Thermal mapping of the airways in humans

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*Shipley Institute of Medicine and Departments of Medicine, Brigham and Women's Hospital
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McFadden, E. R., Jr., B. M. Pichurko, H. Frederick Bowman, Edward Ingenito, Steven Burns, Neil Dowling, and Julian Solway. *Thermal mapping of the airways in humans*. J. Appl. Physiol. 58(2): 564–570, 1985.—To characterize the intrathoracic thermal events that occur during breathing in humans, we developed a flexible probe (OD 1.4 mm) containing multiple thermistors evenly spaced over 30.2 cm, that could be inserted into the tracheobronchial tree with a fiberoptic bronchoscope. With this device we simultaneously recorded the airstream temperature at six points from the trachea to beyond the subsegmental bronchi in six normal subjects while they breathed ambient and frigid air at multiple levels of ventilation ($\dot{V}_E$). During quiet breathing of room air the average temperature ranged from 32.0 ± 0.05°C in the upper trachea to 35.5 ± 0.3°C in the subsegmental bronchi. As ventilation was increased, the temperature along the airways progressively decreased, and at a $\dot{V}_E$ of 100+ l/min the temperature at the above two sites fell to 29.2 ± 0.5 and 33.9 ± 0.8°C, respectively. Interval points were intermediate between these extremes. With cold air, the changes were considerably more profound. During quiet breathing, local temperatures approximated those recorded in the maximum $\dot{V}_E$ room-air trial, and at maximum $\dot{V}_E$, the temperatures in the proximal and distal airways were 20.5 ± 0.6 and 31.6 ± 1.2°C, respectively. During expiration, the temperature along the airways progressively decreased as the air flowed from the periphery of the lung to the mouth: the more the cooling during inspiration, the lower the temperature during expiration. These data demonstrate that in the course of conditioning inspired air the intrathoracic and intrapulmonic airways undergo profound thermal changes that extend well into the periphery of the lung.

airway temperatures; thermal changes in lungs; respiratory heat exchange

EARLY EFFORTS TO DEFINE THE ROLE of the respiratory tract in heating and humidifying inspired air have suggested that direct involvement is limited to the extrathoracic extrapulmonic airways (3, 4, 10, 11, 17). Whereas this is certainly the case at rest, particularly with nose breathing, recent studies with mouth breathing using varied levels of ventilation and inspired air temperatures have demonstrated that when large minute ventilations are respired, the temperature in the esophagus adjacent to the trachea falls, suggesting that the capacity of the upper airway to condition inspired air may be overcome (1, 5, 6, 12, 13, 17). In these circumstances, the point at which inhaled gas becomes heated to body temperature and fully saturated with water vapor appears to advance deep into the bronchial tree (14).

To better characterize the dynamic thermal events involved in the conditioning process, we developed a flexible probe containing multiple thermistors that could be safely inserted into the tracheobronchial tree of normal subjects. With this device we made simultaneous temperature recordings from the glottis to the distal bronchi under different inspired air conditions and over a range of ventilations, thereby constructing thermal maps of the airways. Our observations form the basis of this report.

METHODS

Thermal probe. The thermal probe consisted of a 270-cm-long flexible polyvinyl tube (OD 1.4 mm) that contained seven small thermistors (250-μm diam) placed distally 30.2 cm (Fig. 1). The thermistors were evenly spaced at 4.3-cm intervals and arranged in a spiral pattern on the probe. Each was fixed into the base of a small notch with epoxy glue and thermally and electrically isolated from its neighbor. The electrical connections were passed through the base of the notch and into the lumen of the tube, where they were gathered into a plug at the proximal end. The spiral pattern and recess design were incorporated to minimize contact of the thermistors with the walls of the bronchi. The thermal isolation of the thermistors was tested by applying a known temperature to each one and recording both the local response and that of its neighbors.

Each thermistor was excited in sequence with a 100-μA precision current source. The voltage drops across the thermistors were sampled ~8 times/s with an analog-to-digital converter coupled to a PDP-11 computer; the digitized data were stored for later analysis. Analog signals of temperature fluctuations were reconstructed and displayed on a cathode-ray tube, thereby permitting breath-by-breath visualization of the temperature within the airstream. The thermistors were calibrated electronically, and their digital output agreed to within <0.1°C with a Bureau of Standards thermometer over a temperature range from 0.0 to 40.0°C. The 63% response time of the probe was 0.250 s in stirred water.

Subjects. Six normal humans (5 males and 1 female)

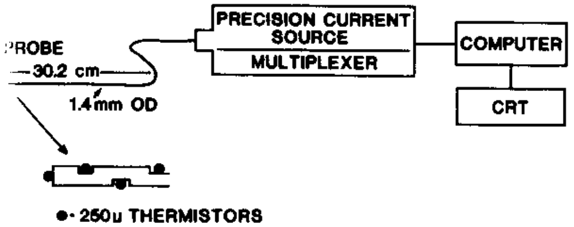

FIG. 1. Schematic representation of thermal probe assembly. Seven small thermistors (250 μm in diameter) are evenly spaced in a spiral fashion over distal 30.2 cm of a 270-cm-long flexible polyvinyl tube (1.4 mm OD). Thermistors were excited in sequence with a precision current source, and output passed through a multiplexer and analog-to-digital converter into a PDP-11 computer. CRT, cathode-ray tube.

with a mean age of 30.7 ± 3.7 yr (SE) served as our subjects. After informed consent was obtained, the nose and throat of each subject were anesthetized with 2% lidocaine, and a fiber-optic bronchoscope was inserted through the nasopharynx into a subsegmental bronchus of the anterior segment of the right lower lobe. As the scope was passed, distances were recorded from the tip of the nose to major anatomical landmarks from the glottis to the orifice of the subsegmental bronchi. The thermal probe was passed beside the bronchoscope by grasping a fine thread (tied around the end of the probe) with a biopsy forceps and then retracting the forceps into the suction channel of the scope. When the tip of the bronchoscope was in position the forceps was advanced and used to direct the probe until it wedged beyond the orifice of a subsegmental bronchus. The distance from the nose to the proximal end of the probe was recorded, and the bronchoscope was carefully removed, leaving the probe undisturbed. The probe was then slowly withdrawn until the most distal thermistor showed fluctuations in temperature with a deep breath, thus confirming an unobstructed bronchus. The length of probe withdrawn was recorded again, and the probe was securely fastened to the subject's nose to prevent movement. By knowing the length of the probe, the distance the tip was inserted, and the location of each landmark relative to the tip of the nose, the position of each thermistor within the tracheobronchial tree could be determined.

The approach used in the current study represents a modification of our previous technique in which a probe was threaded through the suction channel of the bronchoscope and the latter was withdrawn into the subglottic area (14, 16). In the present study the endoscope was removed completely to avoid the laryngeal irritation that can occur with high minute ventilations ($\dot{V}_E$) when the bronchoscope is left in the upper trachea (16). Minimal anesthesia was used during the bronchoscopy, and once in place, the probe was well tolerated. The stability of the position of the probe was verified by direct visualization of the thermistors during hyperpnea in preliminary experiments and by monitoring temperatures at given locations in all experiments. Intentional mouthward or distal movement of the probe resulted in a readily detectable decrease or increase, respectively, in the temperature recordings from the most proximal thermistor.

Experimental protocol. After the thermal probe was in position, the subjects performed eucapnic hyperventilation while they inhaled frigid air or air at room conditions. In the first situation, dry compressed air was cooled to subfreezing temperatures by passage through a heat exchanger that incorporated a Freon-containing refrigeration coil (8, 16). Previous experience has shown the water content of air treated in this fashion to be <0.05 mgH_2O/l, which for the purpose of this study was considered to be zero (8). In the room air experiments, the inspirate was preconditioned to duplicate typical ambient laboratory conditions of temperature and humidity by having the subjects inhale through a second heat exchanger in series with a bubble humidifier (18). The temperature of the humidifier's water bath was set to produce a water content of 8–9 mg/l of air. The air leaving the humidifier was warmed to ~26°C in the exchanger. In both circumstances, inspired air temperatures were recorded continuously by thermocouples in the airstreams of the exchangers. The order of study with respect to room or frigid air was randomly determined.

Eucapnic hyperventilation was performed as reported previously (7). In brief, expired gas was directed away from the heat exchanger into a reservoir balloon that was being constantly evacuated at a known rate through a calibrated rotameter. The subjects were asked to respire so as to keep the balloon filled. In so doing, their $\dot{V}_E$ could be set to any desired rate. End-tidal CO_2 concentrations were monitored with a Beckman LB-2 analyzer, and sufficient CO_2 was added to the inspiratory port of the exchanger to maintain end-tidal CO_2 concentrations at resting eucapnic levels.

The target $\dot{V}_E$ chosen for each study were 15, 30, 60, and 100 l/min, performed first in ascending and then descending order. (In 2 subjects, the maximum $\dot{V}_E$ was 120 l/min.) In this fashion the reproducibility of the temperature measurements could be determined. Each level of $\dot{V}_E$ was maintained for 2 min, with 2-min periods of quiet breathing interspersed between hyperpnea trials. One subject had difficulty sustaining the maximum $\dot{V}_E$ during the first descending experiment because of laryngeal irritation, so this particular $\dot{V}_E$ was not repeated with the other inspired air condition in the descending trial. The temperatures within the airways were recorded continuously during hyperventilation. The *no. 4* thermistor malfunctioned in the first trial, so no data were taken from it during any of the subsequent experiments.

The data were analyzed by paired *t* tests and one-factor analysis of variance (ANOVA).

RESULTS

The individual positions of the anatomical landmarks in our subjects are presented in Table 1. The average distances from the tip of the nose to the glottis and main carina of the trachea were 18.2 ± 0.6 and 31.4 ± 1.2 cm, respectively. The orifice of the right lower lobe bronchus (RLL) was 37.3 ± 1.4 cm from the nose, and those of the anterior segment (AS) and first subsegmental bronchi (seg − 1) were 39.4 ± 1.4 and 41.2 ± 1.6 cm, respectively. The most distal thermistor was 5.8 cm beyond seg − 1 on average (Figs. 2 and 3).

Results from the room air studies are shown in Fig. 2. The average temperature of the inspired air was 26.7 ±

0.5°C with an H_2O content of 8.8 ± 0.3 mg/l. At a $\dot{V}_E$ of 15 l/min the end-inspiratory temperature (T_{insp}) 2 cm below the glottis (most proximal thermistor) averaged 32.0 ± 0.5°C, and as the air moved toward the periphery of the lung, T_{insp} progressively rose as heat was transferred from the airway walls. At the carina, seg − 1, and the most distal thermistor, T_{insp} was 33.2 ± 0.5, 34.3 ± 0.5, and 35.5 ± 0.3°C, respectively. The distribution of the temperatures along the airways was significant by one-factor ANOVA ($F = 8.84$; $P < 0.001$). As $\dot{V}_E$ was increased, T_{insp} progressively decreased at each location. At about the level of the seg − 1, T_{insp} tended to rise more steeply with increasing $\dot{V}_E$, giving rise to a change in slope of the curves. As $\dot{V}_E$ was elevated, at all positions except at the most distal thermistor, the T_{insp} at each $\dot{V}_E$ were significantly different from each other. In the periphery, significant changes only occurred at 60 and 100+ l/min. During the maximum $\dot{V}_E$ trial ($\dot{V}_E$ = 100+ l/min), T_{insp} at the most proximal thermistor and carina were 29.2 ± 0.5 and 30.2 ± 0.4°C, and those at seg − 1 and the furthermost recording site were 31.6 ± 0.5 and 33.9 ± 0.8°C, respectively. At the intermediate levels of $\dot{V}_E$, T_{insp} at each recording site were intermediate between the extremes.

TABLE 1. *Anatomical landmarks*

Subj. No.	Glottis	Carina	RLL	AS	Seg − 1
1	18.4	31.1	40.0	41.5	44.4
2	17.5	32.5	37.0	39.6	42.0
3	19.5	35.3	40.7	43.0	44.6
4	17.5	28.2	32.5	34.0	35.5
5	16.7	28.7	35.0	37.7	38.4
6	19.8	32.5	38.5	40.5	42.0
Mean ±SE	18.2 ±0.6	31.4 ±1.2	37.3 ±1.4	39.4 ±1.4	41.2 ±1.6

Distances are recorded from the tip of the nares. RLL, orifice of right lower lobe bronchus; AS, orifice at anterior segmental bronchus; seg − 1, orifice of subsegmental bronchus.

During expiration the converse occurred. As the air flowed from the alveoli toward the mouth, heat was continuously given back up to the mucosa. At 15 l/min the temperature at the end of expiration (T_{exp}) fell from 36.3 ± 0.6°C in the periphery to 32.9 ± 0.4°C near the glottis. Again, the distribution of temperatures was significant ($F = 12.92$; $P < 0.001$). Increasing $\dot{V}_E$ increased heat recovery, and T_{exp} decreased progressively at each recording site. Once more, these changes with $\dot{V}_E$ were significant except at the distal two thermistors, where only the values for the two highest $\dot{V}_E$ reached statistical requirements. At maximal $\dot{V}_E$, T_{exp} was 34.9 ± 0.8°C at the distal thermistor and 30.4 ± 0.3°C at the most proximal location.

Switching to frigid air (−18.6 ± 1.2°C) materially accentuated the thermal changes within the lung (Fig. 3). The overall shape and pattern of the curves were the same as in the room air studies, but the temperature-distance slope change was more marked. At all levels of $\dot{V}_E$ and at all recording positions, T_{insp} and T_{exp} were substantially colder than corresponding values in the room air experiments. Unlike the room air trials, factorial analysis demonstrated significant differences in the most distal thermistor for both T_{insp} and T_{exp} as a function of $\dot{V}_E$ (T_{insp} $F = 5.66$, $P < 0.001$, T_{exp} $F = 5.16$, $P < 0.01$).

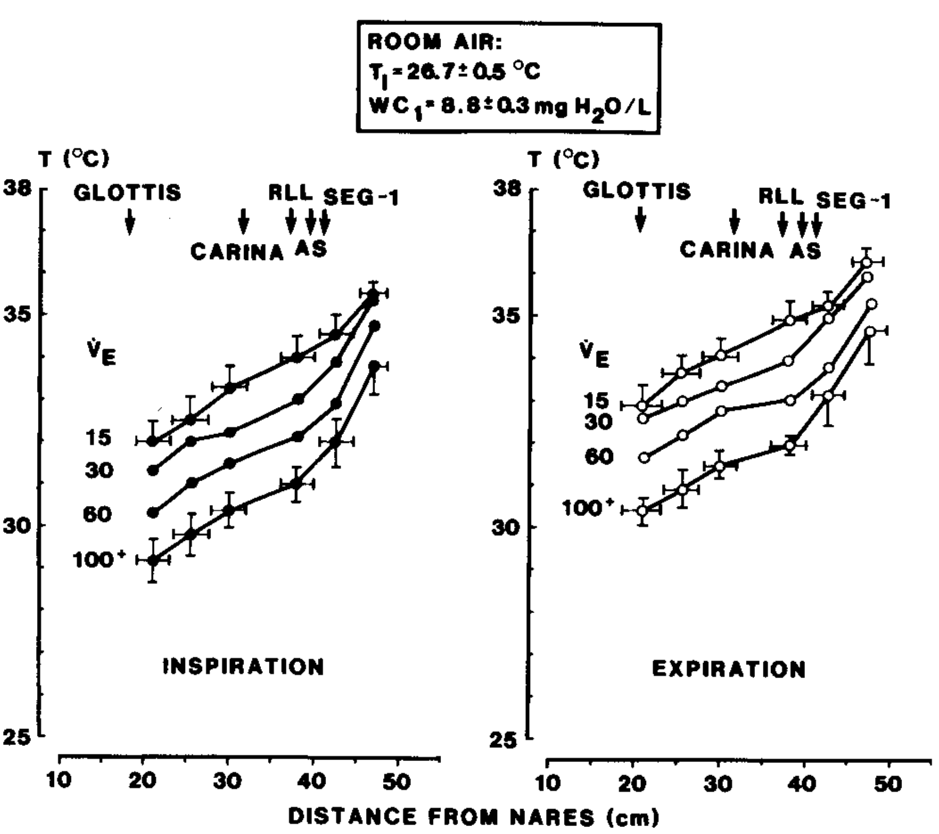

FIG. 2. Inspiratory and expiratory thermal maps while breathing room air at various minute ventilations ($\dot{V}_E$). Mean locations of anatomical landmarks are shown at top of each graph. Data points are mean values recorded from each thermistor and brackets represent one SE. T_I, mean temperature of inspired air; WC_I, mean inspired water content; T, temperature within airstream in tracheobronchial tree; RLL, right lower lobe; AS, anterior segmental bronchus; seg − 1, subsegmental bronchus.

At 15 l/min, T_{insp} ranged between 28.1 ± 0.3 and 35.4 ± 0.4°C from the proximal to the distal thermistor. From the glottis to seg − 1, these values approximated those recorded in the maximum $\dot{V}_E$ room air study: T_{insp} proximal thermistor at 15 l/min cold was 28.1 ± 0.3°C; 100+ l/min room was 30.4 ± 0.3°C (P = NS); seg − 1 15 l/min cold was 32.2 ± 0.7°C; 100^+ l/min room was 31.6 ± 0.5°C (P = NS). At maximum $\dot{V}_E$, T_{insp} in the upper trachea was 20.5 ± 0.6 and 31.6 ± 1.2°C in the distal bronchi. During expiration T_{exp} varied from 36.2 ± 0.3 in the periphery to 29.6 ± 0.2°C below the glottis at the lowest $\dot{V}_E$ and from 32.5 ± 1.2 to 22.5 ± 0.5°C at the highest $\dot{V}_E$ at the same positions.

The changes in airstream temperature as a function of $\dot{V}_E$ during inspiration and expiration are shown in Fig. 4. At any given point in the airways from the glottis to

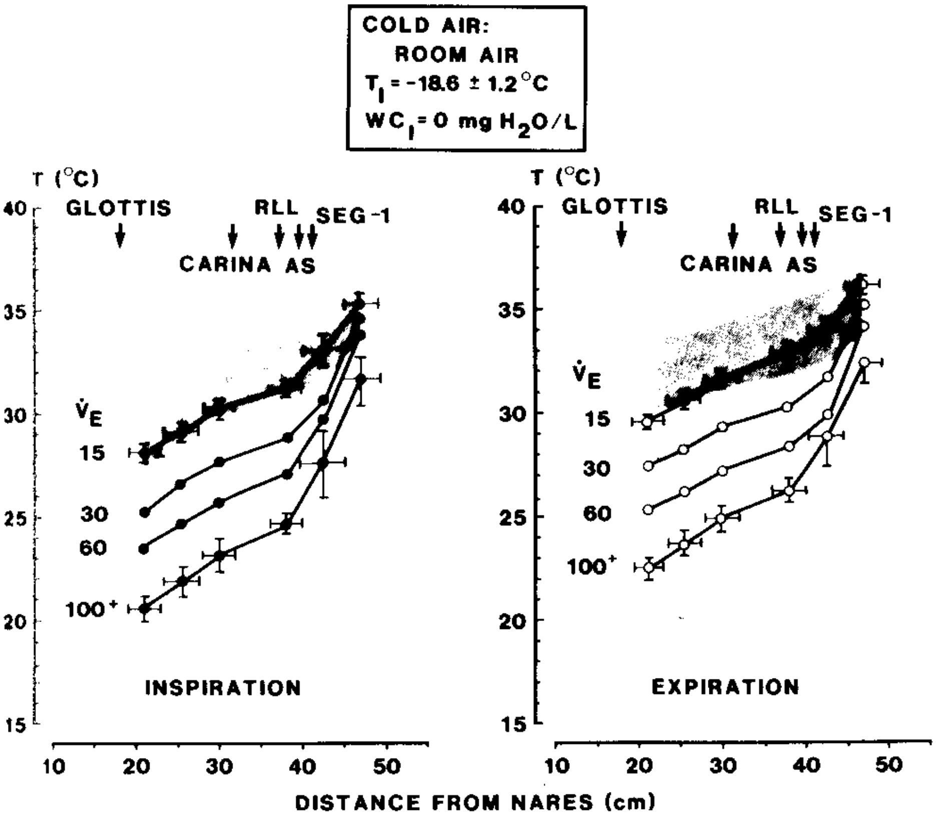

FIG. 3. Inspiratory and expiratory thermal maps while breathing cold air at various minute ventilations ($\dot{V}_E$). Range of temperature found in room air studies is shown by shaded area. Format is identical to Fig. 2.

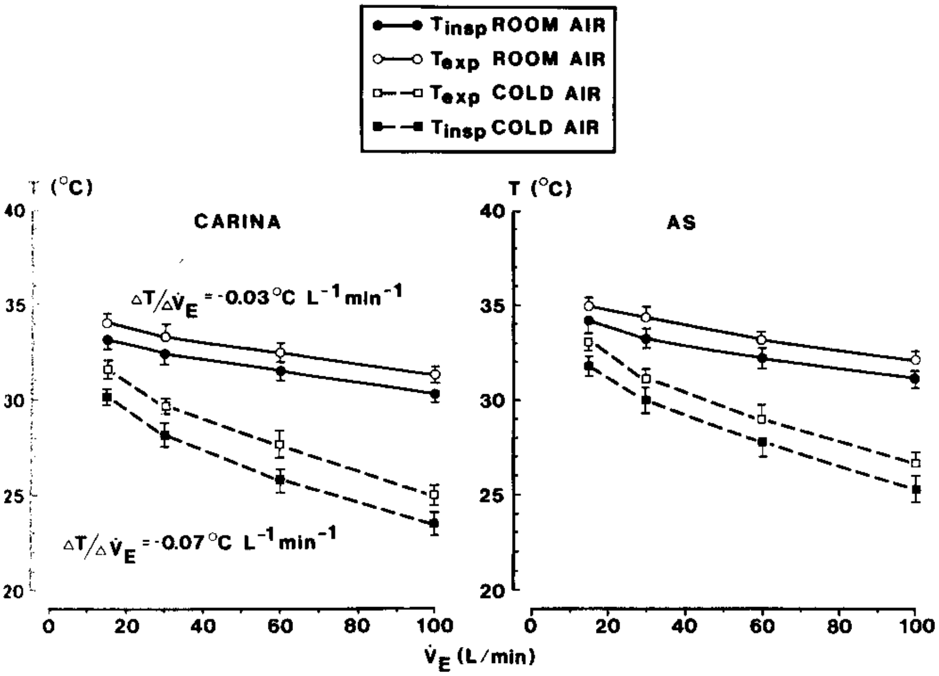

FIG. 4. Temperature of airstream (T) at various levels of tracheobronchial tree as a function of ventilation ($\dot{V}_E$). Data points are mean values and brackets represent one SE. *Closed* and *open* symbols represent end-inspiratory temperatures (T_{insp}) and end-expiratory temperatures (T_{exp}), respectively. *Circles* are room air experiments; *squares* are cold air data. $\Delta T/\Delta \dot{V}_E$, slopes of lines; AS, anterior segment right lower lobe.

the anterior segment (AS) of the RLL, the temperature of the airstream was inversely related to the level of $\dot{V}$E. Under ambient room conditions, the slope of this relationship ($\Delta T/\Delta \dot{V}$E) was $-0.03°C \cdot l^{-1} \cdot min$. While under cold air conditions it decreased to $-0.07°C \cdot l^{-1} \cdot min$. The differences between T_{insp} and T_{exp} increased as the temperature and water content of the inspirate were reduced.

The reproducibility of the temperature measurements is displayed in Fig. 5 for the studies employing maximum $\dot{V}$E. No significant differences from the line of identity were found in either room or cold air trials.

DISCUSSION

The present study characterizes, for the first time, the dynamic thermal events that occur in the intrathoracic and intrapulmonic airways of normal humans under a variety of circumstances ranging from sedentary activity to the simulation of strenuous exertion in ambient and frigid environments. Our findings support and extend previous observations employing single points of measurement (3, 4, 10, 11, 14, 19) and demonstrate that heat exchange is not confined to any particular region of the respiratory tract. Rather, the location and magnitude of transfer change in response to the thermal demands made on the system. In the current investigation during inspiration, temperature of the airstream rose progressively as the air flowed from the mouth to the periphery of the lung under all experimental conditions, demonstrating that the transfer of heat and H_2O is a continuous longitudinally distributed process that can occur anywhere within the tracheobronchial tree as long as thermal gradients exist between the air and the airway mucosa.

The site of the conditioning process is determined during inspiration by the level of $\dot{V}$E, temperature, and H_2O content of the air being respired. With room air at low $\dot{V}$E, the bulk of the conditioning takes place in the upper airways as expected (3, 4, 10, 11, 19); however, the colder (therefore drier) the inspirate and/or the greater the $\dot{V}$E, the more other regions begin to participate. As this occurs, the temperature within the intrathoracic airways falls dramatically and large gradients develop between the glottis and the subsegmental bronchi, indicating a transfer of heat from airway walls to the airstream in these areas (Figs. 2 and 3). The degree of cooling that occurs with the combination of high $\dot{V}$E and frigid air can be substantial, as evidence by the average T_{insp} of 20.5 and 23.5°C in the upper and lower trachea, respectively. The magnitude of this cooling would not have been apparent from the indirect measures of airway temperatures that have been used in previous investigations (1, 5, 6, 12, 13). Although the temperature in the retrotracheal esophagus falls with exercise and hyperventilation (1, 5, 6, 12, 13, 17), comparison of the magnitude of cooling with that shown in Figs. 2 and 3 demonstrates that gradients of 8–9°C can exist between the lumena of these structures with cold air breathing (6, 13). Thus the utility of these indirect techniques is limited to qualitative rather than quantitative assessment of the thermal changes in the airstream of the intrathoracic airways.

One reason why hyperpnea has such a profound influence on T_{insp} is that the more $\dot{V}$E is elevated, the greater the volume of air to be conditioned and the less the residence time at any given point. Hence there is less warming that occurs in the mouth, pharynx, and major intrathoracic airways. Consequently, heat transfer is forced to take place further along the tracheobronchial tree, and incompletely conditioned air must penetrate deeply into the distal airway segments before being brought to body conditions. The progressive decrease in airstream temperature measured at the most distal thermistor with increasing $\dot{V}$E clearly illustrates this phenomenon, particularly with cold air. The temperature at this recording site could only have fallen if less heat had been added to the air before it reached this location. In addition, it is clear that final conditioning must take place at some point in the bronchi beyond the tip of the probe.

These findings on penetrance agree qualitatively and

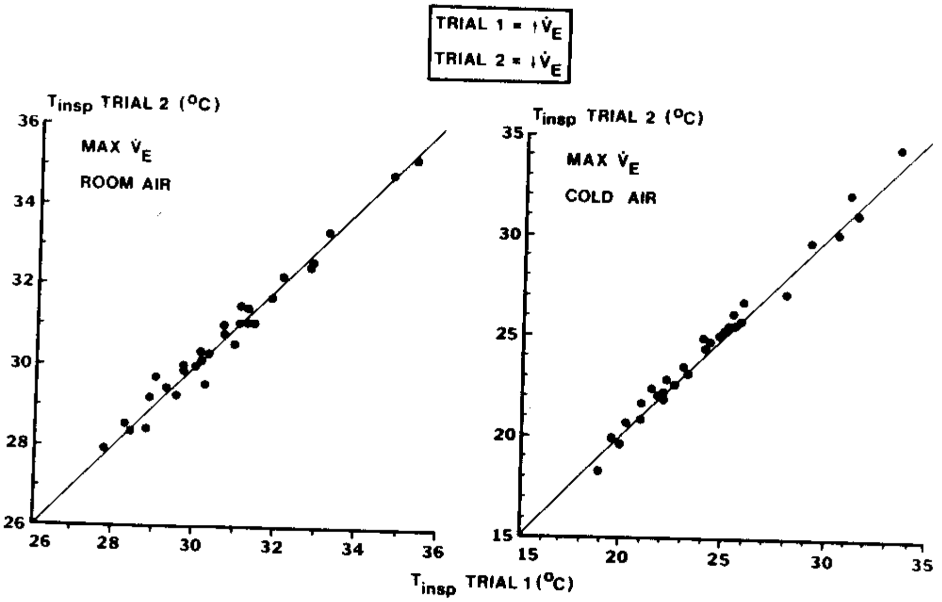

FIG. 5. Reproducibility of intrathoracic temperature measurements during maximum ventilation ($\dot{V}$E) in room and cold air experiments. *Trials 1* and *2* represent experiments in which $\dot{V}$E had been increased and decreased, respectively. T_{insp}, end-inspiratory temperature. Data points are individual values from each thermistor.

quantitatively with the results of an earlier work (14) and confirm that heat exchange can readily take place in distal parts of the tracheobronchial tree. Our results are in conflict, however, with the conclusions of Gross et al. (9). These authors introduced thermistors tied to a biopsy forceps into the tracheobronchial trees of several individuals and were unable to observe any fluctuations in temperature with respiration at distance 10–12 cm beyond the carina. In this particular study, the diameter of the temperature probe was relatively large (>2 mm), and based on the anatomical data in Table 1 it is likely that it was inserted into a subsegmental bronchus where it filled most of the airway. Hence it is probable that the above findings are derived from either occluding the orifice of the segment totally, or from materially limiting flow to the area.

The exact extent to which incompletely conditioned air can penetrate the bronchi is presently unknown, but when one considers that our approach underestimated airway temperatures, the depth could ultimately turn out to be considerable. Because the 63% response time of the probe was 0.250 s in stirred water, it is likely that it was slower in air. Thus the excursions we measured, if anything, minimized the actual variations in airstream temperatures. In addition, as the airways branch into the lung, the probe progressively occupies a larger part of the airway lumen. This factor, by slowing flow and/or changing flow profiles in the distal airways, promotes conductive and convective transfers and so artificially raise T_{insp} at these points. The abrupt changes in temperature-distance slopes shown in the curves in Figs. 2 and 3 probably result from this source.

It has been recognized for some time that the temperature of the air exiting the nose or mouth decreases as a direct function of environmental temperature and indirectly with $\dot{V}_E$ (2–4, 19), and from these observations it has been deduced that the respiratory tract undergoes cooling to facilitate heat recovery. Our study supports these speculations and demonstrates that this phenomenon is not the result of a purely local event within the upper airways but, rather, is a continuous process that begins in the periphery of the lung. From our data it appears that the air leaving the alveoli gradually undergoes a decrease in temperature as it passes through the bronchial tree, and this effect is dependent on the temperature and volume of the air that had previously been inspired. The further the air penetrates unconditioned during inspiration, the earlier recovery begins in expiration; the colder the airstream at any point in inspiration, the more heat is transferred back to the mucosa during expiration. As the temperature of the gas decreases, its ability to hold moisture changes in concert, so water condenses back to the airway surface as well. Thus the fall in T_{exp} is an important mechanism for the conservation of heat and water, and it can only occur if the temperature of the mucosa is lower than that of the air at any given point.

The mechanism by which these gradients are achieved and maintained is unknown. It is important to realize that a continuous source of heat is not required to warm the incoming air. Cole (2) has found that breathing through a glass tube containing moist blotting paper will condition air as effectively as the upper respiratory tract, so a blood supply to the exchanging surface is not necessary. In fact, warming the mucosa may even be detrimental, for if the airways were to have the heat they gave up to the air replenished from the circulation, recovery during expiration could be seriously jeopardized, and more heat and water would be lost to the environment. As discussed previously, since esophageal temperatures fall when the thermal burden on the airways is increased (1, 5, 6, 12, 13, 17), it is possible that the bronchial circulation may be thermally sensitive and so may play a role in respiratory heat exchange. If this vascular bed were to constrict in response to cooling in a fashion analogous to the vessels in the skin, mucosal temperatures could reach, and be held at, levels sufficiently low to facilitate recovery. In support of this possibility, we have recently been able to show that that the generating of heat and the increases in cadiac output that develop with moderately severe exercise do not raise the temperature within the airways over that seen with voluntary hyperventilation at matched $\dot{V}_E$ (15). Thus the local need to recover heat and water may be a prime determinant of regional blood supply.

In summary, our data demonstrate that respiratory heat exchange is a dynamic process that produces profound thermal changes in the intrathoracic and intrapulmonic airways. We believe that the techniques and observations described in the present report may begin to make it possible to come to a better understanding of the factors controlling this phenomenon.

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