Increasing Mean Skin Temperature Linearly Reduces the Core-temperature Thresholds for Vasoconstriction and Shivering in Humans

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Background: The contribution of mean skin temperature to the thresholds for sweating and active precapillary vasodilation has been evaluated in numerous human studies. In contrast, the contribution of skin temperature to the control of core responses such as arteriovenous shunt vasoconstriction and shivering is less well established. Accordingly, the authors tested the hypothesis that mean skin and core temperatures are linearly related at the vasoconstriction and shivering thresholds in men. Because the relation between skin and core temperatures might vary by gender, the cutaneous contribution to thermoregulatory control also was determined in women.

Methods: In the first portion of the study, six men participated on 5 randomly ordered days, during which mean skin temperatures were maintained near 31, 34, 35, 36, and 37°C. Core hypothermia was induced by central venous infusion of cold lactated Ringer’s solution sufficient to induce peripheral vasoconstriction and shivering. The core-temperature thresholds were then plotted against skin temperature and a linear regression fit to the values. The relative skin and core contributions to the control of each response were calculated from the slopes of the regression equations. In the second portion of the study, six women participated on three randomly ordered days, during which mean skin temperatures were maintained near 31, 35, and 37°C. At each designated skin temperature, core hypothermia sufficient to induce peripheral vasoconstriction and/or shivering was again induced by central venous infusion of cold lactated Ringer’s solution. The cutaneous contributions to control of each response were then calculated from the skin- and core-temperature pairs at the vasoconstriction and shivering thresholds.

Results: There was a linear relation between mean skin and core temperatures at the response thresholds in the men: $r = 0.90 \pm 0.06$ for vasoconstriction and $r = 0.94 \pm 0.07$ for shivering. Skin temperature contributed 20 ± 6% to vasoconstriction and 19 ± 8% to shivering. Skin temperature in the women contributed to 18 ± 4% to vasoconstriction and 18 ± 7% to shivering, values not differing significantly from those in men. There was no apparent correlation between the cutaneous contributions to vasoconstriction and shivering in individual volunteers.

Conclusions: These data indicate that skin and core temperatures contribute linearly to the control of vasoconstriction and shivering in men and that the cutaneous contributions average 20% in both men and women. The same coefficients thus can be used to compensate for experimental skin temperature manipulations in men and women. However, the cutaneous contributions to each response vary among volunteers; furthermore, the contributions to the two responses vary within volunteers.

(THERMOREGULATORY responses can be characterized by thresholds (temperatures triggering response), gain (increase in response intensity for a given temperature increment), and maximum response intensity.† Because thresholds depend on both skin and core temperatures,‡ core-temperature thresholds usually are reported at a specified skin temperature.

The contribution of mean skin temperature to the core-temperature thresholds for sweating and active
SKIN TEMPERATURE, VASOCONSTRICTION, AND SHIVERING

Precapillary vasodilation\textsuperscript{1,4} has been evaluated in numerous human studies. Most find that skin contributes 5–20% to the control of each thermoregulatory response and that the relation between mean skin and core temperatures at response thresholds is linear.\textsuperscript{5–9} A 1°C increase in skin temperature reduces the sweating and active capillary vasodilation thresholds (expressed in terms of core temperature) by 0.05–0.2°C. Arithmetically, this relation takes the form:

\[
\text{thres}_{\text{MBT}} = \beta T_{\text{skin}} + (1 - \beta) T_{\text{core}},
\]

where \text{thres}_{\text{MBT}} = \text{the sweating or vasodilation threshold in terms of mean body temperature (degrees Celsius)}; \ T_{\text{skin}} = \text{mean skin temperature (degrees Celsius)}; and \ T_{\text{core}} = \text{core temperature (degrees Celsius)}; and \ \beta = \text{the proportionality constant. In this case, the proportionality constant is 0.05–0.2.}

Because the cutaneous contribution to the control of warm responses such as sweating and active vasodilation is thought to be relatively consistent, some investigators have used equation 1 to compensate for experimentally induced changes in skin temperature.\textsuperscript{10} This technique allows researchers to estimate what the sweating thresholds might have been were it possible to keep skin temperature constant throughout a study.

In contrast to sweating\textsuperscript{6,7} and active vasodilation,\textsuperscript{5,7–9} the contribution of skin temperature to the control of cold responses such as arteriovenous shunt vasoconstriction\textsuperscript{11} and shivering is less well established. Controversy remains because it has proven difficult in humans to independently cool the core at various (relatively high) skin temperatures. It thus remains unclear to what extent skin temperature alters core temperature thresholds for vasoconstriction and shivering and even whether the relation between skin and core temperatures is linear for each threshold. Accordingly, we tested the hypothesis that mean skin and core temperatures are linearly related at the vasoconstriction and shivering thresholds in men.

Women and men control body temperature with comparable precision,\textsuperscript{12} but the setpoint is \(\approx 0.3°C\) greater in women—even during the follicular phase of the menstrual cycle.\textsuperscript{10,12–14} The interthreshold range (temperatures not triggering autonomic thermoregulatory responses\textsuperscript{1}) is further elevated \(\approx 0.5°C\) during the luteal phase.\textsuperscript{15} Furthermore, women have lower basal skin blood flow,\textsuperscript{6} produce less sweat during heat exposure,\textsuperscript{17} and consequently tolerate heat stress with greater difficulty than do men.\textsuperscript{18} Cold defenses are equally gender-dependent.\textsuperscript{19} Given these differences, one cannot assume that skin temperature contributes comparably to thermoregulatory control in men and women. We therefore also determined the extent to which skin temperature contributes to thermoregulatory response thresholds in women.

Materials and Methods

With approval from the Committee on Human Research at the University of California, San Francisco, we studied six male volunteers having the following morphometric characteristics: age 31 ± 7 yr; height 175 ± 6 cm; and weight 77 ± 7 kg. Their percentage of body fat was 27 ± 6 as determined using infrared interactance (Futrex 1000, Futrex, Hagerstown, MD).\textsuperscript{20} We also studied six female volunteers with the following morphometric characteristics: age 28 ± 4 yr; height 164 ± 6 cm; weight 54 ± 6 kg, and percentage of body fat 29 ± 4%. These volunteers were not conditioned athletes. None was obese, taking medication, or had a history of thyroid disease.

The volunteers were advised to eat lightly before arriving at the laboratory. They were minimally clothed during the protocol and rested supine on a standard operating room table. To avoid circadian fluctuations, studies were scheduled so that thermoregulatory responses were triggered at nearly the same time on each of the study days.

On the 1st study day, a 16-G catheter was inserted into the superior vena cava via the right internal jugular vein. Echo sonography was used to locate the internal jugular vein and decrease risk of the procedure. The catheter was left in position for a maximum of 3 consecutive days.

Treatment Protocol: Men

In a randomly assigned order, mean skin temperatures were maintained near 31, 34, 35, 36, and 37°C. Each volunteer experienced each target skin temperature on a separate study day. Designated skin temperatures were maintained by manipulating temperature of an air stream directed into a disposable patient cover (full-body cover, Augustine Medical, Eden Prairie, MN). Warm air was provided by a warmer (Bair Hugger, Augustine Medical) modified to allow continuous temperature adjustment\textsuperscript{15}; cold air was provided by a prototype forced-air cooling device (Augustine Medical). In addition, the temperature of a circulating water mattress (Blanketrol II, Maxi-Therm blanket, Cincinnati
Sub-Zero, Cincinnati, OH) was set to the designated skin temperature on each study day.

The arms were protected from active warming and cooling to avoid locally mediated vasomotion. Cardboard shield were positioned to prevent inadvertent heating by the forced-air warmer. (Both arms were treated similarly to maintain side-to-side symmetry.) However, all other skin below the neck was exposed to a comparable temperature throughout each study day. Skin temperatures were not identical in each volunteer, but skin temperatures were maintained within a few tenths of 1°C once established on any given study day.

Volunteers were then cooled by central venous infusion of lactated Ringer’s solution at \( \approx 3^\circ C \), as previously described.\(^2\) The solution was cooled by passing it through an aluminum cardiopulmonary bypass heat exchanger immersed in an ice-and-water slurry. The infusion rate was initially 10 ml/min and adjusted at 1-min intervals to maintain a core cooling rate near 1.6°C/h. We have previously demonstrated that this cooling rate does not trigger dynamic thermoregulatory responses.\(^1\)

In general, we continued core cooling until the shivering threshold was identified. However, to minimize fluid administration (and therefore risk to the volunteers), we made no effort to record shivering at the highest skin temperature. Similarly, the volunteers already demonstrated vasoconstriction before fluid administration at the lowest skin temperature. Thresholds for each response were therefore determined at four skin temperatures in most volunteers.

**Treatment Protocol: Women**

In a randomly assigned order, mean skin temperatures were maintained near 31, 35, and 37°C; each target temperature was evaluated on a separate study day. The women were then cooled by central venous infusion of lactated Ringer’s solution at \( \approx 3^\circ C \). Fluid initially was administered at a rate of 10 ml/min and subsequently adjusted at 1-min intervals to maintain a core cooling rate near 1.3°C/h.

Core cooling continued until the vasoconstriction threshold was identified at the highest skin temperature (\( \approx 37.5^\circ C \)). We made no effort to record shivering at this skin temperature, thereby limiting fluid administration (and risk to the volunteers). Core cooling continued until both the vasoconstriction and shivering thresholds were identified when the target skin temperature was 35°C. At the lowest target skin temperature (31°C), the volunteers vasoconstricted before fluid administration began. Consequently, thresholds for each response were determined at two different skin temperatures in each volunteer.

**Measurements**

Core temperature in the men was measured in the distal esophagus using disposable thermocouple probes (Mon-a-Therm, Mallinckrodt Anesthesiology Products, St. Louis, MO). Optimal insertion length of the esophageal probe was calculated using the formula of Mekjavic and Rempel.\(^3\) Body temperature in both men and women was measured at the right tympanic membrane using thermocouples (Mon-a-Therm, Mallinckrodt Anesthesiology Products). The aural probes were inserted by the volunteers until they felt the thermocouple touch the tympanic membrane and then were maintained in that position; appropriate placement was confirmed when the volunteers easily detected a gentle rubbing of the attached wire. The probe was then securely taped in place, the aural canal occluded with cotton, and a gauze bandage positioned over the external ear. We have previously demonstrated that distal esophageal and tympanic membrane temperatures are virtually identical under the circumstances of this study.\(^1\)

Arca-weighted, mean skin-surface temperatures were computed from measurements at 15 sites by assigning the following regional percentages: head 6%, upper arms 9%, forearms 6%, hands 2.5%, fingers 2%, back 19%, chest 9.5%, abdomen 9.5%, medial thigh 6%, lateral thigh 6%, posterior thigh 7%, anterior calves 7.5%, posterior calves 4%, feet 4%, and toes 2%.\(^2\) Temperatures were recorded from thermocouples connected to two calibrated 16-channel electronic thermometers having an accuracy of 0.1°C and a precision of 0.01°C (Iso-Thermex, Columbus Instruments, Columbus, OH). Individual and averaged temperatures were displayed on a computer at 1-s intervals. Ambient temperature was recorded from a probe positioned at the level of the volunteer, well away from any heat-producing equipment.

Absolute right middle fingertip blood flow was quantified using venous-occlusion volume plethysmography at \( \approx 1 \)-min intervals, as previously described.\(^2\) Oxygen consumption was measured using a canopy-based metabolic monitor (Deltatrac, SensorMedics, Yorba Linda, CA). The system was calibrated daily using a known mixture of gases and also calibrated numerous times.

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by burning ethanol. Measurements were averaged over 1-min intervals.

Data Analysis
Thresholds are most formally defined by the initiation of protective responses. However, it often requires considerable judgment to identify the beginning of a response, particularly when the responses are intrinsically variable. We thus chose objective definitions to minimize potential for bias in determining the sometimes subtle initiation of vasoconstriction and shivering.

As in a previous study, the core-temperature vasoconstriction threshold was defined as the core temperature producing a sustained decrease in fingertip blood flow to <0.25 ml/min. This flow corresponds to early vasoconstriction (a forearm minus fingertip, skin-temperature gradient near 0°C) but is considerably less than the values resulting from respiratory variation or rhythmic oscillations in sympathetic tone. We have previously shown that a calf-minus-toe, skin-temperature gradient of 0°C correlates with the core-temperature plateau and is therefore clinically important.

Electromyography is a common method of detecting shivering and is one we have used extensively. The technique is sensitive but perhaps more subject to artifact in the form of muscle tension resulting from positional discomfort or even nervousness. Consequently, we identified the core temperature triggering a sustained 40% increase in oxygen consumption as the core-temperature shivering threshold. The gains of both vasoconstriction and shivering are high. That is, the intensity of each response increases rapidly once the triggering threshold is reached. Consequently, core temperatures change little between the first detectable response and the strict criteria used here. Shivering thresholds would thus be similar had we chosen a smaller (i.e., 25%) or larger (i.e., 50%) increase.

Core-temperature thresholds from each man were plotted against mean skin temperature at the times of vasoconstriction and shivering, and a least-squares linear regression was fit to the values to obtain the relation:

\[ T_{core} = ST_{skin} + K. \] (2)

where S = the slope of the regression equation. The slope thus indicated the extent to which skin warming increased thermoregulatory tolerance for core hypothermia (i.e., how much skin warming was required to reduce the vasoconstriction and shivering thresholds). To determine the fractional contribution of skin temperature to the thermoregulatory control of vasoconstriction and shivering (the proportionality constant \( \beta \)), we rearranged equation 1:

\[ T_{core} = \frac{-\beta}{1 - \beta} T_{skin} + \frac{\text{thres}_{MB}}{1 - \beta}. \] (3)

Combining equations 2 and 3 gives

\[ S = \frac{-\beta}{1 - \beta}, \] (4)

and consequently that

\[ \beta = \frac{S}{S - 1}. \] (5)

The correlation coefficients for the skin versus core regressions indicated the extent to which the vasoconstriction and shivering thresholds were linear functions of skin and core temperatures. To further evaluate the extent to which skin and core temperatures were linearly related, we calculated the residuals (difference between measured and predicted core temperatures). The residuals for each response were then plotted against skin temperature. These values, in turn, were fit using a linear, least-squares regression. Nonlinearities in the cutaneous contributions might be identified on these plots by significantly nonzero slopes. Other types of nonlinearities (such as a U-shaped curve) might produce near-zero slopes but would be apparent by visual inspection.

To determine the cutaneous contributions to the vasoconstriction and shivering thresholds in the women, we first determined the slope by dividing the difference of the triggering core temperatures by the difference in the triggering skin temperatures for each response. Subsequently, the fractional cutaneous contribution was determined from equation 5.

Ambient temperature on each study day was first averaged within each volunteer; the resulting values were then averaged among volunteers. Results for each study day were compared by using analysis of variance and Scheffé's F tests. Results are expressed as means ± standard deviation; differences were considered significant when \( P < 0.05 \).

Results

Men
One man shivered during cold fluid administration at the highest skin temperature; another did not become
Table 1. Ambient Temperature and Core Cooling Rates in the Men on the 5 Study Days

<table>
<thead>
<tr>
<th></th>
<th>Mean skin temperature (°C)</th>
<th>Ambient temperature (°C)</th>
<th>Core cooling rate (°C/h)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>31.0 ± 0.2</td>
<td>21.5 ± 1.9</td>
<td>1.6 ± 0.8</td>
</tr>
<tr>
<td></td>
<td>33.6 ± 0.7</td>
<td>21.0 ± 1.3</td>
<td>1.6 ± 0.3</td>
</tr>
<tr>
<td></td>
<td>35.0 ± 0.4</td>
<td>19.2 ± 1.2</td>
<td>1.3 ± 0.3</td>
</tr>
<tr>
<td></td>
<td>35.7 ± 0.4</td>
<td>22.3 ± 0.5</td>
<td>1.3 ± 0.3</td>
</tr>
<tr>
<td></td>
<td>36.9 ± 0.3</td>
<td>21.2 ± 0.6</td>
<td>1.0 ± 0.1</td>
</tr>
</tbody>
</table>

Per protocol, mean skin temperatures differed significantly among the study days. Core cooling rates did not differ significantly on the study days. Data are presented as mean ± SD.

sufficiently hypothermic to shiver at the second highest target skin temperature, even after administration of 5 l of lactated Ringer's solution. Their shivering regressions were thus calculated using five and three thresholds, respectively. Another man was unable to tolerate the esophageal temperature probe. We thus recorded core temperature only from his tympanic membrane. Ambient temperatures and core cooling rates were similar on the 5 study days (table 1).

There was a linear relation between mean skin and core temperatures at the vasoconstriction and shivering thresholds in each man: \( r = 0.90 ± 0.06 \) for vasoconstriction and \( r = 0.94 ± 0.07 \) for shivering. The slope of the residual regression for vasoconstriction was 0.007; similarly, the slope of the residual regression for shivering was 0.004. Visual inspection of the residuals from the skin- versus core-temperature regressions also indicated that the data were linear (fig. 1).

The cutaneous contribution to thermoregulatory control, however, differed among men and was not necessarily the same for vasoconstriction and shivering. Skin temperature contributed 20 ± 6% to vasoconstriction and 19 ± 8% to shivering (table 2 and fig. 2). There was no apparent correlation between cutaneous contribution to vasoconstriction and shivering in individual men \((r = 0.3)\) (fig. 3).

Women
In the women, core cooling rates were comparable on the 3 study days (table 5). Hemodynamic responses and ambient temperature and humidity also did not differ significantly on the study days. Skin temperature in these women contributed 18 ± 4% to vasoconstriction and 18 ± 7% to shivering (table 4). These values did not differ significantly from those in the men.

As in the men, the cutaneous contribution to thermoregulatory control differed among the women and was not necessarily the same for vasoconstriction and shivering. Consequently, there was a poor (and negative) correlation between the cutaneous contributions to the vasoconstriction and shivering thresholds (in

Table 2. Correlation Coefficients and Cutaneous Contributions to Vasoconstriction and Shivering in Each Man

<table>
<thead>
<tr>
<th>Volunteer No.</th>
<th>Vasoconstriction r</th>
<th>Skin (%)</th>
<th>Shivering r</th>
<th>Skin (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.90</td>
<td>20</td>
<td>0.98</td>
<td>14</td>
</tr>
<tr>
<td>2</td>
<td>0.95</td>
<td>15</td>
<td>0.98</td>
<td>18</td>
</tr>
<tr>
<td>3</td>
<td>0.94</td>
<td>32</td>
<td>0.97</td>
<td>29</td>
</tr>
<tr>
<td>4</td>
<td>0.90</td>
<td>21</td>
<td>0.83</td>
<td>11</td>
</tr>
<tr>
<td>5</td>
<td>0.78</td>
<td>19</td>
<td>0.99</td>
<td>28</td>
</tr>
<tr>
<td>6</td>
<td>0.91</td>
<td>15</td>
<td>0.88</td>
<td>14</td>
</tr>
</tbody>
</table>

Mean ± SD 0.90 ± 0.06 20 ± 6 0.94 ± 0.07 19 ± 8

Skin and core temperatures contributed linearly to control of vasoconstriction and shivering in men. However, cutaneous contribution to control of vasoconstriction and shivering was not necessarily the same in individual volunteers. Furthermore, the cutaneous contribution varied considerably among volunteers. Data are presented as mean ± SD.

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Fig. 1. The residuals (difference between measured and predicted core temperatures) at the vasoconstriction thresholds were plotted against skin temperature to confirm the linear relation between skin- and core-temperature contributions to the control of vasoconstriction in men. The slope of the residual regression for vasoconstriction was 0.007 (top); the slope of the residual regression for shivering was 0.004 (bottom).
Skin temperature, vasoconstriction, and shivering

Fig. 2. Core and skin temperatures at the vasoconstriction and shivering thresholds were linearly related in men. The correlation coefficients averaged 0.90 ± 0.06 for vasoconstriction and 0.94 ± 0.07 for shivering. The extent to which mean skin temperature contributed to central thermoregulatory control (the proportionality constant \( \beta \)) was calculated from the slopes (S) of the skin-temperature versus core-temperature regressions using the formula \( \beta = S/(S-1) \). Cutaneous contribution to vasoconstriction averaged 20 ± 6%, which did not differ significantly from the contribution to shivering, which was 19 ± 8%.

\( ^\circ\text{C} \): vasoconstriction = -1.5 \cdot shivering + 0.4; \( r = 0.73 \).

Discussion

Our hypothesis was that skin and core temperatures contribute linearly to the control of vasoconstriction and shivering in men. Both the high correlation coefficients and residual analysis indicate that the cutaneous contribution to vasoconstriction and shivering thresholds indeed is linear. It remains possible and perhaps even likely that skin and core temperatures no longer contribute linearly at extreme skin temperatures. However, the range of temperatures tested in this study (roughly \( 5 \)°C for vasoconstriction and \( 5 \)°C for shivering) spans that typically experienced in daily life and certainly exceeds that observed during routine clinical practice.

Skin temperature contributed \( \approx 20\% \) each to the control of vasoconstriction and shivering in men. This value exceeds most of those reported for sweating and active vasodilation in humans, but is less than the \( \approx 30\% \) cutaneous contribution to metabolic heat production observed in goats. (That it should be greater in a smaller species is typical.) It is, however, consistent with our previous observation that lower-body skin contributes \( 11 \pm 3\% \) to the control of shivering in humans.

The cutaneous contributions to control of vasoconstriction and shivering in women were \( 18\% \), which is similar to the values we reported previously in men. That the contributions were comparable is convenient and might be considered the "expected" result. However, similar contributions in men and women could not be assumed a priori, because thermoregulatory responses display considerable gender-specificity under numerous circumstances. Similar cutaneous contributions indicate that the same coefficients can be used to compensate for experimental skin temperature manipulations in men and women. Had the con-

Table 3. Ambient Temperature and Core Cooling Rates in the Women on the 3 Study Days

<table>
<thead>
<tr>
<th></th>
<th>Mean ± SE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean skin temperature ( ^\circ\text{C} )</td>
<td>31.0 ± 0.0, 35.1 ± 0.1, 37.5 ± 0.1</td>
</tr>
<tr>
<td>Ambient temperature ( ^\circ\text{C} )</td>
<td>21.6 ± 0.7, 22.1 ± 0.8, 22.3 ± 0.6</td>
</tr>
<tr>
<td>Core cooling rate ( ^\circ\text{C/h} )</td>
<td>1.2 ± 0.2, 1.3 ± 0.2, 1.4 ± 0.2</td>
</tr>
</tbody>
</table>

Per protocol, mean skin temperatures differed significantly on the 3 study days. Core cooling rates did not differ significantly on the study days. Data are presented as mean ± SD.
Table 4. Core Temperatures Triggering Vasoconstriction and Shivering at Designated Skin Temperatures and the Cutaneous Contributions to Each in the Women

<table>
<thead>
<tr>
<th>Volunteer No.</th>
<th>( T_{\text{Core}} ) (°C) at ( T_{\text{Skin}} ) = 35°C</th>
<th>( T_{\text{Core}} ) (°C) at ( T_{\text{Skin}} ) = 37.5°C</th>
<th>( \beta ) (%)</th>
<th>( T_{\text{Core}} ) (°C) at ( T_{\text{Skin}} ) = 31°C</th>
<th>( T_{\text{Core}} ) (°C) at ( T_{\text{Skin}} ) = 35°C</th>
<th>( \beta ) (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>36.69</td>
<td>36.09</td>
<td>19</td>
<td>36.75</td>
<td>35.98</td>
<td>16</td>
</tr>
<tr>
<td>2</td>
<td>36.67</td>
<td>36.31</td>
<td>13</td>
<td>37.09</td>
<td>35.58</td>
<td>27</td>
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<td>3</td>
<td>36.88</td>
<td>36.35</td>
<td>19</td>
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<td>4</td>
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<td>36.35</td>
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<td>36.93</td>
<td>36.49</td>
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<td>13</td>
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<td>35.72</td>
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<td>6</td>
<td>37.04</td>
<td>36.33</td>
<td>22</td>
<td>36.78</td>
<td>36.05</td>
<td>15</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>36.8 ± 0.2</td>
<td>36.3 ± 0.1</td>
<td>18 ± 4</td>
<td>36.9 ± 0.1</td>
<td>36.0 ± 0.3</td>
<td>18 ± 7</td>
</tr>
</tbody>
</table>

The core temperature required to trigger vasoconstriction was \(-0.5\)°C less when the skin temperature was \(-37.5\)°C than when it was \(-35\)°C. Similarly, the core temperature required to trigger shivering was \(-0.9\)°C less when the skin temperature was \(-35\)°C than when it was \(-31\)°C. The cutaneous contribution to each response (\( \beta \)) was comparable, \(-18\)%. Data are presented as mean ± SD.

Contributions differed, women still would be able to participate in such studies, but the appropriate correction factors would be required.

In the women, we determined the fractional contribution of skin temperature from only two sets of data for each response. Consequently, we assumed that the relationship between skin and core temperature was linear in our female volunteers. This assumption is justified because numerous studies have shown that onset of sweating is a linear function of skin and core temperatures.\(^6\)\(^{-8}\)\(^{-12}\) (In contrast, intensity of thermoregulatory responses are not linear functions of core temperature.\(^6\)\(^{-13}\)\(^{-14}\) Furthermore, the vasoconstriction and shivering thresholds were linearly related to skin temperature in men. It is thus unlikely that the shape of this relationship differs in men and women.

Skin covering the upper chest, neck, and face contributes roughly three times as much as other skin to the control of thermoregulatory responses.\(^35\)\(^{-37}\) Although forehead skin temperature was recorded and included in our computation of mean skin temperature, the head was not directly warmed or cooled in our study. It is thus likely that cutaneous contributions would have been somewhat greater had facial temperature also been manipulated.

The cutaneous contributions to the control of vasoconstriction and shivering differed among the volunteers: skin temperature contributed \(15-32\)% to vasoconstriction and \(14-29\)% to shivering in men and was comparably variable in the women. These data suggest that the cutaneous contribution to thermoregulatory control varies considerably, even among relatively similar persons. It is possible that variations as a function of age are even greater.

The cutaneous contribution to the control of vasoconstriction and shivering differed even within a given volunteer. These data thus suggest that even within the category of cold responses, thermal afferent signals may be integrated differently. The possibility of independent integration modes is consistent with the impression of some investigators that the spinal cord contributes more to the control of shivering than to other thermoregulatory responses.\(^38\)\(^{-39}\)

For the purpose of this study, we considered all thermal afferent signals to be “skin” or “core.” However, it is likely that tissues throughout the body contribute to thermoregulatory control.\(^30\)\(^{-31}\)\(^{-32}\) Furthermore, various structures probably contribute in different proportions, depending on their site and mass. Our two-compartment model is thus necessarily a substantial simplification.

The cutaneous- and core-temperature contributions to vasoconstriction and shivering remained linear, despite this degree of simplification. However, it remains possible that the observed variability in cutaneous contributions to each response among volunteers and the variability between responses within individual volunteers might have been less had we used a more complex model. Nonetheless, in most cases, only core and skin temperatures are readily accessible; our results apply in such situations.

We induced core hypothermia (while maintaining designated skin temperature) by central venous infusion of cold fluid. At times, fluid at \(-3\)°C was infused at rates approaching 100 ml/min. Nonetheless, it is unlikely that this infusion produced significant local cooling because blood flow in the superior vena cava is typically \(2\) l/min. Furthermore, evidence suggests

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that veins have limited ability to detect thermal manipulations. 

Core cooling rates were restricted to $<1.7^\circ C/h$ because we previously demonstrated that such rates do not trigger dynamic thermoregulatory responses. However, it is well established that rapid (skin) temperature changes provoke aggressive thermoregulatory responses. Consequently, our results should be applied with caution to situations involving rapid thermal perturbations. Similarly, we studied young women during the follicular phase of their menstrual cycles; cutaneous contributions may differ during the luteal phase of the cycles, or in the elderly.

Defining the fractional contribution of cutaneous temperature to the thermoregulatory control of shivering has distinct practical implications. Shivering during recovery from general anesthesia is a common complication of intraoperative hypothermia. It is potentially dangerous because it substantially increases oxygen consumption and plasma catecholamine concentrations, which may mediate hypothermia-induced perioperative myocardial ischemia. In addition, postoperative shivering increases intraocular and intracranial pressures and may aggravate wound pain by stretching incisions.

Postoperative shivering can be prevented by maintaining core normothermia or can be treated with drugs including meperidine and clonidine. However, shivering also can be rapidly treated, without risking pharmacologic complications, by warming the skin. Cutaneous warming is effective because thermoregulatory tolerance for core hypothermia increases at higher skin-surface temperatures. Our results indicate that each degree Celsius of cutaneous warming will compensate for $\approx 0.2^\circ C$ core hypothermia. Even with forced-air warming, it is difficult to increase skin temperature more than $3^\circ C$. In the absence of residual anesthetic effects, our data thus suggest that cutaneous warming will prevent postoperative shivering only when core temperature is within $\approx 0.6^\circ C$ of the normal shivering threshold ($\approx 36^\circ C$).

In summary, there was a linear relation between mean skin and core temperatures at the response thresholds in each man: $r = 0.90 \pm 0.06$ for vasoconstriction and $0.94 \pm 0.07$ for shivering. Skin temperature contributed $20 \pm 6\%$ to vasoconstriction and $19 \pm 8\%$ to shivering in the men. Skin temperature contributed $18 \pm 4\%$ to vasoconstriction and $18 \pm 7\%$ to shivering in women. These values not differing significantly from those in men. The same coefficients thus can be used to compensate for experimental skin temperature manipulations in men and women. However, the cutaneous contributions to each response vary between volunteers; furthermore, the contributions to the two responses vary within volunteers.

The authors appreciate the assistance of Andrew M. Sessler, Ph.D. (Senior Scientist, Lawrence Berkeley Laboratory). They thank Mallinckrodt Anesthesiology Products for donation of the thermocouples and Cincinnati Sub-Zero for the loan of a Blanketrol II circulating water mattress.

References

14. Havenith G, van Midendorp H: The relative influence of physical fitness, aclimatization state, anthropometric measures and gender

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47. Frank SM, Beattie C, Christopher RN, Norris EJ, Perler BA, Williams GM, Gottlieb SO. Unintentional hypothermia is associated with postoperative myocardial ischemia. Anesthesiology 78:468–476, 1993
50. Joris J, Banache M, Bonnet F, Sessler DI, Lamy M. Clonidine and ketanserin both are effective treatments for postanesthetic shivering. Anesthesiology 79:532–539, 1993
53. Sharkey A, Lipton JM, Murphy MT, Giesece AH. Inhibition of postanesthetic shivering with radiant heat. Anesthesiology 66:249–252, 1987

Anesthesiology. V 82. No 5, May 1995