Mechanisms Airway Effects and Cutaneous Reflex 

Weather in COPD: The Roles of Direct Bronchoconstriction due to Cold 

Heikki O. Koskela, Anna K. Koskela and Hannu O. Tukiainen 

Chest 1996;110;632-636 
DOI 10.1378/chest.110.3.632 

The online version of this article, along with updated information and services can be found online on the World Wide Web at: 
http://chestjournal.org/cgi/content/abstract/110/3/632
Bronchoconstriction due to Cold Weather in COPD*

The Roles of Direct Airway Effects and Cutaneous Reflex Mechanisms

Heikki O. Koskela, MD; Anna K. Koskela, MD; and Hannu O. Tukiainen, MD

To clarify how cold weather may induce bronchoconstriction in patients with COPD, a series of challenges were performed in 20 patients with COPD in stable condition as well as in 13 healthy subjects. A whole-body exposure to -17°C during resting nasal breathing was performed to study the reflex effects of facial cooling on lung function. In addition, a near-maximal hyperventilation of cold air was performed in a warm room to study the direct airway effects of cold air. The whole-body exposure to cold air induced statistically significant bronchoconstriction in both groups, the maximal decrements in FEV₁ being 9.4±1.4% in the patients with COPD and 10.3±0.8% in the healthy subjects (p=NS). The whole-body exposure to cold air also increased the resting ventilation. The hyperventilation challenge induced bronchoconstriction only in the patients with COPD, the maximal decrements in FEV₁ being 8.0±1.3% and 1.5±1.0%, respectively (p<0.01). These results suggest that cooling of the facial skin is predominantly responsible for the bronchoconstriction due to cold weather both in patients with COPD and in healthy subjects. At high ventilation level, as during heavy exercise, the direct airway effects of cold air may also contribute to the bronchoconstriction in patients with COPD. Some patients with severe COPD might benefit from wearing protective clothing over their face in cold weather.

(CHEST 1996; 110:632-36)

Key words: bronchial hyperreactivity; cold air hyperventilation; cold climate; COPD; facial cooling

According to common clinical experience, patients with COPD often complain of excessive exercise dyspnea under conditions such as those encountered in the Scandinavian winter. How cold weather increases dyspnea in patients with COPD is unknown. However, the most important disturbance of respiratory function in COPD is generalized airway obstruction. Thus, one could assume that the excessive dyspnea in cold weather might be due to cold air-induced bronchoconstriction.

When a person exercises in cold weather, bronchoconstriction may develop due to two basic mechanisms, which probably operate simultaneously. First, cold ambient air cools the skin of the face, which may induce bronchoconstriction via a vagal reflex. Second, if the heat-exchanging capacity of the upper airways is overcome, the cold inhaled air can have direct effects on the lower airways.

In asthma, the most potent stimulus for the bronchoconstriction under such circumstances is the direct airway effect of cold air, facial cooling being a weaker stimulus. Less is known about the effects of cold weather in patients with COPD. They usually do not respond to cold air hyperventilation. To our knowledge, the effects of a whole-body exposure to cold air have not been studied in patients with COPD. Thus, the effects of cooling of the face and the total effects of cold weather are unknown in this disease.

The primary aim of the present study was to determine the roles of direct airway effects and cutaneous reflex mechanisms in bronchoconstriction due to cold weather in COPD. A better understanding of this issue would be useful when advising the patients with COPD on how to protect themselves from the bronchoconstrictive effects of cold weather. Another aim was to study the effect of a whole-body exposure to cold air on minute ventilation.

Material and Methods

Subjects

Twenty patients in stable condition who all met the American Thoracic Society criteria for chronic bronchitis and/or emphysema participated in the study. All had a history of cigarette smoking, mean 38 pack-years (range, 10 to 80). Eleven patients had stopped smoking. Table 1 shows their basic characteristics. Patients with evidence of asthma (FEV₁ increase >15% after inhalation of 0.6 mg...
of rimiterol; spontaneous diurnal variation of peak expiratory flow >20% were excluded.

In addition, 13 healthy volunteers (3 women and 10 men) were recruited as a control group. They all were lifelong nonsmokers, free of respiratory symptoms, and had no history of any atopic disease. Their mean (SD) age was 63.5±8.7 years. The two groups were thus comparable with respect to sex distribution and age. All subjects gave their informed consent for participation in the study. The study was approved by the ethical committee of the University of Kuopio.

The patients were not allowed to take β₂-agonists for 6 h (in the case of salmeterol, 12 h), anticholinergic agents for 8 h, and theophylline preparations for 24 h before each challenge. However, because of severe COPD, 4 patients (patients 2, 3, 11, and 16) could abstain from treatment with anticholinergic drugs only for 6 h and 2 of these were allowed to continue to take their theophylline preparations throughout the study. The use of inhaled or oral corticosteroids was unchanged. None of the patients had experienced any exacerbation of their disease for at least 1 month before the study.

**Study Design**

To study the effects of facial cooling on lung function, a whole-body exposure to cold air during resting nasal breathing was carried out in an environmental chamber. To study the direct airway effects of cold air, an isocapnic hyperventilation of cold air was carried out in a warm room. The challenges were performed on separate days, in a random order, always at the same time of day. Before each experiment, the subjects had to rest for at least 30 min at room temperature.

In addition, another whole-body exposure to cold air was carried out to study the effects of a whole-body cold exposure on resting ventilation. This was done on the same day as the first whole-body exposure to cold, at least 30 min apart, in 25 subjects and on a separate day in 6 subjects. Because of technical problems, this exposure could not be carried out in two patients (patients 5 and 9).

**The Whole-Body Exposure to Cold Air During Resting Nasal Breathing: Effects on Airflow Parameters**

Three technically satisfactory flow-volume curves were obtained with a pneumotachograph spirometer (Medikro 909; Medikro LTD; Kuopio, Finland) and the temperature of the skin of the right cheek was measured (GTH 1200 Digitalthermometer; Greisinger Electronic; Regenstauf, Germany), while the subjects were sitting at room temperature and humidity. The subjects then dressed as they felt appropriate for a cold wintry day. They wore woolen hats and gloves, but the face was always uncovered, thus being the only exposed area of the skin. They then entered an environmental chamber of 32 m³ volume. The mean temperature in the chamber was –17.0°C (range, –17.4 to –16.2°C) and there was a 2 to 4 m/s turbulent airflow to mimic wind in the chamber. A transmural breathing system in the chamber allowed the measurements of spirometric values during the exposure. The subjects were sitting for 10 min in the chamber breathing cold air tidally through the nose. The temperature of the skin of the face and at least 2 technically satisfactory flow-volume curves were obtained at 3 and 7 min during the exposure, immediately after the exposure, and 4, 8, 12, 16, and 20 min after the exposure. During the maximal expiratory maneuvers, the subjects wore nose clips. The recovery time was spent at room temperature and humidity.

**The Whole-Body Exposure to Cold Air: Effects on Resting Ventilation**

Before the exposure, the resting ventilation and the respiratory frequency were measured at room temperature with the spirometer. During the exposure, the patients were dressed as in the first visit to the chamber. The mean temperature in the chamber was –17.0°C (range –17.4 to –16.6°C). The total length of the exposure was 5 min. The patients breathed cold air through the nose while sitting at rest for the first 4 min. The ventilation and the respiratory frequency were again measured during the fifth minute in the chamber. During the measurement, the subjects wore nose clips and breathed warm air from the outside of the chamber by using the transmural breathing system in the chamber.

**Isocapnic Hyperventilation of Cold Air**

At least three technically acceptable baseline flow-volume curves were obtained with the spirometer. By using the largest FEV₁ value, the target minute ventilation was set to FEV₁×30. If the subject could not maintain that level, the airflow was diminished to FEV₁×25. Carbon dioxide (CO₂) was added to the inspired air and the flow was calculated as follows: target minute ventilation ×0.05. The flow of CO₂ was further adjusted during the hyperventilation according to the end-tidal CO₂ measurements at the expiratory limb of the mouthpiece (Engström Eliza; Engström Medical LTD; Stockholm, Sweden). Air containing less than 1.75 mg H₂O/L was cooled in a heat exchanger (Jaeger RHES; Erich Jaeger GmbH & CoKG; Germany) and released through a mouthpiece. The subjects wore nose clips during the hyperventilation. At the inspiratory port of the mouthpiece, 8 cm from the mouth, the temperature of the inspired air was monitored continuously (GTH 1200 Digitalthermometer; Greisinger Electronic) and was mean of –12.9°C (range –15.4 to –10.2) during the hyperventilation. During the second

<table>
<thead>
<tr>
<th>Patient/Age, yr/Sex</th>
<th>Medication*</th>
<th>Symptoms in Cold Weather</th>
<th>FEV₁, L (% pred)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1/43/M</td>
<td>No</td>
<td>No</td>
<td>3.75 (88)</td>
</tr>
<tr>
<td>2/71/M</td>
<td>A S T Cl⁺ₒ</td>
<td>Yes</td>
<td>0.71 (21)</td>
</tr>
<tr>
<td>3/68/M</td>
<td>A B T Cl⁺ₒ</td>
<td>Yes</td>
<td>0.80 (28)</td>
</tr>
<tr>
<td>4/60/M</td>
<td>B T Cl</td>
<td>Yes</td>
<td>1.49 (42)</td>
</tr>
<tr>
<td>5/63/M</td>
<td>B</td>
<td>No</td>
<td>2.61 (70)</td>
</tr>
<tr>
<td>6/46/F</td>
<td>A B</td>
<td>No</td>
<td>2.50 (81)</td>
</tr>
<tr>
<td>7/71/M</td>
<td>A B Cl</td>
<td>No</td>
<td>0.92 (31)</td>
</tr>
<tr>
<td>8/55/M</td>
<td>A S Cl</td>
<td>No</td>
<td>2.45 (65)</td>
</tr>
<tr>
<td>9/67/M</td>
<td>A B Cl</td>
<td>No</td>
<td>0.70 (20)</td>
</tr>
<tr>
<td>10/57/M</td>
<td>No</td>
<td>No</td>
<td>1.95 (59)</td>
</tr>
<tr>
<td>11/71/M</td>
<td>A B Cl</td>
<td>Yes</td>
<td>0.60 (18)</td>
</tr>
<tr>
<td>12/77/F</td>
<td>B Cl</td>
<td>Yes</td>
<td>1.16 (58)</td>
</tr>
<tr>
<td>13/69/M</td>
<td>B Cl</td>
<td>Yes</td>
<td>1.54 (47)</td>
</tr>
<tr>
<td>14/77/M</td>
<td>No</td>
<td>Yes</td>
<td>0.91 (31)</td>
</tr>
<tr>
<td>15/64/M</td>
<td>No</td>
<td>No</td>
<td>2.29 (67)</td>
</tr>
<tr>
<td>16/77/M</td>
<td>A B Cl</td>
<td>Yes</td>
<td>0.66 (21)</td>
</tr>
<tr>
<td>17/76/M</td>
<td>B S T</td>
<td>Yes</td>
<td>0.64 (21)</td>
</tr>
<tr>
<td>18/59/F</td>
<td>A B Cl</td>
<td>Yes</td>
<td>1.59 (71)</td>
</tr>
<tr>
<td>19/48/M</td>
<td>B</td>
<td>No</td>
<td>2.42 (62)</td>
</tr>
<tr>
<td>20/67/M</td>
<td>A</td>
<td>Yes</td>
<td>1.32 (38)</td>
</tr>
</tbody>
</table>

Mean±SD

64.3±10.4 yr: 11Y, 9N
3F/17M

4.0±23

*A=inhaled anticholinergic agent; B=inhaled β₂-sympathomimetic agent; Cl=inhaled corticosteroid; Co=continuous oral corticosteroid; T=theophylline preparation; S=salmeterol.

†Symptoms in cold weather: an answer to the question: Does cold weather worsen your feeling of dyspnea when walking outdoors?
minute of the hyperventilation, the minute ventilation was measured from the expired air by the spirometer. The duration of the hyperventilation was 3 min. At least 2 technically satisfactory maximal expiratory flow-volume curves were obtained at 3, 5, and 10 min after the end of hyperventilation. The subjects wore nose clips during the forced expiratory maneuvers. The mean temperature in the room was 24.9°C (range, 21.7 to 27.5°C) and the mean humidity was 29.7% (range, 12.2 to 41.8%).

Analysis

The largest FEV$_1$ of the three baseline flow-volume curves was recorded. At each timepoint during and after the experiments, the larger FEV$_1$ of the two values was recorded. All figures in the “Results” section are means and SEs, and a p value <0.05 was accepted as a level of significance.

The responses to the experiments were analyzed by analysis of variance with repeated observations. If this analysis showed significant changes in FEV$_1$, the FEV$_1$ values at different time points were compared with the baseline values using Student’s paired t tests with the Bonferroni correction for multiple comparisons. Linear regression analysis was used to test the relationship of the responses and the baseline FEV$_1$. This analysis was applied separately in the healthy persons and in the patients with COPD. In addition, paired and unpaired Student’s t tests were applied when appropriate.

Results

The whole-body exposure to cold air cooled the skin of the face similarly in the healthy persons and in the patients with COPD (Fig 1, top). This challenge induced statistically significant bronchoconstriction in both groups. The magnitude of the responses did not differ significantly between the groups, although there was a tendency to larger responses in the healthy subjects (Table 2). However, the response was longer in the healthy persons than in the patients with COPD. In the patients with COPD, FEV$_1$ had returned to the baseline level immediately after the exposure whereas in the healthy persons, FEV$_1$ was significantly lower than the baseline value as late as 12 min after the end of the exposure (Fig 1, bottom). The bronchial responses to the whole-body exposure to cold air did not correlate with the baseline FEV$_1$.

The whole-body exposure to cold air at rest also increased the resting ventilation (from 12.3±0.7 L/min to 14.6±1.1 L/min in the patients with COPD, p<0.01; and from 14.2±1.6 to 15.7±1.9 in the healthy persons, p<0.05). The respiratory frequency did not increase, but the tidal volumes increased significantly in both groups.

During the isocapnic hyperventilation of cold air, only 3 patients with COPD could not maintain the minute ventilation level of FEV$_1$×30 and their target ventilation was diminished to FEV$_1$×25. As expected, the minute ventilation of the patients with COPD was lower than that of the healthy subjects (50.0±6.1 L/min vs 88.0±4.8 L/min, p<0.001). However, the hyperventilation induced statistically significant bronchoconstriction only in the patients with COPD (Fig 2, Table 2). There was, again, no association between the response and the baseline FEV$_1$.

The patients with COPD were divided into those 11 individuals who told that cold weather increases their exercise-associated dyspnea and those 9 individuals without such a history. The responses to the challenges did not differ between these subgroups. However, baseline FEV$_1$ was significantly lower in the former subgroup (1.05±0.1 L and 2.18±0.3 L, respectively, p<0.01). All patients with a history of an enhanced exercise-induced dyspnea in cold weather had their baseline FEV$_1$ below 1.6 L.

The baseline FEV$_1$ values did not differ significantly

---

**Table 2—Maximal Changes in FEV$_1$**

<table>
<thead>
<tr>
<th></th>
<th>Healthy Subjects, %</th>
<th>Patients With COPD, %</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Whole-body exposure to cold air</td>
<td>-10.3±0.8</td>
<td>-9.4±1.4</td>
<td>NS</td>
</tr>
<tr>
<td>Cold air hyperventilation</td>
<td>-1.5±1.0</td>
<td>-8.0±1.3</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>p value</td>
<td>&lt;0.001</td>
<td>NS</td>
<td></td>
</tr>
</tbody>
</table>
between the challenges. Omitting those patients who could not completely withhold treatment with their medication did not alter any results.

**Discussion**

This study shows that in patients with stable COPD, cooling of the face by cold air is capable of inducing eventually great bronchoconstriction as near-maximal hyperventilation of cold air. If one assumes that such a high level of ventilation rarely occurs in everyday life, we propose that cooling of the face is usually predominantly responsible for the bronchoconstriction due to cold weather in patients with COPD. At high ventilation level, as during heavy exercise, the direct airway effects may also contribute to the bronchoconstriction.

A whole-body exposure to cold air during resting nasal ventilation suits well for studying the facial cooling-induced reflex bronchoconstriction. Under such conditions, direct effects of cold air on the lower airways are unlikely, since even subfreezing air is almost completely conditioned when it has passed the nasal cavity. Cooling of the upper airways does not contribute to the bronchoconstriction. This challenge is also physiologic, since even under arctic conditions, the clothing usually leaves the face exposed. Under such conditions, the cooling of the face appears to be a stimulus for bronchoconstriction also in patients with COPD, although their responses tended to be slightly smaller and shorter than those of the healthy control subjects. The reason for this difference may be the parasympathetic autonomic neuropathy of COPD since the bronchial response to facial cooling is mediated via the vagus nerve.

The responses to facial cooling were surprisingly large in the healthy, elderly subjects, with a mean 10% fall in FEV1. In our previous study, the mean decrement in FEV1 was 5% to similar challenge in healthy subjects who were about 30 years younger than the healthy subjects in the present study. Thus, it seems that the bronchial response to facial cooling increases with age. As the responses to cold air hyperventilation were negligible in the healthy subjects, our results suggest that in healthy, elderly persons, facial cooling is the sole stimulus for bronchoconstriction due to cold weather.

Facial cooling was found to induce bronchoconstriction during the exposure to cold, which is in contrast to the effects of hyperventilation and exercise, which usually induce bronchoconstriction after the challenge. This finding highlights the importance of cutaneous reflexes, since a bronchoconstriction during exercise probably affects the exercise capacity more than bronchoconstriction after it has been completed.

In addition to its bronchoconstrictive effects, the whole-body exposure to cold air also increased the resting ventilation. There are several reports of similar responses in healthy persons. The immediate increase in ventilation in cold environment is thought to be a reflex response to cooling of the skin. In contrast, if only the inhaled air is cooled, the ventilation decreases, also in patients with COPD. The effect of cold environment on ventilation is important in COPD, since any factor tending to increase ventilation at a given exercise level will contribute to a reduction in the total exercise capacity, often to a marked degree.

The ventilation level for the hyperventilation challenge was set close to the maximal predicted breathing capacity of the subjects to reach maximal responses to direct airway stimulation. These responses tended to be smaller than the responses to facial cooling, although the difference was not statistically significant in the patients with COPD. We assume that in everyday life, the minute ventilation is usually much lower than what we used. Thus, it seems that direct airway effects of cold air usually play a minor role in bronchoconstriction due to cold weather both in patients with COPD and in healthy persons.

However, we found that the patients with COPD were significantly more responsive to cold air hyperventilation than the healthy subjects. In 7 of 20 patients with COPD, the fall in FEV1 was more than 9%, that is, in the asthmatic range. Consistently, in the study of Arnup et al., 6 of 26 patients with COPD responded to cold air hyperventilation and in the study of Ramsdale et al., 3 of 27 patients responded. Thus, among patients with well-defined COPD, there are individuals who respond to cold air hyperventilation. This finding should be taken into account when using cold air hyperventilation in the diagnosis of asthma.

The results of the present study cannot directly be

**Figure 2.** The effect of the isocapnic hyperventilation of cold air on FEV1 in patients with COPD (closed circles) and in healthy subjects (open circles). The bold line on the time axis indicates the duration of the hyperventilation.
applied to the situation in everyday life, since the bronchodilating effect of exercise was not taken into account in our study. In addition, little is known on how the cutaneous reflex mechanisms and the direct airway mechanisms operate simultaneously. However, it seems that cold weather is capable of worsening the FEV₁ almost 10% in patients with COPD, even at rest. Such a bronchoconstriction is unlikely to cause symptoms for a person with a large ventilatory reserve, but may incapacitate a patient whose exercise capabilities are limited by the ventilatory impairment. In such patients, the FEV₁ is usually under 1.6 L. In our study, all patients who reported that cold weather worsened their exercise-associated dyspnea had FEV₁ values under 1.6 L.

In conclusion, facial cooling seems to be the most important trigger for the bronchoconstriction due to cold weather in patients with COPD and may also contribute to the increased ventilation under such conditions. Cold weather seems to worsen the exercise-associated dyspnea, especially in those patients with the most impaired ventilatory reserve. Theoretically, such patients might benefit from wearing protective clothing over their face in cold weather.

References

Bronchoconstriction due to Cold Weather in COPD: The Roles of Direct Airway Effects and Cutaneous Reflex Mechanisms
Heikki O. Koskela, Anna K. Koskela and Hannu O. Tukiainen
*Chest* 1996;110;632-636
DOI 10.1378/chest.110.3.632

This information is current as of May 7, 2008

<table>
<thead>
<tr>
<th>Updated Information &amp; Services</th>
<th>Updated information and services, including high-resolution figures, can be found at: <a href="http://chestjournal.org">http://chestjournal.org</a></th>
</tr>
</thead>
<tbody>
<tr>
<td>Permissions &amp; Licensing</td>
<td>Information about reproducing this article in parts (figures, tables) or in its entirety can be found online at: <a href="http://chestjournal.org/misc/reprints.shtml">http://chestjournal.org/misc/reprints.shtml</a></td>
</tr>
<tr>
<td>Reprints</td>
<td>Information about ordering reprints can be found online: <a href="http://chestjournal.org/misc/reprints.shtml">http://chestjournal.org/misc/reprints.shtml</a></td>
</tr>
<tr>
<td>Email alerting service</td>
<td>Receive free email alerts when new articles cite this article sign up in the box at the top right corner of the online article.</td>
</tr>
<tr>
<td>Images in PowerPoint format</td>
<td>Figures that appear in CHEST articles can be downloaded for teaching purposes in PowerPoint slide format. See any online article figure for directions.</td>
</tr>
</tbody>
</table>