Absence of Nonshivering Thermogenesis in Anesthetized Adult Humans

James M. Hynson, M.D.,* Daniel L. Sessler, M.D.,† Azita Moayeri, B.S.,‡ Joseph McGuire, B.S.‡

Background: Typically, core temperature rapidly decreases after induction of anesthesia, but reaches a stable plateau after several hours. This plateau typically occurs in conjunction with the onset of thermoregulatory vasoconstriction. Decreased heat loss, caused by vasoconstriction, may not be sufficient to establish thermal steady state without a concomitant increase in heat production. Accordingly, the authors tested the hypothesis that nonshivering thermogenesis contributes to thermal steady state during anesthesia. Rewarming from hypothermia is often associated with an afterdrop (a further reduction in core temperature, despite cutaneous warming). Because total body heat content increases during cutaneous warming, heat storage during afterdrop must reflect increased temperature and heat content of the peripheral tissue mass. Thermal balance was measured during rewarming to estimate the thermal capacity of the peripheral tissues.

Methods: Five volunteers were anesthetized with isoflurane and paralyzed with vecuronium. Oxygen consumption was measured during cooling to a core temperature at least 1°C less than that which triggered vasoconstriction. Volunteers were subsequentlyrewarmed using a circulating-water blanket and forced-air warmer. Oxygen consumption and cutaneous heat flux were measured to assess thermal balance and peripheral tissue heat storage during rewarming.

Results: The core temperature threshold for vasoconstriction was 35.2 ± 0.8°C. Oxygen consumption decreased 9 ± 5%/°C during active cooling before vasoconstriction and 9 ± 3%/°C after vasoconstriction. After the start of rewarming, core temperature continued to decrease for an additional 32 ± 8 min. The magnitude of this afterdrop was 0.6 ± 0.1°C. Peripheral tissue heat storage measured from the start of rewarming until the first net increase in core temperature was 144 ± 60 kcal, which approximately equals 2 h of resting metabolic heat production.

Conclusions: The authors concluded that nonshivering thermogenesis is not an important thermoregulatory response in adults anesthetized with isoflurane. Afterdrop and delayed core temperature recovery during rewarming reflect the large heat storage capacity of peripheral tissues. (Key words: Heat measurement; thermal flux transducers. Hypothermia. Oxygen consumption. Rewarming. Temperature, measurement: skin; tympanic membrane. Temperature, regulation: nonshivering thermogenesis; setpoint; threshold; vasoconstriction.)

CORE temperature during general anesthesia usually follows a characteristic pattern: a rapid, 1–2°C decrease in the first hour after induction, followed by a gradual linear decrease. Typically, after 3–4 h of anesthesia, core temperature reaches a plateau and decreases no further. Peripheral thermoregulatory vasoconstriction often coincides with the onset of this central temperature plateau.

Thermal steady state requires that heat production equals heat loss to the environment; thus, a core temperature plateau during anesthesia indicates a reduction in heat loss, an increase in metabolic heat production, or a change in body heat distribution. During isoflurane anesthesia, thermoregulatory vasoconstriction decreases total cutaneous heat loss ≈ 25%; however, this decrease may not be sufficient to explain a core temperature plateau, particularly during major surgery, during which substantial evaporative heat loss continues. Consequently, increased metabolic heat production in response to hypothermia during anesthesia must also be considered.

A thermoregulatory increase in metabolic heat production not associated with muscle activity is known as nonshivering thermogenesis. Although it is an important homeostatic mechanism in neonates and in small animals, its role in adult humans is probably less important. However, Jessen et al. reported an increase in oxygen consumption of 30–41% in awake, hypothermic adult volunteers who were not visibly
shivering,\textsuperscript{13} and an increase of 25\% in comatose head trauma patients made hypothermic while paralyzed with curare.\textsuperscript{14} We, therefore, tested the hypothesis that nonshivering thermogenesis also occurs in response to hypothermia in adults during general anesthesia.

Core temperature afterdrop is a well known phenomenon associated with skin-surface warming for the treatment of accidental hypothermia.\textsuperscript{15} Afterdrop refers to the tendency for core temperature to continue decreasing despite initiation of cutaneous warming. In victims of accidental hypothermia, afterdrop is an important consideration because any further reduction in core temperature may be associated with serious consequences, including cardiac irritability.\textsuperscript{16} Afterdrop is classically attributed to the initial cooling of blood flowing through cold vasodilated tissue.\textsuperscript{17} However, continued conductive heat loss from the core to the periphery may also contribute.\textsuperscript{18}

Regardless of the exact mechanism of afterdrop, conservation of energy requires that it involves a net transfer, or redistribution, of heat from central to peripheral tissues (because total body heat content is simultaneously increasing). The magnitude of afterdrop is, therefore, largely determined by the amount of heat that can be transferred from central to peripheral tissues. Similarly, the magnitude of hypothermia caused by redistribution of body heat after induction of anesthesia is dependent on the extent to which peripheral tissues can accept heat from the core. Accordingly, we assessed the thermal capacity of peripheral tissues, by measuring thermal balance and peripheral tissue heat storage during rewarming from hypothermia.

Materials and Methods

After approval of the University of California, San Francisco, Committee on Human Research and informed consent, we studied five young, healthy volunteers. None was obese or taking prescription medications. All abstained from food and liquids for 8 h before the study. Volunteers wore only shorts or a bathing suit, and were studied in an operating room with an ambient temperature near 20° C. An intravenous catheter was placed peripherally, and lactated Ringer’s solution was administered at \( \approx 1 \text{ ml} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}. \)

Study Protocol

Anesthesia was induced using 70\% nitrous oxide in oxygen followed by isoflurane, 3–4\% inspired concentration. Nitrous oxide was discontinued before intubation of the trachea. After intubation, paralysis was imposed by administration of an intravenous bolus of vecuronium, 2 mg, followed by an infusion of 2 mg/h; the vecuronium infusion rate was adjusted to maintain a single-twitch response to a supramaximal train-of-four electrical stimulus of the ulnar nerve. End-tidal isoflurane concentrations were maintained near 1.1\%, as measured by a mass spectrometer (Medspect, St. Louis, MO).

A Siemens Servo Ventilator 900-C (Schaumburg, IL) was used to deliver isoflurane in air at a controlled rate and tidal volume. Minute ventilation was adjusted periodically to maintain end-tidal P\textsubscript{CO\textsubscript{2}} near 35 mmHg. Passive airway heating and humidification were provided by placing a heat-and-moisture exchanger between the Y-piece of the breathing circuit and the endotracheal tube. Blood pressure was measured oscillogmetrically (Dinamap 1846 SX; Critikon, Tampa, FL). Standard monitoring included electrocardiography, pulse oximetry, and capnography.

To minimize the initial hypothermia from internal redistribution of body heat, preinduction skin-surface warming was administered for \( \approx 45 \) min before induction of anesthesia using a forced-air warmer set on “high” (Bair Hugger; Augustine Medical, Eden Prairie, MN; air temperature \( \approx 43^\circ \text{C} \)).\textsuperscript{19} Warming was discontinued upon induction. Volunteers were allowed to remain normothermic for 45 min (control period), but then were actively cooled using two full-length circulating-water blankets (Blanketrol; Cincinnati Sub Zero Products, Cincinnati, OH) set at 5° C, one applied to the chest and one under the back.

Cooling continued until core temperature was at least 1° C less than that which triggered thermoregulatory vasoconstriction. Thermoregulatory vasoconstriction was prospectively defined as a forearm minus fingertip, skin-temperature gradient \( \geq 4^\circ \text{C} \).\textsuperscript{20} Cooling to a core temperature less than the threshold for vasoconstriction was considered necessary, because vasoconstriction is the earliest regulatory response to hypothermia; the threshold temperature for nonshivering thermogenesis would probably be slightly less than that for vasoconstriction.\textsuperscript{21}

Each volunteer was then actively rewarmed (to a tympanic membrane temperature within 1° C of the unanesthetized, normothermic control value) using two forced-air warmers set on “high,” with covers applied to the anterior surface of the trunk and legs. The temperature of the circulating-water blanket under the
back was set to 40°C for rewarming. General anesthesia was maintained during rewarming. Thermoregulatory vasodilation during warming was defined as a forearm minus fingertip, skin-temperature gradient ≤0°C. After adequate rewarming, anesthesia was discontinued and the volunteers’ tracheas were extubated.

Measurements
Core temperature was measured using a Mon-a-Therm (St. Louis, MO) thermocouple placed adjacent to the tympanic membrane. The auditory meatus was covered with cotton. The forearm minus fingertip, skin-temperature gradient was measured using Mon-a-Therm skin-surface thermocouples, one placed on the tip of the middle finger and one on the volar surface of the forearm midway between the wrist and elbow. Mean skin temperature was determined from the weighted average of ten sites.1 The percentage of body fat in each volunteer was determined by infrared intertactance (Futrex 1000; Futrex, Hagerstown, MD).

Oxygen consumption was determined at 10-min intervals from inspired and mixed expired oxygen and nitrogen concentrations (measured by mass spectrometry, Medspect) and expired minute ventilation (as measured by the calibrated Siemens ventilator).22 Mixed expired gas measurements were made after passing expired gases through a mixing chamber. Adequate mixing was assured by verifying that the carbon dioxide waveform at the expiratory end of the mixing chamber remained constant throughout the ventilatory cycle. The average of two oxygen consumption measurements during the 45-min normothermic control period was considered the baseline value.

Total cutaneous heat loss was calculated from the area-weighted heat flux measured from ten anatomically distributed thermal flux transducers.23 Heat flux measurement sites were identical to those used for mean skin temperature. Heat flux was defined as positive when heat was lost from the body to the environment. Analog data were recorded at 5-min intervals using a previously described data acquisition system.23

Data Analysis
Changes in temperature for each volunteer were defined with two references: 1) preinduction (baseline) normothermic tympanic membrane temperature; and 2) tympanic membrane temperature at the onset of vasoconstriction (individual thermoregulatory vasoconstriction threshold). Rate of temperature change was determined at 10-min intervals. The magnitude of the afterdrop was calculated as the change in core temperature from the start of rewarming to the nadir. Oxygen consumption (ml/min) was converted to a percentage of the oxygen consumption measured at the time of significant vasoconstriction, thereby compensating for differing baseline metabolic rates and vasoconstriction thresholds.

A database program was used to sort and average data recorded from each volunteer using change in tympanic membrane temperature (in 0.5°C intervals) as the sorting parameter. Oxygen consumptions at 1.0°C, 0.5°C, and 0°C greater than the vasoconstriction threshold were used to determine the relationship between change in temperature and oxygen consumption before vasoconstriction. Similarly, the relationship between oxygen consumption and change in central temperature after vasoconstriction was determined using oxygen consumption at 0°C, −0.5°C, and −1.0°C (relative to the vasoconstriction threshold). The average slope for the individual regression lines was determined and compared before and after vasoconstriction. Statistical significance was evaluated using a paired t test. During rewarming, oxygen consumption and cutaneous heat loss data were sorted by time and averaged into 10-min epochs.

Peripheral tissue heat storage capacity was determined by measuring heat balance during the time interval from the start of rewarming until the first net increase in core temperature. This time interval included not only the afterdrop duration, but also the time necessary for core temperature to return to that measured at the start of rewarming. Because core temperature was the same at the beginning and end of this period, positive heat balance reflects heat storage in the peripheral tissues.

Heat storage was calculated as the time integral of the sum of metabolic heat production and cutaneous heat gain. Oxygen consumption (ml/min) was converted to equivalent metabolic heat production (W) assuming the caloric value of oxygen to be 4.82 kcal/l (respiratory quotient = 0.82),24 and using a conversion of 1 kcal/h = 1.16 W. We chose a standard value for the respiratory quotient because the caloric value of oxygen varies only slightly over the full range of respiratory quotients; thus, the use of a standard value introduces minimal error in the calculation of metabolic heat production.24 Evaporative heat loss from the skin was not measured, but would be small under hypothermic conditions. Respiratory evaporative heat
Table 1. Core Temperature, Oxygen Consumption, and Forearm Minus Fingertip, Skin-Temperature Gradient during Active Cooling

<table>
<thead>
<tr>
<th>Time (h)</th>
<th>Tm (°C)</th>
<th>∆V̇o₂ (ml/min)</th>
<th>Gradient (°C)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Start of cooling</td>
<td>0</td>
<td>35.8 ± 0.1</td>
<td>-1.6 ± 1.0</td>
</tr>
<tr>
<td>Vasoconstriction</td>
<td>1.7 ± 0.6</td>
<td>35.2 ± 0.8</td>
<td>4.0 ± 0.0</td>
</tr>
<tr>
<td>End of cooling (start of rewarming)</td>
<td>2.6 ± 0.7</td>
<td>35.0 ± 0.6</td>
<td>5.0 ± 0.9</td>
</tr>
</tbody>
</table>

Tm = tympanic membrane temperature; ∆V̇o₂ = oxygen consumption.

loss is minimal when a passive heat-and-moisture exchanger is used.²⁵
Peripheral tissue heat storage was also estimated from the change in mean body temperature calculated with the formula: 

\[ \Delta T_b = 0.66 \times (\Delta T_{im}) + 0.34 \times (\Delta T_{sk}) \]

and using an average specific heat for the human body of 0.83 kcal kg⁻¹ °C⁻¹.²⁶ Because, by definition, core body temperature was the same at the start of rewarming and at the end of the afterdrop recovery period, \( \Delta T_{im} = 0 \), and the equation simplifies to \( \Delta T_b = 0.34 \times \Delta T_{sk} \).

Core temperature and heat balance data during rewarming were analyzed using repeated-measures ANOVA and Dunnett’s tests for means comparisons. Data obtained during the first 10 min of warming was considered the reference for comparison. Average rate of core temperature change for the last two 10-min intervals before the start of rewarming and the first two 10-min intervals after the start of rewarming were compared using a paired t test. Measured heat storage was similarly compared to heat storage calculated from mean body temperature. All data are expressed as mean ± SD. Differences were considered statistically significant when \( P < 0.05 \).

Results

The age of volunteers was 25 ± 3 yr, height was 170 ± 10 cm, and weight was 75 ± 18 kg. The group consisted of four men and one woman. Heart rate and systolic and diastolic blood pressures less than 15% during active cooling.

Cooling (Nonshivering Thermogenesis)

During the normothermic control period, mean tympanic membrane temperature was 37.1 ± 0.4 °C. The duration of time from the start of active cooling until the start of active warming was 159 ± 44 min (table 1). Significant vasoconstriction occurred at 35.2 ± 0.8 °C (\( \Delta T = -1.9 ± 0.9 \) °C), after 99 ± 38 min (table 1). Mean skin temperature at vasoconstriction was 25.9 ± 2.2 °C.

Oxygen consumption progressively decreased during active cooling (fig. 1). In one individual, oxygen consumption increased slightly at the time of vasoconstriction, but fasciculations in the pectoral muscles consistent with shivering were noted at this time (despite a single-twitch response to supramaximal train-of-four stimulus of the ulnar nerve). Administration of an additional 2 mg vecuronium abolished muscular movement; oxygen consumption then continued to decrease as in the other volunteers.

The effect of progressive hypothermia on oxygen consumption and the forearm minus fingertip, skin-temperature gradient is shown in figure 2. The slope

![Diagram](http://anesthesiology.pubs.asahq.org/pdfaccess.ashx?url=/data/journals/jasa/931312/)  

Fig. 1. Baseline oxygen consumption varied among volunteers because of differences in body size. In one individual, volunteer 2, a slight increase in oxygen consumption associated with mild shivering was noted at the time of vasoconstriction (-1.5 °C). Oxygen consumption continued to decrease after administration of additional vecuronium. Labeling of volunteers corresponds to that given in table 2. Change in tympanic membrane temperature (ΔTemp) is calculated with reference to the preinduction temperature. Labeling of volunteers corresponds to that given in table 1.

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Fig. 2. Oxygen consumption decreased in proportion to core temperature. The slopes of the lines of regression were similar before and after vasoconstriction: 9 ± 5 versus 9 ± 3%/°C (P = NS). Change in tympanic membrane temperature (ΔTemp) in this graph was calculated relative to the individual volunteer's threshold for vasoconstriction (average threshold 35.2 ± 0.8°C). Oxygen consumption is expressed as a percentage of the oxygen consumption measured at the individual vasoconstriction threshold temperature. The onset of peripheral thermoregulatory vasoconstriction is indicated by a forearm minus fingertip, skin-temperature gradient = 4°C at ΔTemp = 0°C (by definition).

of the regression lines for the percentage of oxygen consumption versus change in temperature was 9 ± 5%/°C before vasoconstriction and 9 ± 3%/°C after vasoconstriction (P = NS).

Rewarming (Heat Storage)
Temperature and heat storage data during rewarming are shown in table 2. Actual core temperature for each volunteer for 2 h before, and 2 h after, the start of warming is shown in figure 3. A significant afterdrop, ΔT = −0.6 ± 0.1°C, was observed after the start of skin-surface warming.

The average rate of temperature change during the two 10-min epochs before the start of surface warming was −1.3 ± 0.5°C/h. During the first two 10-min epochs after the start of skin-surface warming, the rate was significantly greater, −1.9 ± 0.7°C/h. The time required to reach the core temperature nadir (afterdrop duration) was 32 ± 8 min. Subsequently, core temperature increased; the maximum rate of increase during rewarming was 2.2 ± 0.3°C/h. In two volunteers, peripheral vasodilation (gradient < 0°C) occurred shortly after the start of warming and before the minimum temperature was reached.

Heat flux, metabolic heat production, and heat storage (cumulative heat transfer) during rewarming are shown in figure 4. Total cutaneous heat flux became negative during active warming, i.e., heat was transferred into the body across the skin.

Measured peripheral tissue heat storage capacity was 144 ± 60 kcal (602 ± 251 kJ), or 1.9 ± 0.5 kcal/kg total body weight. Heat storage calculated from the formula for mean body temperature was not significantly different, 155 ± 81 kcal (652 ± 339 kJ), or 2.0 ± 0.6 kcal/kg. Measured and calculated peripheral tissue heat storage capacities correlated strongly with body weight, r = 0.97 and r = 0.96, respectively.

Discussion

Nonsivering Thermogenesis
Metabolic heat production during isoflurane anesthesia did not increase even when core body temperature was driven 1°C less than the vasoconstriction threshold. Our results, thus, indicate that nonsivering thermogenesis is not an important response to hypothermia in adults anesthetized with isoflurane.

The threshold for nonsivering thermogenesis is similar to the vasoconstriction threshold in unanesthetized12 and anesthetized (Bissonnette and Sessler, unpublished data) human infants. However, to overcome the possibility that the threshold for nonsivering thermogenesis was lower than that of vasoconstriction in adults, we actively cooled our volunteers to a core temperature 1°C below their individual vasoconstriction thresholds. Although it remains possible that nonsivering thermogenesis would have been detected at even lower temperatures, its clinical relevance would be questionable, because few patients become that hypothermic.28

Our observation of an ≈ 9%/°C decrease in oxygen consumption during progressive hypothermia is slightly greater than that reported by others. Data compiled by Orkin from various sources indicate that metabolic rate decreases ≈ 5%/°C in animals.29 In the current study, an exaggerated effect may have been caused by our aggressive surface cooling, which probably decreased mean body temperature more rapidly than core temperature.

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Table 2. Morphometric and Thermal Balance Data

<table>
<thead>
<tr>
<th></th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>Average ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td>M</td>
<td>M</td>
<td>F</td>
<td>M</td>
<td>M</td>
<td></td>
</tr>
<tr>
<td>Age (yr)</td>
<td>25</td>
<td>29</td>
<td>21</td>
<td>25</td>
<td>26</td>
<td>25 ± 3</td>
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<tr>
<td>Fat (%)</td>
<td>15</td>
<td>18</td>
<td>27</td>
<td>17</td>
<td>22</td>
<td>20 ± 5</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>69</td>
<td>79</td>
<td>56</td>
<td>62</td>
<td>102</td>
<td>75 ± 18</td>
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<tr>
<td>Tm at warming (°C)</td>
<td>34.1</td>
<td>33.9</td>
<td>34.5</td>
<td>33.0</td>
<td>34.7</td>
<td>34.0 ± 0.6</td>
</tr>
<tr>
<td>Tm minimum (°C)</td>
<td>33.5</td>
<td>33.1</td>
<td>33.7</td>
<td>32.4</td>
<td>34.2</td>
<td>33.4 ± 0.6</td>
</tr>
<tr>
<td>Afterdrop duration (min)</td>
<td>24</td>
<td>28</td>
<td>24</td>
<td>24</td>
<td>22</td>
<td>23 ± 8</td>
</tr>
<tr>
<td>Tm cold (°C)</td>
<td>30.7</td>
<td>26.8</td>
<td>29.3</td>
<td>27.6</td>
<td>26.4</td>
<td>28.2 ± 1.8</td>
</tr>
<tr>
<td>Tm warm (°C)</td>
<td>35.6</td>
<td>35.6</td>
<td>35.7</td>
<td>33.9</td>
<td>36.4</td>
<td>35.4 ± 0.9</td>
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<tr>
<td>Tp cold (°C)</td>
<td>33.0</td>
<td>31.5</td>
<td>32.8</td>
<td>31.2</td>
<td>31.9</td>
<td>32.1 ± 0.8</td>
</tr>
<tr>
<td>Tp warm (°C)</td>
<td>34.6</td>
<td>34.5</td>
<td>34.9</td>
<td>33.3</td>
<td>35.2</td>
<td>34.5 ± 0.7</td>
</tr>
<tr>
<td>ΔQmeasured (kcal)</td>
<td>119</td>
<td>214</td>
<td>92</td>
<td>93</td>
<td>203</td>
<td>144 ± 60</td>
</tr>
<tr>
<td>ΔQcalculated (kcal)</td>
<td>93</td>
<td>192</td>
<td>102</td>
<td>107</td>
<td>280</td>
<td>155 ± 81</td>
</tr>
</tbody>
</table>

Mean skin temperature (Tm) and mean body temperature (Tp) are given at both the beginning and the end of the interval from the start of rewarming until the first net increase in core temperature (after recovery from the afterdrop). By definition, therefore, Tm was the same at both times.

ΔQmeasured = the change in heat storage as determined from the change in mean body temperature during this same time interval; afterdrop duration = the time from the start of rewarming to the central temperature nadir.

Our results contrast with those of Jessen et al.13,14 The absence of significant nonshivering thermogenesis in anesthetized and paralyzed adults versus those who were awake or comatose may be caused by anesthetic-induced inhibition of nonshivering thermogenesis. However, we have previously observed that, although thresholds for thermoregulatory vasoconstriction and sweating are altered by volatile anesthetics, maximum response intensities remain nearly normal. The results of Jessen et al. in unanesthetized humans may have been complicated by increased muscle tone not detectable as shivering. Moreover, detection of increased oxygen consumption caused by nonshivering thermogenesis in comatose patients may have been confounded by metabolic disturbances or infectious processes common in such patients.

In neonates, nonshivering thermogenesis is associated with increased plasma norepinephrine concentrations. Evidence for a stimulus to nonshivering thermogenesis may have been detected in the current study had we measured plasma norepinephrine levels. However, we did not observe increases in heart rate or blood pressure indicative of increased sympathetic nervous system activity. Our measurement system may have failed to detect small changes in oxygen consumption (< 5%). However, such slight increases in oxygen consumption would be of little clinical or physiologic significance.

We did not decrease the isoflurane concentration as temperature decreased. Because the potency of isoflurane increases approximately 5%/°C with decreasing temperature,22 depth of anesthesia may have increased slightly as our volunteers became progressively cooler. General anesthesia with volatile gases reduces metabolic rate by up to 25%.33 However, any effect of increasing depth
of anesthesia on metabolic rate would probably be insignificant compared with the direct effect of temperature on tissue metabolic rate.

Thermoregulatory vasoconstriction occurred at a higher temperature in the current study than that previously reported for similar concentrations of isoflurane, although this difference was not statistically significant (35.2° C vs. 34.5° C). Skin temperature is known to influence thermoregulatory responses; thus, a slightly higher vasoconstriction threshold is consistent with the ≈ 10% contribution of skin temperature on thermoregulatory control.34

**Heat Storage**

Investigations and discussions of heat balance and thermoregulation in humans often implicitly refer to a two-compartment model composed of a core and peripheral compartment. Core temperature is assumed to be nearly uniform and closely regulated, whereas temperature of peripheral tissues is considered less well regulated. Peripheral tissue temperature may range anywhere from nearly core temperature to nearly ambient temperature, depending on the thermoregulatory state and physical relation to the core. Consequently, heat content of peripheral tissues is also variable over a wide range.

Prolonged exposure to a cold environment is associated with relatively less peripheral tissue heat content (heat debt),35 whereas exposure in a warm environment is associated with greater heat content (heat storage).26 The peripheral tissue heat content and capacity to accept heat from the core is probably an important factor in determining the magnitude of afterdrop during rewarming from hypothermia. Similarly, peripheral tissue heat content appears to be an important factor modulating the extent of redistribution hypothermia observed with induction of anesthesia, because preinduction skin-surface warming significantly reduces this effect.19

By measuring thermal flux and metabolic heat production during rewarming of hypothermic volunteers, we were able to determine the heat storage capacity of the peripheral tissues. Core temperature initially decreased during rewarming (afterdrop). Nevertheless, effective heat transfer and ongoing metabolic heat production resulted in net positive heat storage for the entire body. During the time interval from the start of rewarming until the first net increase in core temperature, measured heat storage reflects increased temperature and heat content of only peripheral tissues (because core temperature was the same at the beginning and end of this period). The measured heat storage, ≈ 1.9 kcal/kg total body weight, indicates that heat storage capacity of peripheral tissues is quite large. This value is equivalent to ≈ 2 h of basal metabolic heat production (≈ 1 kcal·kg⁻¹·h⁻¹),24 and, if evenly distributed to body tissues, would raise mean body temperature ≈ 2.3° C (assuming an average specific heat for the human body of 0.83 kcal·kg⁻¹·° C⁻¹).27

Romet showed that the rate of cooling initially increased after the start of surface warming in hypothermic volunteers, indicating that increased convective heat transfer contributes to afterdrop.17 Alternatively, afterdrop may result because externally applied heat
initially increases temperature of only the most peripheral tissues, while core tissues continue to equilibrate through conductive transfer with more proximal "peripheral" tissue. Webb provided evidence to support this theory by producing afterdrop in a physical model lacking a circulatory component.

In our study, the rate of central cooling initially increased. However, peripheral vasodilation was only evident in two of five volunteers during the afterdrop, indicating that a sudden increase in skin blood flow in response to forced-air warming does not occur. A larger afterdrop may have been observed had vasodilation been more complete. Immersion in warm water is likely to produce more profound vasodilation. Nevertheless, the magnitude of the afterdrop that we observed is consistent with that reported by Romet in volunteers rewarmed by water immersion. Although surface warming initially resulted in an increased rate of cooling, cutaneous heat transfer was high; afterdrop was, therefore, small.

A potentially important difference between forced-air warming and warm water immersion is that, in the latter, venous return is augmented by hydrostatic pressure. It is likely that increased venous return would increase the initial rate of temperature decrease during the afterdrop. Skin-surface warming using a forced-air warmer and circulating-water blanket may allow more time for warming of cutaneous venous blood before it returns to the central circulation.

Vigorous surface warming may be avoided in cases of accidental hypothermia because of the fear that any further decrease in core temperature may cause arrhythmias or other physiologic disturbances. Our results indicate that only a small afterdrop occurs during rapid skin-surface warming with a forced-air warmer and circulating-water blanket. Although an additional 0.6°C of hypothermia could potentially lead to complications, it is unlikely that it can be avoided by any other means of peripheral rewarming, including spontaneous rewarming. In Romet's study, afterdrop was more pronounced, and of longer duration, when volunteers were warmed by spontaneous shivering versus warm-water immersion. Moreover, exercise has been shown to exaggerate afterdrop. Effective methods of core rewarming, e.g., peritoneal lavage or cardiopulmonary bypass, take longer to initiate and cannot be started in the field. Core rewarming via heated humidification of inspired air is advocated by some, although others debate its efficacy. Although it is not possible to transfer much heat via the airway, the heat is transferred directly to the central compartment and may, therefore, be more effective than expected.

Heat storage calculated using an estimate of mean body temperature agreed closely with that measured from heat transfer and metabolic heat production. We did not expect such close agreement, because mean body temperature estimated from the formula: \[ T_b = X \cdot T_{sk} + (1 - X) \cdot T_{core} \] depends on the value of the coefficient, X, which may vary depending on the individual's thermal state. Other investigators have reported poor correlations under different circumstances.

In summary, oxygen consumption decreased 9%/°C before and after peripheral vasoconstriction in volunteers anesthetized with isoflurane and cooled using circulating-water blankets. We conclude that nonshivering thermogenesis is not an important thermoregulatory response during isoflurane anesthesia in adult humans. Heat storage capacity of peripheral tissues measured during rewarming was 1.9 kcal/kg body weight. The large capacity of peripheral tissues to absorb heat contributes to core temperature afterdrop during treatment of hypothermia. However, the magnitude of afterdrop is small during rewarming by forced-air and circulating-water.

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References


ABSENCE OF NONSHIVERING THERMOGENESIS

32. Vitez TS, White PF, Eger EI II: Effects of hypothermia on halothane MAC and isoflurane MAC in the rat. ANESTHESIOLOGY 41:80–81, 1974
34. Hales JBS, Jesson C, Fawcett AA, King RB: Skin AVA and capillary dilatation and constriction induced by local skin heating. Pflugers Arch 404:203–207, 1985

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