Byssinosis: Airway Responses in Textile Dust Exposure

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Byssinosis, an occupational respiratory disease, has been found in workers processing cotton, hemp and flax. Although those working in the initial stages of fiber-processing (e.g., carding) areas are at greatest risk, employees in other types of dusty work may develop the disease. The inhalation of an aerosolized cotton or hemp dust extract causes the same symptoms as dust inhalation, i.e., chest tightness accompanied by a decrease in ventilatory capacity.[1-3] Byssinosis starts as a transitory acute response to dust exposure and may progress to chronic disease with more or less severe disability. The disease can be detected by measuring lung function changes over a work shift on Monday and other working days. A larger acute decrease in lung function has been found in those with byssinosis symptoms, but a decrease has also been recorded in those who do not have such a history.[4 5] Although the symptoms of byssinosis are clearly recognizable, the specific agent responsible for the symptoms has not yet been defined.

In order to obtain more information on the mechanism of textile dust effects we conducted studies with hemp dust and hemp dust extract after pretreatment of the subjects with different drugs: propranolol, an antihistamine drug, ascorbic acid, and disodium cromoglycate (Intal, Aarane).

Subjects and Methods

Ten nonsmoking healthy subjects (age: 20 to 26 years) were included in laboratory studies on the effect of propranolol, of an antihistamine drug, and of ascorbic acid on ventilatory function after hemp dust extract (HDE) exposure. HDE was prepared in a concentration of 1 g hemp dust and 6 ml Tyrode solution and sterilized by filtering through a special 0.45 · micron-grid membrane (Nalge Sybron Corp.). Subjects were exposed for 10 minutes to hemp dust extract aerosolized by a Dautrebande D-30 nebulizer with an air pressure of 10 psi. The experiments were always conducted with at least five-day intervals between each experiment. Propranolol (80 mg) was given 90 minutes before HDE exposure, an antihistamine drug solution (methdilazine-hydrochloride) (8 mg) 60 minutes before, and ascorbic acid (1 g) two hours before HDE exposure. The same experiments were conducted with a placebo instead of each drug.

Another group of ten healthy nonsmoking subjects (age: 20 to 26 years) participated in the experiment with disodium cromoglycate (DSCG). Twenty mg DSCG or a placebo (sodium sulphate 5 mg, lactose 35 mg) was administered to each subject by spinhaler 30 minutes before HDE exposure, which was performed as described above.

In addition, the preventive effect of 20 mg DSCG was studied in a group of 17 female nonsmoking workers in the hemp industry. DSCG or a placebo was administered by spinhaler 30 minutes before work shift on two consecutive Mondays.

In all experiments with HDE, lung function was measured before and over a 30-minute period after exposure. Partial and maximum expiratory flow-volume (PEFV and MEFV) curves were recorded on a Brush 500 High Performance XY Recorder (Gould, Inc.) with lung volume changes on the abscissa and expiratory flow rate on the ordinate. Subjects first inspired to about 60% of vital capacity (VC) and then expired to residual volume (RV), immediately followed by full inspiration to total lung capacity (TLC) and maximal expiration to RV. The first maneuver gives the PEFV curve and the second the MEFV curve (Fig 1). At least three blows were made and the mean of the two highest blows was used. From PEFV curves we read maximum expiratory flow rate at 40% of the control VC [MEF40%(P)], i.e., TLC minus 60% of the control VC. Recently, Bouhuys et al.[6] demonstrated that changes of flow rates of PEFV curves were more sensitive than those of flow rates on MEFV curves and FEV_1 in assessing constrictor effects of textile dust. Changes in TLC after dust exposure are very small and not significant.[7]

In female hemp workers MEFV curves were recorded before and after work shift on a portable flow-volume spirometer.[8] Flow rates at 50% of the control vital capacity (MEF50%) were read from these curves.

Results

The inhalation of hemp dust extract aerosol caused acute decreases of MEF40%(P) in all studied subjects. Figure 2 presents the relative mean acute reductions of MEF40%(P) in ten subjects after prior administrations of a placebo, propranolol, methdilazine-HCl and ascorbic acid. In all experiments, after HDE inhalation following pretreatment with a placebo, statistically significant ($P < 0.01$) acute reductions of MEF40%(P) in relation to pre-exposure control values were recorded over each entire 30-minute experiment. After pretreatment with 80 mg propranolol (Fig 2A) flow rates decreased considerably more in comparison with placebo (difference statistically significant up to 10 min.). Pretreatment with 8 mg methdilazine-HCl (Fig 2B) and with 1 g ascorbic acid

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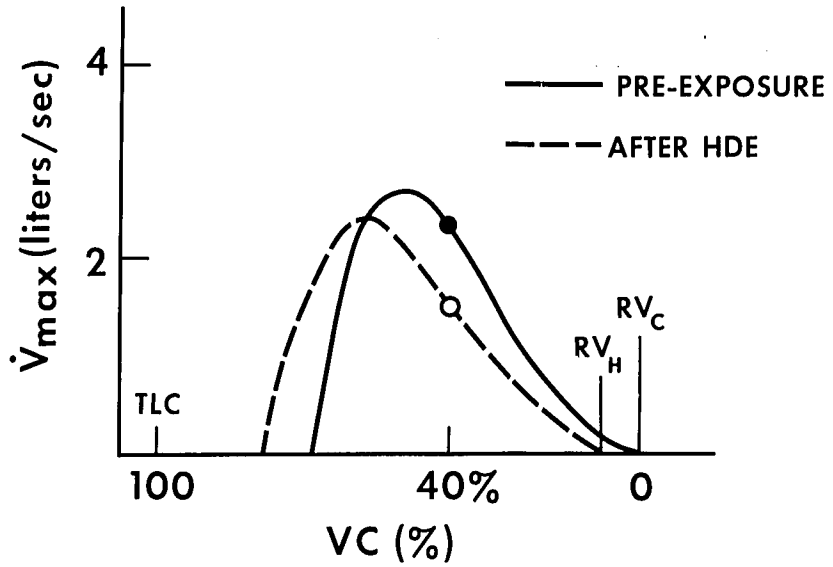

Fig 1. — Partial expiratory flow-volume (PEFV) curves from healthy subject before and 20 minutes after exposure to hemp dust extract (HDE). Lung volume scale is expressed in percentage of vital capacity with the point of maximum inspiration (TLC) and maximum expiration (RV). RVc = residual volume on control curve; RVH = residual volume after HDE. Ordinate: expiratory flow rate (lit/sec).

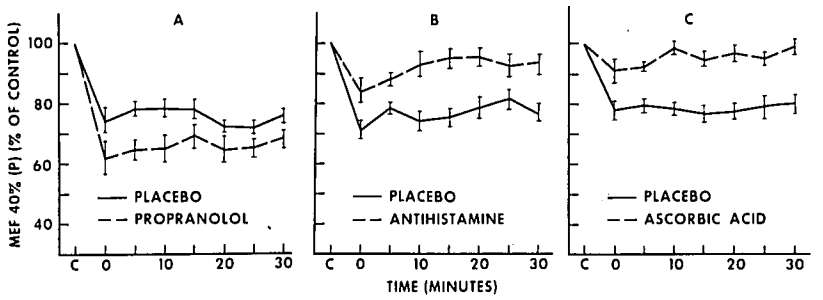

Fig 2. — The mean relative changes in MEF40%(P) ± SE in 10 healthy subjects after hemp dust extract (HDE) exposure following pretreatment with a placebo, 80 mg propranolol, 8 mg antihistamine drug, and 1 gram ascorbic acid.

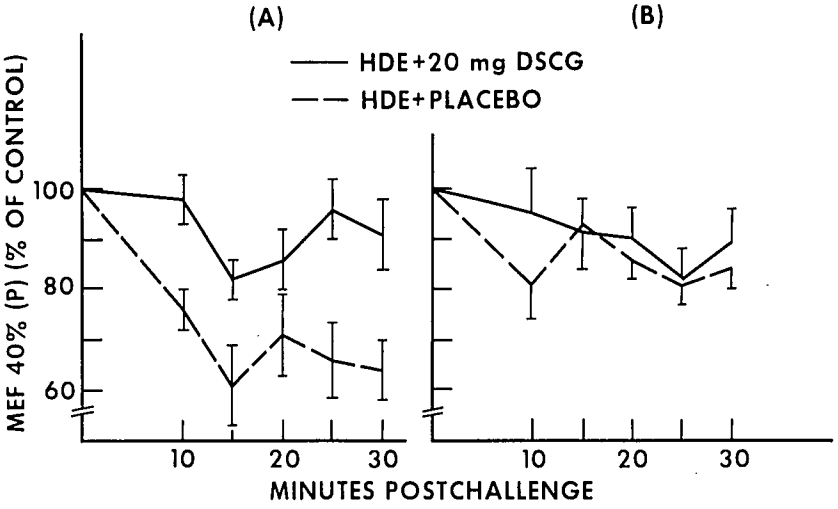

Fig 3. — The mean relative changes in MEF40%(P) ± SE in ten subjects after hemp dust extract (HDE) exposure following pretreatment with a placebo and 20 mg DSCG. Figure 3A in four subjects with acute reductions larger than 20%; Figure 3B in six subjects with less than 20%.

(Fig 2C) significantly diminished the acute reductions in comparison with those after the placebo over the entire 30-minute experiment.

Figure 3 shows the mean acute changes in MEF40%(P) in ten subjects after HDE exposure following pretreatment with either a placebo or 20 mg DSCG. After pre-exposure administration of 20 mg DSCG four subjects out of ten with mean acute reductions in MEF40%(P) of 20% or more over the 30 post-exposure minutes had significantly diminished acute reductions over the entire experiment (Fig 3A). Those with acute reductions of less than 20% (Fig 3B) had significant protection only up to 10 minutes.

Among 17 female textile workers, 6 (35%) workers with large (-29.9%) acute reductions in MEF50% after placebo were completely protected (+4.7%) by the preshift administration of 20 mg DSCG ($P < 0.01$).

Discussion

Our data and those of Bouhuys et al.,[9] show that flow rate changes following dust exposure can be potentiated by propranolol. Propranolol, by blocking β-adrenergic receptors, appears to displace the vagal - β - adrenergic balance in the direction of vagal preponderance, and in this condition small airway constriction during hemp dust extract exposure is potentiated. In contrast, atropine leads to β-adrenergic preponderance and protects the small airways from being constricted by HDE.[10] This observation suggests that the response of the airways to dust is mediated, at least in part, by a parasympathetic postganglionic efferent pathway. There is an individual difference in sensitivity to textile dust. According to Bouhuys,[10] subjects may be classified as "reactors" who experience a flow rate response, i.e. small airway constriction accompanied by chest tightness, or "nonreactors" with a conductance response resulting from a narrowing of relatively large airways. The balance between vagal and sympathetic impulses which impinge on airway smooth muscle appears to be important in determining the lungs' responses to the textile dust inhalation.

The results in this study are in agreement with the previous experiment of Bouhuys[11] and Valic and Zuskin[12] showing that flow rate changes after dust exposure may be prevented by a small oral dose of an antihistamine drug. There

is evidence that textile dusts contain a pharmacologically active agent capable of releasing histamine and that this, at least in part, explains the airway constrictor effect.[1,10] Experiments with aqueous extracts of cotton bracts and hemp dust[2] have shown that extracts of cotton bracts, boiled bracts, hemp dust, and boiled hemp dust released histamine while the distillate, ether extracts, and charcoal-treated bracts possessed no in vivo bronchoconstrictor activity. A correlation between bronchoconstriction in vivo and histamine release in vitro suggests that the same agent(s) may cause these responses. This agent appears to be a highly water-soluble, heat-stable, and low-molecular-weight compound.

DSCG has been shown in previous studies to prevent changes in lung function during antigen provocation.[13-16] The present data demonstrate that DSCG can protect against airway responses to hemp dust, as well as against HDE, particularly in those subjects with large acute reductions in flow rates. Since DSCG prevents the release of chemical mediators from mast cells,[17] this finding is consistent with the hypothesis that flow-rate responses are dependent on the release of histamine.

Previous experiments with ascorbic acid on histamine-induced airway obstruction[18] in humans suggested that ascorbic acid probably has a direct effect on airway smooth muscle since pretreatment with propranolol did not diminish the relaxant effect of ascorbic acid. In the present study we have shown that a single dose of 1 g ascorbic acid inhibits the constrictor effects of hemp dust extracts on airways of human subjects. These results are in agreement with those of Valic and Zuskin,[12] who demonstrated that ascorbic acid (500 mg orally) significantly prevented acute reductions of expiratory flow rates in flax workers.

In the prevention and control of byssinosis in the textile industry one should consider both appropriate medical surveillance and engineering controls. The British Occupational Hygiene Society Committee on Hygiene Standards[19] suggested routine preemployment examination including measurement of FEV_1. They also advised that periodic examination of textile workers, including the measurement of lung function before and after shift, should be performed at intervals of no more than three years. In addition we suggest that the controlled preshift administration on working days of drugs such as DSCG and ascorbic acid (both with no side effects in most people), particularly in "reactors" with large acute reductions in ventilatory capacity, may be worthwhile considering.

Summary

The inhalation of textile dusts causes bronchoconstriction in textile workers and in healthy experimental subjects. The airway responses to these dusts are potentiated by propranolol and inhibited by an antihistamine drug and by ascorbic acid. Administration of 20 mg disodium cromoglycate by spinhaler 30 minutes prior to challenge with hemp dust or hemp dust extract protected a small number of subjects against the airway constrictor effect, mostly those with a large acute reduction in flow rates. Textile dust extracts contain a histamine-releasing agent, which explains their airway constrictor effect. This agent is a highly water-soluble, heat-stable, low-molecular-weight compound which has not yet been chemically identified. In the prevention and control of byssinosis, the administration of drugs such as ascorbic acid or disodium cromoglycate should be considered in addition to engineering methods.

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