Isoflurane-induced Vasodilation Minimally Increases Cutaneous Heat Loss

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Central body temperature, which usually is well controlled, typically decreases more than 1° C during the 1st h of general anesthesia. This hypothermia has been attributed partially to an anesthetic-induced peripheral vasodilation, which increases cutaneous heat loss to the environment. Based on the specific heat of humans, heat loss would have to increase more than 70 W for 1 h (in a 70-kg person) to explain hypothermia after induction of general anesthesia. However, during epidural anesthesia, sympathetic blockade increases heat loss only slightly. Furthermore, thermoregulatory vasoconstriction in unanesthetized humans decreases heat loss to the environment only 15 W. Therefore, we tested the hypothesis that the hypothermia that follows induction of general anesthesia does not result from increased cutaneous heat loss. Heat loss and skin-surface and tympanic membrane temperatures, before and after induction of isoflurane anesthesia, were measured in five minimally clothed volunteers. Peripheral skin blood flow was evaluated with venous-occlusion volume plethysmography and skin-surface temperature gradients. Cutaneous heat losses in watts were summed from ten area-weighted thermal flux transducers. Tympanic membrane temperature, which was stable during the 30-min control period preceding induction, decreased 1.2 ± 0.2° C in the 50 min after induction. Isoflurane anesthesia decreased mean arterial blood pressure approximately 20%. Average skin-surface temperature increased over 15 min to 0.5° C above control. Heat loss from the trunk, head, arms, and legs decreased slightly, whereas loss from the hands and feet (10.5% of the body surface area) doubled (P < 0.01). Total heat loss increased only 7.3 ± 5.4 W (P < 0.01), and the increase was not sustained during the study period. Therefore, central hypothermia after induction of isoflurane anesthesia does not result from increased cutaneous loss of metabolizable heat to the environment. (Key words: Anesthetics, volatile; isoflurane. Brain: hypothalamus. Hypothermia. Measurement techniques: thermal flux transducers; plethysmography. Temperature, measurement: skin; tympanic membrane. Temperature, regulation: setpoint, threshold. Thermoregulation: vasoconstriction.)

COLD OPERATING ROOM environments trigger normal thermoregulatory defenses, including, in most patients, peripheral vasoconstriction. General anesthesia produces vasodilation by central thermoregulatory inhibition,¹–³ and to a lesser extent, by a direct effect on sympathetic ganglia and vascular smooth muscle.⁴ Central body temperature usually decreases more than 1° C during the 1st h of general anesthesia, a decrease that has been attributed partially to the anesthetic-induced peripheral vasodilation and the subsequent increase in cutaneous heat loss to the environment.⁵,⁶

Cutaneous heat loss from minimally dressed humans in a typical operating room is near 125 W (1 W = 1 J/s),⁷ which only slightly exceeds their estimated metabolic heat production.⁸ Central temperature remains constant in this environment because the excess heat is lost from the peripheral thermal compartment.⁹ Since 1 W = 0.86 kcal/h, and the specific heat of humans is approx.0.85 kcal·kg⁻¹·°C⁻¹,¹⁰ heat loss must increase more than 70 W for 1 h (in a 70-kg person) to cause a decrease of 1° C in mean body temperature.

However, during epidural anesthesia, sympathetic blockade increases heat flux (net rate of transfer of heat from an organism or object to the environment) only slightly.⁹,¹¹ Furthermore, thermoregulatory vasoconstriction in unanesthetized humans decreases heat loss to the environment by only 15 W.¹² Therefore, we tested the hypothesis that the hypothermia that follows induction of general anesthesia does not result from increased cutaneous heat loss.

Materials and Methods

With approval from the University of California, San Francisco, Committee on Human Research and written informed consent from volunteers, we evaluated isoflurane-induced cutaneous vasodilation in one woman and four men aged 24–37 yr. (Although morphometrically similar, these were not the same volunteers who participated in our previous heat balance study.¹³) None was obese or taking medication, and none had a history of smoking, thyroid disease, dysautonomia, hypertension, alcoholism, or Raynaud’s syndrome. Volunteers refrained from coffee, tea, and food during the 8 h preceding the study. Each study began at approximately 10:30 AM.

All volunteers were minimally clothed and reclined on their backs on a standard operating room table with a 5-cm-thick foam mattress. Warm lactated Ringer’s solution (<500 ml) was infused intravenously in each volunteer. After 30 min of control measurements and without any preanesthetic medication, anesthesia was induced by inhalation of isoflurane 3–4%, nitrous oxide 70%, and oxygen. Thiopental and opioids were not administered.
Nitrous oxide was discontinued, and the trachea of each patient was intubated without the assistance of a muscle relaxant at approximately 15 min after induction.

Anesthesia was maintained for the duration of the study with isoflurane (≈1.2%) in 30% oxygen and air; mechanical ventilation was adjusted to maintain end-tidal Pco2 near 35 mmHg. Respiratory gas concentrations were quantified by means of a Datex Capnomac® end-tidal gas analyzer (Datex Medical Instrumentation, MA). Prior to each study, the Capnomac® was calibrated with a known gas combination. Blood pressure was measured with a strain gauge attached to a radial artery catheter.

Heat flux in watts per square meter was measured directly from ten skin-surface sites by means of thermal flux transducers (Concept Engineering, Old Saybrook, CT). These values were converted into watts per site by multiplying by the calculated body surface area (area [m²] = weight[0.425] [kg] · height[0.725] [cm] · 0.007184) of each volunteer and assigning the following regional percentages: head = 6%; upper arms = 9%; forearms = 6%; hands = 4.5%; back = 19%; chest = 9.5%; abdomen = 9.5%; thigh = 19%; calves = 11.5%; and feet = 6%. 13

The transducer measuring heat loss from the head was placed in the middle of the forehead; others were placed in the center of each anatomic area. All transducers (except for the one between the back and mattress) were exposed to ambient air during the study. We defined flux as positive when heat traversed skin to the environment. We have described thermal flux measurements in detail previously. 7,12

Temperatures were monitored with Mon-a-Therm® (St. Louis, MO) tympanic membrane and skin-surface thermocouple probes connected to Mallinckrodt® model 8700 (St. Louis, MO) two-channel electronic thermometers with analog output. The manufacturer specifies that these thermometers have an accuracy of near 0.1°C. Thermocouple probes were placed in contact with the tympanic membrane and also under each thermal flux transducer. Analog data from the thermometers and heat flux transducers were acquired at 1–5 min intervals with a previously described “virtual instrument” (computer program that emulates hardware). 7,8

Fingertip blood flow (resulting primarily from increased arteriovenous shunt flow 14–16) was quantified by means of venous-occlusion volume plethysmography at 5–10 min intervals. 17 Volume plethysmography is probably the most reliable technique for evaluating peripheral blood flow. For comparison, we also evaluated peripheral flow by using forearm-to-fingertip skin-surface temperature gradients; we have demonstrated previously that this index correlates well with laser Doppler flowmetry and volume plethysmography. 2,18 As in our previous studies, 2,18 significant vasoconstriction was prospectively defined as a skin-temperature gradient of ≥4°C.

Data recorded from each volunteer at 1–10 min intervals were averaged into 10-min epochs with a database program; these individual averages were used to calculate the means (± SD) for the entire group of volunteers. Changes in skin temperature, thermal flux, fingertip blood flow, and skin-temperature gradient were analyzed by repeated-measures analysis of variance and Dunnett’s tests. The last 10 min acquisition epoch prior to the induction of anesthesia was considered the reference for intragroup comparisons. P < 0.01 identified significant differences.

Results

The mean age of the volunteers was 31 ± 5 yr, weight 76 ± 12 kg, height 172 ± 8 cm, and body surface area 1.9 ± 0.2 m². Average ambient temperature was 21.7 ± 1.2°C during the control period. Ambient temperature remained constant (average change < 0.1°C) during the first 50 elapsed min. Ambient temperature then increased to 0.9°C above control during the 50–70 min period of elapsed time (P = not significant [NS]) and to 0.6°C above control during the final 10 min of the study (P < 0.01).

Fingertip blood flow and skin-surface temperature gradients (forearm temperature — fingertip temperature)

![Fig. 1. Changes in fingertip blood flow and skin-surface temperature gradients (forearm — fingertip temperature). Isoflurane anesthesia started at 30 min and continued for 50 min. Fingertip blood flow increased ≈13-fold within a few minutes after induction and then remained approximately constant for the duration of the study. Skin-temperature gradients decreased from 7.2 ± 2.2°C (values exceeding our prospectively defined index of significant vasoconstriction), to <0°C C = 15 min after induction of anesthesia. Values significantly different (P < 0.01) from the control epoch just prior to isoflurane administration (20–30 min) are indicated by an asterisk.](image)
are shown in figure 1. Fingertip blood flow increased \( \approx 15 \)-fold within a few minutes after induction of general anesthesia and remained elevated for the duration of the study \( (P < 0.01) \). Skin-temperature gradients decreased from 7.2 \( \pm \) 2.2\(^\circ\) C (values exceeding our prospectively defined index of significant vasoconstriction) to \( < 0^\circ\) C \( \approx 15 \) min after induction of anesthesia \( (P < 0.01) \).

End-tidal isoflurane concentration was 2.2 \( \pm \) 0.74\% during the first 20 min of anesthesia (induction and intubation) and then remained constant at 1.2 \( \pm \) 0.4\%. Mean arterial blood pressure remained constant during the first 10 min of anesthesia and then decreased about 21 \( \pm \) 10\% for the remainder of the study (fig. 2). Average skin-surface temperature increased over 15 min to \( \approx 0.5^\circ\) C above control \( (P < 0.01) \). The most prominent increase in skin temperature occurred in the hands and feet (fig. 3). Tympanic membrane temperature decreased 1.2 \( \pm \) 0.2\(^\circ\) C during the 50 min after induction of anesthesia \( (P < 0.01) \) (fig. 4).

Total heat loss decreased 6 \( \pm \) 4 W during the 30-min control period. Total loss then increased 7\% (7.3 \( \pm \) 5.4 W) \( (P < 0.01) \) in the 30 min after induction of anesthesia (fig. 4). Heat fluxes from the ten measured sites were grouped to indicate losses from the trunk and head (forehead, back, chest, and abdomen); the arms and legs (upper arm, lower arm, thigh, and calf); and the hands and feet. Heat loss from the trunk, head, arms, and legs decreased slightly, whereas loss from the hands and feet (10.5\% of the body surface area) doubled \( (P < 0.01) \) (fig. 5). Heat loss from the trunk was less than might be expected because only a few watts were lost from the back, though the 5-cm foam padding covering the operating room table.

Isoflurane-induced cutaneous vasodilation produced little change in the distribution of heat loss except from the hands and feet (table 1). For example, 10\% of the heat loss was from the head (which represents \( \approx 6\% \) of the body surface area) before induction, and 8\% after induction. However, heat loss from the hands and feet \( (\approx 10.5\% \) of the body surface area) increased from 8\% of the total loss to 15\% \( (P < 0.01) \).

**Discussion**

Cutaneous heat loss is determined primarily by the difference between skin and ambient temperatures.\(^{18}\) Skin temperature is determined by ambient temperature, cutaneous blood flow, and other factors.\(^{19,20}\) Heat loss through the skin cannot be calculated accurately without measuring numerous factors, including air speed, skin temperature, mean radiant temperature, and covering insulation.\(^{19,21}\) Furthermore, heat loss cannot be deduced from fluctuations in central temperature alone because central temperature itself is influenced by alterations in

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**Fig. 2.** Induction of anesthesia with isoflurane decreased mean arterial blood pressure approximately 20\% from control values. Values significantly different \( (P < 0.01) \) from the control epoch just prior to isoflurane administration (20–30 min) are indicated by an asterisk.

**Fig. 3.** Average skin-surface temperature increased to \( \approx 0.5^\circ\) C above control in the 15 min after isoflurane administration. The most prominent increase in skin temperature occurred in the hands and feet (consistent with the known distribution of thermoregulatory arteriovenous shunts). Values significantly different \( (P < 0.01) \) from the control epoch just prior to isoflurane administration (20–30 min) after indicated by an asterisk. A few of the error bars for arms and legs and for hands and feet are omitted for graphic clarity. At 75 min, skin temperature of the arms and legs was 30.5 \( \pm \) 0.8\(^\circ\) C, and temperature of the hands and feet was 31.0 \( \pm \) 1.2\(^\circ\) C.
metabolic rate and redistribution of heat within the body. Therefore, we measured cutaneous heat loss directly by using thermal flux transducers.

Our data indicate that induction of isoflurane anesthesia increased cutaneous heat loss by only 7.3 ± 5.4 W. (This increase is similar in magnitude to the heat savings produced by passive airway humidification with a heat and moisture exchanger.) A minimal increase in thermal flux from the skin during general anesthesia is consistent with our previous studies showing that cutaneous heat flux is increased only slightly by high thoracic sympathetic blockade during epidural anesthesia and is decreased slightly by thermoregulatory vasoconstriction in the unanesthetized state.

A 7-W increase in heat loss sustained for 1 h (in a 70-kg individual in thermal steady state) would decrease mean body temperature by only about 0.1° C. Thus, increased heat loss to the environment cannot explain the observed 1.2 ± 0.2°C decrease in tympanic membrane temperature. Although decreased metabolic heat production during isoflurane anesthesia contributes to hypothermia, near cessation of heat production would be required to explain the observed hypothermia. Most probably, central hypothermia results primarily from redistribution of heat from the warm central thermal compartment to cooler peripheral tissues. Peripheral compartment warming was manifested in the current volunteers by an increase in average skin-surface temperature after induction of anesthesia.

Redistribution of heat within the body, and not increased heat loss or decreased heat production, also is a primary cause of central hypothermia during epidural anesthesia. It is likely that central hypothermia resulting from redistribution of heat within the body will be less pronounced in patients who are vasodilated (with warm peripheral tissues) before induction of anesthesia. Central temperature may be better preserved during surgery with anesthetics that do not inhibit thermoregulatory vasoconstriction.

The fractional increases in heat flux during vasodilation were largest in the hands and feet—tissues known to have thermoregulatory arteriovenous shunts. After induction of anesthesia, 67% of the total heat flux occurred across the extremities, which represent 56% of the body surface area. These data suggest that the extremities (including the distal parts) should be covered if maximum heat retention is desired. In contrast, only 12% of the lost heat crossed the skin on the head and back, although they

FIG. 5. Heat fluxes from the ten measured sites were grouped to indicate losses from the head and trunk (head, back, chest, and abdomen), legs and arms (upper arm, lower arm, thigh, and calf), and hands and feet. Total heat flux and flux from the arms and legs increased 7% (7.3 ± 5.4 W) in the first 30 min after induction and then returned to control values in the remaining 20 min of the study. Heat loss from the trunk, head, arms, and legs decreased slightly, whereas loss from the hands and feet (10.5% of the body surface area) doubled (P < 0.01). Values significantly different (P < 0.01) from the control epoch just prior to isoflurane administration (20–30 min) are indicated by an asterisk. Heat losses indicated in the lower three curves (arms and legs, trunk and head, hands and feet) constitute the total loss indicated at the top of the figure.
TABLE 1. Percentage of Total Body Surface Area and Heat Loss

<table>
<thead>
<tr>
<th>Surface Area</th>
<th>Control</th>
<th>Isoflurane</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arms &amp; Legs</td>
<td>45.5</td>
<td>52</td>
</tr>
<tr>
<td>Hands &amp; Feet</td>
<td>10.5</td>
<td>15</td>
</tr>
<tr>
<td>Head</td>
<td>6</td>
<td>8</td>
</tr>
<tr>
<td>Trunk</td>
<td>38</td>
<td>25</td>
</tr>
</tbody>
</table>

The percentages of total heat flux from the ten measured sites were grouped to indicate losses from the trunk and head (forehead, back, chest, and abdomen), arms and legs (upper arm, lower arm, thigh, and calf), and hands and feet. Total heat flux increased 7% (7.3 ± 5.4 W) in the 30 min after induction of anesthesia (P < 0.01). Isoflurane-induced cutaneous vasodilation produced little change in the distribution of heat loss, except from the hands and feet. For example, 10% of the heat was lost from the head (which represents ∼6% of the body surface area) before induction, and 8% after induction. Loss from the hands and feet (∼10.5% of the body surface area) increased from 8% of the total to 15%. Heat loss from the trunk was less than might be expected because only a few watts were lost from the back through the 5-cm-thick foam padding that covered the operating room table.

The back (5 cm of foam) was trivial, suggesting that circulating water blankets will be more effective placed over rather than beneath patients. We have demonstrated previously that a full-length circulating water blanket positioned over volunteers decreases total cutaneous heat loss nearly to zero.7

Cutaneous heat loss from the head (6% of the body surface area) remained throughout the study at near 9% of the total loss. Actual loss was smaller than the measured loss because the insulating properties of hair were not considered. Thus, for adult patients, covering the head will increase heat retention only minimally in a typical operating room environment. In contrast, in an arctic environment, heat loss from the head can be a large fraction of the total loss when the rest of the body is well covered.24 Additional heat is lost from the head by respiration, but this loss cannot be prevented by putting on a hat.

In a previous study, we induced thermoregulatory vasoconstriction by intravenous infusion of iced saline.12 Those volunteers were maintained in a 30.8°C environment to provoke peripheral vasodilation. Because the skin-to-ambient temperature gradient was lower, total heat loss was about half that observed in the current study. However, with iced saline, cutaneous heat loss decreased 25% (15.5 ± 0.3 W), representing a considerably larger change than the 7% (7.3 ± 5.4 W) increase observed in our current investigation.

Several factors may have contributed to the greater change in heat loss in volunteers given iced saline. The first is that central hypothermia (∼1.5°C) in unanesthetized humans is a greater thermoregulatory stimulus than is simple exposure to an ∼22°C environment. Thus, cutaneous vasoconstriction after iced saline administration was greater than it was in the control period before isoflurane administration. (Arteriovenous shunt flow was minimal in both cases, but capillary flow in the trunk skin may have been particularly low during central hypothermia.)

A second factor may be that thermoregulatory vasoconstriction decreases blood flow through peripheral arteriovenous shunts more than ten-fold but decreases capillary flow only minimally.15,25 In contrast, active vasodilation during heat stress increases capillary flow dramatically.15,16 (Blood flow through the top millimeters of the skin can reach 7.5 l/min during intense heat stress.26) General anesthesia, which inhibits active vasoconstriction, probably also prevents active vasodilation; thus, in a 31°C environment, cutaneous blood flow likely is higher in unanesthetized volunteers than in those given isoflurane. As a result, the change in skin blood flow (and consequent heat loss) may be greater when vasoconstriction is triggered in a warm environment than when general anesthesia is induced in a cold environment.

Hypotension is the third factor that may contribute to the difference results with iced saline versus isoflurane anesthesia. As is common during clinical anesthesia, systemic blood pressure in our volunteers decreased ∼20% after induction of anesthesia. (Blood pressures actually were slightly high during the control period and decreased to "normal" values during anesthesia.) The effect of isoflurane-induced hypotension on cutaneous blood flow is unclear because hypotension results both from direct myocardial depression and from anesthetic-induced peripheral vasodilation. The increase in cutaneous blood flow (and consequent heat loss) may have been greater if control blood pressure had been maintained (by administration of less isoflurane, by use of a different anesthetic technique, or by the adrenergic stimulation of surgery).

Previous studies in unanesthetized humans indicate that there is a peripheral thermal buffer with a capacity of approximately 120 kcal.27 Thus, when the central and peripheral thermal compartments are well separated by thermoregulatory vasoconstriction, large amounts of heat can be lost from the periphery without altering central temperature. When an unanesthetized normal volunteer is placed in a typical operating room environment, heat loss exceeds metabolic heat production by approximately 25 W; central temperature, however, remains unchanged, because heat is being lost largely from the peripheral compartment. Since heat is being lost at a rate of 25 W from a peripheral compartment with a capacity of approximately 120 kcal, thermal steady state may not be reached for many hours. It is therefore extremely difficult to provide a true thermal steady state in any but a ther-
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moneutral environment, and our current volunteers were not in steady state. However, small changes in baseline flux would not obscure a heat loss that increased <10% of the amount needed to explain the observed decrease in central temperature.

Isoflurane produced considerable peripheral cutaneous vasodilation (in tissues with arteriovenous shunts). However, most cutaneous heat loss occurs from tissues without shunts and therefore depends on capillary flow. Capillary blood flow measurements were not necessary because we quantified heat loss directly.

Extrapolation from ten thermometers and thermal flux transducers introduced some error in our regional heat flux measurements, but the error was minimized by distributing a large number of sensors on skin surfaces in which changes were greatest. Evaporation of sterilizing scrub solutions during surgery is an additional route of heat loss, but we did not evaluate it in this study. However, since surgical skin preparation usually lasts only 10 min and covers only a limited surface area, it is unlikely that evaporation of preparation solutions contributes substantially to overall heat balance.

Average ambient temperature remained constant during the first 50 min of study, but then increased to 0.3 and 0.6°C above control values during the last portion of the study. Such an increase is typical in operating suites because metabolic heat generated by the surgical care team and operating room equipment is not fully dissipated by the air-conditioning system. Because cutaneous heat loss is determined largely by the difference between skin and ambient temperature, losses would have been slightly greater had room temperature remained constant. It is likely that the slight increase in ambient temperature caused the heat flux to return toward control values during the last 30 min of the study.

We conclude that isoflurane-induced vasodilation increased cutaneous heat loss only 7% (7.3 ± 5.4 W) during the 30 min after induction of anesthesia. Total heat loss then returned to control values during the remaining 20 min of the study, probably because ambient temperature increased 0.6°C. These data indicate that increased heat loss to the environment did not contribute importantly to the observed 1.2 ± 0.2°C central hypothermia. Most likely, central hypothermic resulted from redistribution of heat within the body. The largest fractional increase occurred in skin known to have thermoregulatory arteriovenous shunts. The slight change in cutaneous heat loss after induction of isoflurane anesthesia was consistent with the minimal changes previously observed during high thoracic epidural anesthesia11 and during thermoregulatory vasoconstriction in the unanesthetized state.12

Thermal flux from various body surfaces was roughly in proportion to the area represented by each surface (except in those areas known to have thermoregulatory arteriovenous shunts). Only about 9% of the total cutaneous heat loss traversed the head.

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References


