

## Facial cooling, but not nasal breathing of cold air, induces bronchoconstriction: a study in asthmatic and healthy subjects

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*Facial cooling, but not nasal breathing of cold air, induces bronchoconstriction: a study in asthmatic and healthy subjects. H. Koskela, H. Tukiainen. ©ERS Journals Ltd 1995.*

**ABSTRACT:** Reflex-mediated bronchoconstriction in cold climates may be more important than it has previously been thought. This issue has seldom been studied using physiological methods. We wanted to investigate, using physiological methods, what triggers the bronchoconstriction occurring at cold ambient temperature during resting nasal ventilation: cooling of the skin of the face or cooling of the nasal cavity.

Three experiments were carried out in 15 stable asthmatics and 10 healthy volunteers: 1) a whole-body exposure to subfreezing temperature in an environmental chamber, during which the subjects breathed cold air through the nose; 2) a similar exposure to subfreezing temperature except that the subjects now breathed warm air through the mouth from outside the chamber; and 3) nasal breathing of subfreezing air from a heat exchanger whilst the subjects sat at room temperature. Spirometric values and facial skin temperature were measured both during and after the exposures.

Maximal decrements (means  $\pm$  standard errors) of forced expiratory volume in one second (FEV<sub>1</sub>) in experiments 1, 2 and 3 were:  $5.8 \pm 0.8$ ,  $5.1 \pm 0.7$  and  $2.1 \pm 0.5\%$ , respectively ( $p < 0.001$ ). Only the two experiments in the environmental chamber induced significant bronchoconstriction. All responses were of similar magnitude in the asthmatic and the healthy subjects.

The cooling of the skin of the face seems to be the trigger for the bronchoconstriction during resting nasal ventilation at cold ambient temperature both in asthmatic and nonasthmatic subjects.

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It is well-known that hyperventilation of cold air through the mouth can induce bronchoconstriction in certain asthmatic patients [1]. The stimulus is thought to be the cooling [2] or the drying [3] of the bronchial mucosa, and these mechanisms probably, mainly, explain the enhancement of the exercise-induced bronchoconstriction by cold air [4].

In addition, there are other, probably reflex-mediated, mechanisms by which cold may induce bronchoconstriction even without hyperventilation. Cooling the nasal cavity by spraying freons into the nose has been found to cause bronchoconstriction [5]. Consistently, nasopharyngeal anaesthesia has been found to inhibit the bronchoconstriction induced by cold ambient air [6]. In addition, a small bronchoconstriction can be induced by cooling the skin of the face by ice packs [7–9]. Such studies, however, are highly experimental, and it is difficult to estimate the significance of the results in physiological conditions.

In our previous study, 19 asthmatic patients were exposed to  $-20^{\circ}\text{C}$  in an environmental chamber whilst

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breathing tidally through the nose. This experiment induced a greater decrease in forced expiratory volume in one second (FEV<sub>1</sub>) than did a moderate 10 min treadmill exercise at room temperature [10]. Since, at resting ventilation rates, even subfreezing air is almost completely conditioned when it has passed the nasal cavity [11–13], neither cooling nor drying of the bronchial mucosa were likely to have taken place during the exposure to cold air. According to the above-mentioned experimental studies, one could presume that the trigger for the bronchoconstriction in a cold environment was either the cooling of the nasal cavity whilst the cold air was inhaled or the cooling of the skin of the face.

The present study was designed to find out, using physiological methods, the trigger-site for the bronchoconstriction associated with a whole-body exposure to cold air during resting nasal ventilation. The answer might help some patients with respiratory disorders to protect themselves against the bronchoconstrictive effects of cold weather.

## Materials and methods

### Subjects

The patients were recruited from the out-patient clinic of Pulmonary Diseases of Kuopio University Hospital. Fifteen clinically stable asthmatics were recruited in to the study, 8 males and 7 females. The mean age of the patients was 35 yrs (range 21–53 yrs). Their mean ( $\pm$ SD) FEV<sub>1</sub> was  $96 \pm 11\%$  of predicted (range 75–113%). Eleven patients were atopic (at least one positive skin reaction to common allergens) and only one was a current smoker. All patients used inhaled beta<sub>2</sub>-agonists, 11 patients used inhaled steroids, three used oral theophylline preparations, and one used ipatropium bromide. Nine patients reported breathing difficulties during cold weather, and six did not.

In addition, 10 healthy volunteers were recruited as a control group. They were all nonsmokers, free of respiratory symptoms, and had no history of atopic disease. The two groups were comparable with respect to sex distribution and age.

The asthmatics were not allowed to take beta<sub>2</sub>-agonists for 6 h, anticholinergic agents for 24 h, and theophylline preparations for 24 h before each challenge. They had not used any short-term oral corticosteroid therapy for at least 1 month before the study. The use of inhaled corticosteroids was unchanged. No control subjects used any of the above-mentioned drugs. All subjects gave their informed consent to the study. The study was approved by the Ethics Committee of the University of Kuopio, Finland.

### Study design

The study consisted of three different experiments carried out on separate days, always at the same time of day. The experiments were carried out in a random order. Before each experiment, the subjects had to spend at least 30 min at room temperature.

The first experiment was a whole-body exposure to subfreezing ambient temperature. The subjects sat in an environmental chamber, volume 32 m<sup>3</sup>, for 10 min whilst breathing the cold air around them through the nose. There was a 2–4 m·s<sup>-1</sup> turbulent airflow to mimic wind in the chamber. The second experiment was designed to cool the skin of the face but not the nasal cavity. The subjects were similarly exposed to subfreezing temperature but now breathing warm air from the outside of the chamber through the mouth. In this experiment, the subjects wore noseclips continuously. In the third experiment, the subjects breathed subfreezing air for 10 min through a heat exchanger *via* a nasal mask whilst sitting at room temperature. This experiment was designed to cool the nasal cavity but not the skin of the face.

In the two experiments in the environmental chamber, the subjects were dressed as they felt appropriate for a cold winter day. They wore woollen hats and gloves, but the face was always uncovered. In the experiment with the heat exchanger, the subjects were lightly dressed in a

way they considered appropriate for room temperature. In each experiment, the subjects were instructed to perform spontaneous tidal breathing.

### Methods

To permit the subject to breathe warm air and to be able to perform spirometry during the whole-body exposure to subfreezing temperature, the equipment presented in figure 1 was constructed. The equipment consisted of a heavily insulated tube of 28 cm length projecting into the environmental chamber. In the bottom of the tube was a smaller plastic tube, which is an original part of the pneumotachograph spirometer used in all three experiments (Medikro 101, Medikro Ltd, Kuopio, Finland). The subjects could breathe warm air from outside the environmental chamber *via* this smaller tube. In the first experiment, the subjects breathed through the wall of the chamber only during the forced expiratory manoeuvre. Meanwhile, the small tube was plugged. During the second experiment, the subjects breathed continuously through the wall. The pneumotachograph was connected to the small tube only during the measurements. The volume calibration of the pneumotachograph was performed both through the wall of the chamber and outside the chamber. The height of the chair was always adjusted individually.

To allow the subject to breathe cold air nasally without cooling the skin of the face, the equipment illustrated in figure 2 was constructed. The nasal mask was modified from a mask used in the treatment of obstructive sleep apnoea syndrome (Silicone Contour Mask, size small, Respiration Inc.®, Murrysville, USA). The valve (Spira®,

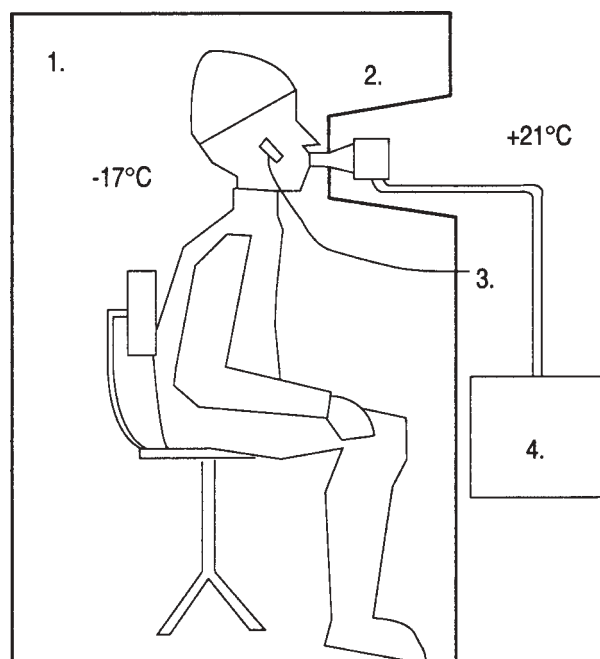


Fig. 1. – A schematic representation of the environmental chamber with the transmural breathing equipment. 1: environmental chamber; 2: heavily insulated tube projecting into the chamber; 3: thermocouple to measure the temperature of the facial skin; 4: spirometer with pneumotachograph. See text for detailed explanation.

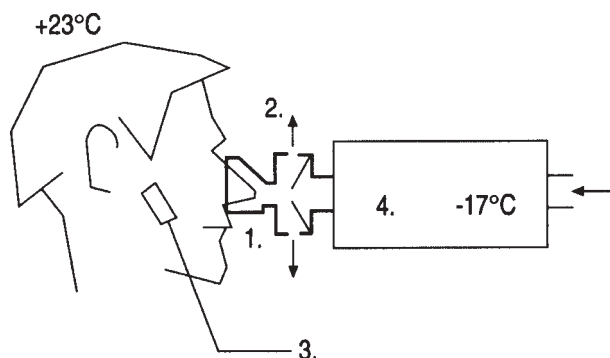


Fig. 2. – A schematic representation of the equipment used to permit the subject to breathe cold air nasally but not to cool the skin of the face. 1: nasal mask; 2: valve; 3: thermocouple to measure the temperature of the facial skin; 4: heat exchanger. The bridge of the nose inside the mask was covered so that only the nostrils were exposed to cold. See text for detailed explanation.

Hengityshoitokeskus, Hämeenlinna, Finland) between the heat exchanger (Jaeger RHES, Erich Jaeger GmbH & CoKG, Germany) and the mask allowed the subfreezing air to come into the mask and the warm expired air to escape without mixing of the gases. The dead space of the system was about 60 cm<sup>3</sup>. Inside the mask, the bridge of the nose was covered with an individually-shaped, 3 mm thick piece of insulation material, so that only the nostrils were exposed to cold. The air breathed by the subjects was room air, which passed through the heat exchanger.

### Measurements

The temperature of the air inside and outside the environmental chamber and in the room with the heat exchanger was measured (fig. 1). The temperature of the cooled air from the heat exchanger was measured with a thermocouple (GTH 1200 Digitalthermometer, Greisinger electronic, Germany) in the following way. Before the experiment, air was blown at a rate of 15 L·min<sup>-1</sup> through the exchanger with the nasal mask connected to it. The temperature of the air was measured near the Spira® valve inside the nasal mask. The temperature of the skin of the face was measured during all experiments with the thermocouple taped to the right cheek of the subject. The value was recorded just before each exposure, at 3

and 7 min during the exposure, and at 4 min after the exposure.

Before each exposure, three maximal expiratory flow-volume curves were determined with the spirometer. Two curves were determined at 3 and 7 min during the exposures, immediately after the exposures, and at 4, 8, 12, 16 and 20 min after the end of the exposures.

### Analysis

The largest forced expiratory volume in one second (FEV<sub>1</sub>), area under the expiratory flow-volume curve (AUC) and forced vital capacity (FVC) of the three baseline flow-volume curves were recorded. At each time-point during and after the experiments, the better FEV<sub>1</sub>, AUC and FVC of the two values was recorded. All figures in the results section are means and standard errors and a p-value of less than 0.05 was accepted as a level of significance. The asthmatic and the healthy subjects were analysed together unless otherwise expressed.

The influences of each experiment, separately, on FEV<sub>1</sub> were analysed by the repeated measures analysis of variance (ANOVA). Between the experiments, baseline FEV<sub>1</sub> values, percentage changes in FEV<sub>1</sub> at all time-points, and percentage maximal changes in FEV<sub>1</sub> were compared by ANOVA. Between the two whole-body exposures to subfreezing temperature, the correlation of the maximal decrements of FEV<sub>1</sub> was tested by linear regression analysis. Between the asthmatic and the healthy persons, the responses to the experiments were compared by Student's t-test (unpaired).

### Results

Table 1 shows the characteristics of the ambient and inhaled air during the experiments, the maximal effect of each experiment on facial skin temperature and lung function, and the baseline FEV<sub>1</sub> values.

Only the two experiments in the environmental chamber, in which the skin of the face was cooled (fig. 3a), caused significant bronchoconstriction (p<0.01 for the whole-body exposure to subfreezing temperature whilst breathing subfreezing air; p<0.001 for the whole-body exposure to subfreezing temperature whilst breathing

Table 1. – Characteristics of the ambient and inhaled air, the maximal effect of each experiment on facial skin temperature and lung function, n=25

Variable	Cc	Cw	Wc	p-value
Ambient temperature °C	-17.1 (0.06)	-17.1 (0.07)	23.1 (0.14)	
Inhaled air temperature °C	-17.1 (0.06)	20.8 (0.2)	-17.2 (0.56)	
Inhaled air humidity %	*	33.8 (2.6)	*	
Lowest skin temperature °C	15.4 (0.8)	13.6 (0.7)	33.8 (0.2)	<0.001
Baseline FEV <sub>1</sub> L	3.93 (0.15)	3.95 (0.14)	4.00 (0.17)	0.27
Maximal fall in FEV <sub>1</sub> %	-5.8 (0.8)	-5.1 (0.7)	-2.1 (0.5)	<0.001

Values are presented as mean and SEM in parenthesis. Cc: a whole body exposure to subfreezing temperature whilst breathing subfreezing air; Cw: a whole body exposure to subfreezing temperature whilst breathing warm air; Wc: nasal breathing of subfreezing air whilst sitting at room temperature; FEV<sub>1</sub>: forced expiratory volume in one second. Inhaled air humidity is expressed as relative humidity. \*: the water content of subfreezing air is near zero irrespective of the relative humidity.

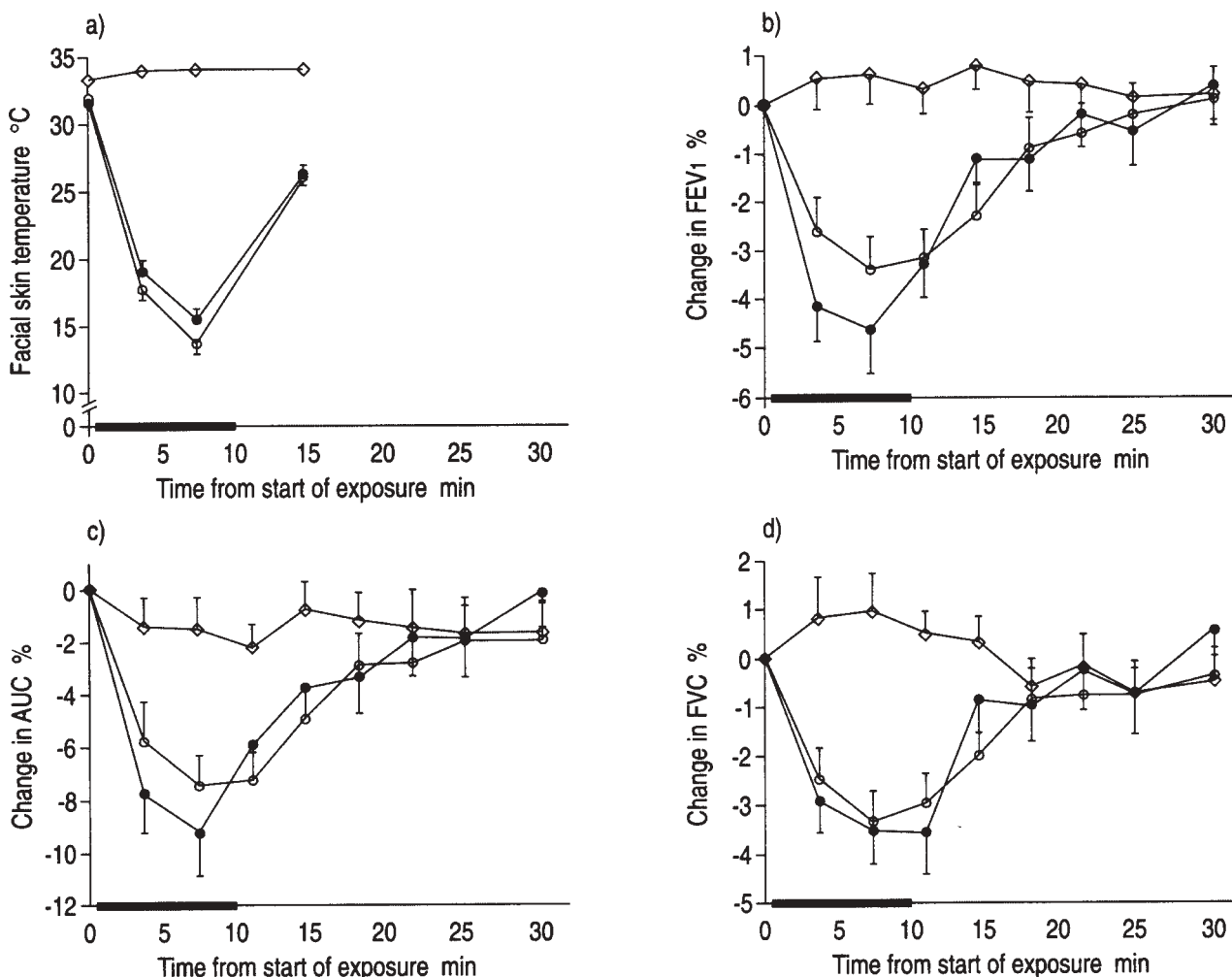


Fig. 3. – Effect of different exposures on: a) facial skin temperature; b) forced expiratory volume in one second (FEV1); c) area under the flow-volume curve (AUC); and d) forced vital capacity (FVC). —●—: whole body exposure to subfreezing temperature whilst breathing subfreezing air; —○—: whole body exposure to subfreezing temperature whilst breathing warm air; —◇—: nasal breathing of subfreezing air whilst sitting at room temperature. The bold line on the abscissa indicates the duration of the exposures, n=25.

warm air). The responses during and after these two experiments were similar at all time-points, in spite of the great differences in the temperatures of the inhaled air. The nasal breathing of subfreezing air through a heat exchanger had no effect on facial skin temperature or the spirometric indices. The time-courses of the changes in FEV1 (fig. 3b), AUC (fig. 3c) and FVC (fig. 3d) closely mirrored the changes in the facial skin temperature. AUC was the most sensitive indicator of bronchoconstriction. The individual responses between the two whole-body exposures to subfreezing temperature correlated well (fig. 4).

The bronchoconstriction associated with facial cooling began rapidly, was greatest during the exposure to cold, and vanished in 12 min after the end of exposure. The bronchoconstriction was usually slight, but some individuals showed considerable responses. The largest individual fall in FEV1 was 19% in the whole-body exposure to subfreezing temperature whilst breathing subfreezing air, and 12% in the whole-body exposure to subfreezing temperature whilst breathing warm air. The degree of bronchoconstriction was similar in the asthmatic and healthy persons in all experiments and at all time-points. For example, in the whole-body exposure to subfreezing

temperature whilst breathing subfreezing air, mean maximal falls in FEV1 were  $6 \pm 1\%$  in asthmatic and  $5 \pm 1\%$  in healthy persons ( $p=0.464$ ).

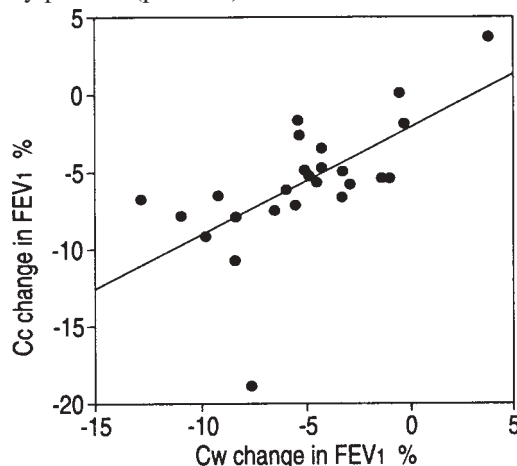


Fig. 4. – Correlation between maximal decrements of forced expiratory volume in one second (FEV1) during whole-body exposure to subfreezing temperature whilst breathing warm air (Cw) and whole-body exposure to subfreezing temperature whilst breathing subfreezing air (Cc) ( $r=0.644$ ;  $p<0.001$ ).

## Discussion

This study shows, that the bronchoconstriction associated with a whole-body exposure to cold air during resting nasal ventilation results from the cooling of the skin of the face. The cooling of the nasal cavity, and thus the actual inhalation of the cold air during the exposure, seems not to be essential to produce this effect. This conclusion is based on the following findings. Firstly, facial cooling produced by subfreezing ambient temperature induced similar bronchoconstriction whether the inhaled air was subfreezing or warm. Secondly, inhalation of subfreezing air *via* the nasal mask had no effect on FEV<sub>1</sub> when the skin of the face remained warm.

The results of the present study are consistent with the findings that application of ice packs on the face of either healthy or asthmatic persons induces a slight bronchoconstriction [7–9]. Similar cooling of other parts of the body seems not to have a bronchoconstrictive effect [9]. However, we think that the results of those studies must be interpreted with caution. With ice packs, the skin of the face cools in an unnatural way, and the possible effects of tactile sensations are difficult to avoid. The present study extends these observations in showing that this phenomenon actually takes place under physiological conditions.

The mechanism leading, from facial cooling to bronchoconstriction has been presumed to be secondary to a neural reflex. The afferent arch of such a reflex is the trigeminal nerve, which innervates the skin of face. The efferent arch is thought to be the vagus nerve [14]. As the responses in the present study were similar in asthmatic and healthy persons, it seems that this reflex is not enhanced in asthma.

The bronchoconstrictive response to facial cooling was very fast and reached its maximum during the exposure to cold. Thus, it is difficult to notice this response if only post-challenge lung function is determined. Many lung function devices, including pneumotachographs, operate well only over a narrow temperature range, thus preventing their use at subfreezing temperatures. To solve these problems, the environmental chamber allowing transmural breathing was constructed.

Our set-up allowed transmural breathing only through the mouth, which was practical for the forced expiratory manoeuvres, but not physiological during the second experiment of the present study, when the subjects breathed continuously transmurally. However, during resting ventilation, the mouth conditions air almost as efficiently as the nose [13, 15]. The drying or cooling of the bronchial mucosa were, thus, equally as unlikely during the second experiment as during the other two experiments.

A whole-body exposure to cold air during resting nasal ventilation is a physiological experiment and safe for all kinds of patients. The individual bronchoconstrictive responses were highly reproducible in our study. Provided with the ability to also determine lung function during the exposure, our method is well suited for studying a facial cooling-induced, reflex-mediated bronchoconstriction.

The set-up allowing nasal breathing of subfreezing air without cooling the rest of the body was thought to be of

importance, since there is evidence to suggest the existence of cold or airflow-sensitive receptors in the nasal cavity [5, 6, 16, 17]. Consistent with these findings, there are reports indicating that cooling of the nasal cavity, and thus the inhalation of cold air through the nose, could induce bronchoconstriction [5, 6, 18]. In our study, however, tidal nasal breathing of subfreezing air without cooling the skin of the face had no effect on FEV<sub>1</sub>. Our results suggest, that under physiological conditions the stimulation of the cold or airflow-sensitive receptors in the nose does not induce bronchoconstriction in man.

One may doubt that the nasal mucosa was cooled sufficiently when the subjects breathed cold air *via* the nasal mask. This might actually explain the lack of bronchoconstrictive response in this experiment. One main reason for the lack of significant cooling of the nasal mucosa is that as much as 40% of the heat supplied to the air by the nasal mucosa on inspiration is returned on expiration [12]. Indeed, an experimental technique has been developed to enhance the cooling of the nasal mucosa. This technique involves inhalation of cold air *via* the nose, and exhalation through the mouth [19]. Our purpose, however, was to study the effects of cold air under physiological conditions.

The present study may also be criticized in that minute ventilation was not measured during the experiments. This would have been of interest, since an exposure to cold has been reported to produce an increase in ventilation [20]. We found it technically difficult to measure minute ventilation when the subjects breathed the cold air in the environmental chamber *via* the nose; and, thus, decided not to do so in the other two experiments either. As the breathing of warm air did not diminish the bronchoconstriction during the whole body exposure to subfreezing temperature, we do not think that the bronchoconstriction observed was a result of an increased ventilation of cold air.

Although the cooling of the skin of the face induced considerable decrements in FEV<sub>1</sub> in some subjects, the bronchoconstriction was usually small. It has previously been shown in asthmatic patients that hyperventilation of cold air through the mouth clearly causes greater bronchoconstriction than application of ice packs on the skin of the face [9]. In the present study, only one asthmatic patient developed symptoms, namely a severe cough, after both whole-body exposures to subfreezing air. It is of interest that the temperature of the inhaled air had no effect on her cough, and that the nasal breathing of subfreezing air did not induce her cough.

The scarcity of symptoms was not surprising, since our subjects all had normal or near normal baseline ventilatory function. However, in patients with severely impaired lung function, even a relative small change in bronchial calibre may have subjective importance [21]. This is often the case in severe chronic obstructive pulmonary disease (COPD). In particular patients and in certain situations, protecting the skin of the face from cooling might have clinical significance. This idea, however, needs to be confirmed by further studies.

In conclusion, this study has shown, that mild bronchoconstriction develops during a whole-body exposure to cold air during resting nasal ventilation, possibly resulting from a reflex initiated by the cooling of the skin of the face. It appears that this reflex is not enhanced in asthma. The cold-sensitive receptors in the nasal cavity do not contribute to the bronchoconstriction observed under these conditions. A whole-body exposure to cold air during resting nasal ventilation is well-suited for studying the facial cooling-induced reflex bronchoconstriction, provided that lung function is measured both during and after the exposure.

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