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Dependence of human respiratory thermal washout on extrathoracic airway conditions

J.W. Kaufman

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ABSTRACT: Thermal washout curves have been proposed as noninvasive tools for analysing lower airway dimensions and pulmonary blood flow, but how upper airway heat transfer affects these washout curves is unclear. The present study was designed to compare extrathoracic and tracheobronchial contributions to thermal washout curves.

Respiratory frequency, air ambient temperature, and body core temperature (t_c) were varied in six male subjects before and after immersion in cold (1.1°C) water for up to 2 h under three conditions: 1) control: ambient temperature (t_{amb}) = 25°C, rectal temperature change (Δt_{re}) = 0°C; 2) pre-immersion: t_{amb} = 4°C, Δt_{re} = 0°C; and 3) post-immersion: t_{amb} = 25°C, Δt_{re} = -0.7°C. Both peak expiratory nasal (t_{pn}) and oral (t_{po}) airstream temperatures were measured. Each subject was tested twice.

Expiratory t_{po} was generally higher than t_{pn} in all conditions. Increasing breathing rates lowered t_{pn} and t_{po} in the control and cold air environments. Orifice temperatures, which are presumed to reflect upper airway blood temperatures, correlated with both t_{pn} and t_{po}. Lowering t_c had no effect on washout curves during quiet breathing and affected only t_{pn} during rapid breathing.

The results suggest that while tracheobronchial conditions may contribute to thermal washout curves, extrathoracic conditions predominate. Strong correlations between orifice temperatures, peak expiratory nasal temperatures and peak expiratory oral temperature demonstrate the dominant role of upper airway heat exchange in determining thermal washout curves.

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Naval Air Warfare Center Aircraft Division, Human Performance Technology Branch, Warminster, PA 18974-0591, USA.

Correspondence: J.W. Kaufman
South Engineering Centre/Crew Systems
Naval Air Warfare Center Aircraft Division
Bldg 2187 Suite 2280
48110 Shaw Rd Unit 5
Patuxent River
MD 20670-1906
USA

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Respiratory thermal exchange plays a major role in cold-induced bronchospasms [1], airway particle [2] and vapour deposition [3]. Increasing our understanding of respiratory heat and water loss can lead to improvements in predicting health risks associated with hygroscopic particle inspiration and the treatment of cold-induced asthma. Directly measuring bronchial heat and water losses is beyond current capabilities, so investigators have begun to use temperature washout curves to estimate bronchial thermal conditions in a noninvasive manner [4, 5].

Respiratory washout curves represent expired airstream composition as a function of expired volume during single or multiple exhalations. The shape of these curves resembles an exponential form (fig. 1) and are characterized by their rise times and plateau values. Nitrogen and CO_2 washout curves are commonly used to quantify lung volumes in health and disease. Temperature washout curves have been proposed as an alternative to N_2 and CO_2 washout curves because their measurement requires less sophisticated equipment and techniques [4]. In addition to measuring lung volumes, SERIKOV *et al.* [6] recently suggested that temperature washout curves can be used to determine pulmonary blood flow and lung tissue mass.

Like N_2 and CO_2 washout curves, temperature washout curves are probably affected by changes in pulmonary blood flow and tissue volume. Since gas exchange only occurs in the lung parenchyma, however, N_2 and CO_2 washout curves are unaffected by conditions in the extrathoracic airways. This is probably not true with temperature washout curves because the upper airway is

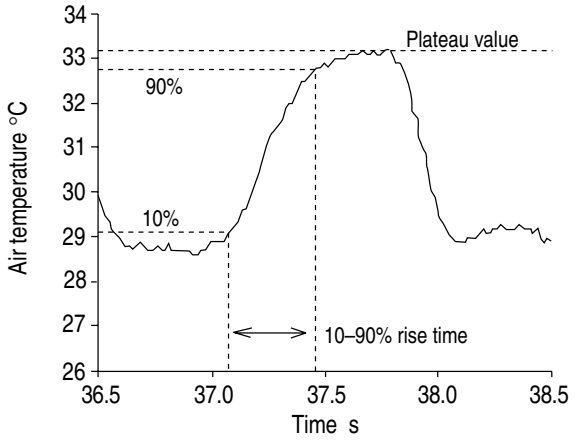

Fig. 1. – Respiratory washout curve obtained during rapid breathing (~30 breaths·min^{-1}) demonstrating how plateau values and 10–90% rise times are determined from an expiratory temperature curve. Expired temperatures representing 10% and 90% of the difference between the minimum and maximum air temperatures during the single breath are indicated. Peak expired temperatures represent plateau values on temperature washout curves.

thought to largely determine expired airstream temperatures [7].

Human airway temperature data suggest that these predictions are accurate during quiet breathing. This is a consequence of expired air passing out of the lung at 37°C; a decline in airstream temperature will not occur until a temperature gradient exists between the airstream and airway mucosal surface. During quiet nasal breathing, airstream cooling will occur proximal to the pharynx, since this is where inspired air reaches the body core temperature (t_c) of 37°C, even at low ambient temperatures (t_{amb}) [7–9]. Oral breathing shifts cooling of expired air to the level of the carina, the point at which inspired air temperature reaches 37°C during quiet breathing [10].

Hyperventilation, however, may cause orally inspired air to pass to at least the 5th bronchial generation before it reaches t_c [11]. It is reasonable to assume that hyperventilation during nasal breathing will also shift the point at which inspired air warms to t_c distally. Under these conditions, considerable heat exchange will occur within the lung (at least during oral breathing) and thermal washout curves may reflect lung volumes, as suggested by SERIKOV *et al*. [6].

The present study was designed to compare upper and lower airway contributions to thermal washout curves by varying respiratory frequency (f_R), t_{amb} and t_c. These variables were chosen because increasing f_R was assumed to increase pulmonary heat exchange, while lowering t_c decreases pulmonary heat exchange. Breathing cold air should reduce upper airway surface temperatures without affecting lung temperatures [9]. Corresponding changes in washout curve shape parameters were quantified by comparing the 10–90% rise times and peak expired air temperatures.

Materials and methods

Subjects

Six nonsmoking males (table 1) with a mean (±SEM) age 33±3.7 yrs, height 177.8±3.5 cm, and weight 74.4±4.6 kg volunteered to participate as subjects after being fully informed of the details of the experimental protocol and associated risks. These procedures were approved by the Naval Air Warfare Center Advisory Committee for the Protection of Human Subjects.

Apparatus

Determination of changes in airstream washout temperatures required the development of a temperature sensor that permitted normal breathing, had a small mass to minimize heating of inspired air [12], and could provide simultaneous measurements of airstream and airway orifice surface temperatures during nasal or oral breathing. Each of the sensors used in this study consisted of a wire ring made of 24 American wire gauge (AWG) stainless steel wire onto which four thermocouples (44 AWG welded bead, type T) were attached (fig. 2). The nasal sensor had a ring diameter of 13 mm while the oral sensor had a 28 mm diameter. On both sensors, two thermocouples were attached to 26 AWG teflon coated wire and mounted in the centre of the ring to measure airstream temperatures. The other two themocouples were attached directly to the ring to measure surface temperatures. This design permitted normal breathing while simultaneously measuring surface and airstream temperatures when the sensor was placed against the perimeter of an airway opening.

Table 1. – Physical description of subjects participating in study

Subject No.	Age yrs	Height cm	Weight kg
1	32	175	70
2	50	168	63.4
3	34	191	84.6
4	24	175	71.8
5	30	173	65
6	28	185	91.4
mean±SEM	33±3.7	177.8±3.5	74.4±4.6

Thermocouple output was directed to an amplifier (Model Tc.4; Bendec, Santa Ana, CA, USA) with an electronic reference junction and a bandwidth of 2.5 Hz. Thermocouples were calibrated at 0°C (Model K140-4; Kaye Instruments, Bedford, MA, USA) and 29.8°C (Model 17402 Gallium Temperature Standard; Yellow Springs Instruments, Yellow Springs, OH, USA).

The time response (τ) of the temperature measurement system was determined using the method of RAY *et al*. [13]. The sensor was placed at the opening of a

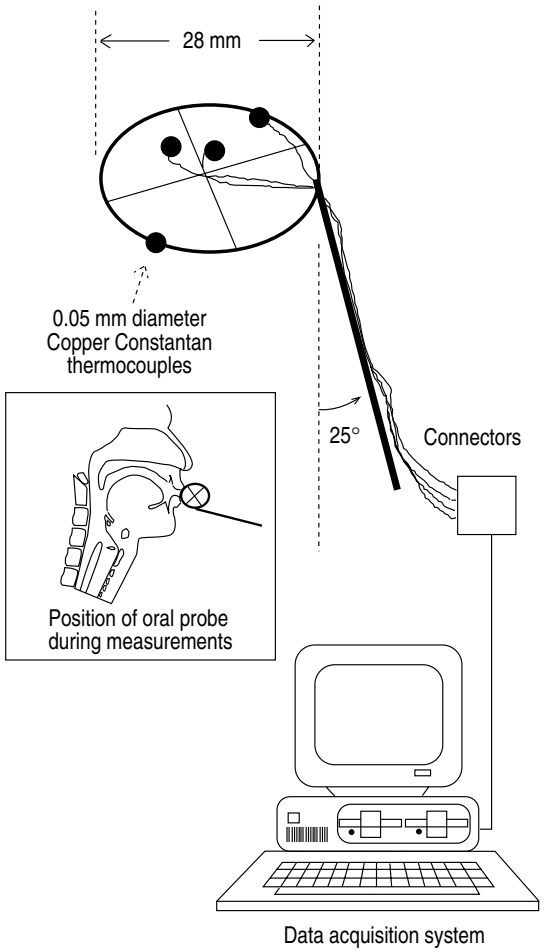

Fig. 2. – Schematic drawing of the temperature sensor used to measure expired and orifice temperatures simultaneously. The wire ring served to correctly position the thermocouples during breathing. The oral probe dimensions are depicted. Nasal probe ring diameter = 13 mm.

14.9 cm tube with a diameter of 1.8 cm. The investigator held the opposite end of the tube to his lips and slowly exhaled (air temperature measured to be 32°C) followed by a rapid inhalation of ambient air (22–25°C). The temperature response of the system was measured with a digital oscilloscope (model HP 54501A; Hewlett-Packard, Palo Alto, CA, USA) and the time to reach 63.2% of the ambient temperature calculated. This technique produced highly variable results depending upon the expired minute ventilation (V'_E) and how quickly flow was reversed. Based on the 10 fastest responses, τ was found to be 46 ms. The slower response times were assumed to be due to a slower transition from expiration to inspiration.

Temperature measurement error (ξ), caused by τ can be characterized by the difference between measured, Δt_{meas}, and actual, Δt, temperature changes during sinusoidal temperature oscillations:

$$\xi = \frac{\Delta t_{meas}}{\Delta t} = \frac{1}{\sqrt{1 + (\omega\tau)^2}} \quad (1)$$

where ω=angular frequency [14].

Δt is underestimated by <5% for f_R <70 breaths·min^{-1}, given τ=0.046 s. Assuming that 5% measurement error is acceptable, the measurement system appears adequate for all f_R observed in this study (table 2). However, temperature measurement error increases to 21–28% when modelling breathing as a series of periodic square waves under the same conditions and approximating square waves by the first order harmonic. Physiologically, higher frequency components of the expiration temperature profile occur during the initial washout of upper airway and proximal bronchial gases and are probably best represented by square waves. This suggests that measured dynamic responses probably underestimate actual rise times and that measured rise times can be interpreted as first order approximations. A data sampling rate of 64 Hz was used during the experimental trials to further minimize measurement error.

Experimental procedures

This study was conducted during a thermal evaluation of anti-exposure protective clothing, with each subject participating in two exposures. Subjects reported to the laboratory at the same time of day for each trial (either morning or afternoon). Prior to dressing in the experimental anti-exposure equipment, the control temperature washout measurements were obtained at a mean (±SD) t_{amb} of 23.0 (±0.7)°C. Airway temperature measurements were obtained by placing the nasal or oral sensor against the nares or lips and breathing through it for 60 s. Subjects kept their mouths closed during nasal breathing, while during oral breathing a noseclip occluded the nasal passages. The following sequence was used in obtaining temperatures: 1) right nares, quiet breathing; 2) left nares, quiet breathing; 3) right nares, rapid breathing; 4) left nares, rapid breathing; 5) oral, quiet breathing, and 6) oral, rapid breathing. Subjects were dressed in medium weight clothing and a dry-type anti-exposure garment and fitted with electrocardiogram (ECG) electrodes and rectal and skin surface thermocouples.

Following dressing, subjects were preconditioned to the cold by resting in a room at 4.7±0.6°C for 20 min. Pre-immersion airway temperatures were measured about 5 min after entering the room using the sequence described above. Immediately afterwards, subjects were immersed neck deep in a pool (1.5 m deep × 2.4 m diameter) of stirred 1.1±0.2°C water for up to 2 h. Some exposures were terminated at less than 2 h because the subject or attending physician elected to stop the exposure. Following removal from the water, the anti-exposure garment was removed from the subject, who was then quickly dried with towels. Post-exposure airway temperature measurements were obtained after any obvious shivering had subsided at t_{amb} of 22.9±0.6°C. A summary of environmental air temperatures and changes in core temperature during exposure to each environment is given in table 3.

Data analysis

The dependent variables used in the analyses were nasal and oral peak expired temperatures (t_{pn} and t_{po}, respectively) and nasal and oral 10–90% rise times. The 10–90% rise times were defined as the expiratory time necessary to rise from 10 to 90% of the difference between minimum inspiratory and peak expiratory temperatures (fig. 2). The 10–90% rise times represent the period during expiration where the greatest rate of temperature change is observed. f_R was calculated from the peak to peak frequency of t_{pn} and t_{po}. Multivariate analysis of variance was used to assess the significance of subject, type of breathing (nasal *versus* oral), t_{amb}, and f_R on peak expired temperature (Statistica for Windows, 1994, StatSoft, Tulsa, OK, USA). Missing data precluded a comparison between right and left nostrils, so data were pooled when available from both nostrils. Linear regression analysis was performed to assess whether orifice (nares or lip) temperature or changes in rectal temperature (Δt_{re}) influenced t_{pn} and t_{po}. A p-value of less than 0.05 was considered significant.

Table 2. – Respiratory frequencies observed during exposure to each experimental condition

Respiratory pattern	Respiratory pattern	Respiratory frequency		
		Pre-exposure breaths·min^{-1}	Cold exposure breaths·min^{-1}	Post-exposure breaths·min^{-1}
Nasal	Quiet	21.2±0.3	24.2±0.3	25.3±0.3
	Rapid	39.9±0.4	35.3±0.4	35.0±0.4
Oral	Quiet	20.8±0.4	24.5±0.4	23.2±0.4
	Rapid	35.3±0.5	37.2±0.5	35.2±0.4

Values are presented as mean±SEM.

Results

Figure 3 shows the relationship between mean t_{pn} and

Table 3. – Experimental conditions in which measurements of air temperature and drop in rectal temperature (Δt_{re}) were obtained

Environment	Air temperature°C	Δt_{re} °C
Control	23.0±0.7	0
Cold air	4.7±0.6	0
Post-exposure	22.9±0.6	-0.7±0.1

Post-exposure Δt_{re} was due to cold water immersion prior to obtaining respiratory air temperatures.

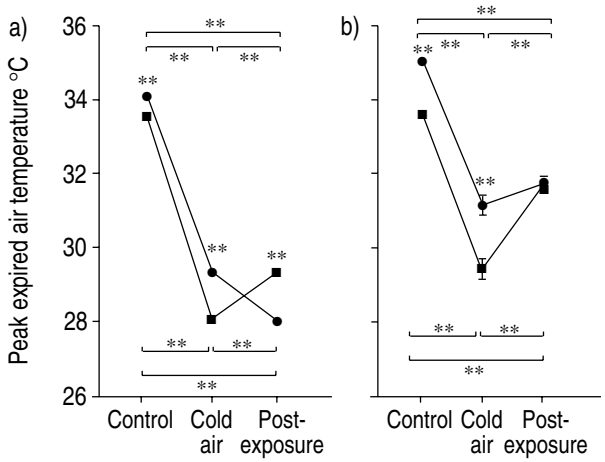

Fig. 3. – Mean peak expiratory airstream temperatures measured during: a) nasal; and b) oral breathing. Rapidly breathing cold air produced significantly lower peak expired temperatures than rapidly breathing warm air with a normal or reduced body care temperature ($p<0.01$). ● : quiet breathing; ■ : rapid breathing. Values are presented as mean±SEM. Missing error bars indicate that the SEM was too small to be displayed on the figure. Horizontal bars at the top of the figures indicate differences during quiet breathing and those at the bottom represent differences during rapid breathing. Statistical symbols adjacent to the values represent comparison of quiet and rapid breathing. **: $p<0.01$.

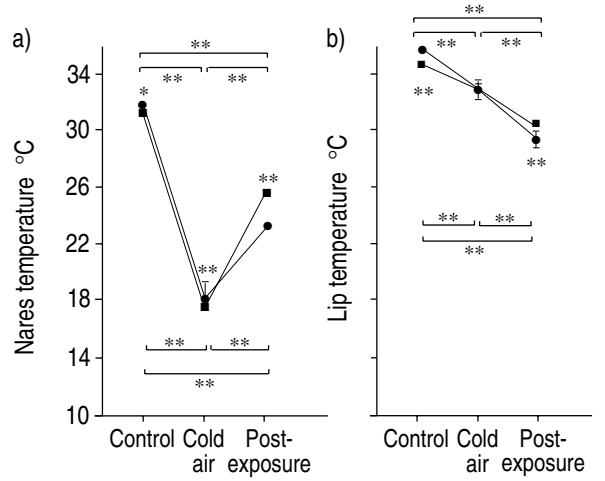

Fig. 4. – Mean orifice temperatures measured: a) at the nares; and b) at the lips, during nasal and oral breathing. Lip temperatures were significantly higher than nares temperatures under all conditions ($p<0.01$). Values are presented as mean±SEM. *: $p<0.05$. For further descriptions of statistical symbols see legend to figure 3.

t_{po} and experimental conditions during nasal and oral breathing. Both experimental conditions caused significant drops in t_{pn} and t_{po} compared with control conditions ($p<0.01$). The value of t_{po} was significantly higher than t_{pn} in all conditions ($p<0.01$) except when subjects were breathing rapidly in the control environment. In addition, increasing f_R significantly lowered t_{pn} and t_{po} in the control and cold air environments ($p<0.01$). Conversely, rapid breathing with a lowered t_C significantly increased t_{pn} ($p<0.01$), while having no effect on t_{po}.

Figure 4 shows how lip and nares temperatures varied in the experimental conditions during oral and nasal breathing. Orifice temperatures, which are assumed to reflect upper airway blood temperatures, correlated with both t_{pn} and t_{po} (fig. 5). This explains why t_{po} was significantly higher than t_{pn} because lip temperatures were significantly higher than nares temperatures in all con-

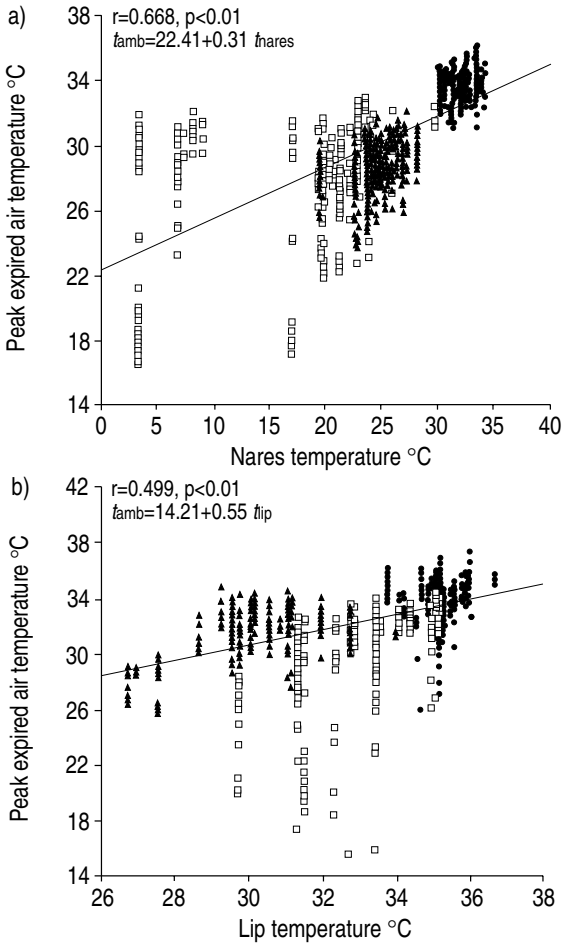

Fig. 5. – Correlations between orifice and peak expired air temperatures during: a) nasal; and b) oral breathing. The apparent bimodal nares temperature results observed during cold air exposures probably result from the probe being improperly placed. Holding the probe such that the ring, but not the thermocouples, contact the nares would expose thermocouples to cold ambient air without actually contacting the nares. This may also have occurred to a lesser extent during oral breathing. ● : control; ❑ : cold air; ▲ : postexposure. t_{amb}: ambient air temperature; t_{nares}: temperature at the nares; t_{lip}: temperature at the lips.

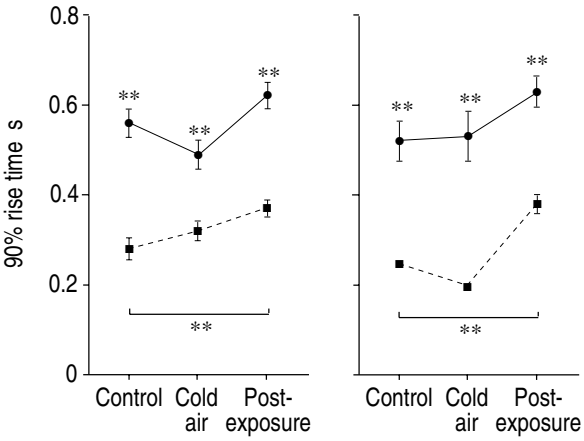

Fig. 6. – Mean 10–90% rise times measured during: a) nasal; and b) oral breathing. No significant differences in 10–90% rise times were observed between oral and nasal breathing except during rapid breathing of cold air ($p<0.01$). ● : quiet breathing; ■ : rapid breathing. Values are presented as mean±SEM. Statistical symbols adjacent to the values indicate comparison of quiet and rapid breathing. Horizontal bars at the bottom of the figures indicate differences during rapid breathing. **: $p<0.01$.

ditions ($p<0.01$). In addition, orifice temperatures fell significantly from control levels in the experimental conditions ($p<0.01$) (fig. 4).

Expired temperature differences across experimental conditions cannot be attributed to expiratory time because no significant correlation between 10–90% rise times and t_{pn} or t_{po} was observed. Figure 6 shows how increasing f_R significantly decreased both t_{rn} and t_{ro} ($p<0.01$). In addition, significant increases in 10–90% rise times were observed when t_c was reduced compared with control conditions during rapid breathing ($p<0.01$).

Discussion

The present study was designed to compare upper and lower airway contributions to thermal washout curves by assessing f_R, t_{amb}, and t_c affected 10–90% rise times t_{pn} and t_{po}. The results suggest that while thoracic conditions may contribute to thermal washout curves, extrathoracic conditions predominate. The strong correlation between orifice temperatures and t_{pn} and t_{po} demonstrates the dominant role that upper airway heat exchange plays in determining thermal washout curves and is consistent with the finding of HOPPE [15].

The rise time data tend to confirm the importance of upper airway heat transfer. Physiologically, rise times reflect the intra-airway temperature profiles at the end of inspiration. Expired air moving outward along the airway reaches some point at which airway wall temperatures steadily decline below t_c. From this point, expired air temperatures are determined by a combination of radial temperature gradient and airstream velocity. A shorter rise time indicates that wall temperatures rise steeply from the airway orifice or that airway velocity has increased. In this study, increasing f_R allowed warm expired air to pass more quickly out of the airway causing significant differences between quiet and rapid breathing. During quiet breathing, however, the insignificant differences in nasal and oral 10–90% rise times between experimental conditions suggest that airway temperature profiles distal to the upper airway were relatively unaffected.

Lowering t_c, however, lessens the axial wall temperature gradient. Expired air passing out of the airway under these conditions cools more gradually causing rise times to increase. During quiet breathing, this was not enough to significantly affect rise times. Reducing t_c during rapid breathing, however, apparently attenuates the affect of increasing f_R enough to significantly increase rise times compared to control conditions.

A caveat must be added to this interpretation, however, because of measurement error associated with dynamic temperature changes. Given the near-square wave temperature changes, thermocouples may respond too slowly to detect rapidly rising air temperatures in the colder expired airstream. Consequently, longer rise times may be measurement artefacts. A t_c difference of 1–2°C is unlikely, however, to affect thermocouple thermal inertia. Therefore, measured differences between rise times probably reflect actual heat exchange differences while not representing actual magnitudes. Likewise, while actual frequency dependent nasal and oral rise time magnitudes are probably underestimated because rise times probably decrease proportionate to f_R, the observed relative differences probably reflect actual physiological differences.

The general drop in t_{pn} and t_{po} as f_R increases provides further evidence for the relative importance of upper airway heat exchange. Increasing f_R reduces extrathoracic heat transfer efficiency by reducing residence time, allowing inspired cold air to penetrate deeper into the airway and increase convective cooling of the conducting airway walls [11, 16]. A corresponding reduction in expiratory heat transfer efficiency should allow warmer expired air to penetrate more proximally and cause t_{pn} and t_{po} to be greater with increasing f_R, assuming expired air temperatures primarily reflect pulmonary conditions. Since t_{pn} and t_{po} generally decrease at elevated f_R, however, airstream heat losses increase during rapid expiration as shown by CALDWELL *et al.* [17]. This increase in expiratory heat loss probably results from the increased extrathoracic airway cooling during rapid inspiration. The greater proportion of upper airway surface area cooled during inspiration causes radial temperature gradients to exist along a greater distance during expiration.

One exception to this relationship was observed, however, when lowering t_c caused t_{pn} to increase along with f_R. This anomaly probably relates to thermoregulatory control of nasal vascular smooth muscle. KAUFMAN [7] and WEBB [9] showed that nasal vasoconstriction during quiet cold air breathing would be minimal because inspired air is rapidly warmed to >33°C after passing 6.0 cm into the nasal passage. Vasoconstriction would allow cold air to penetrate more deeply. However, reducing t_c lowers t_{pn} more than breathing cold air during quiet breathing, demonstrating the major role submucosal blood temperature plays in nasal heat exchange. Cold exposure sufficient to lower t_c by 1°C causes vasoconstriction in most or all of the peripheral circulation and possibly in the nasal vasculature as well [18]. Increasing respiration in relatively warm air after such severe cold exposure will warm nasal surfaces and relax nasal vasculature smooth muscle. Warm nasal surfaces will consequently warm expired air, producing results consistent with the correlation between orifice and expired air temperatures.

Generalized vasoconstriction in the nasal vasculature, however, may not be necessary to explain how t_{pn} increases with f_R. Structural differences between the vasculature of the external nares and nasal mucosa suggest differences in thermoregulatory responses to cold. Lowering t_c by 1°C may cause arteriovenous anastamoses in the external nares to vasoconstrict in a manner analogous to peripheral skin. Conversely, patency in the sinusoids commonly found in nasal mucosa may be unaffected by t_c which is suggested by cranial sinusoidal patency being unresponsive to cold stimuli. An increase in f_R under these conditions would decrease the time warm expired air is exposed to cooler nares temperatures and result in elevated t_{pn}.

A similar increase in t_{po} associated with increasing f_R was not observed during oral breathing. Greater airway cooling due to rapid breathing, as described above, may reduce heat exchange efficiency during oral breathing. Another possibility is that oral heat transfer is more sensitive to changing t_{amb} than nasal heat transfer. FOUKE *et al.* [19] demonstrated that buccal blood flow and surface temperatures drop following cheek cooling.

This suggests that vasoconstriction in the peripheral vasculature reduces contiguous airway surface temperatures. Since a greater proportion of oral surfaces (buccal walls) are adjacent to external surfaces than nasal surfaces (nasal vestibule), t_{amb} would probably have a greater impact on oral heat transfer. Entering a warm environment quickly warms cheek temperatures despite a reduced t_c and independent of f_R. Consequently, vasoconstriction in both the external cheek and buccal vasculature probably accounts for the equivalent t_{po} observed during quiet and rapid breathing.

Altering tidal volume (V_T) by lowering t_{amb} or t_c provides an alternate hypothesis for explaining t_{pn} and t_{po} differences between experimental conditions. HANSON [21] showed that t_c alters pulmonary heat exchange and expired air temperatures but could not separate these effects from temperature-dependent increases in V'_E. Lowering t_c might produce a similar confounding effect in the present study, with heat exchange altered by both lower blood temperatures and reduced V'_E. To minimize this effect, f_R was controlled by volition and was analysed as an independent variable. V_T was not directly measured because spirometry alters orifice heat exchange and cold water immersion, producing shivering and shifting impedence bands, precluded impedence plethysmography. However, the lack of significant correlation between 10–90% rise times and t_{pn} or t_{po} suggests that breathing pattern was not responsible for t_{pn} and t_{po} differences between experimental conditions.

This work also raises the question of whether the nasal passage exchanges heat more efficiently than the oral cavity. VARENE *et al*. [21] found that t_{pn} and t_{po} did not significantly differ in subjects breathing room (21°C) air. Sensible heat losses were calculated to be far less than latent heat losses and they concluded that oral and nasal heat exchange efficiency was roughly equivalent [21]. However, mean t_{pn} and t_{po} were approximately 4.5 and 3.5°C lower, respectively, than comparable temperatures found by HOPPE [15] or in the present study. Temperature differences between studies are at least partially attributable to heat exchange between thermocouples and tubing in the apparatus used to measure airstream temperatures. Higher t_{pn} and t_{po} will more than double nasal and oral sensible heat losses, resulting in sensible heat losses contributing at least 50% to total expiratory heat exchange. This apparent inconsistency in oral and nasal heat exchange efficiency between studies suggests that more research is needed in this area.

In summary, this study demonstrates the significant role extrathoracic conditions have on respiratory heat exchange. It also shows how nasal blood supply is more important than ambient conditions in nasal heat exchange. Conversely, oral blood temperature appears to be less important than ambient conditions in oral heat exchange. Underlying these relationships may be the degree to which the nasal and oral vasculature is vasoconstricted. This study also shows that using temperature washout curves to determine lower airway heat transfer requires a far greater understanding of extrathoracic heat exchange than is currently available.

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