Effects of the combination of skin cooling and hyperpnea of frigid air in asthmatic and normal subjects

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McDonald, James S., Joann Nelson, K. A. Lenner, Melissa L. McLane, and E. R. McFadden, J. R. Effects of the combination of skin cooling and hyperpnea of frigid air in asthmatic and normal subjects. J. Appl. Physiol. 82(2): 453–459, 1997.—To investigate whether reducing integumental temperatures influences pulmonary mechanics and interacts with inhaling cold air, 10 normal and 10 asthmatic subjects participated in a three-part trial in which cooling the skin of the head and thorax and isocapnic hyperventilation of frigid air were undertaken as isolated challenges and then administered in combination. Integumental cooling for 30 min caused airway obstruction to develop in both populations [change in 1-s forced expiratory volume (ΔFEV₁) asthmatic subjects = 10%; normal subjects = 6%]. Hyperventilation, however, only affected the asthmatic subjects (ΔFEV₁ asthmatic subjects = 18%; normal subjects = 3%). In contrast to expectations, the combined challenge did not produce a summation effect (ΔFEV₁ asthmatic subjects = 21%; normal subjects = 7%). These data demonstrate that the skin of the trunk and head is cold sensitive and when stimulated causes similar degrees of bronchial narrowing in both normal subjects and patients with airway disease independent of any ventilatory effect. They also indicate that cooling of the skin does not add to the obstructive consequences of hyperpnea.

asthma; cold exposure; airway obstruction

EXPOSURE TO FRIGID AIR is a common environmental occurrence that can produce a series of physiological or pathological adaptations. In normal subjects (24) and in some individuals with chronic obstructive pulmonary disease (COPD) (26), facial contact with, or inhaling, cold air can provide relief from breathlessness, whereas in asthmatic subjects and others with COPD, such events can induce acute airway narrowing (2, 11, 21, 28). The latter phenomenon seems to be the more frequent. In a survey of 430 consecutive asthmatic patients referred to us for care, 354 (82%) reported that exposure to cold would result in paroxysms of cough, wheezing, and/or dyspnea. By way of contrast, only 35% developed these complaints with aeroallergens. In fact, in our population, cold air ranked third behind upper respiratory tract infections and exercise as an asthma precipitant. As with other triggers of airflow limitation, cold historically has little effect in normal individuals (3, 4, 6, 12, 20, 32).

Despite the apparent high prevalence of airflow limitation, its mechanism has proven difficult to investigate in the laboratory. The available studies have uncovered few sensitive subjects, and, even in them, the effects of reducing skin temperature and/or inhaling frigid air at resting ventilation [in contrast to hyperpnea (6–10, 28)] have been inconsistent or low grade (3, 4, 6, 20, 23, 30, 32). Part of the difficulty, particularly with respect to integumental exposure, may lie in the manner in which the investigations were performed. Typically, stimulus intensity has been quite variable in magnitude and/or duration, and in some trials only limited areas of the body were exposed (10, 20, 23, 30). Furthermore, there has been little effort to ascertain whether an interaction existed between skin and airway cooling, as would occur when a patient enters a frigid environment (5). Thus the situations that induce symptoms in the lives of patients with obstructive lung disease may not have been appropriately simulated.

The present study focused on skin chilling and addressed the above difficulties by having a group of asthmatic and normal subjects wear a thermal garment that circulated a coolant around their heads and upper torsos while they breathed either ambient or freezing air. In this fashion, the temperatures over a large surface area could be altered with and without the addition of airway cooling. The hypotheses being tested were that stimulating a large area of integument would cause airway narrowing and the combination of skin and airway cooling would produce more obstruction than would either site alone. Our observations form the basis of this report.

MATERIALS AND METHODS

Ten asymptomatic asthmatic volunteers (8 women and 2 men; mean age 23.3 ± 1.1 (SE) yr) and 10 normal individuals (7 women and 3 men; mean age 24.6 ± 1.2 yr) served as our subjects. All were nonsmokers. None of the asthmatic subjects used glucocorticoids, cromolyn sodium, or long-acting bronchodilators, and each refrained from taking any short-acting airway agents for 12 h before any study day. Neither group reported symptoms of a respiratory tract infection in the 6 wk preceding the investigation. Informed consent was obtained from each participant.

Changes in pulmonary mechanics were measured by having the subjects perform maximal forced exhalations in triplicate with a waterless spirometer. The performance recommendations of the American Thoracic Society were followed (1), and the best effort, as defined by the curve with the largest 1-s forced expiratory volume (FEV₁), was chosen for analysis.

Skin cooling was achieved with a specially designed body suit (Life Support Systems, Mountain View, CA). The garment consisted of a jacket that covered the chest and back, a cap for the head, and separate wrappings for the forearms, thighs, and abdomen. In each section there were multiple conduits through which a liquid coolant circulated from a central compressor. Each unit was detachable so that the
temperatures of desired areas could be reduced as required. The suit was worn next to the bare skin, and the subjects donned a lightweight cotton shift over it to preserve their modesty. Integumental temperatures were monitored at the surface of the chest and back by matched shielded thermisters (Omega 709 probes; accuracy ± 0.15°C from -30 to +10°C) interfaced to a dedicated digital processor (DP81 Omega Engineering, Stamford, CT). The temperature probes were placed on the pectoral and infrascapular areas of the right hemithorax and secured with tape. A third probe was attached to the interior surface of the jacket. Body core temperature was measured in the auditory canal by an IVAC thermometer (IVAC, San Diego, CA). The accuracy of the thermisters and thermometers was verified to be within 0.1°C of a Bureau of Standards precision thermometer. The cold suit was comfortable to wear and permitted skin temperatures to be reduced slowly and steadily without producing "cold burns" or evoking a ventilatory response, such as shivering or hyperpnea (14). Shivering was also minimized. Spirometry was recorded before and serially during exposure. Temperature and pulmonary mechanical data were obtained every 4 and 5 min, respectively. Only the data at the 30- and 60-min points were shown for the sake of brevity.

Isohyperventilation (HV) of frigid air was performed with a heat exchanger by using standard techniques (6, 7, 9, 10). The HV challenge began with a minute ventilation (VE) of 20 l/min and was raised in 20 l/min increments every 4 min until the level of hyperpnea could no longer be sustained or until a value of 80 l/min was reached. As has been our standard approach, spirometry was performed before and at 5 min after each VE interval (6, 7, 9, 10). Expired air was directed away from the heat exchanger into a reservoir balloon that was being constantly evacuated at a known rate through a calibrated rotameter (6, 7, 9, 10). The subjects were coached to keep the balloon filled, and in so doing, VE could be controlled at any desired level. End-tidal PCO2 tensions (PETCO2) were continuously measured at the mouth by a Beckman LB-2 analyzer (Beckman Instruments, Fullerton, CA). At the inspiratory port of the exchanger, a mixing valve allowed CO2 supplementation to maintain the PETCO2 at resting levels.

The investigation was performed in three parts, in which skin cooling and HV were undertaken as isolated challenges and then administered in combination. The first segment was designed to determine whether exposure of large areas of the integument to cold altered airway caliber. During this experiment, each subject sat quietly for 60 min in a neutral thermal environment on two occasions and breathed room air while wearing the cap and vest of our garment (the average temperatures of the laboratory during these trials ranged between 22.6 ± 0.4 and 23.3 ± 0.3°C). In one instance, the coolant was circulated through the suit while in the other it was not. The latter served as a control, and the order of study was randomly determined. On another day, the subjects undertook the HV challenges to quantitate their sensitivity to airway cooling (6, 7).

When the above sections were completed, the participants returned to the laboratory for examination of whether simultaneously cooling the skin and airways interacted positively. In these trials, skin temperature was lowered as above except that the duration of exposure was shortened to 30 min. This time was chosen because it coincided with the maximum pulmonary response seen in the first set of experiments. At the 30-min point, the subjects hyperventilated frigid air at the level of VE previously determined to produce the largest fall in FEV1. Spirometry was measured before and at the end of skin cooling and every 5 min after HV for 20 min.

The baseline data for the FEV1 for both groups of subjects for each set of experiments are shown in Fig. 1. The mean values for the asthmatic subjects are 3.09 ± 0.2 (93% predicted), and the values are 3.19 ± 0.26, 3.18 ± 0.16, and 3.29 ± 0.15 liters (98% predicted) for the cold exposure, control, hyperpnea, and hyperpnea plus cold exposure trials, respectively. The data for the same trials in the normal subjects are 3.72 ± 0.26, 3.53 ± 0.5 (103% predicted), 3.69 ± 0.25, and 3.86 ± 0.32 (112% predicted), respectively. There were no significant between-trial differences in either group (asthmatic subjects F = 0.2; normal subjects F = 0.18).

The temperatures of the suit (T5), backs (T9), and chests (TC) of the subjects for the cold and control experiments in both populations are shown in Figs. 2 and 3. In the control trial in the asthmatic subjects, T5 rose 0.9°C (from 31.4 ± 0.8 to 32.3 ± 1.0°C) over the period of observation (Fig. 2). In concert, TB and TC also increased 1.0 and 1.3°C, respectively. Activation of the compressor for the cold trial caused T5 to fall substantially (T5 at 60 min = 10.5 ± 1.3°C). The greatest effect occurred in the first 30 min, where T5 decreased 19.9°C from baseline. Thereafter, it stabilized and over the next 30 min changed only an additional 0.8°C. As the suit was cooled, T9 and TC progressively fell. By the end of the experiment, the temperatures in these sites had both reached 29.9°C (P < 0.001 for both). Body core temperature remained constant (body temperature in cold trial at time 0 = 37.0 ± 0.1; 60 min = 37.3 ± 0.1°C).

A similar pattern developed in the normal subjects (Fig. 3). T5, TB, and TC fell slightly in the control period...
and fell significantly when the cooling fluid was circulated [change in (Δ) Ts = 19.1°C; minimal Ts at 60 min = 11.9 ± 1.5°C; ΔTb = 6°C; ΔTc = 3.8°C]. Tc tended to be warmer because the suit opened in the front and was not taped closed in a few of the early experiments. Again, body core temperature was unaffected (Δbaseline to 60-min cold = 0.1°C).

Figure 4 displays the impact of cold exposure on pulmonary mechanics. As expected, there were no significant changes in the control trials; however, skin cooling caused bronchial narrowing in both groups. The effect was slow to develop and reached its nadir at 30 min. In the asthmatic subjects, FEV1 decreased an average of 0.34 ± 0.15 liter (10.2%; P, 0.05) at this point and did not change thereafter. In the normal subjects, the effect was statistically similar [ΔFEV1 at 30 min = 6.0% (0.23 ± 0.06 liter); P, 0.005]. There were no additional alterations with further exposure in either group.

The consequences of inhaling cold air while keeping skin temperatures at ambient levels are presented in Fig. 5. Hyperventilation to a mean V̇E of 61.1 ± 8.5 l/min by the asthmatic subjects reduced the FEV1 by 0.58 ± 0.09 liter (18.2%); P < 0.001. In contrast, little happened in the normal subjects (ΔFEV1 at 80 l/min = 3.3%; P = not significant).

In the interaction experiments, Ts, Tb, and Tc were within 2°C of those in the first trial and resulted in similar changes in pulmonary mechanics (Fig. 6). In the asthmatic subjects, the FEV1 decreased 20.6 ± 4.3% from baseline in the combined trial (P < 0.001). This value was not significantly different from that found with HV alone. Although the response of the normal subjects was twice that observed when HV was performed without exposing the skin to cold (i.e., 7.6%), the increase did not reach statistical significance (P < 0.08) and equaled that found with skin cooling.

DISCUSSION

Patients with asthma are historically quite sensitive to low ambient temperatures and can develop respiratory embarrassment with minimal contact, such as walking into an air-conditioned room or while experiencing the passage of a cold front through their locales (11, 20, 29). The mechanisms underlying this phenomenon have thus far escaped detection, but entering into a cold environment sets in motion two potential sources of
stimulation to the tracheobronchial tree. Exposure of the skin at the face can produce reflex bronchial narrowing while the inspiration of frigid air can directly reduce airway caliber (3, 6, 19, 25, 31). Of the two, the latter has been thought to be the most important (3). For example, only facial icing has been consistently found to raise airway resistance in asthmatic and normal people, but the effect is uniformly small and not associated with symptoms (3, 13, 19). Stimulation of the skin in other areas of the body is generally without effect, even in sensitive subjects; thus the role of integumental cooling has been viewed as inconsequential (3). Furthermore, because the obstructive consequences of breathing cold air at rest are also clinically minor (6, 25, 31), it has been suggested that hyperpnea is necessary to produce meaningful changes in lung function (5). The findings of the present study, however, indicate that this position needs to be reevaluated. Our data demonstrate that a sustained reduction in the integumental temperatures of the heads and torsos produces clinically relevant airflow limitation in asthmatic subjects and even causes bronchial narrowing in normal subjects. In addition, the present work also shows that the combination of skin and airway cooling does not evoke a synergistic or even additive effect.

The cold challenge we employed was quite moderate and reflected the type of situations that an individual in a temperate climate might encounter in his or her daily life. The temperature of the suit averaged 50°F (9–10°C) and simulated exposure equivalent to going out of doors in the late fall while lightly clad (the temperatures in northern Ohio in October and November of 1995 ranged between lows of 43–34°F and highs of 62–49°F, respectively). In addition, stimulation of the face was deliberately avoided so that we could examine the influence of cooling on less-sensitive areas (3, 13, 19). Despite this exclusion, the physiological impact in the asthmatic subjects was a 10% reduction in FEV1. Although this degree of bronchoconstriction was insufficient to induce a full-blown symptomatic episode, it is similar in magnitude to the effects produced by the inhalation of air pollutants such as SO2 (15). The results in the normal subjects were equally striking; not only did they mirror those in the asthmatic subjects, but, to our knowledge, this is the first time that airway obstruction has ever been found with cooling of the integument of the thorax in this group (14, 32).

Why does such a relatively minor stimulus change pulmonary function in this study when seemingly greater thermal challenges have been without effect in others? We believe the answer can be found in the...
manner in which the exposures were conducted. Simp-
plistically put, the intensity of the stimulus or “dose” of
cold that can be generated is a function of the heat flux
that exists at the thermal boundaries of the donor and
recipient interfaces. Heat exchange is driven by the
absolute temperature differences present, the heat
capacity of the materials involved, their mass, the
surface area exposed, and the length of contact. When
thermal gradients are present, heat will flow from one
surface to another (i.e., the hot body will warm the cold
one) until isothermal conditions occur. The larger the
heat capacity and mass, the greater the amount of
thermal energy required to achieve this point. As the
surface area and time of exposure rise, all else being
equal, the magnitude of the transfers increases propor-
tionately. More heat is lost over a longer period, and so
the cooling of the donor surface is greater. By way of
analogy, if one wanted to induce maximum heat loss
from the skin and, therefore, the greatest stimulus to
airway narrowing, one could readily accomplish this
feat by immersing the person in frigid water suffi-
ciently long to cause body temperature to fall.

By using these concepts, it is possible to place our
findings in perspective with respect to the other obser-
vations in the literature. The distinguishing features of
the present study were the application of cold to a large
surface area for a relatively long duration. The result-
ing changes in pulmonary mechanics developed slowly
and reached their nadir at 30 min. In other studies,
different combinations of intensity, duration, and sur-
face area were employed, and only immediate re-
ponses were sought. For example, Wells and associ-
ates (32), in their pioneering efforts, did not find any
pulmonary consequences of blowing cold air across the
heads and torsos of either their normal or asthmatic
subjects. Although these authors exposed the same
surface area as we did, and used air at −5 to −15°C,
they only continued their experiment for 2 min. Hence,
the stimulus intensity they used was much less than
ours and may not have been sufficient to have provoked
a response. Such considerations also explain why Berk
et al. (3) and others (30) found little effect from applying
ice packs to the thorax or having warmly clad asth-
matic subjects sit in a cold room (20, 23). The area of
integument stimulated in such experiments may be too
small to have much impact. Chen and Horton (4), on the
other hand, induced a 20% fall in FEV1 in asthmatic
subjects by having them shower for 1 min with water at
15°C and then sit for 2 min in front of a fan. In these
circumstances, both the surface area and the thermal
gradients were quite large, but the duration of expo-
sure was short. If our construct is correct, there should
have been little airway narrowing. Yet these investiga-
tors saw a considerable response. Again, the form of
exposure is critical. Abrupt reductions in skin tempera-
ture are known to produce marked alterations in
ventilatory pattern (14, 33), and it is possible that the
observations reported were contaminated by airflow
limitation derived from hyperpnea-induced airway cool-
ing and rewarming (8–10). A subsequent report from
the same group showed that breathing hot humid air
during the above experiments [an intervention that
eliminates the obstructive consequences of airway ther-
mal exchanges (27)] materially decreases the magni-
tude of the airflow limitation (12).

Why should the airways narrow on contact of the
skin with cold air? The precise reasons are unknown,
but there are a number of possibilities. The most
obvious is a thermally sensitive somatic afferent-vagal
efferent reflex. Such reflexes are well described in the
face and upper airways in humans (3, 13, 19, 24, 33),
but their presence in the integument in other parts of
the body are less well established (3, 30). Given that we
did not expose the face or nose to cold, it is unlikely that
we activated the physiological responses seen with the
diving reflex (33). Detailed studies, however, using
appropriate neural pharmacological agents would be
necessary to exclude these events with certainty. An-

Fig. 6. Consequences of hyperventilation with
and without skin cooling. A: asthmatic subjects.
B: normal subjects. Bars are mean values, and
vertical lines above bars are 1 SE. In cold expo-
sure experiments in each group, comparisons
being made are between baseline and 30-min
data point. In hyperventilation (HV) experi-
ments, comparisons are between baseline data
and those 5 min after hyperpnea. Graph is orga-
nized so that results of 2 cold and 2 hyperventila-
tion experiments can be readily contrasted.
%ΔFEV1, percent change in FEV1.
other theoretical postulate is that, because of their proximity to the chest wall, the trachea and bronchi could have been directly cooled. Such an event is unlikely with the magnitude of the stimulus used, but its presence could be definitively established by measuring intra-airway temperatures (10, 18).

From a teleological standpoint, an attractive explanation is that the reduction in bronchial diameter functions as a mechanism to limit respiratory water loss to the environment. Because cold air is essentially a dry gas, \(-44\) mg of water must be vaporized from the mucosa of the respiratory tract to bring each liter of air to full saturation as it enters the alveoli (16, 17). This is virtually double the amount required in the usual temperate environment (16, 17), and if recovery were not facilitated, the extra water would be exhaled. Several processes are known to operate to prevent this from happening. Cooling the skin decreases the temperature of the expired air (31) and promotes vasoconstriction in the distal portion of the nose (5, 22). The first event reduces the quantity of water that the air can physically hold, while the second augments return by forcing some of the remaining water to rain out as the air flows over a cold surface. The present study offers a third possibility. As airway diameters decrease, contact between the airstream and bronchial wall during both phases of respiration is facilitated and the efficiency of conductive and convective transfers rises; thus more heat and water are recovered (16, 17). In the normal subjects, the size of the bronchial response is self-limited as it is in other homeostatic circumstances such as inhaling noxious fumes. The heightened airway responsiveness of asthmatic subjects, however, likely eliminates this control, and the severity of the resulting obstruction is accentuated.

An improvement in respiratory heat exchange also offers an explanation as to why the pulmonary mechanical consequences of cooling the skin and breathing frigid air at elevated levels of ventilation do not sum in this and other studies (32). It is now recognized that hyperpnea produces bronchial narrowing through a sequence of mucosal cooling and rapid rewarming (7–10). Any event that increases heat and water recovery will limit the fall in airway temperature and shift the response to the right so that less obstruction develops for the same \(V_{E}(10)\). Consequently, the bronchoconstriction induced by the first stimulus in this study protected against the effects of the second. It remains to be determined whether such beneficial effects can be seen with other environmental bronchoconstrictors or are unique to thermal precipitants.

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