables 2 and 3). There was no systematic difference between subjects with control FEV_1 that were almost normal and those with lower FEV_1 values; within both groups, the decrease of Pa_{O_2} was larger in the subjects with larger ΔFEV_1 during dust exposure. The correlation between ΔFEV_1 and ΔPa_{O_2} was most significant among the small group with control FEV_1 greater than 70 per cent of predicted.

Changes in arterial blood gas tensions were not measured during a control period in the same subjects. In resting man at sea level, Pa_{O_2} values do not show spontaneous variations of the magnitude seen in the present study (14). It was not considered warranted to perform another series of arterial punctures in the same subjects. The absence of such control data was a drawback of the present study, but it was not believed that this invalidated the conclusions.

A decrease of Pa_{O_2}, combined with a small increase of Pa_{CO_2} occurs when ventilation-perfusion relationships in the lungs are drastically altered. This is illustrated in figure 1, using an alveolar ventilation/perfusion ratio ($\dot{V}_A/Q$) line in the oxygen-carbon dioxide diagram of Rahn and Fenn (14). The curve was drawn for specific conditions of inspired and mixed venous gas tensions and is therefore only valid for these conditions. Here it serves to illustrate the nature of the blood gas changes found.

Before dust exposure, the typical composition of alveolar gas is indicated by point A, where the $\dot{V}_A/Q$ ratio is 1.5. The corresponding arterial gas tensions are indi-

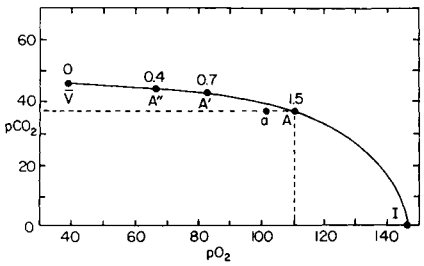

Fig. 1. Oxygen-carbon dioxide diagram of Rahn and Fenn with alveolar ventilation/perfusion ratio ($\dot{V}A/Q$) line (14). I = composition of inspired air. V = composition of mixed venous blood. For further description, see text.

cated by point a, where A-a is the alveolar-arterial oxygen tension difference. During dust exposure, the ventilation of many lung units decrease because their airways become obstructed by airway smooth muscle contraction and possibly by additional mechanisms. As a result, the ventilation of the lungs becomes less uniform, and the $\dot{V}A/Q$ ratio of many lung units decreases considerably. The mean $\dot{V}A/Q$ ratio of the blood that left the lungs might have decreased to values less than 0.4 (A″) in severe cases. Other lung units may maintain or even increase their $\dot{V}A/Q$ ratios, but these do not exert a major effect on the arterial blood because these units with high $\dot{V}A/Q$ probably occupy a small alveolar volume, and second, they probably account for only a small proportion of the pulmonary blood flow. As a result, the preponderant effect seen in the analysis of arterial blood was the decrease of $\dot{V}A/Q$ ratios resulting in a large decrease of Pa_{O_2} and small increase of Pa_{CO_2}. It is clear that gas exchange is often altered drastically during dust exposure, and that these changes can be adequately explained in terms of the shape of the $\dot{V}A/Q$ curve of Fenn and Rahn. The exact shape and position of the $\dot{V}A/Q$ line depends on several variables, such as blood hemoglobin content and acid-base status. This might explain some of the individual variability in the present data. The high control Pa_{O_2} in some subjects was probably related to hyperventilation. The increased Pa_{O_2} and Pa_{CO_2}, after exposure, in Subject 13 were unexplained and might have been due to a technical error in the postdust measurement. Because short-term changes in blood gas tensions were studied, it is not likely that significant changes of hemoglobin or carbon dioxide content in arterial blood influenced the changes in gas tensions during dust exposure. Because only some of the subjects performed physical work during dust exposure, it is also unlikely that differences in alveolar ventilation or cardiac output, or both, between the pre- and postexposure sampling periods had a systematic influence on the results.

Previous studies with the nitrogen washout technique have shown that inhalation of cotton dust (15), flax dust (16), and cotton dust extracts (17) leads to pronounced nonuniform distribution of inspired gas. It is likely that such increased ventilatory nonuniformity can explain most of the present findings. Decreases of $\dot{V}A/Q$ ratios in peripheral lung units would occur if the dust caused vasodilation of pulmonary blood vessels in lung regions where ventilation was decreased through airway obstruction. At the present time, however, there is no evidence of any effect of textile dusts on the pulmonary circulation. It is therefore suggested that the present findings of a large decrease in Pa_{O_2} with concurrent decreases of FEV_1 reflected reversible obstruction of small airways in peripheral lung units caused by an agent in the dust that induced obstruction of small airways (17).

This conclusion also fits in with the finding that ΔFEV_1 and ΔPa_{O_2} correlated best in the group with relatively normal control values of FEV_1. These subjects presumably had a relatively uniform distribution of ventilation before exposure, and dust-induced changes were therefore pronounced. On the other hand, the men with low FEV_1 probably already had some degree of abnormal gas distribution under control conditions, and the effects of dust exposure would therefore not have been as marked as in the other men.

The present study has established that the acute response to textile dust exposure was not merely accompanied by dyspnea and changes of FEV_1. These mechanical distur-

bances are associated with pronounced alterations in gas exchange, often causing severe decreases in Pa_{O_2} in men whose FEV_1 decreased from 0.12 to 1.0 liter. This reinforces a recent recommendation (18) that persons whose FEV_1 regularly decreases 0.20 liter or more while working in risk areas in the textile industry should be removed from these areas and given other, nondusty jobs. Hypoxia can lead to dangerous decrements in performance, and promotes ischemia of the heart and other organs. Environments that induce arterial hypoxemia should be considered hazardous to the worker.

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