Chronic Respiratory Disease in Hemp Workers*

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Respiratory symptoms, smoking habits and ventilatory capacity ($FEV_{1.0}$) were studied in 216 active and retired hemp workers (22.8 per cent of a defined population) and 285 control subjects (farmers, and men from other industries), in and near Callosa de Segura, Spain, formerly a center of soft hemp (Cannabis sativa) processing. The twenty to forty-nine year old hemp workers did not differ from control subjects in that age group. The fifty to sixty-nine year old hemp workers had an extremely high prevalence of chronic cough and phlegm, dyspnea and irreversible pulmonary function loss, compared to control subjects of the same age group. About two thirds of these men had a one second forced expiratory volume ($FEV_{1.0}$) of less than 80 per cent of the expected value; 18.5 per cent were severely disabled by ventilatory insufficiency, with an $FEV_{1.0}$ of 1.00 L. or less. Of the fifty to sixty-nine year old workers, 91 per cent had a history of Monday dyspnea while at work in hemp. Most men without such a history ("nonreactors") had a normal $FEV_{1.0}$ and few symptoms even after a lifetime of exposure to dust.

The chronic and disabling respiratory disease of hemp workers cannot be explained by smoking habits and is attributed to heavy and prolonged exposure to hemp dust. Apparently byssinosis, a disease caused by exposure to hemp and other textile (cotton, flax) dusts, progresses from acute, short-lasting effects of dust exposure (Monday dyspnea) to chronic and permanent lung damage. In view of this progression and the known causal agent, we prefer to diagnose byssinosis, grade 3, rather than unspecified chronic bronchitis in these older hemp workers. Inclusion of retired workers was essential to determine the extent of the problem in Callosa, since the active hemp workers were a self-selected group with less disease.

INHALATION of dust produced during processing of soft hemp fibers (Cannabis sativa) causes acute symptoms of byssinosis in workers engaged in manual batting and hackling of hemp. Previous studies [*1,2*] also showed a high prevalence of chronic respiratory symptoms and irreversible pulmonary function loss among small groups of older retired workers.

Artificial fibers are now replacing soft hemp in most of its applications, and the industry is disappearing, at least in Europe. Further study of hemp byssinosis seemed worthwhile mainly because of its possible importance to the knowledge of cotton workers' byssinosis, which is still widely prevalent in many countries [*3,4,8*].

The hemp trade in Callosa de Segura, Spain,

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employed about 8,000 persons in 1947. Although the trade is now of minor, and still decreasing importance, the town offered a unique opportunity to study the development of chronic lung disease among men who had been exposed to hemp dust for many years.

SUBJECTS AND METHODS

This study was conducted in Callosa de Segura, Spain, during June–August 1967. The working conditions in the Callosa hemp industry have been described previously [*1*]. The methods used were similar to those described before [*2*]. The questionnaire on respiratory symptoms was adapted for coding on punch cards to facilitate data processing by an IBM 1130 computer, to obtain average values, correlation coefficients, analysis of co-variance and χ^2 tests according to standard statistical methods [*3*].

Definitions. As in the previous study [*2*] respiratory symptoms were defined as follows:

Persistent cough and/or phlegm: cough or phlegm production on most days for at least three months each year.

Dyspnea grade 2+: shortness of breath when hurrying on the level, or worse.

Dyspnea grade 4: shortness of breath when walking at own pace on the level.

Dyspnea grade 5: shortness of breath when dressing in the morning.

Past illness from chronic bronchitis: history of chest illness with increased sputum production within the last two years, or history of chronic chest trouble diagnosed as chronic bronchitis by a physician.

Byssinosis grades: 0.5 = occasional chest tightness on Mondays; 1 = chest tightness or difficulty in breathing or both on every Monday at work; 2 = chest tightness or difficulty in breathing or both during work on Mondays and other working days. In retired workers, the byssinosis grade was based on the history of symptoms when last at work in hemp.

Observer Variation. Altogether, six interviewers took part in the study, but two of them saw fewer than twenty persons each. The prevalence of symptoms recorded by the other four interviewers, in the age group fifty to sixty-nine years old, did not differ significantly.

Pulmonary Function. The one second forced expiratory volume ($FEV_{1.0}$) was measured in all subjects with direct reading spirometers with transistorized timers (Poulton & Co., Barry, Glamorgan, U.K.). The mean of the two highest of five measurements was used as the result. This was compared to the expected $FEV_{1.0}$ value according to the V.A. nomogram [*6*], using age at nearest birthday and standing height (without shoes). If the measured value was less than 80 per cent of the expected value, the $FEV_{1.0}$ measurement was repeated fifteen to twenty minutes after inhalation of an isoproterenol-phenylephrine mixture from a pocket nebulizer (Duo-Medihaler®).

TABLE I
CATEGORIES OF HEMP WORKERS

Status	Retired		Active		Disabled		Total
Age (yr.)	20–49	50–69	20–49	50–69	20–49	50–69	
Batters (no.)	222	103	5	2	0	9	341
Hacklers (no.)	450	131	14	7	0	6	608
Spinners (no.)	280	44	19	7	1	2	353
Others (no.)	0	1	6	3	0	0	10
Total (no.)	952	279	44	19	1	17	1,312

NOTE: Retired = No longer employed in the soft hemp industry on June 20, 1967. Active = Employed in the soft hemp industry on June 20, 1967. Disabled = Men awarded a pension for disability attributed to occupational exposure to hemp dust.

Procedure. Since our first study in 1965, the hemp industry in Callosa had contracted further. Several small plants (including plant A on which we reported previously [*2*]) had been closed. A large percentage of the younger male working population is regularly employed in the car industry or in agriculture, elsewhere in Spain, in France and in other Western European countries.

For selection of subjects we used a list of 1,312 men now or previously employed in the Callosa hemp industry (Table 1). We decided to limit our study to those who are or were manual batters or hacklers, since these are the workers most affected by byssinosis [*2*]. The large majority of these men had transferred to types of employment other than hemp work and these are classified as "retired" in Table 1.

Two samples, A and B, of 100 names (twenty in each age decade from twenty to sixty-nine years) were drawn at random from the main list. Thus, 40 per cent of the men in samples A and B were fifty to sixty-nine years old. This overrepresentation of older men in the samples (compare with Table 1) was intentional. We did not want to study the "average" hemp worker, but we wanted to follow the evolution of disease by comparing men in each age decade with control subjects in the same age group. All men in sam-

TABLE II
COMPOSITION OF TWO SEPARATE RANDOM SAMPLES OF HEMP WORKERS

Sample	Age Group (yr.) 20–39	40–59	60–69	Total No. Seen	No. Deaths	No. Absent*	No. Refusals	Total No. in Sample
A	24	28	17	69	5	23	3	100
B	19	30	16	65	4	27	4	100
Total	43	58	33	134	9†	50	7	200

* Includes men who could not be located or who resided elsewhere at the time of study.
† One of byssinosis and four of other lung diseases.

ples A and B were either seen and studied, or the reason for their absence (mainly death or departure from town) was investigated. Home visits were made to reluctant men; refusals were few (Table II).

As control subjects we first used seventy-nine agricultural workers from the same town (group C). These were, in part, volunteer subjects who were invited to participate when they happened to visit the trade union office. Others were selected at random from a list of men employed in farming. Since several of these men had worked with hemp at some time, mostly in the field, other control groups were studied as well. These were (1) a group of thirty-eight agricultural workers seen in another village, Rafal, in 1965, described previously (group D, [2]); (2) 168 workers in a marble-cutting factory (group E) and a shoe factory (group F) in a third town, Monóvar. In groups E and F, the total male population between twenty and sixty-nine years of age, at work on the day of study, was studied.

Previous experience led us to expect to find many disabled older men among the hemp workers. We therefore also solicited participation of active or retired batters or hacklers aged fifty to sixty-nine years not included in the two random samples, without random selection. In this way a total of 146 of the 258 men (51.8 per cent) in this age and job category were seen, compared to seventy of 691 (10.1 per cent) in the age group twenty to forty-nine years.

RESULTS

Respiratory Symptoms. The average prevalence of symptoms and the smoking habits among all men seen are summarized in Table III. Of the 200 men in the two random samples of hemp workers 33 per cent were not seen, mostly because of death or absence from town (Table II). Of the 141 men in the samples who resided permanently or temporarily in or nearby Callosa at the time of study, 95 per cent were seen.

The men in the random samples A and B did not differ with regard to the high prevalence of respiratory symptoms. Since the age distributions within these two samples were also similar (Table II), the two groups were pooled for comparison with the control subjects. Among the control groups, the farm workers in Callosa de Segura (group C) had a significantly higher

TABLE III

CHRONIC RESPIRATORY SYMPTOMS AND SMOKING HABITS AMONG HEMP WORKERS AND CONTROL SUBJECTS

Group	No.	Age (yr.)	Persistent Cough (%)	Persistent Phlegm (%)	Dyspnea Grade 2+ (%)	Dyspnea Grades 4–5 (%)	Past Illness from Chronic Bronchitis (%)	Smoking Habits (gm./wk.) 0 (%)	<50 (%)	>50 (%)	Ex (%)	Cigar and Pipe (%)
(1) Control Subjects												
C	79	47.1	33*	38*	45‡	11†	11‡	13†	8‡	62‡	16‡	1
D§	38	40.4	11	13	18	3	0	13	8	63	8	0
E	92	45.8	12	18	30	3	5	25	18	47	9	1
F	76	43.3	18	20	28	3	7	33	14	47	4	1
(2) Hemp Workers												
A	69	45.8	41‡	49‡	51‡	22‡	32‡	26‡	10‡	46‡	16‡	2‡
B	65	47.4	43	52	55	20	46	17	18	42	20	3
(3) Combined Hemp Workers and Controls												
C+D+E+F	285	44.8	19#	24#	32#	5#	7#	22‡	13‡	54‡	9‡	1
A+B	134	46.5	42	51	54	21	39	22	14	44	18	2

NOTE: Groups A, B = randomly selected hemp workers in Callosa de Segura; group C = farm workers in Callosa de Segura; group D = farm workers in Rafal; group E = marble workers in Monóvar; group F = shoe workers in Monóvar. Significance (χ^2) tests for (1) are for comparison within the control groups (C+E+F). Significance tests for (2) are for comparison of hemp worker groups A and B. Significance tests for (3) are for comparison of all hemp workers with all control subjects.

* $p < 0.01$.

† $p < 0.05$.

‡ Not significant.

§ Smoking habits not recorded in three subjects (8 per cent). This group not included in χ^2 test because of too small expected prevalences.

# $p < 0.005$.

prevalence of most chronic respiratory symptoms; this group also included fewer nonsmokers. Group D was omitted from this comparison within the control groups since their numbers in most categories were too small.

χ^2 tests revealed no significant differences between hemp workers and control subjects with regard to smoking habits. However, the hemp workers had significantly more respiratory symptoms and dyspnea. One fifth of the hemp workers said they were short of breath at rest or during slight exertion (dyspnea grades 4 and 5), whereas only 5 per cent of the control subjects were similarly disabled. These dyspnea grades refer to shortness of breath in the absence of dust exposure.

Hemp workers and control subjects at different ages: The increased prevalence of respiratory symptoms among hemp workers occurs primarily among the older men (Tables IV and V). For men aged twenty to forty-nine years the prevalence of symptoms does not differ significantly between hemp workers and controls (Table IV), although there is a trend towards more symptoms among the forty to forty-nine year old hemp workers. Smoking habits, likewise, do not differ between hemp workers and controls up to age forty-nine.

Among the men aged fifty to sixty-nine years, the prevalence of symptoms and the smoking habits among the randomly selected hemp workers (A and B) are compared with those among the hemp workers who were not thus selected (G and H; Table IV). No significant differences existed between these two groups. Within the various control groups the prevalence of symptoms and the smoking habits were also similar. Therefore, the results in all hemp workers aged fifty to sixty-nine years were pooled and com-

TABLE IV

CHRONIC RESPIRATORY SYMPTOMS AND SMOKING HABITS AMONG HEMP WORKERS AND CONTROL SUBJECTS AT DIFFERENT AGES

Group*	No.	Average Age (yr.)	Persistent Cough (%)	Persistent Phlegm (%)	Dyspnea Grade 2+ (%)	Dyspnea Grades 4–5 (%)	Past Illness from Chronic Bronchitis (%)	Smoking Habits (gm./wk.) 0 (%)	<50 (%)	>50 (%)	Ex (%)	Cigar and Pipe (%)
Age 20–39 Years												
Controls	75	32.7	21†	24†	19†	1‡	3‡	27†	11†	57†	5†	0
Hemp workers	43	29.8	14	16	21	2	12	28	9	49	14	0
Age 40–49 Years												
Controls	83	43.9	12†	18†	27†	5‡	10‡	27†	28†	39†	7†	0
Hemp workers	27	43.1	26	33	41	4	26	19	19	56	7	0
Age 50–69 Years												
Hemp workers (A+B)	64	59.2	67†	81†	81†	41†	61†	12†	16†	36†	31†	5
Hemp workers (G+H)	82	60.0	72	70	84	34	62	20	22	30	22	6
Age 50–69 Years												
Controls	99	57.3	26§	31§	55§	11§	9§	18†	5§	60§	14§	3
All hemp workers (A+B+G+H)	146	59.6	70	75	83	37	62	16	19	33	26	5

* Hemp workers (A+B): persons included in random samples A and B. Hemp workers (G+H): persons who were not randomly selected; fifty to fifty-nine years (G) and sixty to sixty-nine years old (H). Tests of significance (χ^2) were performed for comparison of controls and all hemp workers within each age group, and of hemp workers A+B versus G+H. Other significance tests: Past illness from chronic bronchitis in twenty to forty-nine year old hemp workers versus controls not significant; cough, phlegm, dyspnea 2+ and smoking habits within fifty to sixty-nine year old controls (groups C, E and F), all not significant.

† Not significant.

‡ Not tested because of too low expected prevalences.

§ $p < 0.005$.

TABLE V

SMOKING HABITS AND RESPIRATORY SYMPTOMS AMONG MEN AGED FIFTY TO SIXTY-NINE YEARS

Group	No.	Average Age (yr.)	Persistent Cough (%)	Persistent Phlegm (%)	Dyspnea (%)		Past Illness from Chronic Bronchitis (%)
					Grade 2+	Grade 4–5	
Non- and Light Smokers (<50 gm./week)							
(1) Controls	20	56.3	10 *	15 *	35 *	10 †	15 *
(2) Hemp workers	52	59.0	69	63	81	34	63
Moderate and Heavy Smokers (>50 gm./week)							
(3) Controls	52	57.7	31 *	37 *	63 †	10 ‡	10 *
(4) Hemp workers	47	58.9	66	74	81	30	51
Ex-Smokers							
(5) Controls	14	57.6	36 ‡	36 *	71 †	14 †	21 *
(6) Hemp workers	38	61.2	79	87	87	45	79

NOTE: Controls: groups C, E, and F (described in text). Pipe and cigar smokers excluded from all groups. There were no significant differences between controls (1), (3) and (5), or between hemp workers (2), (4) and (6) (χ^2 test). Significance of differences between controls and hemp workers in each smoking category.

* $p < 0.005$.

† *Not significant.*

‡ $p < 0.01$.

pared with those in the combined control groups. This comparison shows a highly significant difference with respect to all symptoms, as well as significant differences in smoking habits. All respiratory symptoms are more prevalent among the hemp workers; 37 per cent of these men said they were short of breath during slight exertion. Fewer of them were heavy smokers, and 26 per cent had stopped smoking cigarettes, many on doctor's orders or because they thought that smoking increased their symptoms. The men fifty to sixty-nine years of age are compared with respect to occupation and smoking history in Table v. The χ^2 test showed no significant differences among the hemp workers in the three smoking categories for the prevalence of persistent cough and phlegm, past illness from chronic bronchitis and dyspnea. When the hemp workers are compared with the controls within each category of smoking, the prevalence of most symptoms is significantly higher among the hemp workers. Although smoking habits do not seem to affect the prevalence of symptoms among the hemp workers, such an effect seems to be present among the controls. The heavier smoking control subjects and the ex-smokers have more symptoms than the control subjects who do not smoke or smoke less. However, the difference is not statistically significant.

Byssinosis: history of symptoms on Monday (*Table* VI). In all men seen inquiries were made about the occurrence of such symptoms as chest tightness or breathing difficulty on Mondays or on any other workdays. None of the controls had such symptoms. Since most hemp workers (90 per cent) in the random samples A and B and in groups G and H were no longer active in the trade, most answers referred to symptoms experienced in the past. Of all the hemp workers 87 per cent admitted to having had dyspnea on Mondays while at work. This percentage was significantly higher among the older men. The thirteen men aged fifty to sixty-nine years who

TABLE VI

HISTORY OF SYMPTOMS ON MONDAY AMONG HEMP WORKERS

Age Group (yr.)	Negative		Positive		Total
	No.	%	No.	%	(No.)
20–49	15	21	55	79	70
50–69	13	9	133	91	146
Total	28	13	188	87	216

NOTE: χ^2 test: 5.45; $p < 0.05$.

TABLE VII
RESPIRATORY SYMPTOMS AND BYSSINOSIS IN ACTIVE HEMP WORKERS IN 1965 AND 1967

Data	1965	1967
No.	13	37
Age (yr.)		
Mean	45	41
Range	37–61	18–61
Exposure (mean, yr.)	28	27
Byssinosis grade		
0	1(8%)	13(35%)*
0.5–1–2	12(92%)	24(65%)*
Persistent cough (%)	38	43*
Persistent phlegm (%)	69	62*
Dyspnea grade 2+ (%)		
Weekend	46	38*
Monday	92	49†
Past illness from chronic bronchitis (%)	46	13†
Smoking		
gm. per week	94	103
% nonsmokers	38	57*

NOTE: 1965 data from Bouhuys et al. [2]. gm. per week smoking = average for smokers only. Difference between 1965 and 1967 data: * Not significant (χ^2 test); † $p < 0.05$.

had never had dyspnea on Mondays also had fewer chronic respiratory symptoms than their contemporaries with such symptoms in the past.

Random samples and labor migration. A large number of men from Callosa de Segura have their permanent residence abroad or elsewhere in Spain. Absence from town, because of this labor migration, was the main reason why only 67 per cent of all men in the random samples were seen. However, the 134 men from samples A and B whom we did see include forty-four men who stayed in Callosa temporarily, for holidays, but had their permanent residence elsewhere. These forty-four migrants had fewer respiratory symptoms than residents, at similar ages, but the migrants also had fewer years of exposure to hemp dust. When the migrants were compared with residents matched for duration of exposure and age, no difference was found between the two groups, both with respect to symptoms and to the prevalence of low $FEV_{1.0}$ values.

Family history of respiratory disease: A large number of hemp workers said that one or more relatives (parents, siblings or own children) had asthma, bronchitis or both. Among the 134 men in samples A and B, fifty-eight men (43 per cent) gave such a history. However, the majority of these affected relatives worked in hemp. When these were excluded, only nine men (7 per cent) gave a history of asthma or bronchitis among their relatives, probably not related to exposure to hemp dust. Thus, a predisposition towards the development of asthma or bronchitis may exist only in a small minority of the hemp workers.

Active workers: We interviewed thirty-seven hemp batters and hacklers still active in the trade, fifteen of whom were included in sample A, B, G or H. These men work in several small hemp plants or in shops in their own home. The data in these men were compared to those obtained in active workers in 1965 (Table VII). The men active at present are slightly younger and thirty-five per cent have never experienced symptoms on Monday (versus 8 per cent in the 1965 group). They have also had less illness from chronic bronchitis, but the prevalence of other respiratory symptoms is similar for the two

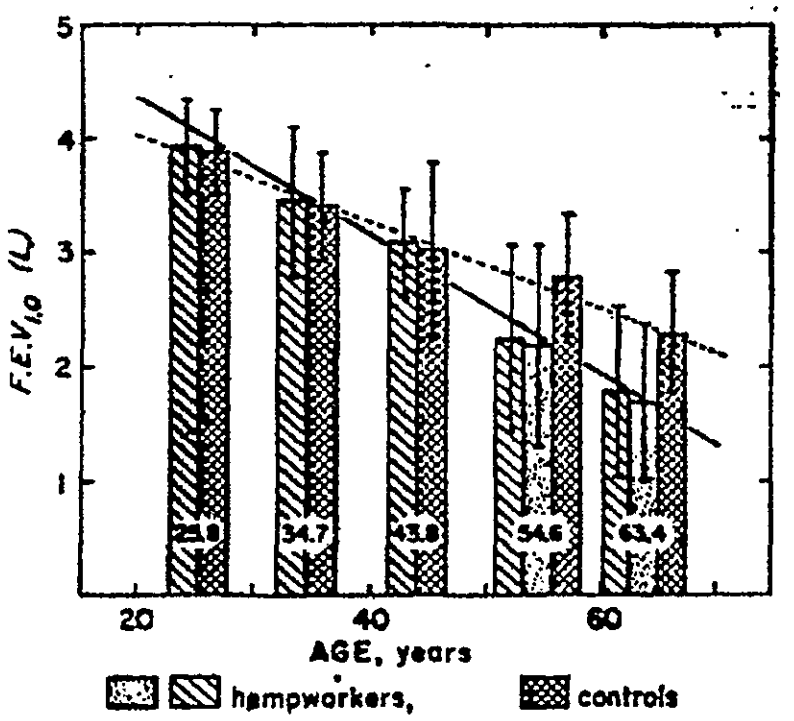

FIG. 1. Bars: mean $FEV_{1.0}$, adjusted for age (at average age shown, for each ten year group, within the bars) and for height (165 cm.). Hatched bars: hemp workers in samples A and B. Gray bars: hemp workers in groups G and H (see Table IV). Cross-hatched bars: control groups C, D, E and F. Lines: broken line, regression of $FEV_{1.0}$ on age, height 165 cm., in control subjects; drawn line, similar for hemp workers. Regression equations: Controls: $FEV_{1.0} = -1.689 + 0.039(\pm 0.010; p = 0.95) \times$ height (cm.) $- 0.038(\pm 0.006; p = 0.95) \times$ age (years). Hemp workers: $FEV_{1.0} = -2.938 + 0.051(\pm 0.017; p = 0.95) \times$ height (cm.) $- 0.059 (\pm 0.009; p = 0.95) \times$ age (years). Terms in brackets are ranges of variation of each of the four coefficients for a probability of 0.95. That is, there is 5 per cent or less chance that the coefficients exceed this range. Difference between mean adjusted $FEV_{1.0}$ for hemp workers and controls aged fifty to sixty-nine years: $F = 38.04$, $p < 0.005$. The similar differences for men aged twenty to forty-nine years are not significant.

groups. Among the men now active fewer have symptoms on Monday than their retired colleagues of the same age, seen in the present study. However, the numbers in each group are too small for detailed analysis.

Pulmonary Function. An analysis of co-variance for $FEV_{1.0}$ as a function of age and standing height was made for the total material and for several subgroups. There were no differences between the hemp worker groups (A and B) or between the control groups (C, D, E and F). Accordingly, these data were pooled into two groups. In Figure 1 the regression data are compared for groups A and B versus groups C, D, E and F. The regression coefficient of $FEV_{1.0}$ on age differed significantly ($F = 12.98$; $p < 0.005$) between controls and hemp workers. $FEV_{1.0}$ decreases more with age among the hemp workers than among the controls.

Within each age decade the effect of age on $FEV_{1.0}$ is no longer different between the controls and hemp workers. Analysis of variance shows that, after removal of the variation due to regression on age and height, the mean adjusted $FEV_{1.0}$ differs significantly between hemp workers and controls in the decades fifty to fifty-nine and sixty to sixty-nine years, but not in the lower decades (Fig. 1). The mean adjusted $FEV_{1.0}$ among the older hemp workers was similar for the randomly selected men (A, B) and the others (G, H).

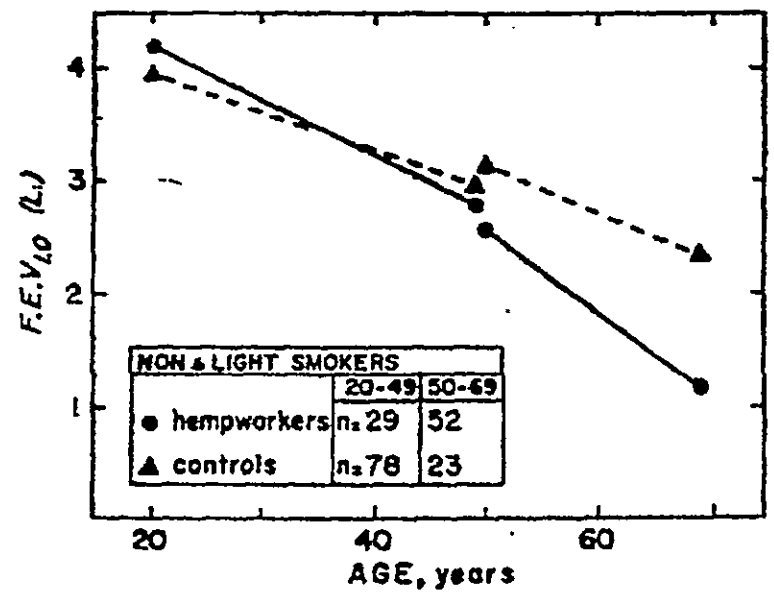

FIG. 3. Regression of $FEV_{1.0}$ on age (for height 165 cm.) in non- and light smokers aged twenty to forty-nine and fifty to sixty-nine years. Drawn lines: hemp workers; broken lines: controls. The slopes of the equations, within each age group, do not differ significantly. The mean adjusted $FEV_{1.0}$ for men aged twenty to forty-nine years is similar for controls and hemp workers ($F = 0.10$; $p > 0.25$); for men aged fifty to sixty-nine years the adjusted $FEV_{1.0}$ values differ significantly ($F = 17.33$; $p < 0.005$).

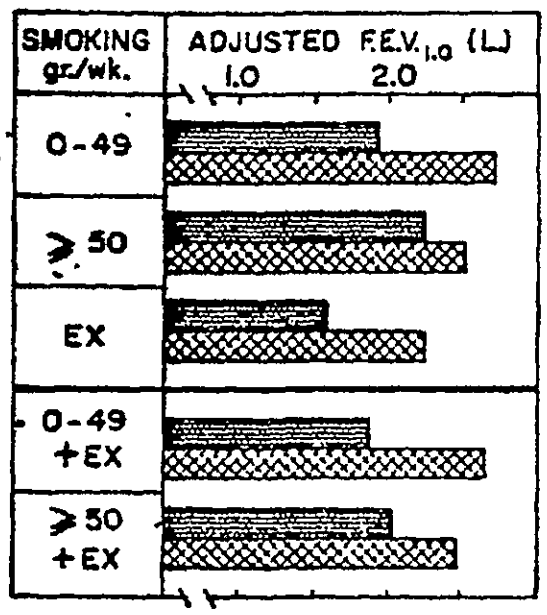

FIG. 2. Mean adjusted $FEV_{1.0}$ (for age fifty-nine years and height 165 cm.) for men fifty to sixty-nine years old, in different smoking categories. Differences between hemp workers and controls are significant in all five categories ($p < 0.025$ to $p < 0.005$). Other significance tests: *Controls:* 0–49 *vs.* ≥50, $p < 0.05$; 0–49 *vs.* Ex, $p < 0.01$; ≥50 *vs.* Ex, not significant; 0–49 + Ex *vs.* ≥50 + Ex, $p < 0.025$. *Hemp workers:* 0–49 *vs.* ≥50, $p < 0.025$; 0–49 *vs.* Ex, not significant; ≥50 *vs.* Ex, $p < 0.005$; 0–49 + Ex *vs.* ≥50 + Ex, not significant. 0–49 and ≥50 indicate present smoking in grams week. Ex = ex-smokers. 0–49 + Ex and ≥50 + Ex indicate all men who now smoke *or* used to smoke 0–49 or ≥50 grams per week, respectively.

We also analyzed the $FEV_{1.0}$ data with respect to smoking habits. In neither smoking category did the regression analysis for $FEV_{1.0}$ on age and height show any significant difference between the twenty to forty-nine year old controls and hemp workers. In contrast, hemp workers aged fifty to sixty-nine years had a significantly lower $FEV_{1.0}$ (after removal of the effect of age and height) than control subjects in the same smoking category. This was true regardless of the manner of grouping, i.e., whether considering ex-smokers as a separate group (Fig. 2, upper half) or whether including them with men of similar habits who still smoked (Fig. 2, lower half).

A surprising feature of the data in Figure 2 is that moderate to heavy smoking hemp workers have a significantly higher $FEV_{1.0}$ than the non-smoking or light-smoking hemp workers. Among the hemp workers the ex-smokers have a much lower $FEV_{1.0}$ than those who still smoke. A

TABLE VIII

ACTUAL $FEV_{1.0}$ VERSUS EXPECTED VALUES IN CONTROL SUBJECTS AND HEMP WORKERS

Group	No.	$FEV_{1.0}$ <80% of Expected (%)	$FEV_{1.0}$ <50% of Expected (%)
	Age 20–39 Years		
Controls	75	4	0
Hemp workers	43	5	0
	Age 40–49 Years		
Controls	83	7	2
Hemp workers	27	15	0
	Age 50–69 Years		
Controls	89	24	4
Hemp workers	146	61*	31*

NOTE: Expected values from Veterans Administration nomogram [6].

* $p < 0.005$.

complete statistical analysis of the relations between smoking, exposure to hemp dust and $FEV_{1.0}$ is reported elsewhere [7].

The effect of exposure to hemp dust *per se* appears most clearly from the $FEV_{1.0}$ data obtained in men who never smoked more than 49 gm. per week (Fig. 3). Between ages twenty and forty-nine years there is no significant difference between controls and hemp workers, but between ages fifty and sixty-nine years the hemp workers have a much smaller $FEV_{1.0}$ than the control subjects. In both age categories the slopes of the regression lines are not significantly different.

Forced expiratory volume compared to expected values: The $FEV_{1.0}$ data were also individually compared to the values expected for age and standing height, from the Veterans Administration nomogram [6]. This allows an analysis in terms of the number of persons with a low $FEV_{1.0}$ among specific subgroups. The percentage of those with low $FEV_{1.0}$ values was similar for the randomly selected older hemp workers and the other hemp workers in age group fifty to sixty-nine; these have therefore been combined in Table VIII. Of the older hemp workers 31 per cent have an $FEV_{1.0}$ less than half the expected value, compared to only 4 per cent of the control subjects of that age. None of the controls, but 18.5 per cent of 146 hemp workers, aged fifty to sixty-nine years, had an $FEV_{1.0}$ of 1.00 L. or less.

Effect of isoproterenol on $FEV_{1.0}$: With few exceptions, men with an $FEV_{1.0}$ less than 80 per cent of expected were given isoproterenol by inhalation, and their $FEV_{1.0}$ was determined again after twenty to thirty minutes. The average increase in $FEV_{1.0}$ induced by isoproterenol was small, and similar for all men with a low $FEV_{1.0}$, whether control subjects or hemp workers (Table IX). The loss in pulmonary function in those with a low $FEV_{1.0}$ seems to be mostly irreversible by a single bronchodilator treatment.

Duration of exposure to hemp dust and $FEV_{1.0}$. An analysis of multiple correlation for $FEV_{1.0}$ with respect to age, height and numbers of years of exposure to hemp dust in the industry showed that the duration of exposure had no significant effect on $FEV_{1.0}$. Nearly all men entered the trade at about the same age (twelve to seventeen years). Duration of exposure and age correlated significantly ($r = +0.89$). Therefore, the effects of age and of duration of exposure are indistinguishable.

$FEV_{1.0}$ and history of dyspnea on Monday: The majority of hemp workers aged fifty to sixty-nine years had an $FEV_{1.0}$ less than 80 per cent of the expected value (Table VIII). Among these were thirteen men who had never had symptoms of byssinosis (Table VI). Of these thirteen men eleven (85 per cent) had an $FEV_{1.0}$ more than 80 per cent of the expected value, i.e., a presumably normal value for their age and height, compared to only 34 per cent among those who did have symptoms on Monday. This difference is significant (Table X).

COMMENTS

Our previous study in Callosa de Segura [2] led us to suspect that there are many respiratory cripples in that town, and that exposure to hemp dust is the most likely cause of the high prevalence of chronic respiratory disease. These

TABLE IX

EFFECT OF ISOPROTERENOL IN MEN WITH DECREASED FORCED EXPIRATORY VOLUMES

Group	No.	Average Control $FEV_{1.0}$ (L.)	$\Delta FEV_{1.0}$ L.	$\Delta FEV_{1.0}$ % Increase
	Age 40–49 Years			
Controls	5	1.92	+0.15	7.8
Hemp workers	4	2.32	+0.19	8.2
	Age 50–69 Years			
Controls	20	1.63	+0.21	12.9
Hemp workers	87	1.25	+0.11	8.8

NOTE: $\Delta FEV_{1.0}$ = increase of $FEV_{1.0}$ after isoproterenol administration.

TABLE X

$FEV_{1.0}$ AND HISTORY OF DYSPNEA ON MONDAY AMONG HEMP WORKERS AGED FIFTY TO SIXTY-NINE YEARS

History of Monday Symptoms	$FEV_{1.0}$ >80% of Expected No.	%	$FEV_{1.0}$ <80% of Expected No.	%	Total No.
No. with symptoms on Monday at present or in past	45	34	88	66	133
No. who never had symptoms on Monday	11	85	2*	15	13
Total no.	56		90		146

NOTE: χ^2: $p < 0.005$.

*One nonsmoker, one light smoker (<50 gm. per wk.); FEV_1 = 65 and 68 per cent of expected.

suspicions have been confirmed by the present study.

Our conclusions may be in error if the methods of selection led to overrepresentation of diseased subjects among the hemp workers or of healthy subjects among the control groups. Such factors are difficult to exclude in transsectional population studies, but we believe they do not operate to any marked extent in our study. Some possible sources of errors will now be discussed.

The results obtained among four different control groups (C, D, E and F) were similar, except for a higher prevalence of some symptoms and a lower percentage of nonsmokers among group C. Control group C and the hemp worker groups G and H (fifty to sixty-nine years old) were selected similarly; the prevalence of symptoms is much greater among the latter than among the farm workers in group C. The higher prevalence of symptoms in control group C than among the other control groups may be due to occasional exposure to hemp dust. Many men in group C had at some time worked with hemp in the field, and may have been exposed to hemp dust for short periods. The $FEV_{1.0}$ in group C did not differ significantly from the values in the other control groups. Any chronic effect of hemp dust in these men is therefore probably not severe enough to depress ventilatory capacity.

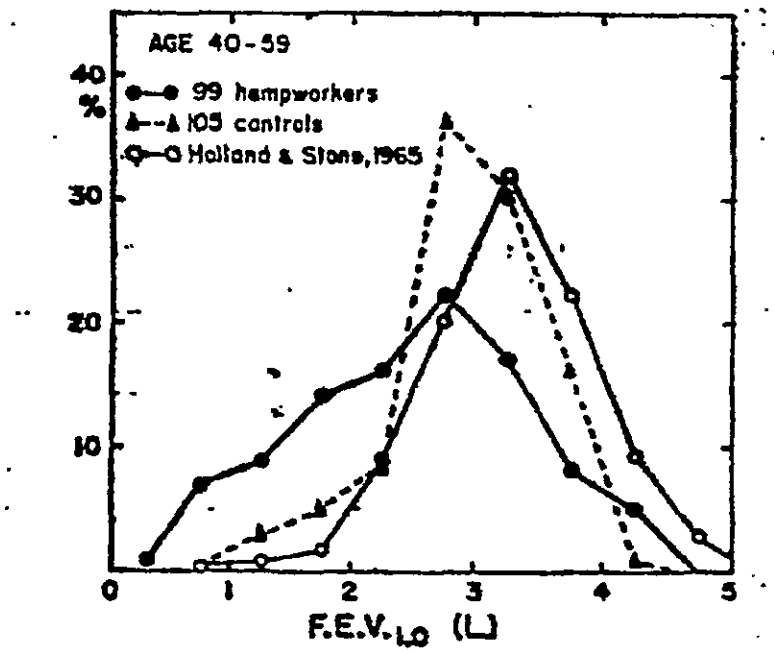

FIG. 4. Frequency distribution of $FEV_{1.0}$ (in intervals of 0.5 L.) in the present subjects (hemp workers and controls) and in 625 U.S. telephone men (Holland and Stone [9]). All three curves show an approximately normal distribution.

The data from control groups E and F might be biased in favor of healthy men since all these subjects were active industrial workers. In contrast, most of our hemp workers were classified as "retired." Actually, the large majority of our hemp workers were gainfully employed in other trades. In agricultural towns, such as Callosa de Segura, old and disabled men are taken care of by their relatives. Even severely disabled men may perform minor jobs. It is therefore difficult to make a sharp distinction between active and retired workers.

The prevalence of symptoms in all the control groups combined is similar to that observed in other studies of men not exposed to occupational inhalation hazards, such as U.S. telephone men [9] and men in a Canadian rural town [10]. In our controls the prevalences of dyspnea grade 4 and 5 was slightly higher and illness from chronic bronchitis slightly more than in the subjects of Anderson et al. [10].

Comparison of the regressions of $FEV_{1.0}$ on age and standing height with those obtained by others also suggest that the present control groups are representative for male populations who smoke but are not exposed to other inhalation hazards. The constants and the coefficients for height are nearly equal to those found in the Veterans Administration cooperative study [6] and by Ferris et al. [11]. The coefficient for age is slightly larger in our material than in these two studies, but is similar to the coefficients found by Huhti [12] for men aged forty to sixty-four years in a Finnish rural community. Our control subjects have $FEV_{1.0}$ values slightly lower than those of the U.S. telephone men studied by Holland and Stone [9] (Fig. 4), probably because of a smaller average body height. Control group E did not differ from the others, although it consisted of men exposed to dust in

marble cutting operations indoors. Review of mass radiography films of 84 per cent of the men in group E did not disclose any gross lesions of the lung which might have been caused by the inhalation of marble dust. Inclusion of group E among the control groups stresses the fact that in hemp workers we are dealing not with effects of any kind of dust, but with effects of a textile dust with special toxic properties.

That selection errors play no appreciable role in the results found among hemp workers is perhaps best shown by the similarity of the data obtained in the fifty to sixty-nine year old hemp workers, regardless of the method of selection: random or by invitation (Table IV and Fig. 1). Labor migration is probably not a serious source of bias, since we have some evidence that the men who were absent because of migration are not a specially selected group. The migrants who returned for their holidays, and who were then available for our study, did not differ, as a group, from the residents when duration of exposure to dust and age were taken into account. Therefore we believe that the lapse rate because of migration does not invalidate our conclusions.

This is the more so since these conclusions are based mainly on the major differences between controls and hemp workers at the age of fifty to sixty-nine years. Seventeen of eighty randomly sampled men in that age group were not seen. Of these, eight had died since the list of workers (Table I) was drawn up. The causes of death were cannabosis (equal to hemp workers' byssinosis [7]) in one, other chronic lung disease (not cancer) in four and nonpulmonary disease in three. Of the remaining nine men, one refused to cooperate, three could not be located and five worked elsewhere. Thus, the number of possibly healthy men in this age group who were not seen is balanced by the number of those who died, and of whom at least five had chronic lung disease according to the death certificates. We therefore believe that lapse because of death or migration does not invalidate the conclusions drawn from our data in the fifty to sixty-nine year old men.

A selection process does appear to determine, in part, which men still work in the hemp trade. More of the men still active in 1967 had never had symptoms of byssinosis on Monday than the men who were active in 1965 (Table VII). Most of the reactors among the men employed in 1965 had a large decrease in $FEV_{1.0}$ during work on Monday; this was less common among the men now active (Table XI). That this difference is not caused by decreased toxicity of the dusty work environments was shown by the results obtained in five now retired workers and one healthy subject, in whom the $FEV_{1.0}$ response to hemp dust was tested in 1965 and in 1967, in the same rooms as the active workers. All reacted at least as severely in 1967. These data suggest that, as the hemp trade in Callosa contracts, the men with byssinosis have more incentive to leave the trade than the men who experience fewer respiratory symptoms. More widespread knowledge among these men about byssinosis as an occupational hazard may have contributed to this. The "nonreactors" might stay partly because hemp work is better paid than farm work in the Callosa area.

TABLE XI

$FEV_{1.0}$ IN ACTIVE HEMP BATTERS AND HACKLERS

Data	1965*	1967†
Number of men	13	23
Average age (yr.)	45	36
Control $FEV_{1.0}$ <80% of expected value	5(38%)	3(13%)
Change of $FEV_{1.0}$ on Monday		
Average change (L.)	−0.33 ($p < 0.01$)	−0.12 ($p < 0.02$)
No change or increase	4(31%)	7(30%)
Decrease <0.20 L.	1(8%)	9(39%)
Decrease >0.20 L.	8(62%)	7(30%)

* Data from Bouhuys et al. [2].

† Present study. $FEV_{1.0}$ was measured before and after about six hours of work in hemp in twenty-three of thirty-seven active workers (Table VII).

The decreased ventilatory capacity of older hemp workers is to a large extent irreversible (Table IX). Sixteen men were treated with bronchodilator drugs during ten days; none of them showed more than a slight improvement in $FEV_{1.0}$ or symptoms. Seven men first seen in 1965, when they worked in hemp, were studied again in 1967. They had retired from hemp work when their plant was closed early in 1966. In none of them had the $FEV_{1.0}$ increased by more than 0.17 L. since 1965 (average for group 2.68 L. in 1965 and 2.72 L. in 1967).

We considered twenty-seven of 146 hemp workers aged fifty to sixty-nine years (18.5 per cent) to be severely disabled by ventilatory insufficiency, since their $FEV_{1.0}$ was 1.00 L. or less. These men also had severe dyspnea and

chronic respiratory symptoms. No such men were found among the control groups. From Table I it can be seen that only fifteen of 949 (1.6 per cent) batters and hacklers had been awarded pensions for disability caused by occupational respiratory disease. Our study suggests that the prevalence of this type disability among the hemp workers of Callosa de Segura is much greater than indicated by the number of pensions. In none of the disabled men did the history suggest nonpulmonary causes of dyspnea or pulmonary function loss. Physical examination showed signs of right heart failure (cyanosis, engorged central systemic veins, enlarged liver and ascites) in only one man. A more complete clinical evaluation of this group of disabled men is now in progress by one of us (A. Barbero).

The majority of men who were hemp batters or hacklers have a less than expected ventilatory capacity at age fifty to sixty-nine. However, some men appear to escape the noxious effects of the dust, in particular those who never experienced dyspnea on Monday while at work (Table X). We believe that these men are nonreactors [*2*]. In men who do not experience the acute symptoms of byssinosis, irreversible pulmonary function changes are apparently unlikely to develop in the long run. This does not prove that the agents responsible for the acute and the chronic effects of the dust are identical. However, the following working hypothesis may be useful for further studies. The acute dust effects are most likely mediated by the release of histamine in lung tissue [*2,13*]. This release process may involve at least temporary damage to mast cells in the lungs. The acute effect of the dust on Monday might represent a micro-insult to lung tissue, and repetition of these micro-insults regularly, over many years, would lead to irreversible damage to the structure of the lungs.

The relationship between smoking habits and $FEV_{1.0}$ among the older controls is in agreement with the view that cigarette smoking causes, in the long run, a slight but significant decrease in ventilatory capacity. The relations among hemp workers are quite different (Fig. 2). We believe that the active smokers among them are selected with respect to the chronic effect of hemp dust [*7*]. Those who are relative "nonreactors" to hemp dust remain healthy and may continue to smoke beyond age fifty. In those who react more severely to hemp dust, chronic obstructive lung disease is likely to develop. This lowers their $FEV_{1.0}$ and compels them to stop smoking. This explains why the actively smoking hemp workers (Fig. 2) have a higher $FEV_{1.0}$ than the nonsmokers and light smokers, whereas the exsmokers have a low $FEV_{1.0}$.

It is of interest that this analysis of $FEV_{1.0}$ data brings out relations which do not show from the analysis of chronic respiratory symptoms in Table V. The present data confirm the results of a previous survey among flax and cotton workers, which showed lower $FEV_{0.75}$ values in these men, compared to control subjects who smoked considerably more than the textile workers [*14*]. In that study, too, the effect of flax or cotton dust inhalation appeared to override the effects of cigarette smoking.

The prevalence of chronic respiratory symptoms and of ventilatory insufficiency (as defined by a low $FEV_{1.0}$) among the older hemp workers is much higher than has been described in any previous population study on respiratory disease. This high prevalence occurs in a rural area with a Mediterranean climate, with few other sources of industrial air pollution and with a low density of motorized traffic. It occurs among nonsmokers or light smokers to the same extent as among heavier smokers. Prevalences among control subjects, living in the same general area, are comparable to those reported by others who studied chronic respiratory symptoms and pulmonary function in occupational or residential populations. Little doubt remains that heavy and prolonged exposure to hemp dust is the cause of the high prevalence of chronic respiratory disease. We would not, however, have realized the magnitude of the problem if we had limited our study to the men who are active in the hemp trade. The men now active are a younger group, probably biased in favor of those who do not react severely to exposure to hemp dust. We were able to see the retired workers as well, and this group presents a quite different picture. We could study these retired men because they live in a town in which the Spanish hemp industry used to be the main trade. In tracing occupational hazards, the need to study men who have left the industry is obvious from our experience in Callosa de Segura.

Many physicians would diagnose the disease of older hemp workers as chronic bronchitis; this diagnosis had been made in many of the men in the present study. Chronic bronchitis, as defined at present, however, is a complex of symptoms rather than a disease with an established pathogenesis. We prefer to diagnose bys-

sinosis grade III (i.e., permanent dyspnea, chronic respiratory symptoms and ventilatory insufficiency caused by textile dust exposure [3]) in the disabled hemp workers. We have presented evidence that the syndrome of "chronic bronchitis" in these men is induced by exposure to hemp dust. Therefore, we believe we are dealing with a disease with an established environmental causation, and a progression from acute, short-lasting effects of dust exposure to chronic and permanent lung damage. It serves little purpose to classify this disease as chronic bronchitis, since that term conveys less information than the diagnosis "byssinosis grade III." The symptom complex of chronic bronchitis is widely prevalent, but our diagnostic efforts should not stop with what essentially is an empiric description of symptoms. We believe that the large group of patients now diagnosed as having chronic bronchitis may include patients with various diseases with specific, possibly environmental causations. Exposure to hemp dust, and (on the basis of previous studies) cotton and flax dust as well, is one specific cause of "chronic bronchitis." Future research may discover other specific causes. Cigarette smoking is probably one of these, although our data suggest it is less deleterious than hemp dust, at least as far as the development of chronic respiratory symptoms and of decreased ventilatory capacity is concerned.

Acknowledgment: This study was made possible by the wholehearted cooperation of many persons in Callosa de Segura and Monovar. Special thanks are due to Dr. A. Flores, A. Ballester, J. Canales, J.A. Delcerro, A. Anton, M. Lopez Serna, A. Canales Belmonte, R. Martinez, J. Bernabeu, the management of Calzados Jesus Gil Ponce S.A., and Marmoles Tortosa S.A., Monovar, and personnel of the Syndical de Obreros de Cañamo, Callosa de Segura. Assistance with data processing was given by Dr. J.A.J. Stolwijk, J. Casby and F.G. Bouhuys.

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