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Byssinosis

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Airway Responses Caused by Inhalation of Textile Dusts

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Inhalation of cotton or hemp dust causes chest tightness and decreases of maximum expiratory flow rates on flow volume curves in the majority of textile workers and healthy subjects exposed to these dusts, or to aerosolized dust extracts. This acute response probably reflects narrowing of small intrapulmonary airways by toxic, histamine-releasing agents in the dust. The symptoms and the flow rate decreases can be potentiated by propranolol and inhibited by atropine. The balance between vagal and sympathetic impulses which impinge on airway smooth muscle appears to be important in determining the lung's response to textile dust inhalation. The role of such interactions between endogenous autonomic activity and other exogenous stimuli (eg, air pollutants) needs to be studied in detail.

SINCE the studies of McKerrow et al[1] it is known that inhalation of cotton dust causes decreases of the ventilatory capacity of the lungs, as well as symptoms of chest tightness and dyspnea. These observations have repeatedly been confirmed. In recent years it has also been shown that byssinosis is highly prevalent among cotton textile workers in the United States.[2,3] These findings have led to increased interest in byssinosis and the nature of the airway responses which accompany inhalation of textile dusts. In this paper I will discuss only responses which occur within a few hours. These may be relevant to acute actions of air pollutants other than textile dusts. In particular, the description of different degrees of individual sensitivity to dust may be of interest.

McKerrow et al[1] showed that the forced expiratory volume in 1 second ($FEV_{1.0}$) is significantly lower at the end of a work shift in a cotton carding room than, in the same worker, at the beginning of the shift. It seemed likely that this effect was due to a pharmacological agent with bronchoconstrictor properties in the dust, because the $FEV_{1.0}$ decreases were reversible. Soon afterwards, it was shown[4] that cotton dust contains water-soluble agents causing reversible prolongation of nitrogen washout in man, suggesting reversible narrowing of small airways. A similar water-soluble fraction of cotton dust caused histamine release from human lung tissue in vitro.[5] Later work[6,7] has confirmed and extended these results. The active principle in cotton dust appears to be contained in the bracts. An aqueous extract of these leaves (which surround the stem of the cotton boll) causes histamine release in human lung in vitro and chest tightness, as well as lung function changes suggestive of airway constriction in man in vivo. Dr. M. Hitchcock, of our laboratory, has recently prepared more concentrated extracts containing the active principle, and its further purification and identification is now being attempted.

This experimental work leads to the fol-

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lowing concept of the acute response to textile dust exposure in man. When small, inhaled textile dust particles settle in small airways, the histamine-releasing agents in the dust can penetrate the airway mucosa and release histamine, principally from mast cells. The released histamine contracts airway smooth muscle, and this results in various pulmonary function changes associated with constriction of small airways, such as prolongation of nitrogen washout, decrease of maximum expiratory flow rates, and decrease of $FEV_{1.0}$.[8]

Textile dust exposure affects some persons much more than others. The individual difference in sensitivity became quite obvious when we began our studies of hemp workers in 1965.[9] In workrooms where some of the men experienced severe chest tightness, accompanied by $FEV_{1.0}$ decreases of as much as 1 liter during the shift, other men were not at all affected. We called these men "reactors" and "nonreactors," respectively.

This intriguing finding was one reason why we performed more complete studies of lung mechanics in a similar group of hemp workers in 1967.[8] We used a body plethysmograph to measure lung volumes, airway conductance, and maximum expiratory flow rates at different lung volumes, before and after exposure to hemp dust. Again we found that some subjects reacted severely to exposures which left others (in the same room, at the same time) unaffected. Those who complained of chest tightness, after dust exposure, also had decreases of maximum flow rates and of $FEV_{1.0}$. Their airway conductance decreased little or not at all. This combination of findings suggests, in line with the previous discussion, that the symptom of chest tightness is accompanied by narrowing of small airways. Because the aggregate cross-section area of airways increases enormously as one proceeds along the bronchial tree towards the alveoli, the contribution of peripheral small airways to airway resistance is minimal. As a result, peripheral airway constriction must be pronounced before it results in measurable changes of airway conductance.

In contrast with this group of men who experienced a "flow rate response" and chest tightness while in dust, a small group of other men had no symptoms of chest tightness, nor a decrease of maximum flow rates and of $FEV_{1.0}$. We concluded that these men were, for unknown reasons, unaffected by the agents in dust that cause small airway constriction. However, the men in this group all showed a moderate decrease of airway conductance. The combination of two findings, decrease of conductance in the absence of flow rate decreases, suggested some degree of large airway narrowing in these men, whom we had previously labelled "nonreactors."

Thus, it became apparent that we were dealing not just with "reactors" and "nonreactors," but with two groups of people with qualitatively different responses to dust. One, the previous "reactors," seemed to experience small airway constriction after dust. This response was associated with chest tightness; the lung function changes could adequately be explained by reversible narrowing of small airways. The $FEV_{1.0}$ test, before and after work, is the most commonly used method to detect this response. The other subjects were, indeed, "nonreactors," as previously defined, judged from the absence of subjective symptoms and of changes in most function tests. The airway conductance measurements, however, demonstrated that the "nonreactors," in fact, did show a response, probably consisting mainly of narrowing of relatively large airways.

If these interpretations of two responses to hemp dust inhalation are correct, why does the same dust cause narrowing of predominantly small airways in some persons, and of large airways in others? Some tentative answers to this question have been discussed elsewhere.[8] By analogy with results of experiments with histamine in guinea pigs, we suggested that the balance between vagal and sympathetic stimuli reaching airway smooth muscle cells might be an important determinant of smooth muscle sensitivity. Predominant effects in small or in large airways could depend on local differences in this balance.

We have recently made further observations in hemp workers which may support these views.[10] Using partial, as well as full maximum expiratory flow-volume curves to assess flow rate responses to hemp dust and to histamine aerosols, we found that a small dose of propranolol (40 mg) administered orally potentiates the effect of histamine aerosol, as well as that of hemp dust. Flow rate responses to dust, as well as chest tightness, could be elicited, after propranolol, in subjects who had no such response nor symptoms under control conditions. In other subjects, propranolol increased the severity of the flow rate response, as well as the severity of chest tightness, after dust. On the other hand, atropine (1 mg administered subcutaneously) exerted a pronounced protective effect against histamine aerosol, as well as against hemp dust. These results in man are similar to previous results in guinea pigs.[11] In these animals. propranolol often potentiated the effect of histamine aerosol, while atropine protected them against histamine.

In principle, thresholds and response rates could differ at each link in the chain of events that leads to the final response, as we observe it. Individual differences in sensitivity to hemp dust could, for instance, be associated with differences in histamine-releasing capacity of most cells, or with differences in smooth muscle sensitivity to histamine. Also, differences in airway wall compliance could lead to varying degrees of airway narrowing, in spite of similar degrees of airway smooth muscle contraction. However, no positive evidence concerning anyone of these possible mechanisms has been available so far.

We believe that our results demonstrate for the first time that alteration of the balance between vagal and sympathetic stimuli which impinge on airway smooth muscle can markedly alter an individual's sensitivity to hemp dust exposure. A drug which blocks β-adrenergic receptors (propranolol) displaces the vagal-sympathetic balance in the direction of vagal preponderance, and in this condition small airway constriction during hemp dust exposure is potentiated. Conversely, atropine leads to sympathetic preponderance, and protects the small airways from being narrowed by hemp dust.

It is not inconceivable that a similar mechanism may determine, at least in part, airway responses to air pollutants other than textile dusts. If so, further work along these lines may help to identify persons who are particularly sensitive to such air pollutants, and may also point to ways of preventing or alleviating the deleterious effects of air pollutants in sensitive persons.

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