

Time course of bronchoconstrictive response in asthmatic subjects to reduced temperature

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Ramsey, J. M. (1977). *Thorax*, 32, 26-28. **Time course of bronchoconstrictive response in asthmatic subjects to reduced temperature.** Thirteen young adults with bronchial asthma and a like number of controls were subjected for 45 minutes to a temperature of 2°C after leaving a temperature of 24°C to which they subsequently returned. Pre-exposure examination included VC, FEV₁, MMEF, FEV₁/VC%, and urinary catecholamines. The pulmonary measurements were repeated at 15, 80, and 200 minutes after exposure. Catecholamines were measured from a second urine sample, the collection of which corresponded to the period during and after the stress.

Controls showed no significant pulmonary changes throughout the time of study, but 15 minutes after exposure the asthmatic subjects showed a significant mean decrease of all pulmonary measurements from pre-exposure values. The controls showed a significant mean increase in urinary catecholamines after the stress, whereas those with asthma showed no significant increase.

Strong statistical correlations have been demonstrated between cold weather fronts and asthmatic bronchoconstriction (Greenburg *et al.*, 1966; Tromp, 1968). Furthermore, statistical data suggest that the distress may persist for a time after the meteorological change (Ramsey, 1976).

The experiments of Wells *et al.* (1960) and Simonsson *et al.* (1967) have shown that when patients with respiratory disease inhaled air at -20 to -30°C for 2-3 minutes, the majority experienced increases in airway resistance that immediately returned to control levels when cold air was no longer being inhaled. Simonsson *et al.* (1967) concluded that cold air sensitises cough receptors which stimulate a localised bronchoconstrictive reflex via cholinergic pathways.

Cabezas *et al.* (1971) have shown that when vagal bronchoconstriction is present in dogs, electrical stimulation of sympathetic nerves reverses the bronchoconstriction. Szentivanyi (1968) has postulated that the basic defect in bronchial asthma is an insufficient adrenergic responsiveness to stress. Mathé and Knapp (1969) reported a less than normal rise in urinary adrenaline levels in six asthmatic patients subjected to controlled psychic stress. Also Barboriak *et al.* (1972) showed that asthmatic subjects fail to exhibit the expected

increase in plasma nonesterified fatty acids in response to exercise, presumably because of decreased release of adrenaline.

The following controlled experiments were designed to resolve whether or not those with asthma show significant bronchoconstriction in response to a single chill stress, and in particular to determine how long the bronchoconstriction persists after the exposure. In addition, the study was to determine if asthmatic subjects show a difference from controls in mobilisation of catecholamines as a consequence of the exposure.

Methods

Thirteen non-smoking university students (4 female) with a diagnosis of bronchial asthma were carefully screened and selected for the study. Those selected were 19-23 years of age, in good health apart from the asthma, and had not been on medication or had asthma attacks for three weeks before the study. Thirteen additional non-smoking subjects of matched age (2 female) and in good health with no evidence of pulmonary disease were recruited as controls. The studies were conducted during the winter when outdoor airborne allergens were not present.

When reporting to the laboratory (one at a time) each subject brought a 24-hour volume of urine and proceeded to acclimatise at rest to a temperature of 24°C and relative humidity of 45%. Total catecholamines were measured from the urine sample by the method of Jacobs *et al.* (1961) and read fluorometrically. Determinations in duplicate were done for vital capacity (VC), forced expiratory volume at 1 second (FEV₁), and maximal midexpiratory flow (MMEF) with a Warren E. Collins 13.5 litre respirometer. Percentages for FEV₁/VC were calculated and all values were corrected to BTPS. Measurements of flow rates were chosen rather than airways resistance in view of the contention of McFadden and Lyons (1968) that airflow obstruction can reside in lower airways despite normality of total airway resistance. Bouhuys *et al.* (1970) also indicate that in many instances of bronchoconstriction there are decreases of VC and maximal flows with little change in resistance.

Each subject was exposed to a temperature of 2°C with a controlled relative humidity of 45% for 45 minutes in a large, well-ventilated, walk-in environmental chamber (Scherer, model CER-810) and then returned to a temperature of 24°C. During the time in the chamber the subject sat at rest. They were reasonably clothed with typical street wear such as a heavy sweater, but the head and hands were bare. Most of them felt cold and tended to shiver by the end of the 45 minutes. Spirometric measurements were repeated at intervals of 15, 80, and 200 minutes after the exposure. A second urine sample (24-hour volume, inclusive of the time of the stress) was collected for catecholamine estimation.

Results

PULMONARY EVALUATION

The time course of means for both groups is shown in Tables 1 and 2. Controls showed no significant changes throughout the time course

Table 1 Time course of mean pulmonary values in 13 controls exposed to a temperature reduction of 22°C for 45 minutes

	Pre-exposure	Postexposure		
		15 min	80 min	200 min
VC (l)	4.84 ± 0.86 ¹	4.89 ± 0.90	4.88 ± 0.99	4.88 ± 0.99
FEV ₁ (l)	4.16 ± 0.59	4.16 ± 0.57	4.10 ± 0.57	4.19 ± 0.69
MMEF (l/sec)	4.76 ± 0.70	4.74 ± 0.80	4.72 ± 0.78	4.71 ± 0.70
FEV ₁ /VC (%)	86.91 ± 7.75	86.66 ± 5.43	86.84 ± 4.87	86.50 ± 5.85

¹Standard deviation.

Table 2 Time course of mean pulmonary values in 13 asthmatic subjects exposed to a temperature reduction of 22°C for 45 minutes

	Pre-exposure	Postexposure		
		15 min ²	80 min	200 min
VC (l)	4.72 ± 1.01 ¹	4.56 ± 0.92	4.67 ± 0.90	4.71 ± 0.99
FEV ₁ (l)	3.78 ± 0.83	3.58 ± 0.77	3.65 ± 0.73	3.72 ± 0.76
MMEF (l/sec)	3.87 ± 1.34	3.50 ± 1.24	3.65 ± 1.03	3.79 ± 1.18
FEV ₁ /VC (%)	80.77 ± 7.65	77.30 ± 7.45	79.18 ± 5.30	79.88 ± 6.31

¹Standard deviation.

²All means significantly different from pre-exposure.

(Table 1). However, 15 minutes after asthmatic subjects had returned to 24°C they showed mean reductions from pre-exposure values that are significant by paired *t* test for VC ($P < 0.01$), FEV₁ ($P < 0.01$), MMEF ($P < 0.001$), and FEV₁/VC% ($P = 0.05$) (Table 2). Twelve of 13 subjects showed a reduction in MMEF, and 11 of 13 experienced a reduction in VC, FEV₁, and FEV₁/VC. Though the means remained lower at 80 minutes than those before exposure (Table 2), the differences were not statistically significant. At 200 minutes the means for pulmonary function approximated those before exposure (Table 2).

CATECHOLAMINE EVALUATIONS

The mean for total catecholamines in controls before cold exposure was 50.9 µg/24-hour volume (SD ± 23.54). Catecholamines from their second urine sample had a mean of 69.8 µg/24-hour volume (SD ± 34.66), an increase that is significant by paired *t* test ($P < 0.05$). The pre-exposure mean for asthmatic subjects was 47.5 µg/24-hour volume (SD ± 29.04), and that of their second sample only 50.3 µg/24-hour volume (SD ± 24.25), which is not a significant increase.

Discussion

Though the sample in this study is not large, it appears that a reduction in ambient temperature is capable of significantly reducing pulmonary flow rates in asthmatic subjects but not in normal individuals. Furthermore, the bronchoconstriction persists for more than 15 minutes after the subject once more inhales warm air. Although residual volume was not measured, the significant reduction in postexposure VC suggests elevation of RV. Permutt (1973) has pointed out that reduction of VC is characteristic of asthmatic distress.

If the bronchoconstrictive effect is mediated by the stimulation of cough receptors, as

postulated by Simonsson *et al.* (1967), then those with asthma either have a lower receptor threshold for initiating the response or less ability to counteract vagal firing. The persistence of the bronchoconstriction for some time after removal of the stimulus could mean either that the receptors remain sensitive or that counteraction, possibly related to adrenergic response, is not as effective in asthmatic subjects. The lesser catecholamine excretion among asthmatic subjects in response to the cold stress in this study is in favour of the latter. Jansky *et al.* (1967) have demonstrated that normally there is a significant release of catecholamines which enhance thermogenesis in animals exposed to cold. Of course other stresses, such as the reaction to coming to the laboratory, may have been a factor affecting catecholamine levels.

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